Harmonized Protocols and Guidelines

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

for Pediatric Ventricular Assist Devices, Mechanical Circulatory Support, Heart Failure, Fontan, and Muscular Dstrophy Programs

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DISCLAIMER

This document is part of the quality improvement, assessment, and peer review activities of the Advanced Cardiac Therapies Improving Outcomes Network (ACTION), headquartered at Cincinnati Children's Hospital Medical Center. The information contained herein is intended solely for the use of the individual or entity to whom it is addressed.

ACTION focuses on quality improvement efforts such as harmonizing best practice protocols, disseminating them across institutions, and supporting centers in improving local care practices. These protocols are developed as consensus tools for pediatric and adult congenital heart disease (ACHD) heart failure programs to standardize care for patients at risk of heart failure. The information in these protocols is based on multi-center practices, expert opinions, clinical experience, and, where available, published literature.

Participating ACTION centers are encouraged to adapt these protocols for inclusion in their center-specific guidelines, with appropriate reference to ACTION. These protocols are intended as guidance tools and are not to be considered standards of care. If centers make modifications, please share a copy with us at *info@actionlearningnetwork.org* so we can continue learning from centers' practices.

PART ONE

Pediatric Ventricular Assist Device (VAD) & Mechanical Circulatory Support (MCS)

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Antiplatelet Strategies for Paracorporeal VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Antiplatelet initiation and titration plans should be driven by the VAD team and/or dedicated hematology service with special expertise in MCS to maintain consistency and continuity of care.

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OBJECTIVES

No approach to antiplatelet therapy initiation, monitoring, nor titration has been evaluated. There is wide variation among institutional experience and practice with minimal data to support any one method. This document is intended to serve as a guide for suggested approaches to antiplatelet therapy in children supported by paracorporeal VADs. Paracorporeal VADs are defined as pumps outside of the body with either temporary or durable cannula. Thrombogenicity varies by device type, cannula type, and number of connectors, as such variations in antiplatelet therapy may be required for different types of paracorporeal devices. The most common paracorporeal VAD include: Berlin Heart EXCOR with EXCOR cannula and Centrimag/Pedimag/Rotaflow with EXCOR cannula.

In this document, we strive to provide a summary and harmonization of institutional practices that appear reasonable based on the current clinical experience surrounding antiplatelet therapy in the pediatric paracorporeal population.

PROTOCOL

Aspirin (acetylsalicylic acid)

Aspirin induces its platelet inhibitory effect via COX-1 inhibition by irreversibly blocking the arachidonic acid (AA) binding site and reducing the expression of platelet surface GP IIb/IIIa receptors. This effect is irreversible for the life of the platelets exposed (7-10 days in healthy persons, may be shorter in children with inflammation and exposure to extracorporeal circuits due to inflammation-induced COX-2 activation resulting in high on-aspirin platelet reactivity).

Dosing preparations:

- Immediate release (oral 81 mg, 325 mg, 500 mg, enteric coated 81 mg or 325 mg, non-enteric coated/chewable 81 mg; rectal suppositories 300 or 600 mg)
- Delayed release (oral 81 mg or 325 mg, may have lower efficacy when compared to the chewable tablet)

Dosing Suggestions

- *Starting dose: 3-10 mg/kg/dose once daily (minimum 20.25 mg)*
- *Approximate suggested maximum total daily dose: 30 mg/kg/day up to 325 mg per dose*

Adverse effects:

- Tinnitus, diminished auditory acuity
- GI intolerance/ulcers (6-31%)

- Sensitivity/allergies have been described: skin reaction, urticaria, angioedema, agitation, confusion, acidosis, hyperkalemia, hypoglycemia, acetabular bone destruction, rhabdomyolysis, weakness, anemia, DIC, prolonged PT
- There are many medications and foods that can diminish or enhance salicylate effect, see Special Considerations
- No specific antidote

Special considerations:

- Ibuprofen, naproxen and other NSAIDS can reduce the cardioprotective effect of aspirin [Capon 2005; Catella-Lawson 2001].
- If absolutely needed, NSAIDS should be administered 2 or more hours after aspirin [MacDonald 2003].
- Does not require renal dosing, but cautious use if CrCl <10 for worsening nephropathy
- Avoid in severe liver disease
- Aspirin has been associated to prolong PT and can be a cause of thrombocytopenia
- Aspirin can enhance the nephrotoxic effects of ACE-I (*Risk C: Monitor therapy*)
- Aspirin can diminish the therapeutic effect of ACE-I (*Risk C: Monitor therapy*)
- Calcium channel blockers (CCB) can enhance the antiplatelet effect of aspirin
- Aspirin may enhance the adverse effects of corticosteroids related to GI bleeding
- Aspirin can decrease the absorption of ascorbic acid
- Aspirin can diminish the effect of spironolactone
- The following foods can cause salicylate accumulation: prunes, raisins, tea and gherkins, curry powder, paprika, licorice as they contain additional salicylate... DID YOU KNOW the average American diet contains 10-200 mg/day of salicylates?
- The following foods can increase urinary excretion of salicylates: Vitamin C containing fruits
- Unable to achieve “therapeutic aspirin” and/or thrombosis in setting of aspirin:
    - Pharmacogenomics testing for CYP2C9 polymorphism
    - Consider BID dosing (should also be considered in setting of significant thrombocytosis)
    - Consider rectal administration if enteral access (gastric or jejunal) is not feasible or in smaller infants where crushing and diluting the medication leads to loss of some of the needed dose to the tube or cup.
    - Consider adding or transitioning to alternate oral antiplatelet agents (Clopidogrel, Dipyridamole, Ticagrelor)
- Bleeding events/supratherapeutic on aspirin:
    - Pharmacogenomic testing for CYP2C9 polymorphism
    - Review medications or foods that may lead to accumulation of salicylate effect
    - Change formulation (from chewable to enteric coated, or PR)
    - Consider changing to lower BID dosing
- Patients at high risk for thrombosis and bleeding (complex hemostasis), can consider utilizing alternative intravenous reversible antiplatelet agents (ticagrelor, cangrelor, tirofiban, eptifibatide)

Monitoring:

- Thrombelastography with Platelet Mapping – arachidonic acid inhibition greater than 70% is considered therapeutic platelet inhibition with aspirin.
- VerifyNow can be used – Aspirin Reaction Units (ARU) $\leq$ 550 is considered therapeutic platelet inhibition with aspirin.

Clopidogrel (Plavix)

Clopidogrel prevents platelet activation and aggregation by irreversibly blocking the P2Y12 component of adenosine diphosphate (ADP) receptor on the platelet surface. The half-life of the parent drug is 6 hours, but the active metabolite has a half-life of 30 minutes. CYP2C19 inhibitors may reduce the concentration of active metabolites and CYP2C19 polymorphism may affect efficacy.

Dosing preparations:

- Suspension oral 5 mg/ml
- 75 mg and 300 mg tablet that may or may not be film coated (may be crushed)

Dosing Suggestions:

- Starting dose: 0.3-1 mg depending on age mg/kg/dose once daily
- Approximate suggested maximum 75 mg per day (or 1.8 mg/kg/day)

Adverse Effects:

- Bleeding

Special considerations:

- No renal or hepatic dosing adjustment necessary
- Unable to achieve "therapeutic clopidogrel effect" and/or thrombosis in setting of clopidogrel:
    - Pharmacogenomics testing for CYP2C19 poor metabolizer (CYP2C19*2 or *3 carriers)
    - Assess for medications that will decrease effect of clopidogrel: amiodarone, CCB, erythromycin, fentanyl, grapefruit juice, lansoprazole, omeprazole, pantoprazole, morphine
    - Change to alternative oral antiplatelet agents (aspirin or dipyridamole) or consider intravenous antiplatelet agents (ticagrelor, cangrelor, tirofiban, eptifibatide)
- Bleeding events/supratherapeutic on clopidogrel:
    - Pharmacogenomics testing for CYP2C19 hypermetabolizer
- See below regarding important transition recommendations between P2Y12 inhibitors

Monitoring:

- Thrombelastography with Platelet Mapping – ADP inhibition greater than 70% is considered therapeutic platelet inhibition with clopidogrel.
- VerifyNow can be used – P2Y12 Reaction Units (PRU) $\leq$ 194 is considered therapeutic platelet inhibition with P2Y12 inhibitors.

Dipyridamole (Persantine)

Dipyridamole synergistically modifies several biochemical pathways, including: a) inhibition of platelet cAMP-phosphodiesterase; b) potentiation of adenosine inhibition of platelet function by blocking reuptake by vascular and blood cells, and subsequent degradation of adenosine; and possibly, c) potentiation of PGI2 antiaggregatory activity and enhancement of PGI2 biosynthesis.

**Note that dipyramidole has vasodilatory properties including the coronary arteries.*

Dosing preparations:

- Oral suspension 10 mg/ml

- Oral tablets (25mg, 50mg, 75mg)
- IV infusion is available, but generally not used
- Available as combination product with aspirin (Aggrenox)

Dosing Suggestions:

- Starting dose: 1 mg/kg every 6-8 hours.
- Standard suggested maximum: 6 mg/kg/day (divided every 8 hours)
- Higher maximal dose has been reported: 16 mg/kg/day (divided every 6 hours, up to maximum of 100 mg/dose)

Adverse effects:

- Headaches
- Dizziness
- Flushing

Special Considerations:

- It requires no renal or hepatic adjustment

Cangrelor (Kengreal)

Cangrelor is a direct $P2Y_{12}$ platelet receptor inhibitor that blocks ADP-induced platelet activation and aggregation. Cangrelor binds selectively and reversibly to the $P2Y_{12}$ receptor to prevent further signaling and platelet activation. The drug induces peak effect platelet inhibition within 2 minutes and its antiplatelet effect is maintained throughout the duration of the infusion. Upon discontinuation, platelet function returns to normal within 1 hour. The volume of distribution is 3.9 L and is up to 98% protein bound. Cangrelor is rapidly inactivated in the circulation by dephosphorylation to its primary metabolite (a nucleoside which has negligible antiplatelet activity (half-life elimination is 3-6 minutes; urine excretion 58% and fecal excretion is 35%).

Canreglor is a nonthienopyridine antiplatelet agent that is a direct, reversible P2Y12 inhibitor that blocks ADP-induced platelet activation and aggregation. The onset of action is immediate with a time to peak effect within 2 minutes. The half-life elimination ranges between 3-6 minutes as it is rapidly inactivated in the plasma via dephosphorylation to an inactive metabolite. Upon discontinuation, platelet function returns to normal within 1 hour and it is 98% protein bound.

Dosing preparations:

- 200 mcg/mL concentration: 50 mg vial requiring reconstitution with 5mL sterile water to make 10 mg/mL concentration. Additional dilution with 250 mL of normal saline to a final concentration of 200 mcg/mL.
- 400 mcg/mL (0.4 mg/mL) concentration for smaller patients to minimize volume: take 1 mL of reconstituted 10 mg/mL concentration and dilute with 24 mL of normal saline to yield a final concentration of 400 mcg/mL [Vargas 2021].
- Diluted cangrelor is stable at room temperature for 24 hours in normal saline.

Dosing Suggestions:

- 0.5 mcg/kg/min – 2 mcg/kg/min as starting dose [Vargas 2021] [Fahnhorst 2021] [Ghbeis 2021]
- Neonates and infants at high risk for bleeding:
- For infants less than 2 months of age, consider starting at 0.1 mcg/kg/min [Anton-Martin]
- For infants over 2 months and/or patients at low risk for bleeding, start at 0.3 mcg/kg/min [Anton-Martin]

Adverse effects:

- Bleeding

Special considerations:

- Can be utilized in the immediate post-operative period or for preprocedural antiplatelet bridging in patients who are NPO or with impaired enteral absorption.
- It requires no renal or hepatic adjustment
- P2Y12 levels using the VerifyNow technology (see below) should be monitored (goal 100-180) (note: the drug is dephosphorylated in the blood, thus samples must be run as soon as possible after collection).
- P2Y12 levels can be affected by anemia and polycythemia: Hematocrit <30% can lead to artificially elevated levels and hematocrit >45 can lead to artificially low levels.
- check P2Y12 level 1-4 hours post initiation and after each titration
- Contraindications include significant active bleeding and hypersensitivity to cangrelor or any component of the product.
- Transitioning from cangrelor to oral P2Y12 inhibitors
    - Clopidogrel: give clopidogrel dose immediately after cangrelor is stopped. Do not give while infusion is running
    - Ticagrelor: ticagrelor may be initiated at any point prior to cangrelor being stopped or may be given immediately after infusion is stopped
    - Aspirin may be initiated regardless of cangrelor infusion status

Ticagrelor (Brilinta)

Ticagrelor is a nonthienopyridine antiplatelet agent that noncompetitively and reversibly binds and inhibits the ADP-induced platelet activation and aggregation. With a loading dose, the onset of platelet inhibition occurs within 30 minutes (~41%) with a peak effect(~88%) at 2 hours post administration. This level of inhibition is maintained for 2-8 hours post loading dose and 24 hours after the last maintenance dose. It takes ~56 hours post dose to reach a platelet inhibition of ~30%. The half-life elimination of total drug is 7 hours and 9 hours for the active metabolite. It is hepatically metabolized through the CYP3A4/5 pathway into an active metabolite and is excreted primarily through the feces (58%) and urine (26%) and is >99% protein bound.

Dosing Preparations:

- 60 mg and 90 mg tablets (can be crushed)
- No oral suspension available

Dosing Suggestions:

- Adult Dosing recommendations
    - Loading dose: 180 mg x1
    - Maintenance dose: 90 mg every 12 hours. The first dose to start 12 hours after loading dose.
- Dosing extrapolated from management of vaso-occlusive crises in pediatric sickle-cell disease [Heeney 2019].
    - >12 to < 24 kg: 15 mg twice daily
    - >24 to < 48 kg: 30 mg twice daily
    - >48 kg: 45 mg twice daily
    - No data available in patients < 2 years of age and <12kg

Adverse Effects:

- Bleeding

- Bradyarrhythmias
- Dyspnea

Special Considerations:

- It requires no renal or hepatic adjustment
- Transitioning from clopidogrel to ticagrelor: administer ticagrelor dose (loading or maintenance) within 24 hours after the last dose of clopidogrel

Tirofiban (Aggrastat)

Tirofiban is a reversible glycoprotein (GP) IIb/IIIa receptor inhibitor and prevents the binding of fibrinogen to the GP IIa/IIIa receptor to prevent platelet aggregation. Over 90% platelet inhibition is seen within 10 minutes and once stopped, platelet function is restored within 4-8 hours post discontinuation. It has a half-life of 2 hours and has negligible metabolism. It is excreted in the urine (65%) and feces (25%) primarily as unchanged drug and has concentration-dependent protein binding (~65%).

Dosing Preparations:

- IV concentrate: 3.75 mg/15 mL
- IV solution: 5 mg/100 mL NS, 12.5 mg/250 mL NS

Dosing Suggestions:

- Adult Dosing
    - Loading dose: 25 mcg/kg
    - Maintenance infusion: 0.1-0.15 mcg/kg/min [Nei 2020].
- Pediatric Dosing
    - Extrapolated from mBTT shunt data: 10 mcg/kg bolus dose followed by 0.15 mcg/kg/min [Emani 2020]

Adverse Effects:

- Bleeding
- Pelvic pain

Special Considerations:

- Dose adjustments are recommended in a creatinine clearance < 60 mL/min.
- With regards to monitoring, there are no specific recommendations. Monitor for signs of bleeding and possible thrombocytopenia

Eptifibatide (Integrilin)

Eptifibatide is a reversible GP IIb/IIIa inhibitor that blocks the binding site for fibrinogen, von Wilelbrand factor, and other ligands to prevent platelet aggregation. Over 80% platelet inhibition is achieved 5 minutes after the bolus dose with a maximum effect within 1 hour. Platelet function is restored within 4-8 hours following discontinuation. It has a half-life of ~2.5 hours and is metabolized in the plasma to an active metabolite. It is excreted primarily through urine.

Dosing Preparations:

- Premixed IV solution: 200 mg/100 mL 75 mg/100 mL, 20 mg/10 mL

Dosing Suggestions (no pediatric data):

- Bolus dose: 180 mcg/kg (max 22.6mg) followed by infusion of 0.1-2 mcg/kg/min (max 15 mg/hr) [Tellor 2014] [Bitar 2017].

Adverse Effects:

- Bleeding
- Hypotension

Special Considerations:

- Dose adjustments are recommended for a creatinine clearance <50 mL/min
- With regards to monitoring, there are no specific recommendations. Monitor for signs of bleeding

General considerations for initiation of antiplatelet drugs:

Prior to starting antiplatelet therapies, these suggested criteria should be considered:

1. *Patient is tolerating anticoagulation without excessive bleeding as agreed upon by surgical and medical teams.*
2. *Evolution of chest tube output from sanguinous to serosanguinous.*
3. *Suggest stable platelet count over 80 x 10^3/mL.*
4. *Maximum amplitude by heparinase TEG is not below 50 mm and/or does not already exhibit 70% AA or ADP inhibition prior to starting either aspirin or clopidogrel, respectively*

Table of strategy options:

Weight-based strategy	Circuit appearance	Titration based on responsiveness testing

Antiplatelet medications are usually started shortly after achieving a therapeutic PTT.
 	
Medication goals:
 	
Aspirin
• Double dose each day until achieving target
• Target dose: 30 mg/kg/day divided BID
 	
Clopidogrel
• Double dose each day until achieving target
• Target dose: 0.8-1 mg/kg/day, once daily
 	
Caveats:
• The above maximum target doses are typical for Berlin Heart patients that eventually are transitioned to enoxaparin as a chronic anticoagulation agent. While on Bivalirudin, due to its innate antiplatelet effect, we consider lower antiplatelet medication doses (usually half of the maximum above and sometimes no clopidogrel)
• Target TEG MA heparinase (not platelet mapping) of 55-65 but do not titrate on any sliding scale based on those numbers. If greater than 65, assess the clinical picture to see if there is a source of inflammation or if medications can be weight adjusted. In extreme cases with excessive pump thrombosis can go to as high as 1.8 mg/kg/day of clopidogrel. Also consider adding Omega 3 fatty acids 500 mg BID.
• Optimize GI prophylaxis, especially in continuous flow pumps to prevent bleeding, at times dual therapy is needed.
• Clarify your route of administration of these medications. Aspirin, in particular, is tough to give to small babies effectively by mouth/tube as it does not compound and can be gritty and clog up tubes. If possible, to have patients chew their aspirin or if babies consider crushing multiple small dose tablets to increase the amount of powder or consider rectal aspirin for more precise dosing and assurance that what you order is what the patient gets.
	Antiplatelet therapy initiation is suggested once anticoagulation therapy has been therapeutic and stable, based on the appearance of the circuit and bleeding risk profile.
	
	Clean Circuit:
	• Patient is therapeutic and stable on anticoagulation infusion, with no signs of increased bleeding and risk is low
	• Initiate aspirin therapy
	• Monitor for signs of increased bleeding, especially if chest drains still in place, and other sites
	
	Circuit with early postoperative fibrin/thrombus deposition within 24-48 hours of VAD implantation (inflammation, infection, shearing):
	• Patient should be on an anticoagulation infusion, based on bleeding risk profile
	• If not on anticoagulation, consider starting anticoagulation prior to aspirin therapy
	• If patient is subtherapeutic on anticoagulation, optimize therapy and monitor VAD and bleeding
	• If available, send TEG/ROTEM, coagulation profile and platelet function assay to assess reason for fibrin/thrombus deposition
	• If anticoagulation is optimal, and bleeding appropriate, start aspirin therapy irrespective of hardware/tubing, and titrate to target ranges (see monitoring and titration) in discussion with clinical team
	• If available, repeat platelet function assay to assess response
	
	Circuit with delayed fibrin/thrombus deposition, and not on aspirin therapy:
	• If available, send TEG/ROTEM or platelet function assay to assess platelet activity
	• Initiate aspirin therapy and repeat platelet function assay to assess response
	
	On stable anticoagulation and aspirin therapy, with signs of increased fibrin/thrombus deposition:
	• Check anticoagulation parameters with labs, TEG/ROTEM, and platelet function assay
	• Optimize/increase anticoagulation goals if necessary
	• Increase aspirin dose per dosing titration table until either platelet function assay indicates improved response or max dose reached
	
	Subtherapeutic anticoagulation, not on aspirin and evidence of fibrin/thrombus deposition:
	• If anticoagulation therapy is subtherapeutic, continue to titrate to target goals
	• Obtain TEG/ROTEM and platelet function assay
	• Assess for any bleeding (chest tubes, cannula sites, airway, etc.)
	• Initiate aspirin therapy at starting dose and titrate to goal dose
	
	For institutions who give consideration to chest tubes prior to starting aspirin therapy:
	• Patient is therapeutic and stable on an anticoagulation infusion and bleeding risk is not high. If bleeding risk is high, discuss with team best and safest next steps
	• If available, obtain TEG/ROTEM or platelet function assay to assess platelet function
	• Discuss with team initiation of aspirin therapy
	• After initiation of aspirin therapy, monitor chest tube output for increased bleeding
	• Consider removing chest tubes when bleeding remains stable or improves
		Two-step aspirin titration to ensure (1) responsiveness and (2) 24-hour antiplatelet effect:
		
		STEP 1 – responsiveness testing ("peak" effect):
		• Obtain TEG with platelet mapping at 4 hours after first aspirin dose.
		• If platelet inhibition is adequate at 4-hours (>70% AA inhibition), continue to STEP 2.
		• If platelet inhibition is inadequate at 4-hours (<70% AA inhibition), increase next aspirin dose (up to 15 mg/kg/dose or maximum of 81 mg/dose).
		  ○ Re-test TEG with platelet mapping at 4-hours after this increased dose.
		  ○ >70% arachidonic acid inhibition demonstrates adequate "peak" effect of platelet inhibition by aspirin via the AA pathway, proceed to STEP 2.
		
		STEP 2 – 24-hour antiplatelet effect:
		• To ensure long-lasting 24-hour platelet inhibition with aspirin (once responsiveness is established in STEP 1), re-test TEG with platelet mapping at 24 hours after the first dose (prior to the next dose)
		• If platelet inhibition is adequate at 24 hours (>70% AA inhibition), continue once daily aspirin dosing.
		• If platelet inhibition is inadequate and waned at 24 hours (<70% AA inhibition), increase dosing frequency to twice daily (same dose from STEP 1 that demonstrated adequate "peak" inhibition of AA pathway, up to 15 mg/kg/dose BID or maximum of 81 mg/dose BID).
		
		Note: A similar strategy can be utilized with either ROTEM or VerifyNow testing for aspirin responsiveness. The use of multiple modes of testing should be considered; however, fair discordance exists between assays [Lordkipanidzé 2007]

IT IS REASONABLE TO START ANTIPLATELET THERAPY WITH ASPIRIN WITHIN 2-4 DAYS POST-OPERATIVE.
SUGGESTED USUAL SEQUENCE OF ANTIPLATELET THERAPY INITIATION: ASPIRIN, FOLLOWED BY CLOPIDOGREL OR DIPYRAMIDOLE.

Circuit appearance-based strategy:

Recommendations for aspirin initiation in the post-operative pediatric VAD patient, primarily based on circuit appearance and taking into consideration bleeding risk profiles of the patient. Below are recommendations based on circuit appearance, at different clinical times in the patient's course. Always monitor for increase in oozing or bleeding as you add or increase anticoagulation/antiplatelet therapy, assess the VAD frequently per unit protocol, and increase frequency if any fibrin or clots detected. [Steiner 2016 and Rosenthal 2017]

1. **Clean circuit:**
    a. Patient is therapeutic and stable on anticoagulation infusion as set by clinical team, with no signs of increased bleeding and bleeding risk is low
    b. Initiate aspirin therapy
    c. Continue monitoring for any signs of new onset oozing or bleeding, especially if chest drains in place
    d. If oozing or bleeding noted after aspirin initiation, refer to "monitoring"
2. **Circuit with early postoperative fibrin/thrombus deposition within 24-48 hours of VAD implantation** (inflammation, infection, shearing):
    a. Patient should be on an anticoagulation infusion, based on bleeding risk
        - If not on anticoagulation, consider starting anticoagulation prior to aspirin therapy
    b. If patient is not therapeutic on anticoagulation, optimize therapy and monitor VAD and bleeding deposition [Feldman 2013].
    c. If anticoagulation is optimal, and bleeding is within expected parameters, start aspirin therapy irrespective of hardware/tubing, and titrate to target ranges (see monitoring and titration) in discussion with clinical team
    d. If available, repeat platelet function assay to assess response
3. **Circuit with delayed fibrin/thrombus deposition:**
    a. If patient is not on aspirin therapy and fibrin or thrombi deposition noted
        i. If available, Send TEG/ROTEM or platelet function assay to assess platelet activity
        ii. Initiate aspirin therapy and repeat platelet function assay to assess response (see table)
4. **Special Considerations:**
    a. On stable anticoagulation and aspirin therapy, with signs of increased fibrin/thrombus deposition
        i. Check anticoagulation parameters with labs, TEG/ROTEM, and platelet function assay
        ii. Optimize/increase anticoagulation goals if necessary
        iii. Increase aspirin dose per dosing titration table until either platelet function assay indicates improved response or max dose reached
        iv. Look for underlying inflammatory/infectious process
    b. Subtherapeutic anticoagulation, while not on aspirin and evidence of fibrin/thrombus deposition
        i. If IV anticoagulation therapy is subtherapeutic, continue to titrate to target goals
        ii. Obtain TEG/ROTEM and platelet function assay
        iii. Assess for any bleeding (chest tubes, cannula sites, airway, etc)
        iv. Initiate aspirin therapy at starting dose and titrate to goal dose
    c. For institutions who give consideration to chest tubes prior to initiation of aspirin therapy:

i. Patient is therapeutic and stable on an anticoagulation infusion and bleeding risk is not high
   - If bleeding risk is high, discuss with team best and safest next steps

ii. If available, obtain TEG/ROTEM or platelet function assay to assess platelet activation

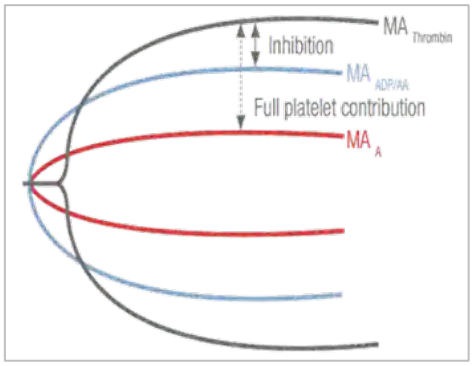
iii. Discuss with team initiation of aspirin therapy

iv. After initiation of aspirin therapy, monitor for signs of increased bleeding while chest tubes are in place

v. Consider removing chest tubes when bleeding remains stable or improves

Titration based on responsiveness testing (TEG with platelet mapping):

Thrombelastography (TEG) is a whole blood viscoelastic hemostatic assay (VHA) that characterizes the life-span of clot formation from the initiation of fibrin cross-link formation through clot breakdown and fibrinolysis. Another commonly-used VHA is rotational thrombelastometry (ROTEM) that produces comparable whole blood hemostatic data merely with altered terminology. The maximal amplitude of the TEG oscillogram (or maximum clot firmness of ROTEM) demonstrates the maximal clot strength achieved by the platelet linking via the interaction of fibrin and platelet surface GP IIb/IIIa receptors. Platelet mapping is performed by comparison of 3 samples from the same patient. $MA_{thrombin}$ demonstrates the maximal clot strength (MA from standard TEG oscillogram) via activation with Kaolin to induce a thrombin response to maximally activate all platelets and convert all fibrinogen to fibrin. MA_A (aka MA_{fibrin}) demonstrates the complete blockade of thrombin (platelets inhibited, fibrin activation only). MA_{AA} samples have arachidonic acid (AA) added (conversion inhibited by aspirin) to demonstrate the ability of non-inhibited platelets to activate. The comparison of the AA-bathed MA_{AA} tracing to the difference between the fully activated $MA_{thrombin}$ and fully-inhibited MA_A tracings demonstrates the % platelet inhibition via the AA pathway in the presence of aspirin. [Whiting 2014 and Luddington 2005]



The antiplatelet effect of acetylsalicylic acid has a half-life of 20 minutes and, thus, remains effective in the circulation for just over an hour (anti-inflammatory effect maintains a longer half-life). New platelets generated after clearance of aspirin will likely remain uninhibited (and thus able to induce thrombosis) until the next dose of aspirin arrives. The increase in aspirin dosing frequency has been demonstrated to provide consistent platelet inhibitory effect in adult patients with inflammation associated with type 2 diabetes [Spectre 2011 and Rocca 2012].

Two-step aspirin titration to ensure (1) responsiveness and (2) 24-hour antiplatelet effect:

1. **STEP 1 – responsiveness testing:**
   a. Obtain TEG with platelet mapping at 4 hours after first aspirin dose.
      i. Initial 4-hour post-aspirin testing is meant to establish adequacy of response to aspirin dose and meant to evaluate the “peak” effect on arachidonic acid (AA) inhibition.
      ii. Aspirin (anti-platelet effect) has a short half-life of 20 minutes (anti-platelet effect). Early post-dosing testing will demonstrate the effect of that initial aspirin dose on the circulating platelets at that time.
   b. If platelet inhibition is adequate at 4-hours (>70% AA inhibition), continue to STEP 2.
   c. If platelet inhibition is inadequate at 4-hours (<70% AA inhibition), increase aspirin dose to next deliverable dose (up to 30 mg/kg/dose).
      i. Re-test TEG with platelet mapping at 4-hours after this increased dose.

ii. >70% arachidonic acid inhibition demonstrates adequate "peak" effect of platelet inhibition by aspirin via the AA pathway, proceed to STEP 2.

2. **STEP 2 – 24-hour antiplatelet effect:**

a. Children after VAD implant are likely to have more-rapid platelet turnover (wound healing, circuit exposure, inflammation, infection). Platelets produced after aspirin has been cleared (t ½ = 20 min) will not be inhibited by the initial aspirin dose.

b. To ensure long-lasting 24-hour platelet inhibition with aspirin, re-test TEG with platelet mapping at 24 hours after the first dose (prior to the next dose):

i. Waning of platelet inhibition prior to the second dose demonstrates less-than-24-hour platelet inhibition with once-daily dosing of aspirin.

ii. Platelet turnover results in production of new (AA pathway not inhibited) platelets after the clearance of the prior aspirin dose.

c. If platelet inhibition is adequate at 24 hours (>70% AA inhibition), continue once daily aspirin dosing.

d. If platelet inhibition is inadequate and waned at 24 hours (<70% AA inhibition), increase dosing frequency to twice daily (same dose from STEP 1 that demonstrated adequate "peak" inhibition of AA pathway).

Note: A similar strategy can be utilized with ROTEM or VerifyNow testing for aspirin responsiveness.

VerifyNow Testing for Aspirin/P2Y12 inhibitor Resistance/Responsiveness:

- The VerifyNow test is a qualitative test to aid in the detection of platelet dysfunction due to aspirin or P2Y12 inhibitor therapy:
  - Test results are reported in Aspirin Reaction Units (ARU) or P2Y12 Reaction Units (PRU) – ARU indicates the amount of thromboxane A2-mediated platelet activation (via GP IIb/IIIa receptors). PRU indicates the amount of ADP-mediated platelet activation.
  - ARU is calculated as a function of the rate and extent of platelet aggregation. Expected values are 350-700 ARU. Therapeutic platelet inhibition with aspirin is at ARU <550.
- Use VerifyNow point of care test alone or in conjunction with TEG with platelet mapping to assess antiplatelet effect of aspirin and/or P2Y12 inhibitors:
  - For aspirin <550 ARU denotes responsiveness:
    - If ≥550 ARU, consider increasing aspirin dose, changing to BID dosing, reviewing medication or food that may diminish effect, and/or adding or converting to another antiplatelet agent
  - For clopidogrel <194 PRU denotes responsiveness:
    - If ≥194 PRU, consider increasing clopidogrel dose, changing to BID dosing, reviewing medication or food that may diminish effect, and/or adding or converting to another antiplatelet agent.
  - For ticagrelor <194 PRU denotes responsiveness:
    - If ≥ 195 PRU, may consider increasing ticagrelor dose, reviewing medication or food that may diminish effect and/or adding or converting to another antiplatelet agent
  - For Cangrelor, 100-180 PRU denotes responsiveness:
    - For >180 PRU, titrate cangrelor appropriately and check 1-4 hours after each titration
  - Consider reduction of aspirin dosing if <350 ARU (aspirin) or <75 PRU for P2Y12 inhibitors).

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 3/6/2024)*

Berlin Heart Blood Pump Assessment & Exchange Guideline

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Historically, there has been significant variability in the management of pulsatile paracorporeal ventricular assist devices (VAD). Typically, management strategies and pump head exchanges were based on a subjective circuit assessment, limited patient risk vs benefit analysis, and non-standardized procedure. Over the last few years, the procedure below and network learnings have been employed to standardize this practice.

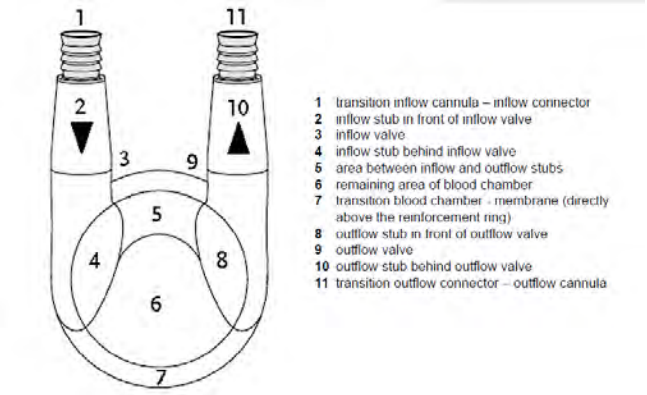
ACTION REVISED DATE: 07/10/2025

OBJECTIVES

To provide a standardized approach to assessing and managing a paracorporeal pulsatile flow VAD, to develop a risk vs benefit analysis patient algorithm, and to complete a protocol for a pump exchange procedure.

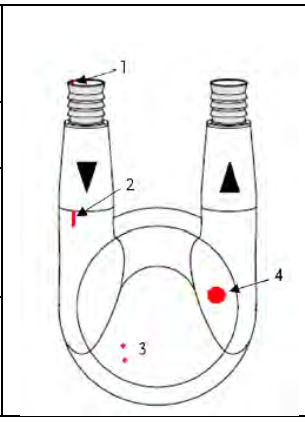
PROTOCOL

The decision to change a Berlin Heart VAD pump in a pediatric patient is generally made by a multi-disciplinary team including CT Surgery, Cardiology (HF/VAD specialist), Cardiac Intensive Care, Perfusionists, bedside nursing, & VAD coordinator.



Berlin Heart EXCOR

1. **Blood Pump Assessment**
    - Assess pump hourly to every four hours starting from inflow cannula, pump head, and outflow cannula. Repeat for BIVAD configuration.
        - Recommend checking more frequently when patient inflamed, febrile, infected, or with high fibrinogen.
    - Document clots using a standardized language
    - Assess the connectors and extension sets for any accumulated fibrin or clots

	Plaque – White punctate deposit		Thrombus- darkened red or black clot deposit
1 & 3 Small	**Individual specks of white deposit < 2mm**		**Individual specks of deposit < 2mm**
2. Strand	**Collection of white deposits that extend across and area of pump**		**Collection of darkened clots that extend across area of pump**
4. Large	**Accumulation of white deposit in one area of the pump >3 mm**		**Accumulation of darkened deposit in one area of the pump >3mm**

2. **Indications for Blood Pump Change**
    - Mobile fibrin or thrombus
    - Thrombus
        - (dark areas 3 mm) - 10 and 15 cc pump. 4 mm for pumps >25 ml
        - Consider change if the location of a smaller thrombus is near the pump outflow
    - Multiple fibrin deposits
    - Risk increased with combination of thrombus or fibrin deposits with inflammation, elevated fibrinogen, fever, or
    - Pump integrity
        - Excessive graphite in air chamber or pitting of membrane concerning for pump membrane rupture
        - Pump membrane rupture
        - Blood, water, or air in membrane between air/blood chambers
        - Damage to pump head
        - Membrane rupture - complete absence of membrane movement due to membrane rupture (emergent)
3. **Pre Blood Pump Change**
    - Discuss augmenting anticoagulation or consider bolus of UFH or Bivalirudin if prolonged pump stasis expected
    - PRN baseline labs (within 24 hours of change): CBC with diff, aPTT*, fibrinogen, ACT
        - Optional labs: TEG with PM, CRP, LDH, HIT screen
    - Document VAD settings, filling/ejecting, clot status per protocol
    - Discuss NPO timing with surgical and CICU team
    - Consider respiratory support management if intubated
    - Discuss whether cardiac anesthesia consult needed
    - Blood available at bedside
    - Ensure adequate line access; create med line
        - Available sedation/analgesia
        - Consider inotropic support syringes in line for labile patients
        - Volume replacement available
        - Sedate patient and remove the chest dressing (optional)
    - Make sure back up console available
    - Pump and Procedure Preparation

- Reference IFU and institutional protocols

4. **Intra-op or Bedside Management**
    - New blood pump prepared ahead of time
    - **TIME OUT #1:** verify patient, procedure (which VAD(s) will be replaced) and cannula position(s); verify cannula/blood pump position with photograph (if available) from patient chart
        - Skin and blood pump(s) prepped appropriately and a sterile field set up per protocol
        - Remove tie bands connecting the blood pump to the cannulae
        - Active driver – remove flow probe for pump prep
    - **TIME OUT #2:** sequence for pump change and plan who is managing console for VAD settings will be confirmed by surgeon. Verify correct pump positioning.
    - Console:

      IKUS: Select **Pause left** or **Pause right**, as required, then press **<Enter>** to confirm. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The selected pump will stop. The view *Pump size and single-step mode* is displayed.

      ACTIVE: Login to the console as 'Expert'. Disconnect flow senor(s). Acknowledge alarm. Stop appropriate pump(s). The *Step* button(s) will now be available.
    - Once pump paused, surgeon will clamp inflow and outflow tubing proximal to patient
        - Old pump head will be removed
            1. Old blood pump will be full of blood
            2. Rinse out and consider saving for education
            3. If there is a suspected membrane rupture, preserve the pump and send to Berlin Heart for further analysis.
    - Connect the new pump to the cannulae using the same orientation as old pump.
    - Once connected, surgeon will remove clamps and ask for pump to be restarted; press step while surgeon de-airs the pump until pump de-aired and then go on full support.
    - Filling and ejection should be closely monitored; pump will be further de-aired if needed.
        - Remove the trocar using precaution from the de-airing nipple as improper removal can cause air entrainment

5. **Early post blood pump change management**
    - Continue bivalirudin peri – pump change
    - Consider obtaining labs (aPTT, PT/INR, fibrinogen, BMP, CBC) within 2 hours of change

- Correct with blood product replacement as needed, being mindful of risk of dilutional coagulopathy with multiple PRBC transfusions, and correct any surgical bleeding as needed
- Sterile dressing placed per Berlin Heart dressing change guidelines
- Monitor neurologic status closely
- Document VAD settings, filling/ejecting, clot status per protocol
- Restart feeds

6. Bivad Considerations:
    - For right sided pump exchange, monitor left pump function.
        - Reduce left sided pump rate if poor filling occurs while right sided has incomplete function.
    - For left sided pump exchange, temporarily decrease the right sided pump rate to prevent pulmonary edema.

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Berlin Heart Emergency Algorithms & Care Guide

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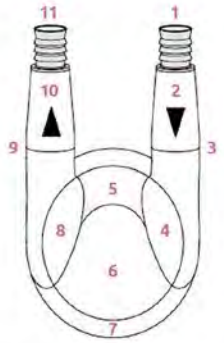
Collaborators: *Berlin Heart*

action

Pump Assessment

1. Transition inflow cannula, inflow connector
2. Inflow stub in front of inflow valve
3. Inflow valve
4. Inflow stub behind inflow valve
5. Area between inflow and outflow stubs
6. Remaining area of blood chamber
7. Transition blood chamber, membrane (directly above reinforcement ring)
8. Outflow stub in front of outflow valve
9. Outflow valve
10. Outflow stub behind outflow valve
11. Transition outflow connector, outflow cannula



Optimizing Pump Function

POOR FILL | **POOR EJECT**

CAUSES

CVP (Central Venous Pressure)

- ↓ Hypovolemia
- ↑ Inflow Cannula Obstruction
- ↑ Tamponade
- ↑ Right Heart Failure

- ↑ Hypertension
- ↑ Outflow Cannula Obstruction
- ↑ Agitation

C.O. (Cardiac Output)

- ↓ Hypovolemia
- ↓ Inflow Cannula Obstruction
- ↓ Tamponade
- ↓ Right Heart Failure

- ↓ Hypertension
- ↓ Outflow Cannula Obstruction
- ↓ Agitation

Patient Treatments

Hypovolemia: ***Give Fluid***
Inflow Cannula Obstruction: ***Evaluate Further***
Tamponade: ***Surgical Drainage***
Right Heart Failure: ***+/- Nitric Oxide & Inotropes***

Hypertension: ***Reduce Afterload***
Outflow Cannula Obstruction: ***Evaluate Further***
Agitation: ***Pain Control/ Sedation***

PUMP FIXES

Decrease Rate
Increase Diastolic Pressure
Decrease % Systole

Increase Systolic Pressure
Increase % Systole

Berlin Heart CPR

Unresponsive Patient
Assess for a palpable pulse!

Pulse Present

Assess pump membrane movement

Assess for other causes of un-responsiveness:
- Stroke
- Hypoglycemia
- Sedative use
- Hypoxemia

Pulse Absent

Immediately begin chest compressions!
- Follow PALS protocol including defibrillation
- DO NOT CLAMP CANNULAE

Assess the following:
- Is the membrane moving, filling/ ejecting adequately?
- Are cannulae or driveline kinked?
- Is the IKUS powered & functioning?

If IKUS not functioning, **use manual hand pump** until back-up IKUS powered and ready for use.
- Hand pump at a rate of 60–80 bpm
- Recheck pulses

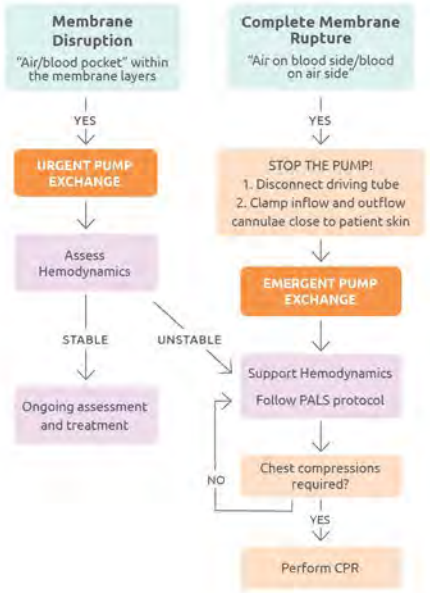
Pulse Absent?
- Resume chest compressions immediately!
- Follow PALS protocol

Notify Cardiovascular Surgery
- Consider ECMO

Pulse Present?
Hand pump at a rate of 60–80 bpm

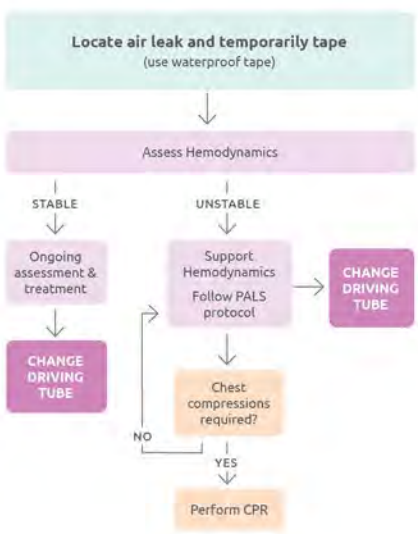
Membrane Malfunction

**Will require urgent/emergent pump exchange*



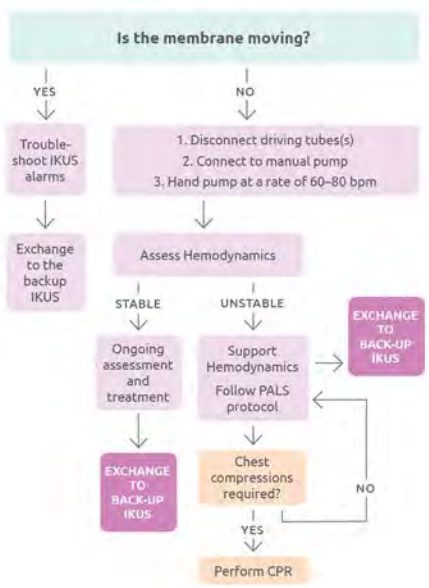
Cracked Driving Tube

**Will require urgent driving tube exchange*

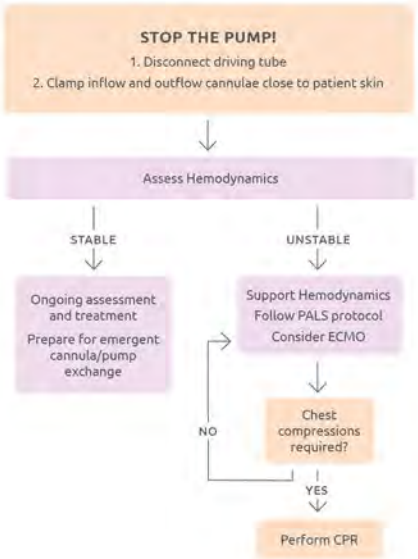


IKUS Malfunction

**Will require urgent IKUS exchange*



Cannula Disruption



BLEEDING PROTOCOL for Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Epistaxis and gastrointestinal bleeding are common complications post VAD implantation due to anticoagulation requirement. The pathophysiology is unclear but acquired von-Willebrand disease, angiodysplasia and formations of arterio-venous malformations have been implicated. This management is complicated as the risk of thrombosis increases if anticoagulation is held.

ACTION REVISED DATE: 03/06/2024

OBJECTIVES

To review the options for management of epistaxis and GI bleeding in patients with VADs based on the severity of the symptoms.

PROTOCOL

EPISTAXIS: Spontaneous non-traumatic

Sporadic episodes:

- Application of direct pressure
  - Pinch at the bottom, soft part of the nose for 10 minutes while keeping head upright, do not let go to check for blood during that time
  - If bleeding continues, soak ½ cotton ball with oxymetazoline and place gently into the bleeding nostril. Continue to pinch nose firmly for 10 minutes.
  - Do not put anything else in the nose to stop bleeding
- Recommend nasal sprays like oxymetazoline (if lasting >5 mins) – if required for > 3 days, consider ENT consultation.
- Avoid NSAIDs and counsel parents/patient about nose picking
- Cool mist humidifier in the home, Q6 hour saline spray and Vaseline or Aquaphor to prevent dryness in nose (esp when admitted in-house)- titrate to Q6-12 hours
- If requiring treatment for >3 days or for larger/uncontrolled bleeds, consider consulting ENT

Chronic significant refractory bleeds: *(Impaired quality of life like loss of school time or with drop in Hb (>1g/dL) or Hct (>3%)*

- Send diagnostic studies CBC, Coagulation profile (PT, aPTT, INR), fibrinogen. Consider sending Thromboelastography (TEG).
- Consult ENT and consider consider topical aminocaproic acid (Amicar) or cauterization with silver nitrate or topical amicar
- If patient on warfarin: Consider lowering goal INR to 2.0-2.5
- If patient on heparin or bivalirudin: Consider lowering aPTT goal to 1.5X-2.5X baseline (DTT 60-75 seconds)
- Consider holding anti-platelet therapy (if multiple agents, reduce to one or discontinue all at physician discretion)
- Recommend hematology consult and consider a work up for acquired vWF

Uncontrolled Bleeding: *(defined by significant drop in Hb >3g/dL or Hct>10%; PRBC transfusion requirement or continuous bleeding not controlled by cauterization)*

- Send diagnostic studies- CBC, TEG Coagulation profile (PT, aPTT, INR), Fibrinogen
- Consider holding all anticoagulation and antiplatelet therapy until bleeding is controlled
- Transfuse for significant drop in hemoglobin and/or if patient is hemodynamically unstable with markers of low oxygen delivery (SvO2, NIRS, etc)
    - Ensure fibrinogen > 100mg/dL
    - In case of derangements of coagulation labs, consider administering Vitamin K/Kcentra and/or FFP replacement
- Consider dissolvable/non-dissolvable hemostatic packing by ENT
- When bleeding is controlled consider slow re-initiation of anticoagulation with modified target dosing
    - Warfarin: Consider reinitiating of warfarin with slow up-titration to a goal INR of 1.8-2.2 when HCT stable for 48 hours (Bridging with LMWH or heparin may not be necessary if held less than 1 week)
    - Heparin/bivalirudin: Consider lowering aPTT goal to 1.5X-2X baseline (DTT 50-70 seconds)
- Consider stopping anti-platelet medication
- Recommend hematology consult and consider a work up for acquired vWF deficiency

GI BLEEDING

GI Bleeding defined according to INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) criteria as clinical evidence of GIB including melena, hematochezia, hematemesis, or rectal bleeding occurring >7 days post-LVAD implantation.

In case of occult bleeding without significant clinical change (hemodynamically stable, no drop in Hb or HCT), recommend to continue monitoring.

First episode:

- Send diagnostic studies – CBC, TEG, Coagulation profile (PT, aPTT, INR), fibrinogen
- Transfuse for significant drop in hemoglobin and/or if patient is hemodynamically unstable with markers of low oxygen delivery (SvO2, NIRS, etc.)
    - Ensure fibrinogen > 100mg/dL
    - Consider checking coagulation labs and in case of derangements– consider stopping bivalirudin/heparin or administering Vitamin K and/or FFP replacement
- Consider consultation with GI team to ensure adequate gastric acid suppression and consider dual therapy to include proton blocker therapy
- If patient on warfarin: Consider reinitiating warfarin to a goal INR of 2-2.5
- If patient on heparin/bivalirudin: Consider lowering aPTT goal to 1.5X-2.5X baseline (DTT 60-75 seconds
- If life-threatening or major bleed (Major bleeding is defined as bleeding into a major organ (including intracranial hemorrhage) or requiring surgery or transfusion of packed red blood cells (PRBC), consider warfarin at a fixed dose (i.e. warfarin 1mg daily)

Recurrent episodes:

- Send diagnostic studies and recommend holding anticoagulation until results
- Ensure adequate gastric acid suppression, consider dual therapy to include proton blocker therapy either intermittent or as a continuous infusion (to be used until bleeding is stabilized).
- Transfuse for significant drop in hemoglobin and/or if patient is hemodynamically unstable with markers of low oxygen delivery (SvO2, NIRS, etc)
    - Ensure fibrinogen > 100mg/dL
    - Consider checking coagulation labs and in case of derangements– consider stopping bivalirudin/heparin or administering Vitamin K and/or FFP replacement

- When bleeding is controlled consider slow re-initiation of anticoagulation with modified target dosing
    - Warfarin: Consider reinitiating warfarin with goal INR of 1.8- 2.2 (may not need bridging) or consider discontinuing warfarin and restarting either reduced dose enoxaparin (0.5mg/kg/day) or continuous short acting heparin or bivalirudin drips.
    - Heparin/bivalirudin: Consider lowering aPTT goal to 1.5X-2X baseline (DTT 50-70 seconds)
- Consider holding anti-platelet therapy (if multiple agents, discontinue all at physician discretion)
- Consider octreotide in consultation with you ICU or GI teams– esp if angiodysplasia bleed suspected.
- If life-threatening or major bleed, consider maintaining warfarin at a fixed dose (i.e. warfarin 1mg daily)
- Recommend hematology consult and consider a work up for acquired vWF deficiency

≥4 episodes:

- Consider discontinuation of all anticoagulation indefinitely
- Start proton pump inhibitor infusion
- Consider octreotide– esp if angiodysplasia bleed suspected.
- Consider last-line therapies such as thalidomide (decrease AVM formation) or estrogen/hormonal replacement therapy
- Consider further investigations like tagged RBC study/EGD/Colonoscopy/CTA or video capsule endoscopy

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Continuous Flow Paracorporeal VAD Circuit Change Guideline

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Historically, there has been significant variability in the management of continuous flow paracorporeal ventricular assist devices (VAD) circuits. Typically, management strategies and circuit changes were based on a subjective circuit assessment, limited patient risk vs benefit analysis, and non-standardized procedure. Over the last few years, the procedure below and network learnings have been employed to standardized this practice.

ACTION REVISED DATE: 07/10/2025

OBJECTIVES

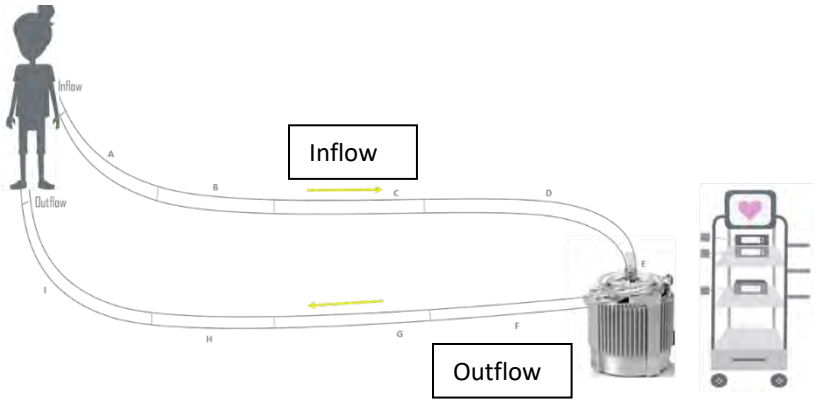
To provide a standardized approach to assessing and managing a paracorporeal continuous flow VAD circuit, to develop a risk vs benefit analysis patient algorithm, and to complete a protocol for a circuit change procedure.

PROTOCOL

The decision to change a VAD circuit in a pediatric patient is generally made by a multi-disciplinary team including CT Surgery, Cardiology (HF/VAD specialist), Cardiac Intensive Care, Perfusionists, & VAD coordinator.

Extracorporeal Centrifugal Continuous Flow Devices

1. **Circuit Assessment**
    - Assess circuit hourly to every four hours starting from venous cannula, pump head, and arterial cannula. Repeat for BIVAD configuration.
    - Document clots using standardized language
        - Plaque or thrombin – small white punctate
        - Thrombus – large dark area



2. **Indications for Circuit Exchange (may also consider removing an affected section if circuit change is not indicated)**
    - Mobile thrombus or fibrin strand
    - Thrombus accumulation > 5mm
    - Unusual vibration or noise from pump head
    - Increased hemolysis markers
        - LDH > 1.5X baseline
        - Plasma free hgb
        - FDP
        - D-Dimer

- Platelet decrease
- Hemaglobinuria

3. **Pre Circuit Change**
    - Continue bivalirudin peri – circuit change
    - Document clot status and VAD settings per protocol
    - PRN baseline labs (within 24 hours of change): CBC with diff, aPTT*, fibrinogen,
        - Optional labs: TEG with PM, CRP, LDH, HIT screen
    - Discuss NPO timing with surgical and CICU team
    - Consider respiratory support management if intubated
    - Discuss whether cardiac anesthesia consult needed
    - Consider steroids
    - Ensure adequate line access; create med line
        - Available sedation/analgesia
        - Consider inotropic support in line for labile patients
        - Volume replacement available
        - Sedate patient and remove the chest dressing (optional)
    - **Equipment & Circuit Exchange Procedure:**
        - Reference circuit's IFU and institutional protocols
4. **Intra-op or Bedside Management**
    - Circuit primed ahead of time
    - Consider ACT 30 mins prior to exchange
    - **TIME OUT #1:** verify patient, circuit to be exchanged
    - Skin and circuit prepped appropriately and a sterile field set up per protocol
    - **TIME OUT #2:** sequence for circuit(s) change and plan who is managing circuit settings will be confirmed by surgeon
    - Once circuit paused, surgeon will clamp tubing
        1. Can cut tube ties during prep phase to reduce the time off support
    - Old circuit will be removed
    - Once connected, surgeon will remove proximal clamp and ask for pump to be restarted
5. **Early post blood pump change management**
    - Continue bivalirudin peri – pump change
    - Consider labs (aPTT, PT/INR, fibrinogen, BMP, CBC, ACT) within 2 hours of change

- Correct with blood product replacement as needed, being mindful of risk of dilutional coagulopathy with multiple PRBC transfusions
- Sterile dressing placed per dressing change guidelines
- Monitor neurologic status closely
- Document VAD settings, clot status per protocol
- Restart feeds
- Monitor patient's temperature closely after circuit exchange. If patient becomes hypothermic due to heat loss through circuit, consider applying external heat (like barehugger) source to gently rewarm patient.

6. Bivad Considerations
    - Monitor the risks and benefits of changing one or both circuits.
    - If changing a single circuit is determined to be the best course of action, be mindful of how the exchange will temporarily affect the flow to the alternate circuit.
        - If changing the circuit supporting the left side, temporarily decreased the flow of the right circuit to prevent pulmonary edema.
        - If changing the circuit supporting the right side, monitor the left side performance and decrease RPMs if the left side begins to chatter or suction.

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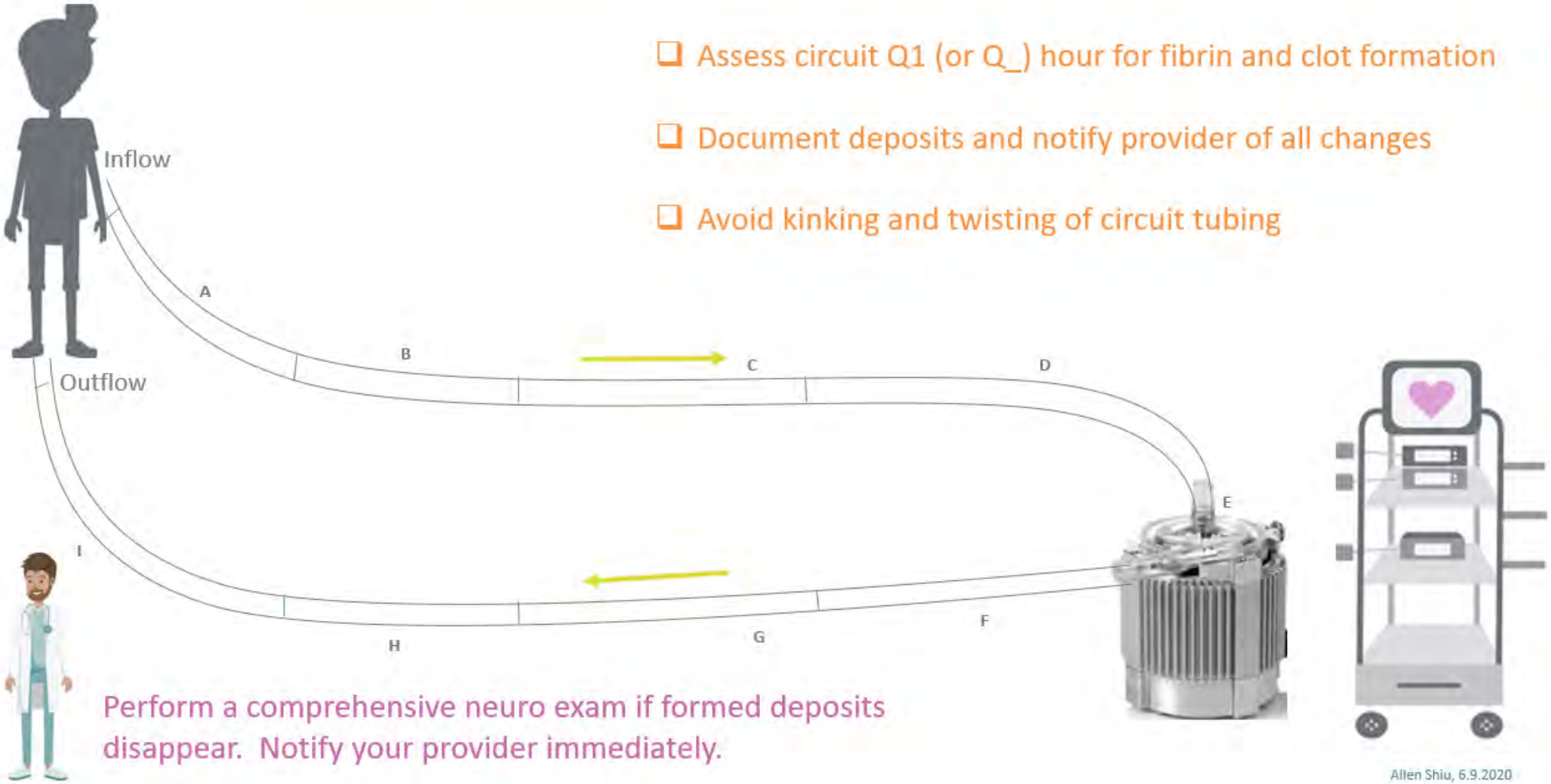
CENTRIMAG Deposit Diagram

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

- ❑ Assess circuit Q1 (or Q_) hour for fibrin and clot formation
- ❑ Document deposits and notify provider of all changes
- ❑ Avoid kinking and twisting of circuit tubing



Perform a comprehensive neuro exam if formed deposits disappear. Notify your provider immediately.

Allen Shiu, 6.9.2020

SECTION

Compassionate Deactivation

ACTION REVISED DATE: 10/07/2024

STEPS FOR POWERING OFF IKUS UNIT

1.In the monitor program, select the option **Drive OFF** (see Fig.1) and press **<Enter>** to confirm.

2. Respond to the prompt in the dialog window by pressing the **<X>** key or the **<1>** key. The system stops operation immediately and writes an operating log.

3. Wait until the log has been completed. When the message **Switch drive off with main switch!** appears, press **<F10>** to shut down the monitor program. Confirm by pressing the **<X>** key or the **<1>** key.

4. Select **3. End** (**<3>**, see Fig. 2) in the start menu and switch off the laptop.

5. Switch the Ikus off by turning the key switch to ***[0]*** position.

Fig.1

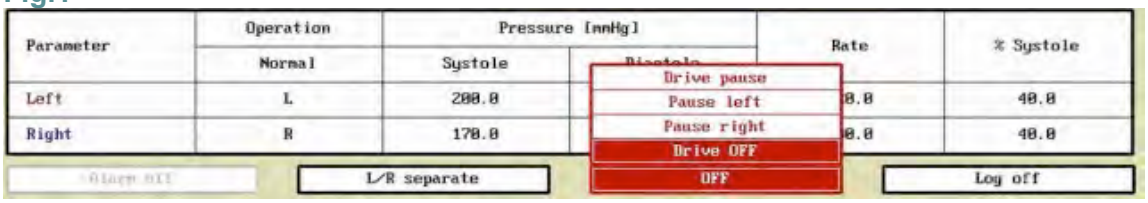
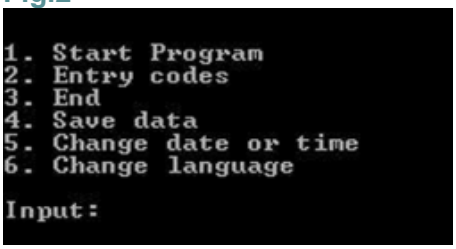


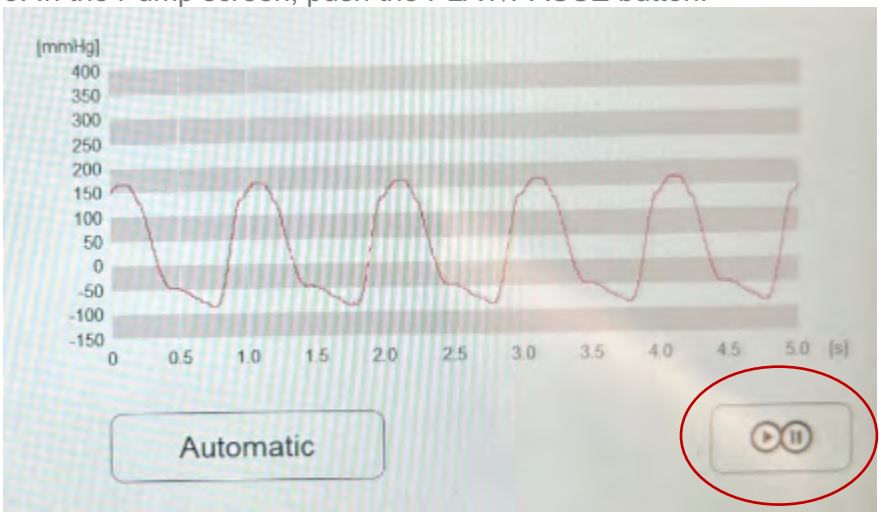
Fig.2



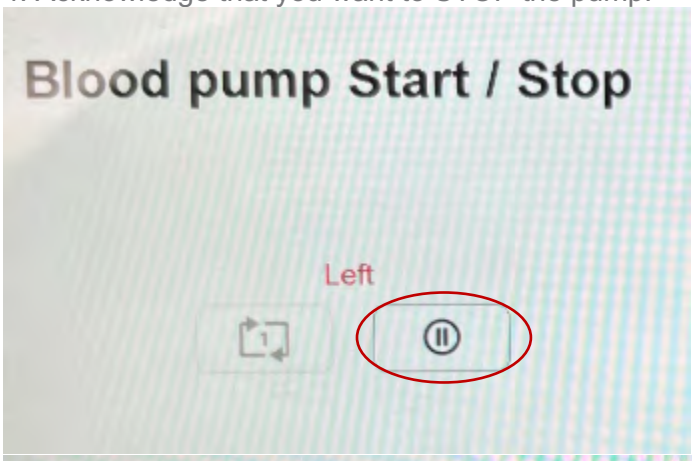
STEPS FOR POWERING OFF ACTIVE DRIVER

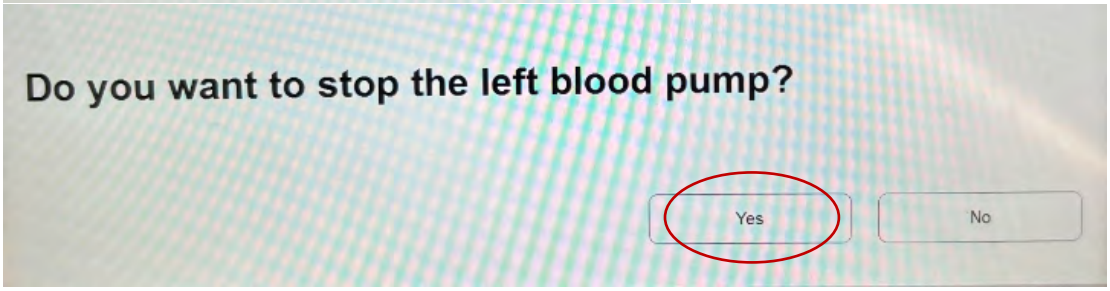
1.In the PC panel, log in as Expert.
2. At the top of the Menu, push the PUMP icon.

3. In the Pump screen, push the PLAY/PAUSE button.



4. Acknowledge that you want to STOP the pump.





5. Once the pump is stopped, disconnect the driveline and flow probe from the driver and remove the driver from the room. The driver can be shut down once outside of the room.

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Compassionate Deactivation of HEARTMATE3 in Children

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

ACTION REVISED DATE: 10/07/2024

STEPS FOR POWERING OFF HEARTMATE 3

Action: Before proceeding, ensure deactivation of pacemaker or ICD (defibrillation and pacing functions) if applicable (item 1.3 of Checklist)

1: Disconnect the Driveline. On the PC back, open the latch lever;  press the Red button while pulling the Driveline connector out.  The VAD is stopped. You may hit the alarm silence button, bell with X thru it, to quite the alarms while you disconnect power.

2: Remove Power from the Controller. Loosen the White / Black Power Connections (unscrew the lock nut) and pull each apart. 

3: Hold down the Battery button until the Controller shuts down ~ 5 seconds.

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ACTION REVISED DATE: 10/07/2024

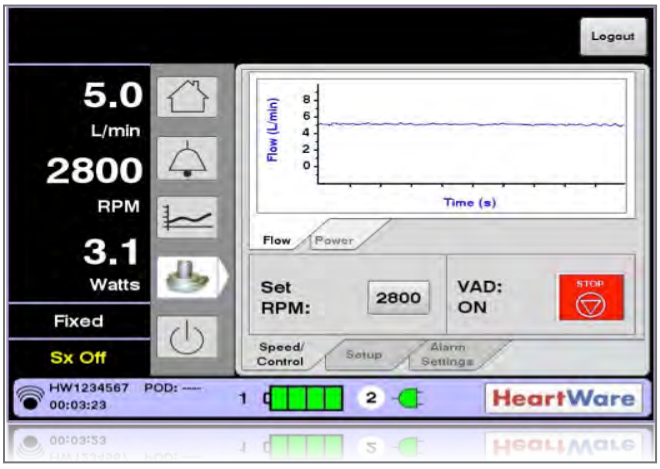
STEPS FOR POWERING OFF HEARTWARE HVAD

Action: Before proceeding, ensure deactivation of pacemaker or ICD (defibrillation and pacing functions) if applicable (item 1.3 of Checklist)

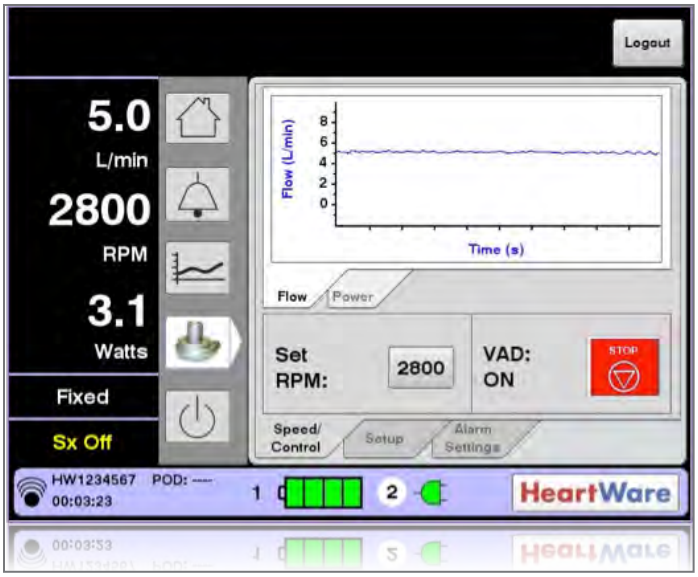
Step 1: Place data/monitor cable to the primary controller

Step 2: Login to the monitor using the pump icon on home screen- password **68773 (Nurse)**, **<enter>**

Step 3: Go to Speed/Control tab



Step 4: Press **Red VAD Stop** button



Step 5: Press **<Yes>**, to confirm you want to stop the VAD

Step 6: Remove data cable, place red alarm adapter to data port

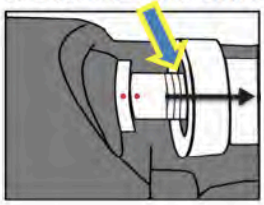
Step 7: Remove both power sources to power down the controller, then remove driveline.

Alternative Steps without monitor:

HVAD Controller:

1: Find and insert the Red Alarm Adapter into the Blue port; line up the arrow and dot then push in.

2: Disconnect the Driveline by sliding the gray boot back; grasp the connector on the ridges / lines and pull back.



3a: Remove both Power Connections by rotating the Black collar CCW and pulling straight back.

3b.If the Red plug is not found press and hold the Alarm silence and Arrow buttons together for 10 seconds THEN DISCONNECT FROM POWER.

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Compassionate Deactivation MCS Checklist

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

ACTION REVISED DATE: 10/07/2024

1. Multi-disciplinary Team Communication and Preparedness Planning: Identify and contact key members listed below

1.1 Primary medical team:

( ) Attending ICU physician
( ) Primary cardiologist and/or On service cardiologist
( ) Cardiothoracic surgeon
( ) VAD coordinator
( ) Bedside nurse and Charge nurse
( ) Respiratory Therapist (RT)
( ) Perfusion Team, if indicated ( ) Child Life Specialists (Patient/sibling support)

1.2 Multi-disciplinary team:

( ) Palliative Care consultant
( ) Social Worker (SW)
( ) Chaplain, as indicated
( ) Ethics consult, as indicated
( ) Bereavement group, as indicated

1.3 Interdisciplinary care plan discussion and preparation for CDMCS

( ) Assess provider comfort level with CDMCS plan and procedure (prepare for substitute staff if needed)
( ) Discuss and plan sequential steps for removal of other life sustaining therapies during CDMCS process
( ) Review each therapy patient may be receiving (Ex: Nutrition, Fluids, Dialysis, Inotropes, inhaled Nitric Oxide, Ventilation)
( ) Review deactivation of pacemaker or ICD (defibrillation and pacing functions) and timing according to steps below
( ) Autopsy

2. Family Meeting:

2.1 Family meeting preparation:

( ) Identify and contact key stakeholders and leader
( ) Identify surrogate decision maker, if required
( ) Call Organ Procurement Organization or appropriate entity: determine candidacy for organ donation

2.2 Meeting content:

( ) Define agenda of the meeting and ask permission to discuss CDMCS process
( ) Review important goals for patient and family
( ) Outline CDMCS process, reiterating commitment to patient's comfort, prioritizing patient's and family's values
( ) Outline comfort-directed therapies that will be continued or started, and therapies to be discontinued (ex.: dialysis, nutrition, ventilation, inotropes, laboratory draws, transfusions, pacemaker or ICD)
( ) Identify which family members plan to be present
( ) Plan religious rites and assistance, as indicated
( ) Explain unpredictability of timing of death (minutes, hours, days) and emphasize continuation of comfort care
( ) Plan care or steps after CDMCS: hospice if indicated, autopsy if indicated and funeral arrangements
( ) Offer resources for bereavement support: environment (respectful silence/ noise control, bereavement rituals with staff if available, family photos and keepsakes if available
( ) Clarify with family date and time for CDMCS
( ) Clarify date and time planned for CDMCS with multi-disciplinary team

2.3 Documentation:

( ) Document legal proxy decision-makers (i.e.: both mother/father, SW as needed)
( ) Document Advanced Directives of Care in accordance with local policies and laws (example below):
( ) Capacitated Patient: Attending must document conversation of patient or surrogate desire to have life-prolonging treatment withheld or withdrawn
( ) Incapacitated Patient: 2 Attending notes documenting terminal/end stage condition and no reasonable probability of recovering capacity or surrogate's desire to have life-prolonging treatment withheld/withdrawn
( ) Document present members and content of family meeting

3. Interdisciplinary end of life care at bedside for CDMCS:

3.1 Delineate team bedside roles and responsibilities:

( ) Review and rehearse planned sequence for deactivation of VAD (specific to VAD type) and other life sustaining therapies discussed in family meeting, including alarm monitoring
( ) Identify member responsible for CDMCS
( ) Certify RT and equipment preparation
( ) Identify responsible bedside nurse and assistant: review medications for comfort at bedside and who will administer

3.2 Orders

( ) Review and discontinue orders that may cause discomfort and align with family wishes (Section 2.2: consider early discontinuation of inotropes to allow natural death to occur when device is turned off)
( ) Review, plan and continue Comfort Care orders:
( ) Ensure privacy (partitions, closed curtains) or consider moving patient to private room if possible
( ) Review PRN medications, doses and titration parameters
( ) Anticipate need of new drips, short acting opioids and benzodiazepines, anti-emetics, anti-pruritus

( ) Write and sign DNR order, if not already done

4. Preparation of family at the bedside:

4.1 Certify available Multi-D Team, as indicated (SW, Chaplain, if desired)

4.2 Patient examination and family support:

( ) Communicate to team important goals outlined by patient and/or family
( ) Exam patient and assess family's perception of patient's level of comfort
( ) Inform family what to expect (ex.: signs of dying and death)
( ) Discuss with family anticipated symptoms and pharmacological and non-pharmacological strategies for discomfort (anxiety, pain, secretions, noises, gasping, skin color changes)
( ) Clarify with patient or family desired attire for CDMCS (example: religious, ethnic or preferred attire)
( ) Inform family when preparation is completed.

5. Post-CDMCS care:

5.1 Hold a team debrief

5.2 Notify appropriate clinical reps of patient outcome

5.3 Complete Simplified Clinical study documentation

AUTHORS

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RESOURCES:

1. Bruce RC, Allen NG, Fahy BN, et al. Challenges in Deactivating a Total Artificial Heart for a Patient With Capacity. CHEST 2014; 145 (3): 625-631
2. Schaefer KG, Griffin L, Smith C, et al. An Interdisciplinary Checklist for Left Ventricular Assist Device Deactivation, Jour of Pall Med, 2014, 17(1): 4-5
3. Hollander SA, Axelrod DM, Bernstein D, et al. Compassionate deactivation of ventricular assist devices in pediatric patients, J Heart Lung Transplant 2016;35:564–567.

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Compassionate Deactivation of Mechanical Circulatory Support in Children

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

The process of compassionate deactivation of mechanical circulatory support (CDMCS) is extremely challenging for families and health care providers. CDMCS is considered to be both legal and ethical, and it is not considered a form of euthanasia because no new pathology is introduced, and the patient dies from the natural progression of his/her underlying disease.

ACTION REVISED DATE: 10/07/2024

OBJECTIVES

1. To provide a preparation guideline for CDMCS as a tool of integration, planning and preparation of patients, families, caregivers, and clinicians.
2. To utilize a standardized pathway that can be tailored to one's individual needs and ensure a comfortable and dignified end-of-life experience for children on VAD support.
3. To provide information about CDMCS of the most common VADs used in children.

PROTOCOL

1. Multi-disciplinary Team Communication and Preparedness Planning: Identify and contact key members listed below

1.1 Primary medical team:

( ) Attending ICU physician
( ) Primary cardiologist and/or On service cardiologist
( ) Cardiothoracic surgeon
( ) VAD coordinator
( ) Bedside nurse and Charge nurse
( ) Respiratory Therapist (RT)
( ) Perfusion Team, if indicated

1.2 Multi-disciplinary team:

( ) Palliative Care consultant
( ) Social Worker (SW)
( ) Chaplain, as indicated
( ) Ethics consult, as indicated
( ) Bereavement group, as indicated
( ) Child Life Specialists (Patient/sibling support)

1.3 Interdisciplinary care plan discussion and preparation for CDMCS

( ) Assess provider comfort level with CDMCS plan and procedure (prepare for substitute staff if needed)
( ) Discuss and plan sequential steps for removal of other life sustaining therapies during CDMCS process
    ( ) Review each therapy patient may be receiving (Ex: Nutrition, Fluids, Dialysis, Inotropes, inhaled Nitric Oxide, Ventilation)
    ( ) Review deactivation of pacemaker or ICD (defibrillation and pacing functions) and timing according to steps below
( ) Autopsy

2. Family Meeting:

2.1 Family meeting preparation:

( ) Identify and contact key stakeholders and leader
( ) Identify surrogate decision maker, if required
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( ) Plan religious rites and assistance, as indicated
( ) Explain unpredictability of timing of death (minutes, hours, days) and emphasize continuation of comfort care
( ) Plan care or steps after CDMCS: hospice if indicated, autopsy if indicated and funeral arrangements

( ) Offer resources for bereavement support: environment (respectful silence/ noise control, bereavement rituals with staff if available, family photos and keepsakes if available
( ) Clarify with family date and time for CDMCS
( ) Clarify date and time planned for CDMCS with multi-disciplinary team

2.3 Documentation:

( ) Document legal proxy decision-makers (i.e.: both mother/father, SW as needed)
( ) Document Advanced Directives of Care in accordance with local policies and laws (example below):
( ) Capacitated Patient: Attending must document conversation of patient or surrogate desire to have life-prolonging treatment withheld or withdrawn
( ) Incapacitated Patient: 2 Attending notes documenting terminal/end stage condition and no reasonable probability of recovering capacity or surrogate's desire to have life-prolonging treatment withheld/withdrawn
( ) Document present members and content of family meeting

3. Interdisciplinary end of life care at bedside for CDMCS:

3.1 Delineate team bedside roles and responsibilities:

( ) Review and rehearse planned sequence for deactivation of VAD (specific to VAD type) and other life sustaining therapies discussed in family meeting, including alarm monitoring
( ) Identify member responsible for CDMCS
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( ) Review, plan and continue Comfort Care orders:
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( ) Review PRN medications, doses and titration parameters
( ) Anticipate need of new drips, short acting opioids and benzodiazepines, anti-emetics, anti-pruritus
( ) Write and sign DNR order, if not already done

4. Preparation of family at the bedside:

4.1 Certify available Multi-D Team, as indicated (SW, Chaplain, if desired)

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( ) Clarify with patient or family desired attire for CDMCS (example: religious, ethnic or preferred attire)
( ) Inform family when preparation is completed.

5. Post-CDMCS care:

5.1 Hold a team debrief

5.2 Notify appropriate clinical reps of patient outcome

5.3 Complete Simplified Clinical study documentation

The full checklist is available via this link, but also copied below for reference: https://public.3.basecamp.com/p/ry93j6WMCihXMVFWRt7FfWa (UPDATE LINKS once posted to Basecamp)

Device-Specific CDMCS (links below to specific documents)

- Berlin Heart: https://public.3.basecamp.com/p/6saWERpJXwcq1RKg3eBVHQ3b
- HeartWare HVAD: https://public.3.basecamp.com/p/vhrwhJFuosyERu11TLpKDLGt
- HeartMate 3: https://public.3.basecamp.com/p/GNvGYUukYH153E99BVq1Snmm
- Pedimag & Centrimag: https://public.3.basecamp.com/p/gtN7vE67mJtAV5BFtWvmBgZU

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Compassionate Deactivation of PEDIMAG & CENTRIMAG in Children

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

ACTION REVISED DATE: 10/07/2024

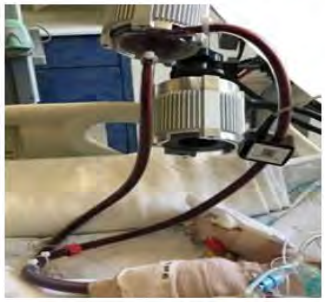
STEPS FOR POWERING OFF PEDIMAG & CENTRIMAG

1. Turn minimal flow limit alarm down to zero

MCS Guideline: Discontinuing PEDIMAG & CENTRIMAG

1. Turn Flow & Flow Alarm to Zero

2. Clamp Return Tubing



3. Decrease RPM to Zero

4. Switch Power off in Back

Move the clear door over the green power button and hold for 5 seconds to power off.

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Direct Thrombin Inhibitor (DTI) Harmonization Protocol for VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Bivalirudin is a direct thrombin inhibitor (DTI). It does not require AT3 for activity. Onset occurs in 2 minutes when given by continuous infusion, with half-life of 26 minutes with normal renal function, and up to 4 hours in severe renal failure. Titration can be done using multiple assays, but has most commonly been performed with aPTT. Steady state requires 4 hours.

ACTION REVISED DATE: 04/24/2020

BIVALIRUDIN

1. **Pre-VAD implantation work-up (<48 hours pre VAD/MCS):**
    - Baseline labs: CBC with diff, aPTT*, PT/INR, fibrinogen, basic metabolic panel (BMP)
    - Optional labs: TEG with PM, CRP, LDH, cystatin C, HIT screen, ROTEM
2. **Intra-op management**
    - Standard heparin anticoagulation for cardiopulmonary bypass with full protamine reversal in OR
    - Standard blood product replacement to normalize coagulation parameters and establish hemostasis in OR
3. **Early post-op management**
    - Labs (aPTT, PT/INR, fibrinogen, BMP, CBC) within 2 hours of arrival to ICU
    - Optional: dilute thrombin time (dTT), TEG ± PM, ROTEM
    - It appears reasonable to start bivalirudin once:
        - Surgical and coagulopathic bleeding resolved (< 2 ml/kg of chest tube output for 4 hours and no other sources of active bleeding)
        - aPTT within 15 sec of baseline* (or institutional normative range)
        - INR <1.3
        - Fibrinogen > 200
        - Platelet count >100,000
    - Correct with blood product replacement as needed, being mindful of risk of dilutional coagulopathy with multiple PRBC transfusions, and correct any surgical bleeding as needed

Standard Goals: In order to learn more about what the ideal level of bivalirudin anticoagulation is, suggested standard goals based on national data have been set as a suggestion. This also helps with clarity for teams at the bedside. Not only are their goal ranges but target PTTs that are central to the range so that patients with a ptt of 61 when the goal is 60-80 will be managed so time within a goal range could possibly be higher.

- **Early Post-op (24-72 hours, high risk for bleeding) target aPTT 55 (goal range 50-60)**
- **Maintenance (standard risk for bleeding) target aPTT 70 (goal range 60-80)**
- **Maintenance (High risk for thrombosis) target aPTT 80(goal range 70-90)**

TABLE 1: Initial Bivalirudin Dosing	
Goal: aPTT • *High risk (of bleeding): aPTT 50-60 sec*	**Goal: dilute thrombin time (dTT)** • *High risk (of bleeding): dTT 50-60 sec*
Renal function (GFR)	Initial dosing
Normal (>60ml/min/1.73 m2)	0.3 mg/kg/hr IV infusion
Mild-moderate (30-60ml/min/1.73 m2)	0.2 mg/kg/hr IV infusion
Severe (<30ml/min/1.73 m2)	0.1 mg/kg/hr IV infusion

- Check aPTT 2 hours after first initiation. Cautious about titrating with first level.
    - If aPTT has jumped dramatically to >2-3 x baseline PTT, then decrease Bival by 50% and recheck in 2-3 hours
    - If PTT has increased to 1-1.5 x baseline, make no adjustment and repeat PTT in 2-3 hours as level may continue to rise

TABLE 2: Maintenance Bivalirudin titration	
Goal: aPTT • *Standard risk: aPTT 60-80 sec* • *High risk (of thrombosis): aPTT 70-90 sec*	**Goal: dTT** • *Standard risk: dTT 60-80 sec* • *High risk (of thrombosis): dTT 70-90 sec*
If aPTT 5 to 15 sec out of range: • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change	***If dTT 5 to 15 sec out of range:*** • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT in target range, no change. • Recheck 2-3 hrs, then can decrease frequency when stable	***If dTT is in target range, no change:*** • Recheck 2-3 hrs, then can decrease frequency when stable
If aPTT ≥15-30 sec out of range • Increase or decrease by 25% (round up to closest 2nd decimal • Recheck 2-3 hours after dose change	***If dTT ≥15-30 sec out of range:*** • Increase or decrease by 25% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT >3x baseline or ~120 sec: • With normal renal function: hold 15 min and reduce by 30% • With mild to moderate renal dysfunction: hold for 45 min and reduce by 40% • With severe renal dysfunction: hold 2 hours and recheck PTT before restarting	***If dTT >100sec:*** • With normal renal function: hold 15 min and reduce by 30% • With mild to moderate renal dysfunction: hold for 45 min and reduce by 40% • With severe renal dysfunction: hold 2 hours and recheck PTT before restarting

SIMPLE TITRATION RULE: Adjust your bivalirudin infusion the same % as the difference between the current aPTT and goal aPTT you are trying to achieve

Example: Goal aPTT 75, and current aPTT 55 (difference of 20), then go up 20%

NOTE:

- **aPTT may be impacted with the following:**
    - heparin contamination (from line) (↑aPTT)** (can use concomitant anti-XA (HAL) and/or INR/PT to identify contamination, since INR/PT will NOT increase with heparin contamination alone, BUT will increase with bival concentration)
    - traumatic phlebotomy, high pressure exerted on syringe during sampling (↑aPTT)
    - Stasis draw - either from a sluggish IV for a lab that sat in the lab for too long can be falsely low
    - low fibrinogen, low FXII, VIII (>30-40% depletion) (Example: chylous effusion, excessive PD drainage, liver dysfunction, consumption within clot) (↑aPTT)
    - plateau aPTT: may be seen at high concentrations of bivalirudin (>1mg/L), consider using PT/INR and/or dTT, or DTI specific assay ecarin TT(Hemoclot, HemosIL DTI) [Stago, or STA-R Evolution]

- **dTT may be impacted by the following:**
    - heparin contamination (from line) (↑dTT)** (can use concomitant INR/PT to identify contamination, since INR/PT will NOT increase with heparin contamination alone, BUT will increase with bival concentration)
    - fibrinogen levels
    - NOT impacted by lupus inhibitors or elevated d-dimer
    - Stasis draw - either from a sluggish IV for a lab that sat in the lab for too long can be falsely low

ARGATROBAN

- Partial hepatic metabolism: no need to dose based on renal dysfunction
- If your hepatic function changes, then you should re-check your levels and titrate more cautiously
- Half life: 39-51 min, may be prolonged further with hepatic dysfunction

The recommended starting dose of Argatroban is 0.5 mcg/kg/min.

- **Titration increments are typically 0.2-0.5 mcg/kg/min with final therapeutic doses typically between 1-5 mcg/kg/min.**
- **Doses as high as 5-8 mcg/kg/min have been used with the recommended maximum in the adult literature of 10 mcg/kg/min.**

TABLE 3: Initial Argatroban Dosing:	
Goal: aPTT • *High risk (of bleeding): aPTT 50-60 sec*	**Goal: dilute thrombin time (dTT)** • *High risk (of bleeding): dTT 50-60 sec*
Initial dosing: 0.5 mg/kg/min IV infusion - consider lower dosing if know hepatic dysfunction with baseline elevated INR	

TABLE 4: Maintenance Argatroban titration	
Goal: aPTT • *Standard risk: aPTT 60-80 sec* • *High risk (of thrombosis): aPTT 70-90 sec*	**Goal: dTT** • *Standard risk: dTT 60-80 sec* • *High risk (of thrombosis): dTT 70-90 sec*
If aPTT 5 to 15 sec out of range: • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change	***If dTT 5 to 10 sec out of range:*** • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT in target range, no change. • Recheck 2-3 hrs, then daily after 2 consecutive in range values	***If dTT is in target range, no change:*** • Recheck 2-3 hrs, then daily after 2 consecutive in range values
If aPTT ≥15-30 sec out of range • Increase or decrease by 25% (round up to closest 2nd decimal • Recheck 2-3 hours after dose change	***If dTT ≥10-20 sec out of range:*** • Increase or decrease by 25% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT >3x baseline or ~120 sec: • With normal hepatic function: hold 15 min and reduce by 30% • With significant hepatic dysfunction: hold 2 hours and recheck PTT before restarting	***If dTT >100sec:*** • With normal hepatic function: hold 15 min and reduce by 30% • With significant hepatic dysfunction: hold 2 hours and recheck PTT before restarting

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Copyright		**Last Modified**	04/2020

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ECHOCARDIOGRAPHY PROTOCOL for Children with Implantable Continuous Flow Ventricular Assist Devices

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

This ACTION harmonization document provides recommendations based on shared practices across ACTION centers and available guidelines on the use of transthoracic echocardiography (TTE) in children with left ventricular assist devices (LVADs).

ACTION REVISED DATE: 6/21/24

OBJECTIVES

To provide guidance on how to use TTE in the management of implantable continuous flow LVADs (Heartmate 3) in children and to suggest a standardized protocol for surveillance.

PROTOCOL

Overall LVAD goals to be assessed by echo:

- Decompression of left ventricle and left atrium
- Maintain neutral and rounded interventricular spectrum (avoid septal bowing into left ventricle)
- Minimize mitral regurgitation
- No more than trivial aortic insufficiency

Key echo findings:

- LV internal dimension at end-diastole (LVIDd)
- LV function
- RV function
- Tricuspid regurgitation
- Aortic insufficiency
- Aortic valve opening (number of times per 10 cardiac cycles)
- Mitral regurgitation
- Presence of pericardial or pleural effusion
- Presence of thrombus (especially around inflow cannula)

The following are SUGGESTED protocols for (1) LVAD surveillance transthoracic echocardiogram and (2) LVAD speed optimization/ramp echocardiogram protocol.

<u>LVAD Surveillance Transthoracic Echocardiogram Protocol</u>

Document baseline blood pressure: _____
Annotate baseline RPM: _____

Parasternal Long-Axis:

1. (2D, 6 beats): Sweep left ventricle
2. (2D, 3 beats): Measure LVIDd x 3 beats (see figure 1)
3. (2D, 3 beats): Sweep aortic root
4. (M-mode, 10 beats, decrease sweep speed): Aortic valve opening (see figure 2)
5. (Color, 3 beats): Sweep aortic valve for regurgitation
6. (Color, 3 beats): Sweep mitral valve for regurgitation
7. (2D, 3 beats): Angle to image apical inflow cannula

8. (Color, 3 beats): Apical inflow cannula
9. (Color, 3 beats): Sweep tricuspid valve for regurgitation
10. (CW): Peak TR velocity (if present)
11. (Color, 3 beats): Sweep pulmonary valve for regurgitation

Parasternal Short-Axis:

12. (2D, 6 beats): Sweep left ventricle
13. (2D, 3 beats): Aortic root
14. (Color, 3 beats): Aortic root
15. (M-mode, 10 beats, decrease sweep speed): Aortic valve opening
16. (2D, 3 beats): Chordal level of LV for septal position
17. (Color, 3 beats): Tricuspid valve for regurgitation
18. (CW): Peak TR velocity (if present)

Right parasternal window:

19. (Color, 3 beats): Outflow cannula into ascending aorta
20. (PW, CW): Outflow cannula

Apical View

21. (A4C, 2D, 6 beats): Sweep both ventricles
22. (A4C, 2D, 3 beats): Septal position, LV function
23. (A4C, Color, 3 beats): Sweep mitral valve for regurgitation
24. (A4C, 2D, 3 beats): Angle to evaluate inflow cannula
25. (A4C, Color, 3 beats): inflow cannula
26. (A4C, PW, CW): inflow cannula
27. (A4C, 2D, 3 beats): RV function
28. (A4C, Color, 3 beats): Sweep tricuspid valve for regurgitation
29. (A4C, CW): Peak TR velocity
30. (A4C, M-mode): lateral annulus of RV for TAPSE measurement
31. (A5C, Color, 3 beats): Sweep aortic valve for regurgitation

Subcostal View:

32. (2D, 6 beats): RV/LV function, assess for pleural effusion
33. (2D, 6 beats): IVC (with sniff if feasible to estimate CVP)

LVAD Speed Optimization/Ramp Transthoracic Echocardiogram Protocol:

- The decision to perform an LVAD ramp study should be made in conjunction with the HF/VAD, ICU and CV surgery teams
- Recommend ramp studies be performed with a member of the VAD team at bedside
- Indications for Ramp Study:
    - Evidence of right heart or left heart failure/persistent symptoms
    - Suboptimal surveillance study findings
    - Suspicion of device thrombus
    - Device speed optimization
- Safety:
    - Ensure patient is on therapeutic anticoagulation
    - Ensure the left ventricle and aortic root are free from thrombus
        - Risk of thromboembolism with reduction in pump speed
    - Allow ≥ 2-minute stabilization between speed changes
        - When decreasing RPMs: monitor for septum shifting rightward, increasing MR, increasing AoV opening, increases in estimated RV pressures, and any symptoms
        - When increasing RPMs: monitor for septum shifting leftward, impedance of flow into inflow cannula, worsening TR, AoV not opening, increase in AI, suction events, and any symptoms.
        - HeartMate3 100 RPM increments
    - Test endpoints: completion of test/desired outcome attained, suction event, hypotension, hypertension, symptoms

See attached worksheet
Annotate RPM on screen with every change (minimum 2-minute stabilization between changes)

Suggested views:

1. PLAX (2D, 3 beats): LVIDd x3 beats
2. PLAX or PSX (M-mode, 10 beats): Aortic valve opening (out of 10 beats)
3. PLAX (Color, 3 beats): degree of AI
4. PLAX or A4C (Color, 3 beats): degree of MR
5. PSAX (2D, 3 beats): septal position
6. A4C (2D, 3 beats): septal position
7. A4C: (2D, 3 beats): RV function
8. PLAX, PSAX or A4C (Color and CW Doppler, 3 beats): degree of TR
9. A4C or PLAX (2D, Color Doppler, PW, CW): inflow cannula

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Adapted from:

Stainback RF, Estep JD, Agler DA, Birks EJ, Bremer M, Hung J, Kirkpatrick JN, Rogers JG, Shah NR and American Society of E. Echocardiography in the Management of Patients with Left Ventricular Assist Devices: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2015;28:853-909.

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LVAD Speed Optimization/Ramp TTE Protocol

Patient Name:_____ Patient MRN:_____ Study Date:_____

	Speed (RPM)	Flow (LPM)	Pulsatility Index (LPM)	Power (Watts)	MAP (mmHg)	CVP (mmHg)	LVIDd (cm)	AoV opening (%)	AI	MR	TR jet	Septum (L/R/N)
Baseline:												

Final Setting:	

Study Comments:

Comments:

2 minute stabilization period between speeds (minimum)

LVIDd: parasternal long axis

AoV opening: % aortic valve opening assessed using M-mode of AoV in parasternal long axis view, at least 10 consecutive cardiac cycles reviewed

AI/MR: graded 0 to 6; 0=none, 1=trace, 2=mild, 3= mild-mod; 4=mod; 5=mod-sev; 6=severe

Septum: bowing leftward (L), rightward (R), or neutral (N)

action
ADVANCED CARDIAC THERAPIES
IMPROVING OUTCOMES NETWORK

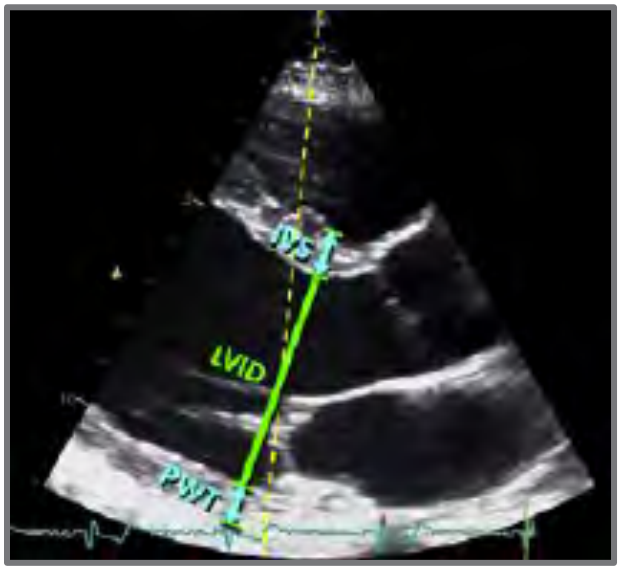

Figure 1. Measure LVIDd parallel to LV long-axis at mitral valve leaflet tips.

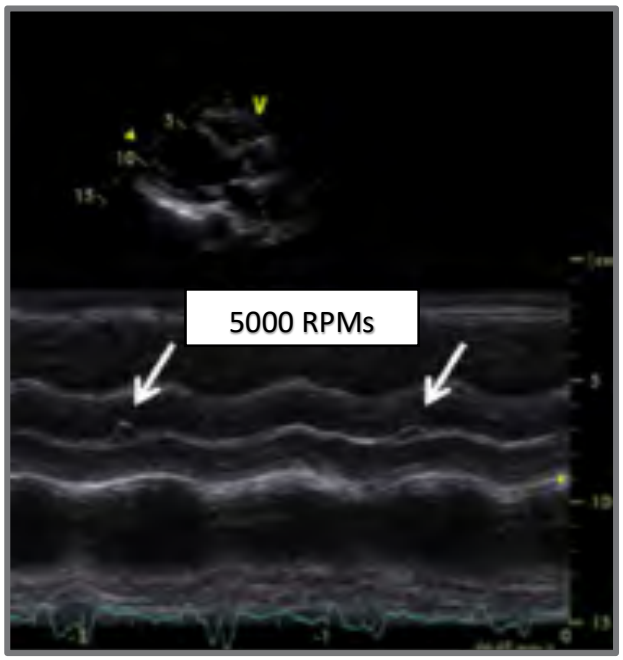

Figure 2. Measure aortic valve opening with m-mode (slow sweep speed). Arrows point to opening of aortic valve. Report number of openings/10 beats. (May be performed in paratsternal long or short axis.) (Stainback et al).

Fontan VAD Management Protocol

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

In select cases of failing Fontan physiology, VAD has been demonstrated to be effective as a form of circulatory support. Physiologic optimization of VAD parameters in this unique population is likely to require individualization. There is limited published literature on VAD support of Fontan patients and we propose these recommendations based on collective clinical experience.

ACTION REVISED DATE: 10/28/2024

OBJECTIVES

1. Optimize physiologic support in post-VAD Fontan patients to include minimization of central venous pressures (CVP) and maximization of effective (non-aortopulmonary collateral) cardiac output.
2. Better define circulatory physiology in post-VAD Fontan patients.

PROTOCOL

PRE-OPERATIVE CONSIDERATIONS

1. Indications.
    a. VAD support can be considered for Fontan patients with:
        i. Signs and symptoms of heart failure or other signs of Fontan failure not responsive to medical management, *and at least one of the following*
            1. Poor systemic ventricular systolic function
            2. Poor systemic ventricular diastolic function
            3. Atrioventricular valve regurgitation
    b. The role of VAD support in individuals with isolated PVR elevation is unclear
2. Pre-VAD Assessment
    a. Cath:
        i. Consider pre-VAD cardiac catheterization to assess pressures, PVR, Fontan obstruction and presence/severity of shunts (ie Aorto-pulmonary (AP) collaterals)
        ii. In some cases, transcatheter closure of AP collaterals may be considered and any significant anatomic obstructions should be addressed, recognizing that gradients may be underestimated in the setting of low flow states and poor cardiac output
        iii. Perform PVR reactivity testing if concern for PVR elevation, to help inform pulmonary vasodilatory use
    b. Imaging:
        i. Ventricular function and distal anatomy may be incompletely characterized by echocardiography
        ii. Consider cardiac MRI to quantify systolic function, volumes, obstruction, flow differential, and collateral burden as well as anatomic data to inform device placement
        iii. In patients who cannot have a CMR, ECG gated CT angiography provides anatomical and some functional data

iv. MRI or CT can be used for 3D modeling and virtual fit

3. Multi-organ system assessment:
    a. Liver disease is not a contraindication to VAD support but extent of liver disease should be thoroughly assessed, including cross-sectional imaging (CT or MRI), assessments for varices and porto-systemic shunts, and evaluation for HCC. If available, obtaining a baseline elastography (ultrasound or MRI) allows for serial evaluations post-VAD with potential prognostic implications
    b. Renal disease may be underestimated by creatinine alone, and other methods for evaluation of renal function are recommended (such as Cystatin C, timed urine collection, or nuclear GFR)
    c. Consider pre-VAD head imaging and detailed neurologic exam.
    d. In patients who are able, consider obtaining baseline functional assessment with cardiopulmonary exercise testing or 6-minute walk
    e. In patients who are able, consider conducting a frailty assessment either using Fried criteria or the Essential Frailty Toolset
    f. Consider obtaining a formal nutritional evaluation
    g. Consider hematology consultation in patients with history of prior thromboembolic events

SURGICAL CONSIDERATIONS

1.) In some centers, a fenestration is created at the time of VAD placement.

Refer to separate *ACTION Harmonized Protocol on Patient and Device Selection*

POST-OPERATIVE CONSIDERATIONS

1. Post-op monitoring
    a. Lines: Optimizing blood flow through the Fontan circuit is critical, and requires in the first 3-5 days post-op:
        i. A reliable CVP catheter, *and either a* pulmonary arterial (PA) Swan-Ganz catheter, *or* an atrial line
        ii. CVP line alone can be considered, especially if low concern for PVR issues.
    b. Monitor NIRS, UOP, and lactate closely in the first 24-48h post-op
    c. Trend mixed venous saturations
    d. If a CardioMems was previously implanted, it can be used to help guide postoperative management
2. Hemodynamic targets
    a. Cardiac index (CI): Recommend initial target of 3.5-4.5 L/min/m^2 including both VAD and native output, to be titrated as needed to the filling pressures and hemodynamic requirements of the individual patient
        i. Patients' native cardiac output will contribute a part of the total CI
        ii. Higher CI may be needed, especially in the presence of significant AP collaterals
        iii. Target A-VO_2 gradient <30%
    b. Blood pressure: May require higher target than other heart diseases post-VAD, as there may be detrimental physiologic changes which occur with excessive vasodilation. Depending on CVP (which typically is >10 mmHg with a Fontan circulation) doppler or mean arterial pressure targets of as high as 100-120 mmHg for continuous flow devices have been reported to be necessary to achieve adequate end-organ perfusion pressure (PP = MAP – CVP).

c. CVP: Target CVP is based on a balance of decreasing systemic venous congestion while maintaining adequate VAD filling. Consider pulmonary vasodilators such as iNO in immediate post-operative period and sildenafil to help lower CVP.

3. Trouble-shooting: In cases of low cardiac output, consider the following:
    a. Inadequate preload
        Causes:
        i. Volume status or bleeding
            1. Signs: Low CVP, low cardiac output, suction events, low flow alarm
            2. Treatment: Volume, hemostasis
        ii. Elevated PVR
            1. Signs: Elevated CVP with low PCWP, hepatic congestion
            2. Treatment: consider pulmonary vasodilator therapy, fenestration creation, optimize ventilation strategy
        iii. Obstruction of pulmonary venous return
            1. Signs: Increased PCWP, increased pulmonary edema on CXR
                a. More frequently encountered with atrial cannulation/smaller patients
            2. Treatment: Surgical revision
    b. Tamponade
        Causes:
        i. Pericardial effusion, tissue edema, oversized intracorporeal VAD
            1. Signs: Increased CVP, increased PCWP, decreased cardiac output
            2. Treatment: Volume resuscitation, opening chest. (Note: because TTE/TEE often inadequate for imaging, treatment of tamponade often requires proceeding with surgical intervention due to high index of suspicion without confirmatory imaging)
    c. Increased afterload
        Causes:
        i. ↑SVR
            1. Signs: Decreased VAD flows, decreased power consumption, increased systemic blood pressure, increased pulsatility
            2. Treatment: Systemic vasodilator
        ii. Thrombus: in either the inflow or outflow, obstructing flow into/out of the device
            1. Signs: uptrending power consumption and evidence of hemolysis
            2. Treatment: increase anticoagulation, thrombolytic therapy, or device change
    d. Ineffective Cardiac output
        Causes:
        i. Excessive aortopulmonary collateral flow
            1. Signs: low Fick cardiac output or low mixed venous oxygen saturations (MVO2) with high VAD flows
            2. Treatment: cardiac catheterization for coiling, increase VAD speed
        ii. Neo/Aortic Insufficiency

1. Signs: low Fick cardiac output or low mixed venous oxygen saturations (MVO2) with high VAD flows
2. TTE for assessment
3. Treatment: Increase VAD flows typically will not overcome valve insufficiency; strongly consider surgical repair/replacement or catheter-based interventions (if thought amenable)

iii. Excessive Vasodilation
1. Signs: end-organ hypoperfusion in the setting of elevated VAD-assessed cardiac output matched by Fick cardiac output. Consider milrinone accumulation (esp if impaired renal function), infection, vasoplegia
2. Treatment: treat underlying etiology (ie, infection), vasopressin, methylene blue

4. Studies:
   a. Echocardiogram:
      i. Used to assess aortic valve opening, aortic and atrioventricular valve regurgitation, ventricular decompression, clots, and fenestration (if present) gradient
      ii. Consider TTE in first 1-3 days post-op and weekly while on vasoactive or respiratory support
   b. Ramp Study (see attached worksheet): Using a ramp study to optimize VAD support can be considered. If performed, recommend using both hemodynamic (cath) and imaging (echo) assessments while VAD settings are titrated
      i. Indications for Ramp Study:
         1. Optimization recommended within 2 weeks post-op, 2-3 months postop or prior to discharge, and 6-12 months post-op
         2. Evidence of heart failure/elevated Fontan pressures, persistent symptoms, or any clinical deterioration
         3. Suspicion for device thrombus
         4. If Swan-Ganz catheter,atrial or CVP line in place, Ramp Study (with echo) recommended early post-op and with any change in clinical status or support
      ii. Goals of Ramp Study:
         1. Decompression of ventricle and common atrium
         2. Minimize atrioventricular valve regurgitation (AVVR)
         3. No more than trivial aortic insufficiency
         4. Intermittent opening of the aortic valve
         5. Optimize Fontan pressures and PCWP
         6. Optimize AVO_2 difference
      iii. Safety:
         1. Ensure the patient is on therapeutic anticoagulation
         2. Ensure the ventricle and aortic root are free from thrombus
            a. Risk of thromboembolism with reduction in pump speed
         3. Allow ≥ 2 minute stabilization between speed changes
            a. When decreasing RPMs: monitor for increasing AVVR, increasing aortic valve opening (AoV), increases in Fontan pressures and PCWP, cyanosis (if fenestration) and any symptoms

b. When increasing RPMs: monitor for impendence of flow into inflow cannula, changes in Fontan pressures and PCWP, cyanosis (if fenestration), AoV not opening, increase in AI, suction events, and any symptoms

4. Test endpoints: completion of test/desired outcome attained, suction event, hypotension, hypertension, increased cyanosis, symptoms

iv. Echocardiography during Ramp Study, suggested views (adapted from *ACTION Harmonized Protocol on Echocardiography for CF-VADs*, refer to this protocol for images):

1. PLAX (2D, 3 beats): Ventricle internal diameter in diastole x3 beats
2. PLAX of PSX (M-mode, 10 beats): Aortic valve opening (out of 10 beats)
3. PLAX (Color, 3 beats): degree of AI
4. PLAX or A4C (Color, 3 beats): degree of AVVR
5. PSAX (2D, 3 beats): function
6. A4C (2D, 3 beats): function
7. PLAX, PSAX or A4C (Color, 3 beats): degree of AVVR
8. A4C or PLAX (2D, Color, PW, CW): inflow cannula
9. A4C or best view of fenestration if present (2D, PW): fenestration gradient

c. Cardiac catheterizations:

i. Recommended as part of Ramp Study as above (at 2 weeks post-op, 2-3 months post-op or prior to discharge, and 6-12 months post-op).

ii. Consider assessing for and addressing AP collaterals, especially if elevated wedge/end-diastolic pressures with evidence of organ hypoperfusion and high VAD output due to AP collaterals based on above assessment.

iii. Consider placement of an implantable pulmonary arterial pressure monitoring device to guide diuretic and VAD management based on findings during in-house RAMP studies.

PARA-CORPOREAL DEVICE CONSIDERATIONS

The above guidelines generally refer to patients with intracorporeal CF devices, though many of the same principles apply to smaller Fontan patients with a para-corporeal device.

1. Fontan patients typically have high CI needs and larger Berlin pumps are required than in patients with biventricular physiology
2. Some centers report starting with a CentriMag (with Berlin cannulas) to determine cardiac output needs and then converting to a Berlin pump
3. Berlin Heart: Blood flow through the Fontan is continuous and if supported with a pulsatile pump, there is no flow into the pump during pump systole. Therefore, to ensure adequate unloading and to minimize atrial/pulmonary venous hypertension, consider targeting ~75% fill and shortening the percent of time in pump systole.

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Ramp Study for Fontan VAD Patients on HW/HM3

Patient Name:_____ Patient MRN:_____

	VAD Settings				Hemodynamics					Echo		
	Speed (RPM)	Flow (LPM)	HW: Pulsatility HM3: PI	Power (Watts)	MAP (mmHg)	Fontan Pressure (mmHg)	PCWP (mmHg)	Ao/O2 sat	MVO2	AoV opening (%)	AI	AVVR
Baseline:												

Final Setting:

Comments:

MAP should be recorded from arterial line or from doppler BP if no arterial access

2 minute stabilization period between speeds (minimum)

AoV opening: % aortic valve opening assessed using M-mode of AoV in parasternal long axis view, at least 10 consecutive cardiac cycles reviewed

AI/AVVR: graded 0 to 6; 0=none, 1=trace, 2=mild, 3= mild-mod; 4=mod; 5=mod-sev; 6=severe

Study Comments:

Impella® CP with SmartAssist®, and 5.5 with SmartAssist®, Management in Pediatric Patient

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Use of mechanical circulatory support in children is restricted to a few devices translated from the adult population. Impella heart pump offers opportunities for mechanical circulatory support in older children. Due to limited pediatric experience with this device, a structured approach to patient selection, assessment and device deployment, followed by careful monitoring and guided therapy de-escalation, is essential.

ACTION REVISED DATE: 4/1/25

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OBJECTIVES

This document will provide an overview of the Impella® CP with SmartAssist®, and Impella® 5.5 with SmartAssist®, devices, patient selection, implantation techniques and management strategies.

PROTOCOL

IMPLANTATION INDICATIONS

As with many temporary and durable mechanical support devices the success of support is dependent on careful patient selection. Current pediatric experience highlights 3 primary disease types that may benefit from Impella support.

1. Support and recovery from acute cardiogenic shock (left sided or biventricular support)[1,2, 18,19]
    a. Acute myocarditis
    b. Acute decompensated heart failure
    c. Acute transplant rejection with graft dysfunction
    d. Malignant arrhythmias

2. Bridge to decision for durable support or transplantation (left sided or biventricular support)[3,4]
    a. Circulatory support and ventricular unloading to enhance the possibility of cardiac recovery
    b. Potential bridge to transplant for patients who are poor candidates for durable VAD due to anatomic or surgical factors
    c. Potential bridge to transplant for adolescents or adults that may have short waitlist time
    d. Left heart unloading to assess PVR response in patients who are poor candidates to transplantation due to elevated PVR of unknown chronicity

3. Left heart unloading on VA-ECMO(ECMO + IMPELLA) [5-8]
    a. Left heart unloading with theoretical goal of maximizing myocardial recovery or in the prescence of acute or ongoing shock
    b. In place of LA vent or balloon atrial septostomy that would subsequently require surgical closure
    c. Facilitate weaning off ECMO in patients with cardiogenic shock

CONTRAINDICATIONS

The following conditions **may not be appropriate for implantation of the Impella system for LV support**.

- Inadequately sized vessels for insertion – will vary based on device type and BSA
- Mural thrombus in left ventricle, [18, 19]
- Moderate to severe aortic insufficiency (echocardiographic assessment graded as ≥+2), [18, 19]
- Presence of a mechanical aortic valve [18, 19]
- Presence of an Atrial or Ventricular Septal Defect (including post-infarct VSD)
- Abnormal arch anatomy precluding catheter advancement, specific to CHD
- Known coagulopathy - should warrant discussion with hematology

PRE-IMPLANTATION EVALUATION AND ASSESSMENT

IMAGING

Echocardiography Assessment and Measurements

Optimal candidacy and device selection will depend on a comprehensive assessment which includes detailed cardiac and vascular imaging.[18, 19]

The following echocardiographic measurements should be performed:

- Assessment of LV or systemic ventricular systolic function [18, 19]
- Measurements of the following cardiac structures are necessary for determining candidacy for Impella insertion:
  - Measure of the systemic ventricular length from the apex to the aortic valve annulus in both an apical 4 chamber view and parasternal long axis view.[18, 19] This is particularly important for smaller patients (<40 kg) as the systemic ventricular length can limit options for device placement.
  - Measure length of the ascending aorta from the aortic valve annulus to the origin of the innominate artery (typically from a high parasternal long axis view). This measurement is not as critical for device selection as the ventricular length.
- Presence of aortic valve insufficiency
  - More than mild insufficiency at baseline could result in worsening AI with Impella placement.
  - Moderate to severe AI is a contraindication to Impella placement.
- Evaluate for any LV or aortic root thrombus. [18, 19]
- For additional diagnostic imaging please refer to publication by Morray et al. 2019[9]

Advanced cardiac imaging

- If any anatomical structures are in question, the assessment should extend to advanced cardiac imaging such as CT chest with contrast. [18, 19]
- Advanced imaging might also be required for planning of surgical implantation to ensure appropriate size of branch vessels as well as determine path of device insertion.[18,19]

Vascular Imaging

- Vascular ultrasound should be used for assessment of potential access sites to exclude presence of any obstruction such as arterial thrombus or arterial collaterals especially in children with chronic illness. For the Impella CP the vessel diameter should be > 5mm.[10, 18]
- Impella 5.5 generally requires larger vessel size (≥ 7 mm)[19] but has been implanted in patients in which the arterial vessels measure smaller than the motor given vessel wall elasticity but should be discussed with surgical team prior to implantation. The Impella 5.5 system consists of a 19Fr microaxial pump and 21Fr cannula mounted on a 9Fr driveline/bearing purge delivery catheter.[11,12,19]
- Caution should be taken in patients with shock on vasopressor support as the access vessel can become much smaller than the native size due to effect of the vasopressors. In these situations nomograms for expected vessel size can be used to determine feasibility of implantation.
- If any suspicion of compromise in distal extremity perfusion (i.e. arterial thrombosis) full assessment for arterial thrombosis in that extremity should be performed prior to device implantation. This might require US doppler at bedside or arterial angiography in interventional suite.

Table 1: Device Critical Dimensions[18, 19]

Dimension	Impella CP	Impella 5.5
Drive Catheter Diameter	9 Fr	9 Fr
Overall Largest Pump Diameter	14 Fr	21 Fr

Cannula Length (cm)	6.7 cm	8.0 cm
Ventricle Length[a] (cm)	8.5 cm	6.0 cm
Aorta Length[b] (cm)	7.0 cm	6.4 cm

a. ventricular length from apex to aortic valve annulus
b. length of ascending aorta from the aortic valve annulus to origin of innominate artery

LABORATORY ASSESSMENT

Table 2: Diagnostics blood tests recommended prior to device deployment

Chemistry and Microbiology				
	☐	Comprehensive Metabolic Panel	☐	Brain Natriuretic Peptide or NT pro-BNP
	☐	Cystatin C	☐	Urinalysis
	☐	CRP	☐	+/- MRSA screen (institutional preference)
Hematology				
	☐	Type and Screen	☐	Plasma-free Hemoglobin
	☐	CBC w/ Differential	☐	LDH
	☐	PT/INR, PTT	☐	Anti-Xa if on heparin
	☐	Fibrinogen, D-dimer	☐	TEG or ROTEM Thromboelastography
	• Consider additional thrombophilia or bleeding work up if concerning family history or clinical course (see Action Pre-Implant Protocol for details)			
Ancillary Studies				
	☐	EKG	☐	Ultrasound Doppler (arterial & venous) to establish vessel size, information on access and line placement
	☐	Echocardiogram	☐	
	• Consider Head CT if patient at high risk (i.e., ECMO) or unable to get reliable neurologic exam • Consider if MRI study (heart or brain) is warranted as cannot be performed after Impella is placed • Consider Chest CT if needed for fit testing/size of heart if anticipate converting to durable VAD later			

MONITORING

- Ensure accurate weight and height is measured and BSA is calculated on the day of procedure.
- The following hemodynamic monitoring should be in place prior to or at the time of Impella implantation:
    - Arterial line
    - Central venous access
    - Swan Ganz catheter in biventricular anatomy and if no contraindications (recommended but may not be utilized in all institutions if experience or training is lacking)
    - Foley catheter
    - Consider tissue oximetry monitoring of the extremity with the implanted device

IMPLANTATION TECHNIQUES

ANTICOAGULATION AT TIME OF IMPLANT

- A bolus dose of heparin should be administered to achieve an ACT >250 seconds prior to introduction of the Impella catheter.[18,19] See below for more information about anticoagulation.

CATHETERIZATION-BASED IMPLANTATION

Femoral Access Approach of the Impella CP with SmartAssist (Impella 5.5 cannot be placed femorally)

- Impella insertion should be performed with fluoroscopic and in most cases, echocardiographic (TTE or TEE) guidance. This is typically done in the catheterization laboratory although implantation in an operating room can be performed with the use of a portable fluoroscopic C-arm. Bedside implantation in an intensive care unit is discouraged. [18, 19]
- The arterial access site may vary depending on the intended duration of support, the size of the patient and size of the pump that will be inserted. [18, 19]
- After ensuring adequate size (>5mm). Access should also be obtained with ultrasound guidance whenever possible. Other imaging techniques, including the use of bony landmarks and angiography may be performed as well. [18, 19]
- Once access is obtained the arteriotomy can be “pre-closed” with 1 or 2 Perclose sutures. This will assist with hemostasis once the device is removed. This has been shown to be helpful in some clinical scenarios but is not in the IFU but described in clinical experience portion of IFU. [18]
- After vascular access is obtained (either percutaneously or via cutdown), appropriately sized peel away sheath is placed in the vessel or chimney graft. This will be peeled away after the Impella CP is in the appropriate position and the repositioning sheath is advanced through the arteriotomy and sutured into position. [18, 19]
- A pigtail catheter is advanced to the systemic ventricle and a guidewire (included with the pump, 0.018 inch Impella wire) is inserted anterior and away from the mitral valve, in the systemic ventricular apex.
- The Impella device is advanced over the guidewire using fluoroscopic guidance and the guidewire removed once the tip of the pigtail is in the systemic ventricular apex. [18, 19]
- The position of the Impella device is verified by echocardiography (see corresponding imaging section). The device may be adjusted if needed using echocardiographic guidance. [18, 19]
- Vessel diameters less than 6 mm may require antegrade perfusion to prevent limb ischemia. [18, 19]
- The Impella repositioning sheath/ may be adjusted (end of sheath is tapered) to optimize distal limb perfusion (based on signal from a distal pulse oximeter and clinical exam).

SURGICAL IMPLANTATION

Right axillary artery approach for Impella CP and 5.5

- Follow institutional practices for pre-op cleansing, anesthesia, time-outs, and ensure appropriate equipment is available.
- Sizes available for this technique: Impella CP and 5.5.
- Pre-op evaluation with CT scan (CTA ideal) to determine the anatomy and largest size Impella device that the vascular access will allow.
- Graft selection: (Hemashield Platinum is the recommended graft). [18, 19]
- Pump standby (CPB), fluoroscopy, and transesophageal echocardiogram are necessary for this

approach.
- Place standard monitoring lines.
- Position patient supine with arms tucked at the side.
- Isolate and expose the axillary artery and obtain control via proximal and distal vessel loops. [18, 19]
- Great care should be taken not to injure or avulse any of the delicate side branches.
- Care is taken to avoid injury to the surrounding axillary vein and brachial plexus located superiorly.
- Isolate and control the right axillary artery using a C-clamp and make an anterior arteriotomy.
- Trim a 10 mm graft[18, 19] to match the arteriotomy and create an end-to-side anastomosis using a running 5-0 Prolene suture to the right axillary artery. Abiomed recommends using at least a 60-degree bevel on the end of the graft to facilitate passage of the rigid motor housing into the artery.
- Great care should be taken to ensure precise suturing and place additional hemostatic sutures as needed as the inferior aspect of the anastomosis is very difficult to see once the graft is tunneled.
- Consider topical hemostatic agents (institutional preference).
- Remove the c-clamp and inspect for hemostasis, while clamping the distal graft.
- Once hemostasis is satisfactory, clamp the proximal graft and tunnel the graft to a remote site (usually anterior to mid-axillary line), bring it out through the skin and temporarily secure it with a clamp.
- Place introducer system in distal graft and de-air.
- Under fluoroscopic guidance (may require cardiac interventionalist or interventional radiology), insert a 0.035 inch diagnostic guidewire with a 4–6 Fr diagnostic catheter into the introducer, Advance the guidewire and catheter into the left ventricle. Remove the diagnostic guidewire and exchange it for a stiff 0.018 inch placement guidewire. With the 0.018 inch placement guidewire properly positioned in the left ventricle, remove the diagnostic catheter. [18, 19]
- Advance the prepped Impella device over the guidewire through the sheath and the graft.
- Confirm Impella device is across the aortic valve and inflow and outflow areas are properly positioned with fluoroscopy and transesophageal echocardiography. [18, 19]
- Confirm that the placement guidewire has been removed and confirm that the controller displays a pulsatile waveform prior to starting the Impella device. The Impella CP will start in AUTO and automatically increase the flow rate over 30 seconds. For the 5.5, slowly increase P-level to desired output/decompression based on position on TEE. [18, 19]
- Reconfirm positioning after final device placement with TEE, as the device has a tendency to advance into the ventricle as flows are increased. Make sure to check positioning again prior to break down of the sterile field at the end of the case.
- Secure the Impella catheter in place to the skin. Catheter fixation accessory may be used to assist in 3-point external fixation of the pump catheter to the patient body. [18, 19]
- Close the right axillary artery cutdown sight in multiple layers and skin.
- Ensure hemostasis of the right axillary artery cutdown site.
- Note the final pump P-level and flow, aortic to mid- inlet measurement by TEE, and pump placement at the cm marker number for changes and repositioning postoperatively.

ECMO + IMPELLA

- Impella can be used in combination with ECMO for left heart decompression.
- Axillary (CP or 5.5) or femoral (CP) approach
- In the circumstance of femoral approach, retrograde insertion of a small caliber sheath in the superficial femoral artery can be performed to augment distal arterial perfusion to the limb and prevent ischemia complications.

POST-OPERATIVE PATIENT AND DEVICE MANAGEMENT

ANTICOAGULATION

Anticoagulation is required to prevent clot formation around the catheter as well as to preserve device motor and pressure monitoring. Optimal anticoagulation is achieved through a combination of purge fluid containing dextrose and heparin or if heparin is contraindicated sodium bicarbinate. and systemic anticoagulation administration. Purge fluid cannot contain NaCl at any point. [18, 19]

Role of Purge Fluid

- Impella pump motors require a constant purge using a dextrose solution in water with heparin (25 or 50 IU/mL) or if heparin is contraindicated, sodium bicarbonate (25 or 50 mEq/L). In addition, Impella pumps are used in conjunction with heparin based systemic anticoagulation therapy. Although direct thrombin inhibitors have been used as an alternative to heparin systemic anticoagulation, this is not aligned with the IFU. During support with Impella pumps, the targeted ACT is 160-180 seconds. [18, 19]
- All Impella pump motors are protected from biomaterial build-up by running fluid through a purge system. The purge fluid is required to maintain function of the device motor and is infused through the internal channel of the catheter, bearings and across the motor. This creates a protective interface or barrier that prevents blood from entering the motor housing. [18, 19]
- Purge system uses a dextrose water solution between D5W and D20W. The solution flows through the internal channel of the Impella catheter in the opposite direction of the blood flow. Through a built-in pressure sensor, the device automatically sets and adjusts the purge flow anywhere between 2 and 30 mL/h to maintain an adequate purge pressure of 300–1100 mmHg.[18, 19] The dextrose concentration of purge fluid determines the viscosity and flow rate. Since the rate of purge fluid is automatically regulated by the controller, the purge infusion rate must be monitored for large changes in dose as this might affect dose of delivered heparin.
- Lower dextrose concentrations, such as 5%, are less viscous and flow more quickly through the purge system, thereby systemically delivering more heparin. Higher (more viscous) concentrations result in a slower purge flow rate and less overall systemic heparin exposure for the patient. Higher dextrose concentrations can also result in more pressure on the pump and should be avoided when possible. The manufacturer recommends a **starting heparin concentration of 25 or 50 IU/mL in a 5% DW as the initial purge solution or if heparin is contraindicated** sodium bicarbonate (25 or 50 mEq/L). [18, 19]
- Since the purge fluid is infused under pressure, care must be taken to document and monitor purge lines and maintain proper fluid and purge cassette change according to institutional guidelines for fluid and line change.
- In 2022 sodium bicarbonate purge solution was approved by FDA as an alternative to heparin, for patients who are intolerant to heparin or in whom heparin is contraindicated (e.g. due to heparin-induced thrombocytopenia or bleeding). The solution is prepared by adding 12.5 mL of sodium bicarbonate 8.4% to a 500 mL solution of D5W.[18, 19]Using sodium bicarbonate purge solution allows for systemic only application of anticoagulation with agents such as Argatroban, Bivalirudin or Heparin.[13-15]
- The Impella catheter has not been tested with any other anticoagulants, such as direct thrombin inhibitors, in the purge solution. Therefore, avoid the use of any alternative anticoagulants in the purge solution to prevent damage to the Impella catheter.[18, 19]

Anticoagulating in Specific Scenarios:

Anticoagulation for isolated Impella CP and 5.5 support

- After implantation of Impella CP, purge fluid is started without any Heparin and should be changed to D5W with 25 or 50 IU/ml heparin **or if heparin is contraindicated** sodium bicarbonate (25 or 50 mEq/L) immediately upon arrival to ICU.
- After implantation of Impella 5.5 the purge fluid should contain Heparin 25 or 50 IU/ml **or if heparin is contraindicated** sodium bicarbonate (25 or 50 mEq/L) upon initiation of support in cardiac cath lab or operating room unless there is concern for significant bleeding.
- In clinical settings where D5W with 25 or 50 IU/ml heparin causes excessive anticoagulation the heparin concentration can be reduced to 12.5 IU/ml or dextrose concentration can be increased to reduce the purge infusion rate. Sodium bicarbonate purge can also be used in this scenario if the reduction of Heparin in purge does not achieve desired anticoagulation goal.
- In situations where D5W with 25 or 50 IU/mL in the purge solution does not allow one to achieve therapeutic goals it is advised to add systemic Heparin drip and titrate that drip to achieve overall therapeutic goals (below).
- Antiplatelet agents are typically not indicated for management of anticoagulation on Impella support.

Anticoagulation on ECMO + Impella

- In the setting of Impella with ECMO support, patients should continue to have purge fluid driven anticoagulation with D5W with 25 or 50 IU /ml heparin and systemic heparin added to achieve desired level of anticoagulation per institutional and patient specific ECMO goals.[16]
- Purge heparin contribution to anticoagulation must be taken into consideration, thus systemic heparin requirements might be lower than prior to Impella insertion.
- Frequent monitoring is recommended especially if the patient is inflamed, infected, coagulopathic or displaying signs of insertion site oozing.
- Sodium bicarbonate purge can also be used in this scenario allowing for use of DTIs for ECMO management.

Initiation and Monitoring of Anticoagulation

- Timing of initiation of heparin purge fluid and systemic heparin (if need additional anticoagulation) may vary based on institutional practice. It is recommended to start anticoagulation as soon as possible.
- Manufacturer recommends maintaining an ACT of 160-180 seconds.[18, 19]
- Institutional practice can include use of PTT or Anti Xa UF Heparin levels for goal anticoagulation (see table below)
- **If the Impella purge system delivers too much heparin**, a purge solution with sodium bicarbonate or a lower heparin concentration (12.5 IU/mL) can be used first followed by increased dextrose concentration to reduce purge infusion rate.

TOTAL HEPARIN DELIVERED TO PATIENT = IMPELLA PURGE HEPARIN + SYSTEMIC IV HEPARIN

Table 3: Anticoagulation lab goals (data taken from Sieg et al. 2015)[17] (Abiomed IFU only recommends monitoring of ACT)[18, 19]

	Anti Xa UF Heparin Level	PTT	ACT
ECMO + Impella	ECMO goals	ECMO goals	ECMO Goals
Impella Support Alone Low risk of thrombosis, short-term use or surgical site bleeding	0.15-0.25	50-60	160-180
Impella Support Alone High risk of thrombosis or long-term use	0.2-0.3	60-70	180-200

LABORATORY MONITORING

Baseline labs post Impella placement: CBC; Chemistry with liver function; Hemolysis labs: plasma Hb, LDH; Coagulation profile: PTT, PT/INR, Fibrinogen, D-dimer, anti-Xa, ACT (POCT), TEG or ROTEM; blood gas with lactate and mixed venous oxygen saturation if available.

Table 4: Recommended laboratory testing following device deployment

Laboratory Markers	24-48h post implantation	Chronic Monitoring
Hematology and Coagulation		
CBC	Q12H	Daily
Plasma free hemoglobin and LDH	Q12H	Daily until stable
DIC Panel	Q24H	Daily until stable
Coagulation panel	Q12H or with every titration	Daily
TEG or ROTEM	Q12H	Daily until stable
Chemistry and Microbiology		
Comprehensive Metabolic Panel	Q24	As indicated
Brain Natriuretic Peptide or NT pro-BNP	Q24	Weekly
Cystatin C	Once	Weekly
Ancillary Studies		
CXR	Daily	Daily
Echocardiogram	Daily	Weekly

These are recommendations only and each center is encouraged to use center-based practice.

Additional Labs:

- Renal panel to assess end organ function
- Hepatic panel to assess end organ function and monitor for hemolysis
- Due to high risk of pancreatitis in patients recovering after cardiogenic shock a pancreatic enzyme panel should be performed and monitored accordingly.

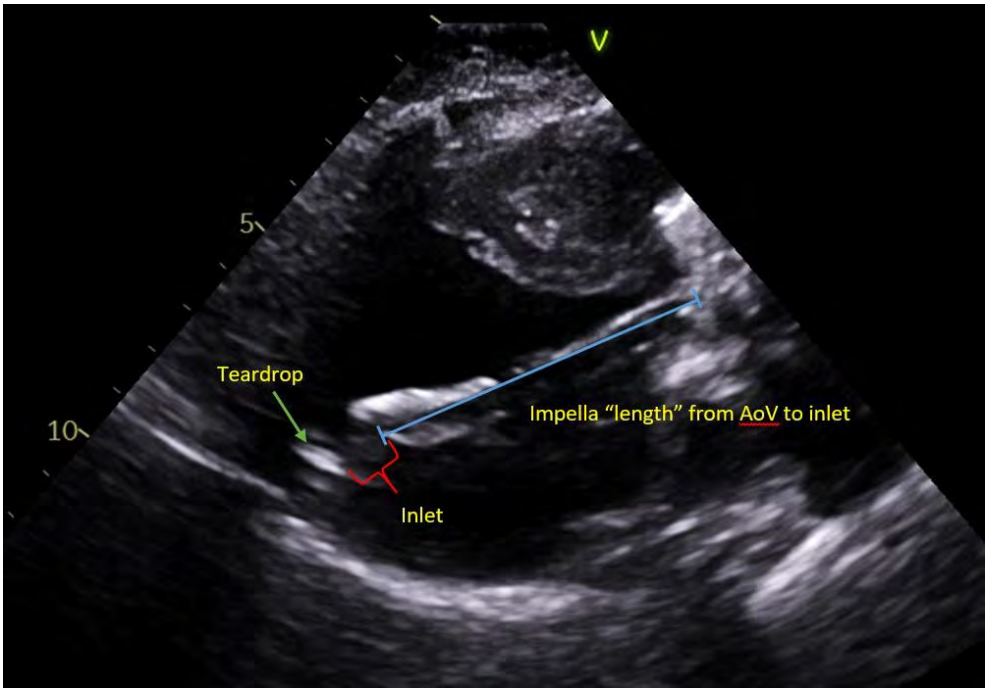
IMAGING TO MONITOR DEVICE POSITION

An echocardiogram provides useful information on Impella positioning for surveillance, if there is an increase in ventricular ectopy, or when evaluating ventricular decompression. [18,19]

Echo Imaging Protocol:

- Positioning of the Impella CP or 5.5 is best seen by echocardiogram in the parasternal long-axis view. To appropriately measure the distance of the Impella in the left ventricle, measure from the aortic valve to the inlet (lucent area prior to teardrop). This will allow for consistent measurements over the patients' course.

Figure 1: Long axis parasternal view delineating intracardiac structures used for measurement of Impella position [18, 19]



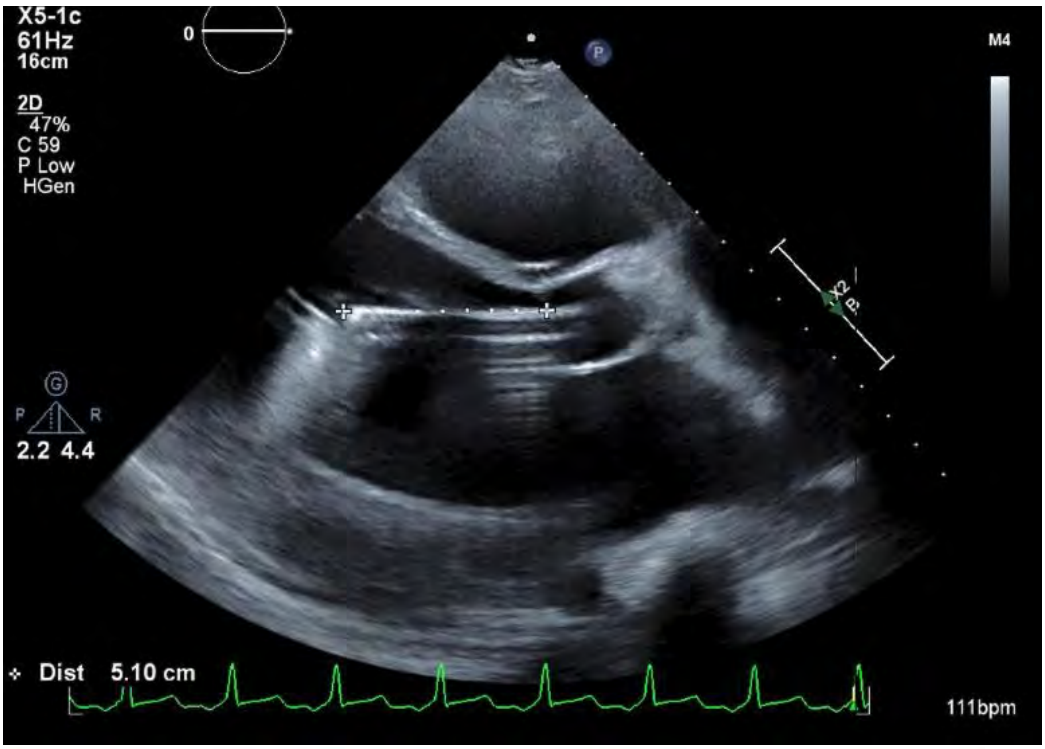
DEVICE POSITION[18, 19]

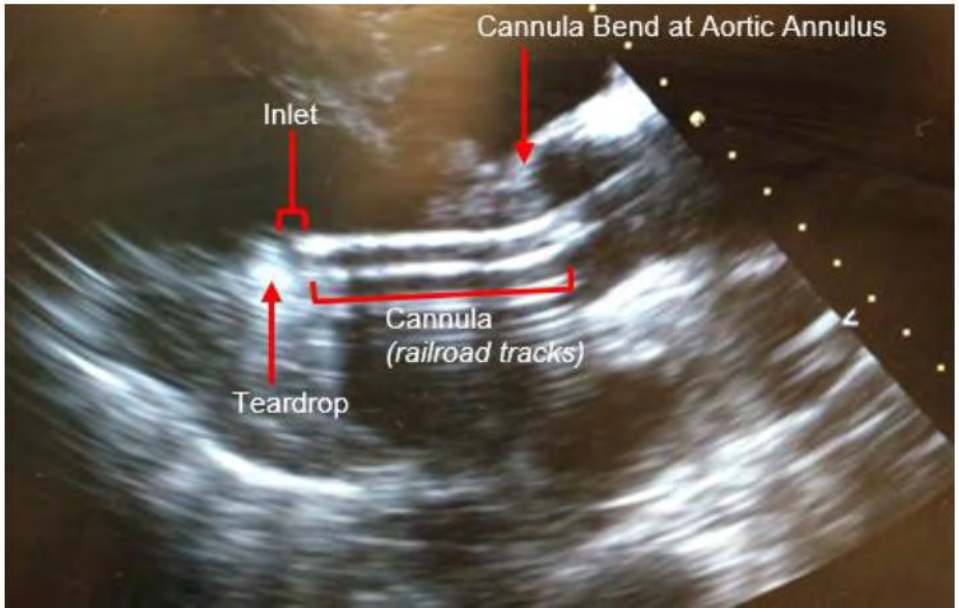
Appropriate device position is crucial for optimal device function. Each device has specific position recommendations which can be found in the imaging section of the IFU.

- Initial device position should be confirmed in the cath lab using fluoroscopy as well as TTE or TEE for correlation.
- It is recommended to re-evaluate the device position upon arrival to ICU and monitor every 48 hours.
- Positioning or suction alarms should prompt a bedside TTE to evaluate device position. The device can be repositioned at the bedside using TTE guidance.
- In smaller patients it may not be possible to place the inlet in the optimal location based on the manufacturer recommendation on distance from AoV to pump inlet. ECHO should be used to ensure the inlet of the device is placed in the mid ventricular cavity, away from cardiac structure, the mitral valve apparatus, and LVOT to avoid suction. The outlet of the device should be a few centimeters above the AoV to ensure uninterrupted flow from the device.

Table 5: Manufacturer recommended device position based on distance of device from the aortic valve to mid-inlet.

Impella Device	CP	5.5
Position below aortic valve per manufacturer IFU	3.5 cm	5.0 cm





DEVICE MONITORING AND MANAGEMENT

DEVICE TERMINOLOGY

- **P-level:** Represents various rotational speed levels at which the device can be programmed to operate. P levels represent range of RPMs that the device will maintain to achieve optimal output (see device manual for specific P-level RPMs and flow rates) [18, 19]

- **Impella Flow (L/min):** Flow is calculated from the current and pressure gradient across the device based on the measured pressure flow curves. Each device is tested in the lab for its performance and accuracy. The flow accuracy is within 10% of max flow error. [18, 19]
- **Motor Current (mA - Green Waveform):** Measures energy required to maintain RPMs, influenced by blood flow, resistance (e.g., thrombus, preload/afterload), and device position. [18, 19]
    - Pulsatility reflects normal systolic/diastolic flow variations.
    - Flat or dampened waveform: Suggests malposition (both inlet and outlet in the same compartment) or severely poor ventricular function.
    - Monitoring: Rising motor current may indicate thrombus formation, device wear, or impending failure, requiring intervention.
- **AO Pacement Signal (mmHg - Red Waveform):** AO Placement signal is measured using an optical sensor at the distal end of the outlet thus measuring aortic pressures. In most clinical cases the waveform should be pulsatile. [18, 19]
    - Impella CP with SmartAssist and Impella 5.5 with SmartAssist contain optical sensors for pressure monitoring directly in the aorta and indirectly in the LV.
    - The AO Placement signal can be used together with motor current waveform to diagnose Impella malposition.
    - The pressure signal can be used together with power waveform to diagnose Impella malposition.
- **LV Placement Signal (mmHg -White Waveform on Impella CP and 5.5):** This signal represents calculated LV pressure. [18, 19]The measurement is deducted from the optical sensor and the derived motor current pressure delta, indirectly measuring LVEDP and LVESP. This feature is available when the P-level is a P-4 or above. The LV placement signal is for informational purposes only and must be validated by an approved clinical diagnostic device.
- **Purge Flow (mL/hr):** The purge flow rate is delivered by purge cassette inside the Automated Impella Control (AIC) and is measured in mL/hr. [18, 19]The purge flow is automatically adjusted by the AIC based on the device needs. **Purge Pressure (mmHg):** The Impella console automatically adjusts the purge flow rate to maintain purge pressures between 300 -1100mmHg.
    - High/low purge pressure alarms should be evaluated by following on-screen instructions.
    - If a ‘purge pressure low’ alarm remains unresolved for more than 20 minutes, the purge cassette will likely need to be changed.

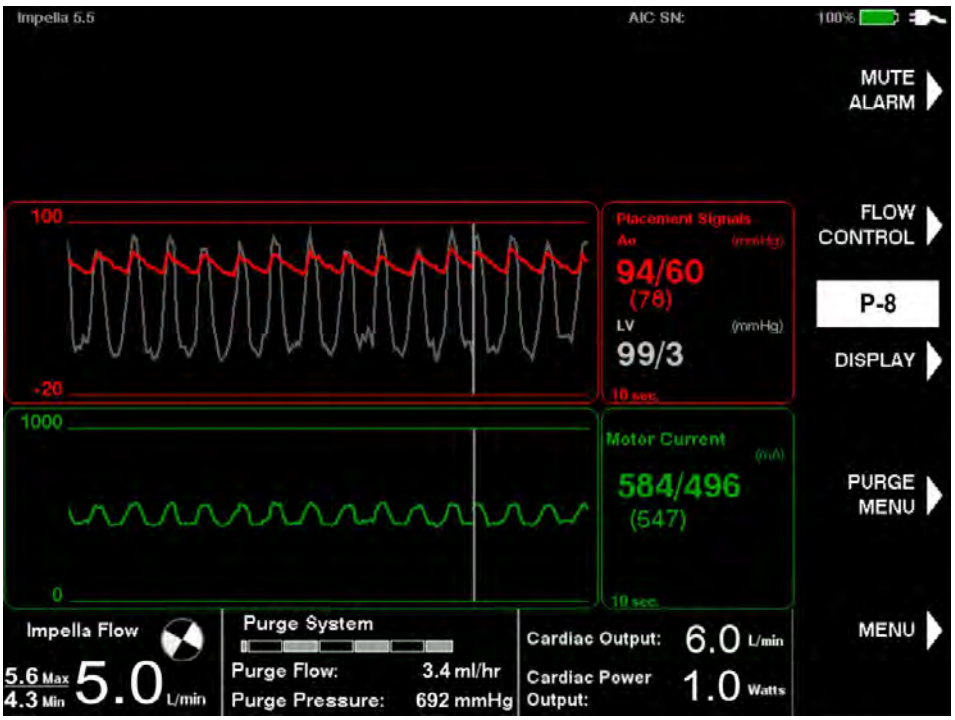


Figure 2: Example of Impella placement screen[18, 19]

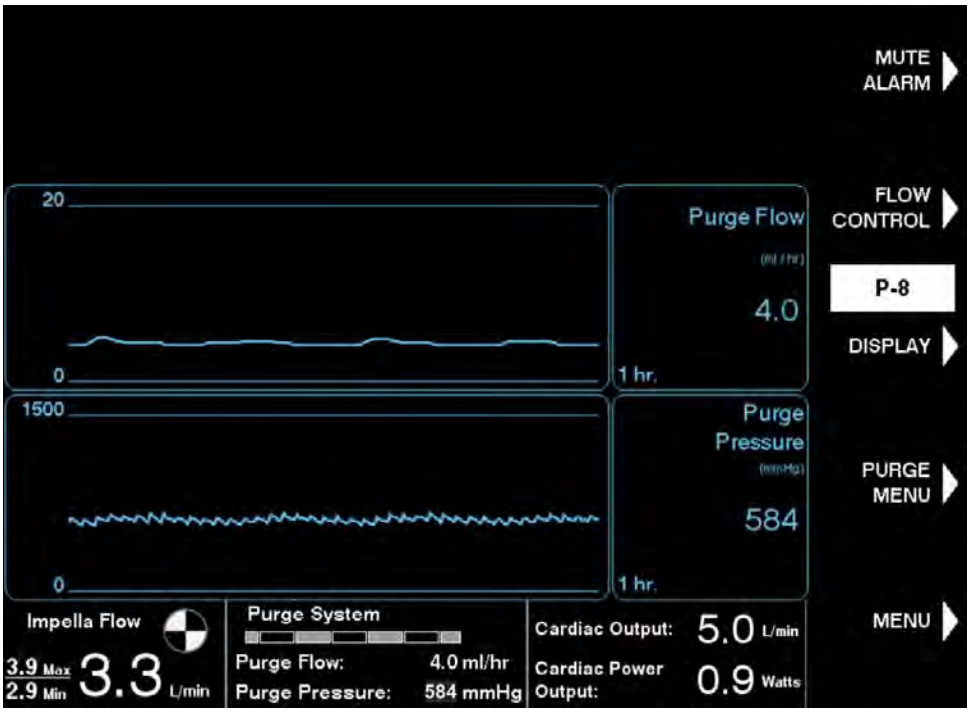


Figure 3: Example of the Impella Purge Screen[18, 19]

MOTOR SPEED[18, 19]

- Motor speed is regulated by P-levels on the controller (P-0 to P-9). Initial P-level after implantation will be in Auto. After 3 hours of operation, the controller automatically switches to P-level mode.
- Optimal lowest P-level should be determined to minimize hemolysis, suction events and other complications, but to maximize cardiac output.

PATIENT MANAGEMENT

DETERMINING OPTIMAL DEVICE SUPPORT:

- Optimal support can change with changes in clinical status (ie. recovery of ventricular function, afterload reduction, intravascular volume status). Advanced hemodynamic monitoring including invasive arterial and venous pressures must be monitored to determine optimal support. PCWP can be directly measured in the cath lab to determine lowest LV filling pressure at the lowest P-level.
- Outside of the cath lab environment, a Swan Ganz (SG) catheter can be used to determine level of LV unloading and optimal speed, as well as the function of the RV. While escalating the P-level, the level of unloading should be measured by monitoring PCWP.
- In addition to the SG catheter, echocardiographic findings can further guide titration of support and monitoring of myocardial response to support.
- Finding the optimal P-level will help minimize hemolysis and optimize device function. The support level should not exceed the required CO for the patient.

ICU ADMISSION [18, 19]

Upon arrival to the ICU, the following should be completed:

- Ensure the AIC is plugged into AC power on arrival to ICU. The controller battery life is only 1 hour.
- The AIC should be positioned at the base of the bed for easy access and screen visibility.
- Device performance and setting should be evaluated and documented.
- ICU nursing should transition to purge fluid per physician order.
- Verify that the Tuohy-Borst connection is tightened to the right and locked in order to prevent catheter displacement or migration (on CP and RPSA/Flex). For the the Impella 5.5, make sure the yellow pin is removed and catheter lock is secured.
- Document insertion length of Impella catheter where the sterile sleeve connects to the sheath.
- Inspect dressing at the insertion site for bleeding and integrity.
- If femoral access, secure the extremity with the knee brace to prevent flexion and injury to the arterial insertion site (see limb care section).

HEMODYNAMIC MONITORING [18, 19]

- Patients in the critical phase of the illness will require more aggressive hemodynamic monitoring than those on long term support.
- Invasive hemodynamic monitoring of arterial blood pressure and central venous pressures is recommended until organ recovery and satisfactory organ function is achieved.
- Hemodynamic parameters and device performance should be documented every hour and as per unit policies.
- Use of a pulmonary artery catheter should be considered; however it must be balanced with experience and training. Parameters (ie. PCWP, PAP, CI) obtained from Swan Ganz catheters can help determine response to device support, need for additional therapies and need for RV support.
- Balance between risk and benefit must be evaluated daily to minimize adverse events associated with invasive monitoring.

The following Impella assessment should be performed at the beginning and end of the shift as well as PRN:

- Device monitoring should include assessment and documentation of the following Q1H:
  - P-level
  - Impella flow (L/min)
  - Motor current (mA -green waveform)
  - AO Placement signal (mmHg -red waveform)
  - Purge pressure (mmHg)
  - Purge flow (ml/h)
  - LV Placement signal
  - Assessment of connections and device alarms
- Verify that the Tuohy-Borst valve (CP) connection is tightened to the right and locked in order to prevent catheter displacement and migration.
- Note and verify the cm marker of the catheter.
- Inspect dressing at the insertion site and confirm securement of Impella catheter.
  - Change dressing as per institutional guidelines.
- Document insertion length of Impella catheter where the sterile sleeve connects to the sheath.
  - Recommended position documentation with any positional changes and patient movement.
- Back-up Impella AIC console should be easily accessible and plugged into AC power.
- Check purge solution
  - Purge solution bag and tubing must be changed per institutional guidleines
  - Ensure one extra Impella tubing cassette is easily accessible
- Reposition patient as per unit protocols.

LIMB CARE, INSERTION SITE AND PERFUSION MONITORING: [18, 19]

The extremity with the Impella insertion site is at a high risk for compromise if there is limited perfusion or nerve compression. Close monitoring and assessment is crucial to minimize these complications.

- If the device is implanted percutaneously in the femoral position, extremity immobilization is recommended.
  - A knee immobilizer can be used to prevent the patient from bending the extremity and causing arterial rupture.
  - Attention must be placed on any pressure points and extremity hyperextension which can result in temporary or permanent foot drop if not recognized early.
  - A physical therapy consult should always be considered for appropriate assessment of knee immobilization.
- **Extremity with Impella must be closely monitored for acute arterial thrombosis or occlusion**. Pulse oximeter provides continuous pulse assessment and local NIRS may be used to monitor deterioration of perfusion. Palpate (or obtain by Doppler) peripheral pulses Q1H. Some institutions use a myometer to monitor loss of neurologic function.
- **Any compromise in perfusion must be immediately addressed**. Potential interventions include arterial jump graft. If unable to improve extremity perfusion, the device must be removed and another MCS strategy considered.
- Observe and document Q1H: Color, capillary refill, warmth, movement, and sensation
- Notify MD if noted signs of diminished peripheral circulation or limb ischemia (i.e. quality of pulses diminished, cool peripheries, change in skin color/mottling or sensory changes including numbness and/or tingling)
- Consider early involvement of physical and occupational therapy to minimize the above complications and address any motor deficiency early
- Observe puncture sites, sheath insertion site or surgical access site for active bleeding, swelling, bruising or hematoma especially when anticoagulation is escalated. Additional bleeding control may be needed by placing mattress sutures at the insertion site.
- With femoral insertion, avoid flexion of leg and keep the head of bed no greater than 30 degrees.

Skin integrity

Due to limitations in patient mobility especially when femoral insertion site is used, close attention must be paid to skin integrity and pressure areas.

- Assess skin integrity Q2H & PRN
- Assess risk of skin breakdown using appropriate pressure ulcer risk assessment tool
- Reposition patient as per hospital protocols

Urine output[18, 19]

Change in urine color can be one of the first indicators of excessive hemolysis indicating device malposition or suction. Foley catheters can be used to diagnose these complications early.

- Observe and document characteristics of urinary output Q1H
- Observe for signs of hemolysis: discoloration of urine, decreasing hemoglobin/hematocrit, increased LDH, plasma free Hgb, AST and bilirubin
- Once stable device position, appropriate hemodynamic status is achieved, and end organ recovery is established, Foley catheter should be removed to minimize risk of infection.

PATIENT TRANSPORT[18, 19]

- Safe transport checklist and expectations should be generated based on intuitional practices with following in mind:
  - Prior to transport, document the insertion length (cm) of the Impella catheter where the sterile sleeve connects to the sheath.
  - A transfer board should be utilized to ensure that the catheter remains in situ and does not kink. The limb with the Impella catheter in situ must remain straight at all times during transport.
  - In preparation for transport the team should check purge fluid, check battery life and that Impella was charging prior to transport, check the catheter connections so as not to dislodge with movement and transfer of patient, monitor urine quality prior and during transport.
  - The Impella controller battery life is 1-hour.

MANAGING COMPLICATIONS AND ADVERSE EVENTS

Potential adverse events include, but are not limited to: aortic valve injury, bleeding, cerebral vascular accident/stroke, hemolysis, limb ischemia, thrombocytopenia, vascular injury and death. [18, 19]

BLEEDING

- Depending on method of Impella insertion, bleeding may occur at the access site and/or surgical sites (subclavian cut down and graft anastomosis). This should always be assessed by the cath or surgical teams and intervened on if needed.
- Compression devices such as safeguard or dressing may be used briefly (<6 hours) and extremity perfusion must be closely monitored during this period and while on support.
- Assess the patient and evaluate the cause of bleeding (over anticoagulation, coagulopathy vs surgical site bleeding).
  - Send labs evaluating for coagulopathy (CBC, PT, PTT, Fibrinogen, Rotem, Anti-Xa) and assess the need for blood transfusions during prolonged periods of bleeding and correct any deficiencies.

Anticoagulation goals may need to be adjusted if there is ongoing bleeding or oozing and the pump itself is otherwise functioning well. Heparin may even need to be held for short periods of time (<6-12 hours) for clinically concerning bleeding. In the event that a patient is intolerant to heparin or in whom heparin is contraindicated (e.g., due to heparin-induced thrombocytopenia or bleeding), sodium bicarbonate (25 or 50 mEq/L) may be added to the purge solution instead of heparin.

- If bleeding continues, consider platelet dysfunction, low fibrinogen, HIT.
- Surgical intervention for bleeding should be considered if bleeding is difficult to control with medical therapies.

HEMOLYSIS[18, 19]

- Some degree of hemolysis may occur at higher P-level settings. It is typical to see some mild hemolysis in the first 24-48 hours of support. This should improve.
- The etiology of hemolysis can be due to the expected mild shearing from the device, from lower than expected flows for the set P-level, suction events, or malpositioning of the Impella device.
- To evaluate the etiology, consider ECHO to assess positioning of cannula, check fluid status, suction events, and P-level setting.
    - P-level setting may need to be adjusted if the setting is too high, as well as fluid administration if patient appears hypovolemic
- If P-level setting and fluid status are unchanged but hemolysis is noted, consider ECHO to assess positioning of cannula. If the Impella has moved further towards the LV apex, the outflow may be close to the aortic valve and cells may be lysed as they exit the outflow of the Impella and hit the aortic valve leaflets. Abiomed recommends repositioning the device, even if the position looks okay.
- Hemolysis is clinically seen as a constellation of findings depending on the degree.
  Mild hemolysis may be seen only with lab findings of elevated LDH or plasma Hb with a stable or slowly decreasing hemoglobin value. Moderate to severe hemolysis manifests with elevated LDH, plasma Hb, elevated bilirubin, AST, and red/tea colored urine with an acute drop in hemoglobin.
- Significant hemolysis can induce AKI, continue to monitor renal function.

DEVICE CLOT

- In the setting of subtherapeutic anticoagulation or periods of profound inflammation, the device is at risk of developing fibrin deposition or thrombus formation, resulting in device failure.
- There may be a rise in purge pressure and drop in purge flow, rise in motor current either acutely or gradually, or drop in device flow overall.
- Consider TPA administration to the device in consultation with Abiomed, or your institution's protocol. Tissue plasminogen activator (tPA) alteplase has been reported to be used for suspected Impella thrombosis (increasing purge pressure, elevated LDH levels).
    - Sterile water is used as the diluent used in the tPA purge solution instead of D5W or normal saline. The solution is prepared by diluting tPA (2 mg) in 50 or 25 ml sterile water for injection in an intravenous piggyback (IVPB) to produce a 0.04 or 0.08 mg/ml solution. The tPA solution replaces the Impella purge anticoagulation solution and runs at the device determined rate while systemic anticoagulation is used to maintain a therapeutic ACT or aPTT. The lower tPA (0.04 mg/hr) purge solution can run over up to 12 hours, or longer if there is improvement but not normalization of the purge pressure. If there is no improvement in purge pressure at 12 hours, the higher tPA (0.08 mg/ml) purge solution can be used for up to 12 hours. Once tPA finishes infusing, the purge solution is switched back to the prior solution. [17]
- If the device stops, support the patient clinically as indicated, and consult interventional cardiology and CT surgery as soon as possible.

DEVICE FAILURE[18, 19]

- This is not a common occurrence with the Impella device, however, when used beyond the indicated device duration of support (≤ 4 days for Impella CP with SmartAssist or ≤ 14 days for Impella 5.5 with SmartAssist), there may be a risk of device failure/stoppage.
- Close monitoring of motor current trends will help to assess the function of the motor.
- Each Impella device has a different motor current upper limit for a P-level setting. If the motor current is approaching the upper limit, notify the ICU and procedural teams. Consult with your Abiomed representative, discuss recommendations for thresholds and potential device exchange.

INFECTION

- As with any foreign indwelling device, there is a risk of infection. Prophylactic antibiotics are not generally recommended for the duration of the device. However, for surgical prophylaxis, cefazolin or other antibiotic covering skin flora may be administered for 24 hours postoperatively.
- Monitor site and continue site care, as described above, continuously evaluating for infection.
- If an infection occurs related to the device, antibiotic regimen to be individualized based on your institution.

SUCTION

- Several factors may cause a suction alarm, including inadequate left ventricular filling or preload, incorrect Impella position against the papillary muscle or the mitral valve, or right ventricular failure. [18, 19]
- Suction may occur if the blood volume available for the Impella catheter is inadequate or restricted. [18, 19]
- Suction limits the amount of support that the Impella can provide to the patient and results in a decrease in expected Impella flow, arterial pressure and cardiac output. It can damage blood cells, leading to hemolysis.
- If a suction alarm occurs, reduce the Impella P-level by 1 or 2 levels, or more, if suction continues. Assess the patient's volume status, assess hemodynamics and RV function, evaluate catheter position using the placement signal, motor current, and imaging. Reposition Impella if necessary. When the suction alarm is resolved, resume pre-alarm flow rate.

OTHER CLINICAL CHALLENGES

Ectopy and arrhythmias

- Periods of ectopy or arrhythmia might be experienced with the Impella device in place. As long as there is preload to the left ventricle, the patient should be adequately supported with the Impella providing continuous flow and perfusion pressure. [18, 19]
- Recurrent refractory ventricular arrhythmias warrant assessment of device parameters and alarms for suction events as well as device position, LV filling and RV function by echo.
- During periods of arrhythmia, the patient may lose synchronous intrinsic contractility and therefore pulsatility, but will have a non-pulsatile blood pressure instead with a mean arterial pressure (MAP). If the MAP range is appropriate during the periods of arrhythmia, the patient is well supported.
- If the patient doesn't have adequate MAPs during periods of arrhythmia, assess RV function, volume status, antiarrhythmic agent and consider adjusting P-level if appropriate to better support the patient clinically while the arrhythmia is being medically managed.

EMERGENCY PROCEDURES

CARDIOPULMONARY ARREST[18, 19]

If your patient arrests and loses blood pressure and perfusion pressure, and CPR is required:

- Decrease P-level of Impella and continue chest compression as usual
- Notify interventional cardiologist and/or surgeon ASAP

During CPR reduce P-level to minimize potential damage due to dislodgement of the device during resuscitation. Once hemodynamics have been restored, an echo should be done to re-confirm placement. Increase P-level by two levels at a time until desired P-level is achieved.

Active CPR maneuvers may change the position of the Impella Device, introducing the risk of cardiac or vascular injury (including ventricular perforation).

DEFIBRILLATION/CARDIOVERSION[18, 19]

If defibrillation and/or cardioversion is required:

- P-level does not need to be adjusted
- Defibrillate/cardiovert as usual
- Image after to confirm accurate device position

DEVICE ALARMS AND MAINTENANCE

The Impella controller will sound an alarm tone, and display both an alarm message and a resolution message on the display screen. Alarm severity is color coded. Please refer to device manual for alarm indications: [18, 19]

Advisory (White)
Serious (Yellow)
Critical (Red)

A few of the alarms are listed below:

Impella Stopped

- Clinically support the patient. If CPR is needed, decrease Impella P-level and perform CPR.
- To troubleshoot the device, check the electric outlet and ensure that the Impella is plugged in. If device is powered off, attempt to restart.
- Replace Impella Controller if there are concerns for Controller Failure.
- Obtain STAT echo and Xray.
- If it restarts, decrease P-level by 1-2 lower than what was set, not going below P-2, and monitor for improvement of flow and function along with patient hemodynamics. If flow resumes at a lower P-level, evaluate the patient's intravascular volume status as well as positioning.
- If flow does not resume at lower P-level or P-2, assess the patient and make sure the patient is stable, call Abiomed, Interventional cardiology and CT surgery STAT for potentially removing and/or replacing malfunctioning Impella. If concerns for clot in device, discuss TPA administration.

Suction

- Clinically support the patient
- Obtain STAT echo and Xray. Decrease P-level by 1-2 lower than what was set, not going below P-2, and monitor for improvement of flow and function along with patient hemodynamics. If flow resumes at a lower P-level, evaluate the patient's intravascular volume status as well as positioning. [18, 19]

Purge Pressure High/Blocked [18, 19]

- Purge pressure is >1100 mmHG with the purge flow <1-2mL/hr
- Check all purge system tubing for kinks or blockages
- Decrease concentration of dextrose in the purge solution
- Replace purge cassette
- High pressure/Blockage may be due to clot. Contact Abiomed representative. Consider TPA administration.

Purge Pressure Low [18, 19]

- Purge pressure is <300 mmHG with the purge flow 30mL/hr
- Check all purge system tubing connections for leaks/damage
- Replace purge cassette
- Increase concentration of dextrose in the purge solution (D5% - D20% acceptable)

Refer to the **QR codes** for additional device alarms in the manufacturer IFU.

Impella CP IFU

Impella 5.5 IFU

MAINTENANCE

Impella Connect System Setup

OVERVIEW: The Impella Connect system consists of two parts: • A web-based user portal that allows authorized users to remotely view the screen of the Automated Impella Controller™ (AIC). The Impella Connect hardware connects to the VGA output of the AIC and transmits the display of the AIC screen to a cloud based server. The transmitted image can be viewed by authorized remote users, which may include hospital clinicians, Abiomed local support staff and Abiomed Customer Support Center (CSC) team members. The Impella Connect only enables passive viewing the AIC video screen. Changes to the controller settings can only be made using the physical controls on the AIC. Impella Connect may be configured and connected to the hospital's secured Wi-Fi network or be plugged in directly via Ethernet cable to the secured hospital network in order to transmit the video image to a web-based portal.
INTENDED USE: Impella Connect is intended to be used to enable remote viewing of the AIC's user interface by clinicians and by trained Abiomed personnel who assist clinicians with troubleshooting AIC alarms or other issues. Impella Connect transfers the video stream from the AIC (via the VGA output) to a cloud-based remote viewing portal. Communication between the AIC and Impella Connect is one-way (AIC to Impella Connect), and the streamed video is limited to Impella device operating parameters and alarm messages with no patient identifiable information. Impella Connect is powered directly by the AIC.
Please contact impellaconnect@its.jnj.com to begin the process of Impella Connect Setup

Transfer from AIC to AIC:

- Please see Instruction for Use or Impella App for detailed instructions

Changing Impella Purge Solution:

- Please refer to Impella App or Impella Instruction for Use

Changing the Impella Purge Cassette and Fluid Bag:

- Please refer to Impella App or Impella Instruction for Use

De-airing the Purge System:

- Please refer to Impella App or Impella Instructions for Use

DEVICE WEANING AND REMOVAL

- Length of use of the devices: please refer to FDA PMA indications on page 1.
- The length of Impella support is dependent on underlying myocardial disease and indications for its use. In setting of acute cardiogenic shock, the length of therapy tends to be short (<5days). In the setting of bridge to decision the length of therapy might be longer depending on the designated destination or recovery.
- In the setting of good hemodynamics and evidence of improved ventricular function, the Impella can be weaned gradually.
- If a patient shows clinical improvement and the care team feels Impella support may no longer be needed, a gradual decrease in P-level settings may be performed first with close monitoring of hemodynamic parameters.
- Impella 5.5 and CP with SmartAssist allows for monitoring of LVEDP trends as long as the P-level is 4 or greater.

Rapid weaning:

If the Impella has been used for temporary circulatory support (<5 days or clinically showing early signs of hemodynamic improvement with ability to wean P-level), the device can be weaned rapidly over the course of 24-48 hours while closely watching hemodynamics and patient tolerance to weaning. While weaning, assess hemodynamics and echocardiograms to assess native heart recovery with decreasing pump flows. If the patient has been weaned successfully to P-2, do not wean further until ready to remove the device. If the patient's hemodynamics remain stable, decrease the P-level to P-2, pull the catheter into the aorta, and stop the motor by decreasing the P-level to P-0.

Weaning on ECMO:

For patients supported with Impella on ECMO the sequence of transition includes weaning Impella to lowest level possible before deciding to wean off ECMO (not lower than P-2). Typically, Impella support is maintained until the patient is liberated from ECMO and then weaned off.

Slow weaning:

- If the patient has been supported by the Impella over a long period of time (>5 days or clinically needing full Impella support and showing slow signs of clinical improvement on Impella support), the Impella should be weaned gradually. Wean the P-level on the Impella 1 or 2 times a day, while closely watching hemodynamics and clinical tolerance. While weaning, assess hemodynamics and echocardiograms to assess native heart recovery with decreasing pump flows. Wean Impella P-level until you've reached P-2 and wean no further unless ready to remove the catheter.
  - On the Impella 5.5, the LVEDP and native cardiac output can be monitored while weaning.
- Monitoring the hemodynamics (blood pressure, perfusion, CVP) are very important at this time.
- Echo guidance during Impella support wean may also be beneficial to evaluate ventricular size and function.
- In the event the patient doesn't tolerate Impella support wean, the team must consider continuation of current therapy versus transition to a durable VAD.

While weaning and once at P-2, if the patient's hemodynamics remain stable and the team is ready to remove the device, decrease to P-1for the 5.5 and to P-2 for the CP, pull the catheter into the aorta and stop the motor (P-0). If the patient's hemodynamics remain stable, follow instructions in the next section for removing the Impella Catheter.

Specific instruction for removal of the device:

- Femoral access:
  - When the device is in the descending aorta turn the device to P-0 and unplug the power cable from the AIC.
  - The catheter shaft is pulled until the motor housing reaches the repositioning sheath at which point the repositioning sheath and the catheter are removed. Apply pressure to the puncture site.
  - If pre-closure sutures have been previously placed, tie down the sutures and observe hemostasis.
  - This can be done in the cath lab or at the bedside for uncomplicated femoral arterial access.

- Axillary access:
  - If the Impella was placed via a graft, device removal should be performed in the cath lab or operating room. The surgeons will assist with removal and control bleeding at the graft before tying off the graft and closing the incision.
  - If the Impella was placed percutaneously, it is advised to remove it in the cath lab. Access can be obtained in the femoral artery and a wire advanced into the axillary artery. This will allow for balloon tamponade of the subclavian to create a dry field for obtaining hemostasis.
  - The Impella pump is removed as described in the femoral access section. Hemostasis can be achieved by pressing the vessel against the second rib. If pre-closure sutures have been previously placed those can be tied down. Again, having another point of access and a compliant balloon in the subclavian artery can allow for tamponade to temporarily control bleeding if necessary.

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 4/1/2025)*

Please refer to the Instructions for Use (IFU) for both CP with SmartAssist and 5.5 with SmartAssist for specific manufacturer recommendations regarding their use.

**Unless expressly noted with an IFU reference, this guideline embodies the best practices as determined by the ACTION Learning Network and NOT Johnson & Johnson MedTech.*

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IMPELLA PERCUTANEOUS TEMPORARY VAD Management in Pediatric Patient

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Use of mechanical circulatory support in children is restricted to few devices translated from adult population. Impella temporary VAD offers opportunities for mechanical circulatory support in older children. Due to limited pediatric experience with this device, a structured approach to patient selection, assessment and device deployment is essential followed by careful monitoring and guided therapy de-escalation.

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OBJECTIVES

This document will provide an overview of the Impella® 2.5®, Impella CP®, Impella CP with SmartAssist®, Impella 5.0®, Impella 5.5 with SmartAssist®, and Impella RP® devices, patient selection, implantation techniques and management strategies.

PROTOCOL

IMPLANTATION INDICATIONS

As with many temporary and durable mechanical support devices the success of support is dependent on careful patient selection. Current pediatric experience highlights 3 primary disease spectrums for left sided support.

1. Support and recovery from acute cardiogenic shock (left sided or biventricular support) [1]
    a. Acute myocarditis
    b. Acute decompensated heart failure
    c. Acute transplant rejection with graft dysfunction
    d. Malignant arrhythmias

2. Bridge to decision for durable support or transplantation [2]
    a. Circulatory support to allow for short term cardiac recovery
    b. LV support to assess response to pulmonary vasodilators when concern for elevated PVR
    c. Potential support for patients who are poor candidates for durable VAD due to anatomical or surgical factors
    d. If concern for RV failure post LVAD implant and consideration of need for BiVAD support, can trial Impella first to see how the RV responds to increased preload

3. Left heart unloading on VA-ECMO support [3–5]
    a. Decompress and unload the left heart and potentially maximize myocardial recovery
    b. Eliminates the need for LA vent or balloon atrial septostomy that would subsequently require surgical closure
    c. Facilitate weaning off ECMO

Right ventricular support can be provided with Impella RP. The following are potential indications for use of Impella RP [6]:

1. Acute right ventricular failure secondary to:
    a. RV failure post LVAD placement
    b. Acute myocarditis
    c. Ventricular arrhythmias

CONTRAINDICATIONS

The following conditions **may not be appropriate for implantation of the Impella system for LV support**.

- Inadequately sized vessels for insertion – will vary based on device type
- Presence of ventricular thrombus
- Presence of severe aortic regurgitation or stenosis
- Artificial aortic valve
- Presence of significant right to left shunts (ie. VSD, ASD)
- Abnormal arch anatomy precluding catheter advancement
- Known coagulopathy - should warrant discussion with hematology
- Anticipated need for durable VAD support (but may use as transition to durable support)
- Manufacturer contraindications: Ventricular long axis length <7cm and aortic valve diameter <1.5cm

The following conditions **may not be appropriate for implantation of the Impella system for RV support.**

- Inadequately sized vessels for insertion
- Presence of RA, RV or PA thrombus
- Presence of moderate to severe pulmonary regurgitation or stenosis or presence of PA conduit
- Mechanical valves in the right heart
- Severe pulmonary hypertension
- Presence of DVT or IVC filter

PRE-IMPLANTATION EVALUATION AND ASSESSMENT

IMAGING

Echocardiography Assessment and Measurements

Optimal candidacy and device selection will depend on a comprehensive assessment which includes detailed cardiac and vascular imaging.

The following echocardiographic measurements should be performed:

- Advanced assessment of LV or systemic ventricular systolic function
- Measurements of the following cardiac structures are necessary for determining candidacy for Impella insertion:
  - Measure of the systemic ventricular length from the apex to the aortic valve annulus in both an apical 4 chamber view and parasternal long axis view. This is particularly important for smaller patients (<40 kg) as the systemic ventricular length can limit options for device placement. The Impella 2.5 pump has a length of 7.5 cm from the pigtail to the aortic valve annulus marker on the motor housing. Implants can be performed in patients with a systemic ventricular length of <7.5 cm but may require angulation of the pigtail in the ventricular apex.
  - Measure length of the ascending aorta from the aortic valve annulus to the origin of the innominate artery (typically from a high parasternal long axis view). This measurement is not as critical for device selection as the ventricular length.
- Presence of aortic valve insufficiency
  - More than mild insufficiency at baseline could result in worsening AI with Impella placement.
  - Moderate to severe AI is a contraindication to Impella placement.
- Evaluate for any LV or aortic root thrombus.
- Evaluate RV function and TR. Biventricular failure may require support of both the LV and RV with a left sided Impella in combination with an RP or with another mode of MCS. Frequently, the RV function can be managed medically and only left sided support is necessary, even in the setting of RV dysfunction.
- For additional diagnostic imaging please refer to publication by Morray et al. 2019 [7]

Advanced cardiac imaging

- If any anatomical structures are in question, the assessment should extend to advanced cardiac imaging such as CT chest with contrast.
- Advanced imaging might also be required for planning of surgical implantation to ensure appropriate size of branch vessels as well as determine path of device insertion.

Vascular Imaging

- Vascular ultrasound should be used for assessment of potential access sites to exclude presence of any obstruction such as arterial thrombus or arterial collaterals especially in children with chronic illness. For the Impella 2.5 and CP the vessel diameter should be >4 mm. [7]
- Larger devices (Impella 5.0 or 5.5) generally require larger vessel sizes but have been implanted in patients in which the arterial vessels measure smaller than the motor given vessel wall elasticity.
- If any suspicion of compromise in distal extremity perfusion (i.e. arterial thrombosis) full assessment for arterial thrombosis in that extremity should be performed prior to device implantation. This might require US doppler at bedside or arterial angiography in interventional suite.

LABORATORY ASSESSMENT

Table 1: Diagnostics blood tests recommended prior to device deployment

Chemistry and Microbiology				
	☐	Comprehensive Metabolic Panel	☐	Brain Natriuretic Peptide or NT pro-BNP
	☐	Cystatin C	☐	Urinalysis
	☐	CRP	☐	+/- MRSA screen (institutional preference)
Hematology				
	☐	Type and Screen	☐	Plasma-free Hemoglobin
	☐	CBC w/ Differential	☐	LDH
	☐	PT/INR, PTT	☐	Anti-Xa if on heparin
	☐	Fibrinogen, D-dimer	☐	TEG or ROTEM Thromboelastography
	● Consider additional thrombophilia or bleeding work up if concerning family history or clinical course (see Action Pre-Implant Protocol for details)			
Ancillary Studies				
	☐	EKG	☐	Ultrasound Doppler (arterial & venous) to establish vessel size, information on access and line placement
	☐	Echocardiogram	☐	
	● Consider Head CT if patient at high risk (i.e., ECMO) or unable to get reliable neurologic exam ● Consider if MRI study (heart or brain) is warranted as cannot be performed after Impella is placed ● Consider Chest CT if needed for fit testing/size of heart if anticipate converting to durable VAD later			

MONITORING

- Ensure accurate weight and height is measured on the day of procedure.
- The following hemodynamic monitoring should be in place prior to or at the time of Impella implantation:
    - Arterial line
    - Central venous access
    - Swan Ganz catheter in biventricular anatomy and if no contraindications (may not be utilized in all institutions)
    - Foley catheter

IMPLANTATION TECHNIQUES

ANTICOAGULATION AT TIME OF IMPLANT

- A bolus dose of heparin should be administered to achieve an ACT >250 seconds prior to introduction of the Impella catheter.
- Depending on the device type, the initial purge fluid containing D5W may be run without heparin during initiation of support but should then be transitioned to purge fluid containing standard concentration of heparin of 25 U/mL depending on the anticoagulation needs of the patient. Discussion with an Abiomed representative is recommended.

CATHETERIZATION-BASED IMPLANTATION

Femoral Access Approach

- Impella implantation should be performed with fluoroscopic and echocardiographic (TTE or TEE) guidance. This is typically done in the catheterization laboratory although implantation in an operating room can be performed with the use of a portable fluoroscopic C-arm. Bedside implantation in an intensive care unit is discouraged.
- The arterial access site will vary depending on the intended duration of support, the size of the patient and size of the pump that will be inserted.
- After ensuring adequate size (> 4mm). Access should also be obtained with ultrasound guidance whenever possible. Other imaging techniques, including the use of bony landmarks and angiography may be performed as well. Percutaneous insertion is performed using the Impella 2.5, CP and RP devices. Surgical implantation (see below) should be used for Impella 5.0 and 5.5 devices.
- Once access is obtained the arteriotomy can be “pre-closed” with 1 or 2 pre-closure sutures. This will assist with hemostasis once the device is removed.
- For implant in smaller patients or for axillary artery implantation of the larger Impella devices (5.0 and 5.5) in adult-sized patients an axillary artery cutdown is performed and a chimney graft is sewn to the vessel (refer to section on surgical implantation). Typically, a Hemashield Platinum or Vascutek Gelweave graft is used. For the Impella 2.5 a 6 mm graft is adequate and for the larger pumps an 8 mm or 10 mm graft is necessary. The graft can then be cut to the appropriate size and tunneled under the skin for enhanced stability
- After vascular access is obtained (either percutaneously or via cutdown) appropriately sized peel away sheath is placed in the vessel or chimney graft. This will be peeled away after the Impella is in the appropriate position and the repositioning sheath is advanced through the arteriotomy and sutured into position.
- A pigtail catheter is advanced to the systemic ventricle and a guidewire (included with the pump, 0.018 Platinum Plus) is inserted anterior and away from the mitral valve, in the systemic ventricular apex.
- The Impella device is advanced over the guidewire using fluoroscopic guidance and the guidewire removed once the tip of the pigtail is in the systemic ventricular apex.
- The position of the Impella device is verified by echocardiography (see corresponding imaging section). The device may be adjusted if needed using echocardiographic guidance.
- Impella can be used in combination with ECMO for left heart decompression. In these circumstances, retrograde insertion of a small caliber sheath in the superficial femoral artery can be performed to augment distal arterial perfusion to the limb and prevent ischemia complications.
- The Impella repositioning sheath/catheter may be adjusted (end of catheter is tapered) to optimize distal limb perfusion (based on signal from a distal pulse oximeter and clinical exam).
- In some older patients, percutaneous axillary artery access may be performed as well. The axillary artery is not an end artery and the arm is generally protected from ischemia due to the subscapular arterial anastomosis. Percutaneous axillary artery access should also be performed using landmarks and ultrasound. For larger patients or those with challenging vascular anatomy, the axillary artery can be visualized angiographically with a catheter advanced from the femoral artery or contralateral radial artery. A wire can then be placed in the axillary artery to provide a fluoroscopic landmark for precise vascular access. A review of this technique is available in publication by Dawson K et al. 2020 [8]

SURGICAL IMPLANTATION

Right axillary artery approach

- Follow institutional practices for pre-op cleansing, anesthesia, time-outs, and ensure appropriate equipment is available.
- Sizes available for this technique: Impella CP, 5.0 and 5.5.
- Preop evaluation with CT scan (CTA ideal) to determine the anatomy and largest size Impella device that the vascular access will allow.
- Graft selection: (Hemashield, Gel-weave) Gel-weave graft has better hemostatic properties than the non-Gel-weave standard Hemashield graft (institutional preference).
- Pump standby (CPB), fluoroscopy, and transesophageal echocardiogram are necessary for this approach.
- Place standard monitoring lines.
- Position patient supine with arms tucked at the side.
- Make an incision 1 fingerbreadth below the clavicle and perform dissection down to the right axillary artery adjacent to the deltopectoral groove.
- The incision is taken to the level of the right axillary artery, and the artery is exposed and encircled with vessel loops in standard fashion. Great care should be taken not to injure or avulse any of the delicate side branches.
- Meticulous hemostasis is critical.
- Care is taken to avoid injury to the surrounding axillary vein and brachial plexus located superiorly.
- Administer heparin dose as per institutional protocol for goal ACT.
- Isolate and control the right axillary artery using a C-clamp and make an anterior arteriotomy.
- Trim an 8 or 10 mm graft to match the arteriotomy and create an end-to-side anastomosis using a running 5-0 Prolene suture to the right axillary artery. The graft should be beveled (based on surgeon preference and vessel size) to create a very gentle curve so as to ease pump head entrance later.
- Great care should be taken to ensure precise suturing and place additional hemostatic sutures as needed as the inferior aspect of the anastomosis is very difficult to see once the graft is tunneled.
- Consider topical hemostatic agents (institutional preference).
- Remove the c-clamp and inspect for hemostasis, while clamping the distal graft.
- Once hemostasis is satisfactory, clamp the proximal graft and tunnel the graft to a remote site (usually anterior to mid-axillary line), bring it out through the skin and temporarily secure it with a clamp.
- Place introducer system in distal graft and de-air.
- Under fluoroscopic guidance (may require cardiac interventionalist or interventional radiology), deliver guide wire into the left ventricle, followed by long sheath for wire exchange and then exchange for a stiff wire.
- Advance the flushed Impella device over the guidewire through the sheath and the graft. It is often helpful to use manual guidance from outside the anastomosis as the device pump reaches the artery, particularly in smaller patients, in order to help the device advance across the anastomosis and into the artery itself.
- Confirm Impella device is across the aortic valve and inflow and outflow ports are properly positioned with fluoroscopy and transesophageal echocardiography.
- Start the Impella LVAD device and slowly increase P-level to desired output/decompression based on position on TEE.
- Reconfirm positioning after final device placement with TEE, as the device has a tendency to advance into the ventricle as flows are increased. Make sure to check positioning again prior to break down of the sterile field at the end of the case.
- Secure the Impella catheter in place to the skin.
- Ensure hemostasis of the right axillary artery cutdown site.
- Close the right axillary artery cutdown sight in multiple layers and skin.
- Note the final pump P-level and flow, aortic to mid- inlet measurement by TEE, and pump placement at the Tuohy-Borst valve cm marker number for changes and repositioning postoperatively.

POST-OPERATIVE PATIENT AND DEVICE MANAGEMENT

ANTICOAGULATION

Anticoagulation is required to prevent clot formation around the catheter as well as to preserve device motor and pressure monitoring. Optimal anticoagulation is achieved through a combination of purge fluid heparin and systemic heparin administration.

Role of Purge Fluid

- All Impella pump motors are protected from biomaterial build-up by running fluid through a purge system. The purge fluid is required to lubricate and maintain function of the device motor and is infused through the internal channel of the catheter, bearings and across the motor. This creates a protective interface or barrier that prevents blood from entering the motor housing.
- Purge system uses a dextrose water solution between D5W and D40W. The solution flows through the internal channel of the Impella catheter in the opposite direction of the blood flow. Through a built-in pressure sensor, the device automatically sets and adjusts the purge flow anywhere between 2 and 30 mL/h to maintain an adequate purge pressure of 300–1100 mm Hg. The dextrose concentration of purge fluid determines the viscosity and flow rate. Since the rate of purge fluid is automatically regulated by the controller, the purge infusion rate must be monitored for large changes in dose as this might affect dose of delivered heparin.
- Lower dextrose concentrations, such as 5%, are less viscous and flow more quickly through the purge system, thereby systemically delivering more heparin. Higher (more viscous) concentrations result in a slower purge flow rate and less overall systemic heparin exposure for the patient. Higher dextrose concentrations can also result in more pressure on the pump and should be avoided when possible. The manufacturer recommends a **starting heparin concentration of 25 IU/mL in a 5% DW as the initial purge solution**.
- Since the purge fluid is infused under pressure, care must be taken to document and monitor purge lines and maintain proper fluid and purge cassette change according to manufacturer recommendations.
- In cases of heparin-induced thrombocytopenia other agents can be considered for anticoagulation and device protection. Please see section below.

Anticoagulating in Specific Scenarios:

Anticoagulation for Impella only support

- After implantation of Impella 2.5, CP, or 5.0, purge fluid is started without any Heparin and should be changed to D5W with 25 units/ml heparin immediately upon arrival to ICU.
- After implantation of Impella 5.5 or RP, the purge fluid should contain Heparin 25units/ml upon initiation of support in cardiac cath lab or operating room unless there is concern for significant bleeding.
- In clinical settings where D5W with 25 units/ml heparin causes excessive anticoagulation the heparin concentration can be reduced to 12.5 units/ml or dextrose concentration can be increased to reduce the purge infusion rate.
- In situations where D5W with 25 units/mL in the purge solution does not allow one to achieve therapeutic goals it is advised to add systemic Heparin drip and titrate that drip to achieve therapeutic goals.
- Antiplatelet agents are typically not indicated for management of anticoagulation on Impella support.

Anticoagulation on ECMO

- In the setting of Impella with ECMO support, patients should continue to have purge fluid driven anticoagulation with D5W with 25 units/ml heparin and systemic heparin added to achieve desired level of anticoagulation per institutional and patient specific ECMO goals.
- Purge heparin contribution to anticoagulation must be taken into consideration, thus systemic heparin requirements might be lower than prior to Impella insertion.
- Frequent monitoring is recommended especially if the patient is inflamed, infected, coagulopathic or displaying signs of insertion site oozing.

Anticoagulation for Impella RP

- Impella RP anticoagulation is also achieved through purge fluid
- Recommended starting purge concentration is D5W with 50 units/mL of heparin and systemic heparin should be added to achieve goal anticoagulation if purge delivered heparin is not achieving therapeutic goals

Initiation and Monitoring of Anticoagulation

- Timing of initiation of heparin purge fluid and systemic heparin (if need additional anticoagulation) may vary based on institutional practice. It is recommended to start Heparin in purge as soon as possible in the cath lab or immediately in the ICU assuming life threatening bleeding is not present.
- Manufacturer recommends maintaining an ACT of 160-180
  - If bleeding is noted one may lower the ACT goal or even briefly hold systemic heparin
  - Subtherapeutic ACT <130 for several consecutive hours might increase risk of pump thrombosis
- Institutional practice can include use of PTT or Anti Xa UF Heparin levels for goal anticoagulation (see table below)
- **If the Impella purge system delivers too much heparin**, a purge solution with a lower heparin concentration (12.5 units/mL) should be used first followed by increased dextrose concentration to reduce purge infusion rate.

TOTAL HEPARIN DELIVERED TO PATIENT = IMPELLA PURGE HEPARIN + SYSTEMIC IV HEPARIN

Table 2 (data taken from Sieg et al. 2015) [9]

	Anti Xa UF Heparin Level	PTT	ACT
ECMO + Impella	ECMO goals	ECMO goals	ECMO Goals
Impella Support Alone Low risk of thrombosis, short-term use or surgical site bleeding	0.15-0.25	50-60	160-180
Impella Support Alone High risk of thrombosis or long-term use	0.2-0.3	60-70	180-200
Impella RP	0.15-0.25	50-60	160-180

Other agents:

The decision to use agents other than Heparin in the purge system should be based on institutional experience with monitoring of the listed agents and careful analysis of risk benefit ratio based on clinical condition. Information presented in this section is based on institutional experience and adult experience from published case reports.

Bivalirudin:

- Bivalirudin can be used in a split-dose protocol which allows for constant infusion of medication in purge solution and additional titration of the systemic bivalirudin. As the purge solution range of flow rates varies, a variation in the dose of anticoagulant delivered to the patient through the purge solution is possible. Three variables should be considered. Total dose of bivalirudin delivered to the patient, the purge fluid flow rate and the concentration of the bivalirudin-based purge solution.

- Appropriate concentration for the purge solution can be made to supply up to a 50% of the required bivalirudin. Different described concentrations used for the purge fluid include 100mg of bivalirudin in 250ml of D5W, 50 mg/500 ml and 20 mg/500 mL. The bivalirudin dose from the purge solution alone can range between 0.015-0.07 mg/kg/h.
- Starting dose of systemic Bivalirudin in pediatrics is 0.3 mg/kg/hr, with the dose adjusted down with renal insufficiency. ACTs or aPTTs are initially monitored every 4 hours. Please refer to the ACTION bivalirudin protocol for more information. [10,11]

Argatroban:

- Argatroban at concentration of 25 mg/25 mL can be added to 475 mL of D5W to produce an argatroban purge solution with a concentration of 50 mcg/mL. Split-dose protocol can be used to deliver constant infusion of medication in purge solution at 50% anticoagulation goal and additional titration of the systemic argatroban. The total argatroban dose is calculated by adding the rate of argatroban purge solution and the systemic argatroban infusion.
- Purge dose is typically 0.05-0.1 mcg/kg/min. Usual systemic dose in pediatrics is 0.5-12 mcg/kg/min (usually <6) with doses titrated by 10-25% to goal activated partial thromboplastin time. While a patient is receiving argatroban purge solution, ACTs or aPTTs should be monitored every 6 hours.
- In hepatic impairment, dose should be adjusted down by 20-50%. [12]

Tissue plasminogen activator (tPA) alteplase:

- Tissue plasminogen activator (tPA) alteplase has been reported to be used for suspected Impella thrombosis (increasing purge pressure, elevated LDH levels)
- Sterile water is used as the diluent used in the tPA purge solution instead of D5W or normal saline. The solution is prepared by diluting tPA (2 mg) in 50 or 25 ml sterile water for injection in an intravenous piggyback (IVPB) to produce a 0.04 or 0.08 mg/ml solution. The tPA solution replaces the Impella purge anticoagulation solution and runs at the device determined rate while systemic anticoagulation is used to maintain a therapeutic ACT or aPTT. The lower tPA (0.04 mg/hr) purge solution can run over up to 12 hours, or longer if there is improvement but not normalization of the purge pressure. If there is no improvement in purge pressure at 12 hours, the higher tPA (0.08 mg/ml) purge solution can be used for up to 12 hours. Once tPA finishes infusing, the purge solution is switched back to the prior anticoagulation solution. [13]

LABORATORY MONITORING

Post Implantation labs obtained should reflect baseline assessment of patient oxygen delivery, coagulation profile, hemolysis, hemoglobin and end organ function, as well as frequency which allows monitoring of the Impella device and patient response to the device and anticoagulation.

Baseline labs post Impella placement: CBC; Chemistry with liver function; Hemolysis labs: plasma Hb, LDH; Coagulation profile: PTT, PT/INR, Fibrinogen, D-dimer, anti-Xa, ACT (POCT), TEG or ROTEM; blood gas with lactate and mixed venous oxygen saturation if available.

Table 3: Recommended laboratory testing following device deployment

Laboratory Markers	24-48h post implantation	Chronic Monitoring
Hematology and Coagulation		
CBC	Q12H	Daily
Plasma free hemoglobin and LDH	Q12H	Daily until stable
DIC Panel	Q24H	Daily until stable
Coagulation panel	Q12H or with every titration	Daily
TEG or ROTEM	Q12H	Daily until stable
Chemistry and Microbiology		
Comprehensive Metabolic Panel	Q24	As indicated

Brain Natriuretic Peptide or NT pro-BNP	Q24	Weekly
Cystatin C	Once	Weekly
Ancillary Studies		
CXR	Daily	Daily
Echocardiogram	Daily	Weekly

These are recommendations only and each center is encouraged to use center-based practice.

Additional Labs:

- Renal panel to assess end organ function
- Hepatic panel to assess end organ function and monitor for hemolysis
- Due to high risk of pancreatitis in patients recovering after cardiogenic shock a pancreatic enzyme panel should be performed and monitored accordingly.

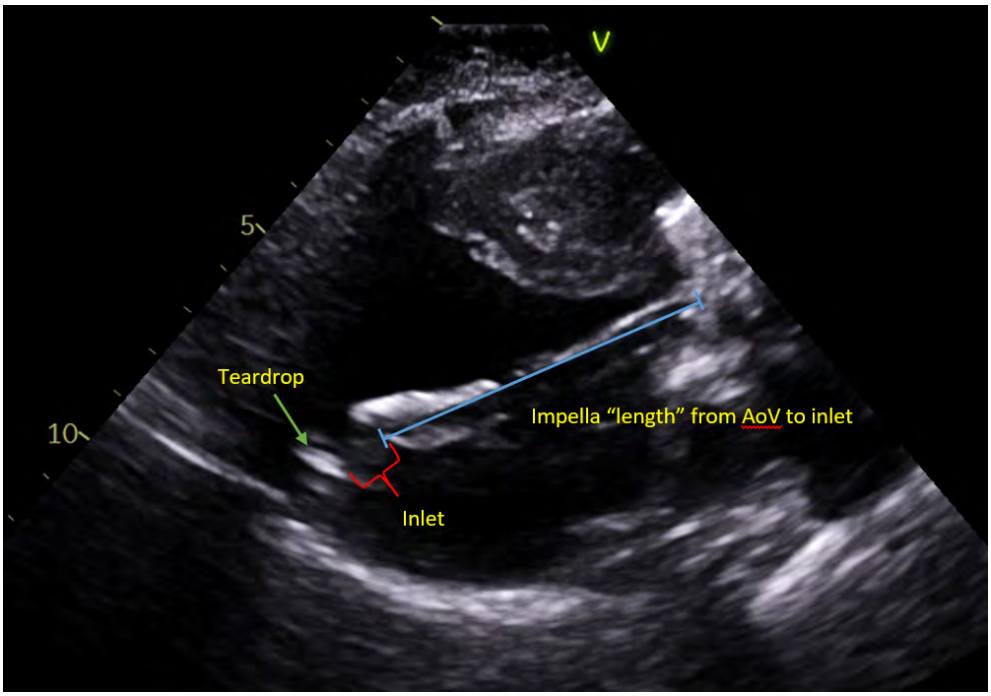
IMAGING TO MONITOR DEVICE POSITION

An echocardiogram provides useful information on Impella positioning for surveillance, if there is an increase in ventricular ectopy, or when evaluating ventricular decompression.

Echo Imaging Protocol:

- Positioning of the Impella is best seen by echocardiogram in the parasternal long-axis view. To appropriately measure the distance of the Impella in the left ventricle, measure from the aortic valve to the inlet (lucent area prior to teardrop). This will allow for consistent measurements over the patients' course.

Figure 1: Long axis parasternal view delineating intracardiac structures used for measurement of Impella position



DEVICE POSITION

Appropriate device position is crucial for optimal device function. Each device has specific position recommendations which can be found in the imaging section.

- Initial device position should be confirmed in the cath lab using fluoroscopy as well as TTE or TEE for correlation.
- It is recommended to re-evaluate the device position upon arrival to ICU and monitor every 48 hours.
- Positioning or suction alarms should prompt a bedside TTE to evaluate device position. The device can be repositioned at the bedside using TTE guidance.
- In smaller patients it may not be possible to place the inlet in the optimal location based on the manufacturer recommendation on distance from AV to pump inlet. ECHO should be used to ensure the inlet of the device is placed in the mid ventricular cavity, away from cardiac structure, the mitral valve apparatus, and LVOT to avoid suction. The outlet of the device should be a few centimeters above the AV to ensure uninterrupted flow from the device.

Table 4: Manufacturer recommended device position based on distance of device from the aortic valve to the inlet.

Impella Device	2.5	CP	5.0	5.5	RP
Position below aortic valve per manufacturer IFU	3.5 cm	3.5 cm	3.5 cm	5.0 cm	Via CXR outlet 2-4 cm above pulmonary valve

DEVICE MONITORING AND MANAGEMENT

DEVICE TERMINOLOGY

- **P-level:** Represents various rotational speed levels at which the device can be programmed to operate. P levels represent range of RPMs that the device will maintain to achieve optimal output (see device manual for specific P-level RPMs and flow rates)
- **Impella Flow (L/min):** Flow is calculated from the current and pressure gradient across the device based on the measured pressure flow curves. Each device is tested in the lab for its performance and accuracy. The flow accuracy is within 10% of max flow error.
- **Motor Current (mA - Green Waveform):** Motor current is the measured amount of energy required to achieve a set range of RPMs.
    - The current value changes based on the amount of blood flowing through the device and other potential resistors (i.e. motor thrombus, afterload and preload).
    - Waveform pulsatility displays the difference in energy requirement to drive the blood across the catheter between the inlet (in the LV) and outlet (in the aorta). Since the amount of flow differs in systole and diastole the current requirement changes reflecting a pulsatile motor current waveform.
    - Motor current provides information regarding catheter placement. When the inlet and outlet of the device are in different compartments (i.e. ventricle and aorta) the change in pressure across these two compartments results in higher or lower amount of blood flowing through the device. This creates a pulsatile current waveform. When a device is malpositioned and migrates into the same compartment (ie aorta or ventricle), the current waveform will disappear. A dampened or flat motor current waveform can be also diagnostic of device malposition (see troubleshooting section).
    - A dampened or flat motor current waveform in the setting of confirmed accurate position of the device might reflect very poor ventricular function.
    - Each Impella device has a different motor current level at specific P settings. Ensure motor current upper threshold parameters for each Impella device and P setting are available to the team. Monitor individual patient/device trends over time as a rise in motor current may be an early sign of device wear or thrombus formation, potentially requiring device exchange.
    - **A rapid rise in motor current may precede or indicate a pending device failure.**

- **Pressure Signal (mmHg - Red Waveform):** Pressure signal differs between various Impella types. Pressure is either measured through direct water column (Impella 2.5 and CP) or using an optical sensor at the motor head thus measuring aortic pressures. In most clinical cases the waveform should be pulsatile.
    - **Direct aortic pressure monitoring (available on Impella 2.5 and CP):** Aortic pressure in these devices is measured by direct pressure measurement using a pressure transducer and pressure bag system. It reflects the true aortic pressure. Care must be taken to maintain constant pressure in the system to prevent lumen obstruction or clotting.
    - Impella CP with SmartAssist and Impella 5.5 with SmartAssist contain optical sensors for pressure monitoring
    - Impella 5.0 and Impella RP use Differential Pressure Sensor
    - The pressure signal can be used together with motor current waveform to diagnose Impella malposition.
- The pressure signal can be used together with power waveform to diagnose Impella malposition (see troubleshooting section).
- **LV pressure Signal (mmHg -White Waveform on Impella 5.5):** This signal is only available on Impella CP and 5.5 with Smart Assist and represents calculated LV pressure. The measurement is deducted from the optical sensor derived by motor current indirectly measuring LVEDP and LVESP. This feature is available when the P level is a P4 of above.
- **Purge Flow (mL/hr):** The purge flow rate is delivered by purge cassette inside the Automated Impella Control (AIC) and is measured in mL/hr. The purge flow is automatically adjusted by the AIC based on the device needs. Higher dextrose concentration of the purge fluid will slow down the purge rate and lower dextrose content will increase purge rate.
- **Purge Pressure (mmHg):** The Impella console automatically adjusts the purge flow rate to maintain purge pressures between 300-1100mmHg.
    - High/low purge pressure alarms should be evaluated by following on-screen instructions.
    - If a ‘purge pressure low’ alarm remains unresolved for more than 20 minutes, the purge cassette will likely need to be changed.

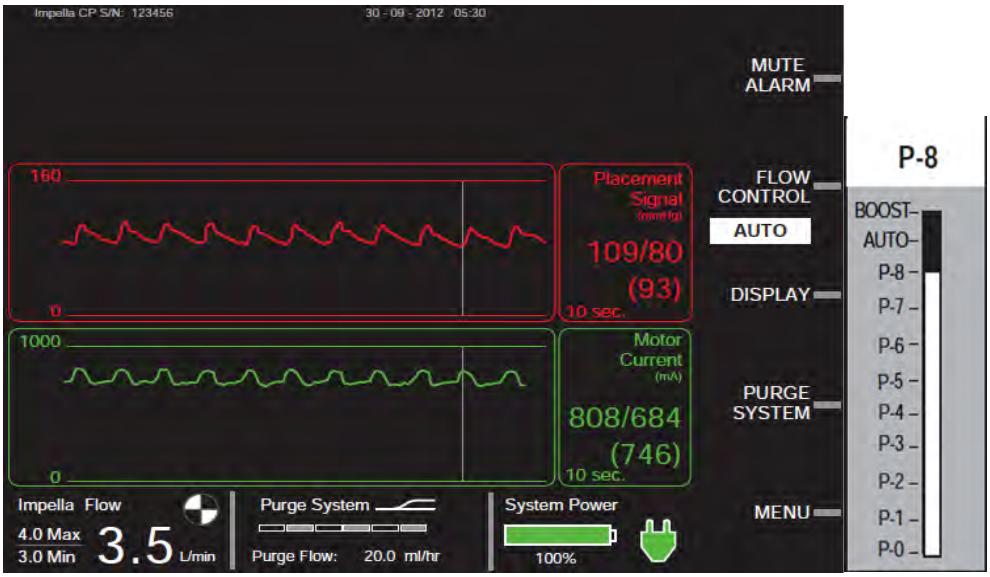


Figure 2: Example of Impella placement screen

Figure 3: Example of the Impella Purge Screen

DEVICE SPEED

- Device speed is regulated by P-levels on the controller (P0-P8) Impella 2.5 and Impella CP. Boost speed (P9) should only be used in the cath lab during high risk procedures. Initial speed after implantation can be at boost level however the device should not be left on boost speed for an extended period of time.
- It is recommended that the device is operated at the lowest speed possible. Optimal lowest speed level should be determined to minimize hemolysis, suction events and other complications.

Determining optimal device support:

- Optimal speed can change with changes in clinical status (ie. recovery of ventricular function, afterload reduction, intravascular volume status). Advanced hemodynamic monitoring including invasive arterial and venous pressures must be monitored to determine optimal support. PCWP can be directly measured in the cath lab to determine lowest LV filling pressure at the lowest P level.
- Outside of the cath lab environment, a Swan Ganz (SG) catheter can be used to determine level of LV unloading and optimal speed, as well as the function of the RV. While escalating the P level, the level of unloading should be measured by monitoring PCWP.
- In addition to the SG catheter, echocardiographic findings can further guide titration of support and monitoring of myocardial response to support.
- Finding the optimal speed will help minimize hemolysis and optimize device function. The support level should not exceed the required CO for the patient.

MALPOSITION

- The device position should be assessed with any device alarms, >20% change in flows, acute onset of hematuria or evidence of hemolysis, or suspected device movement.
- If repositioning is required, it should be done under direct TTE or TEE guidance.
  - **If the device is found to be outside of the LV it should only be repositioned under fluoroscopy guidance.**
  - If the device is found to be deep in the LV, it can be repositioned at bedside with TTE/TEE guidance.

PATIENT MANAGEMENT

ICU ADMISSION

Upon arrival to the ICU, the following should be completed:

- Ensure the AIC is plugged into AC power on arrival to ICU. The controller battery life is only 1 hour.
- The AIC should be positioned at the base of the bed for easy access and screen visibility.
- Device performance and setting should be evaluated and documented.
- For Impella 2.5 and CP, pressure bag systems should be set up as soon as possible.
    - If not started in the cath lab, ICU nursing should transition to heparinized purge fluid.
- Verify that the Tuohy connection is tightened to the right and locked in order to prevent catheter displacement or migration.
- Document insertion length of Impella catheter where the sterile sleeve connects to the sheath.
- Inspect dressing at the insertion site for bleeding and integrity.
- If femoral access, secure the extremity with the knee brace to prevent flexion and injury to the arterial insertion site (see limb care section).

HEMODYNAMIC MONITORING

- Patients in the critical phase of the illness will require more aggressive hemodynamic monitoring than those on long term support.
- Invasive hemodynamic monitoring of arterial blood pressure and central venous pressures is recommended until organ recovery and satisfactory organ function is achieved.
- Hemodynamic parameters and device performance should be documented every hour and as per unit policies.
- Use of a pulmonary artery catheter should be considered strongly, however it must be balanced with experience and training. Parameters (ie. PCWP, PAP, CI) obtained from Swan Ganz catheters can help determine response to device support, need for additional therapies and need for RV support.
- Balance between risk and benefit must be evaluated daily to minimize adverse events associated with invasive monitoring.

The following Impella assessment should be performed at the beginning and end of the shift as well as PRN:

- Device monitoring should include assessment and documentation of the following Q1H:
    - P-level
    - Impella flow (L/min)
    - Motor current (mA -green waveform)
    - Placement signal (mmHg -red waveform)
    - Purge pressure (mmHg)
    - Purge flow (ml/h)
    - Assessment of connections and device alarms

- Verify that the Tuohy connection is tightened to the right and locked in order to prevent catheter displacement and migration.
- Inspect dressing at the insertion site and confirm securement of Impella catheter.
    - Change dressing as per institutional guidelines.
- Document insertion length of Impella catheter where the sterile sleeve connects to the sheath.
    - Recommended position documentation with any positional changes and patient movement.
- Back-up Impella AIC console should be easily accessible and plugged into AC power.
- Check purge solution: Abiomed recommends using a concentration D5W with 25 U/mL Heparin in the purge system.
    - Purge solution bag must be changed Q24H
    - Purge cassette tubing must be changed Q72H (with fluid bag change)
    - Ensure one extra Impella tubing cassette is easily accessible
- Reposition patient as per unit protocols.

LIMB CARE, INSERTION SITE AND PERFUSION MONITORING:

The extremity with the Impella insertion site is at a high risk for compromise if there is limited perfusion or nerve compression. Close monitoring and assessment is crucial to minimize these complications.

- If the device is implanted percutaneously in the femoral position, extremity immobilization is recommended.
  - A knee immobilizer can be used to prevent the patient from bending the extremity and causing arterial rupture.
  - Attention must be placed on any pressure points and extremity hyperextension which can result in temporary or permanent foot drop if not recognized early.
  - A physical therapy consult should always be considered for appropriate assessment of knee immobilization.
- **Extremity with Impella must be closely monitored for acute arterial thrombosis or occlusion**. Pulse oximeter provides continuous pulse assessment and local NIRS may be used to monitor deterioration of perfusion. Palpate (or obtain by Doppler) peripheral pulses Q1H. Some institutions use a myometer to monitor loss of neurologic function.
- **Any compromise in perfusion must be immediately addressed**. Potential interventions include arterial jump graft. If unable to improve extremity perfusion, the device must be removed and another MCS strategy considered.
- Observe and document Q1H: Color, capillary refill, warmth, movement, and sensation
- Notify MD if noted signs of diminished peripheral circulation or limb ischemia (i.e. quality of pulses diminished, cool peripheries, change in skin color/mottling or sensory changes including numbness and/or tingling)
- Consider early involvement of physical and occupational therapy to minimize the above complications and address any motor deficiency early
- Observe puncture sites, sheath insertion site or surgical access site for active bleeding, swelling, bruising or hematoma especially when anticoagulation is escalated. Additional bleeding control may be needed by placing mattress sutures at the insertion site.
- With femoral insertion, avoid flexion of leg and keep the head of bed greater than 30 degrees.

Skin integrity

Due to limitations in patient mobility especially when femoral insertion site is used, close attention must be paid to skin integrity and pressure areas.

- Assess skin integrity Q2H & PRN
- Assess risk of skin breakdown using appropriate pressure ulcer risk assessment tool
- Reposition patient as per hospital protocols

Urine output

Change in urine color can be one of the first indicators of excessive hemolysis indicating device malposition or suction. Foley catheters can be used to diagnose these complications early.

- Observe and document characteristics of urinary output Q1H
- Observe for signs of hemolysis: discoloration of urine, decreasing hemoglobin/hematocrit, increased LDH, plasma free Hgb, AST and bilirubin
- Once stable device position and appropriate hemodynamic status is achieved, and end organ recovery is established, Foley catheter should be removed to minimize risk of infection.

PATIENT TRANSPORT

- Safe transport checklist and expectations should be generated based on intuitional practices with following in mind:
  - Prior to transport, document the insertion length (cm) of the Impella catheter where the sterile sleeve connects to the sheath.
  - A transfer board should be utilized to ensure that the catheter remains in situ and does not kink. The limb with the Impella catheter in situ must remain straight at all times during transport.

- In preparation for transport the team should check purge fluid, check battery life and that Impella was charging prior to transport, check the catheter connections so as not to dislodge with movement and transfer of patient, monitor urine quality prior and during transport.
- The Impella controller battery life is 1-hour.

MANAGING COMPLICATIONS AND ADVERSE EVENTS

Potential adverse events include, but are not limited to: aortic valve injury, bleeding, cerebral vascular accident/stroke, hemolysis, limb ischemia, thrombocytopenia, vascular injury and death.

BLEEDING

- Depending on method of Impella insertion, bleeding may occur at the access site and/or surgical sites (subclavian cut down and graft anastomosis). This should always be assessed by the cath or surgical teams and intervened on if needed.
- Compression devices such as safeguard or dressing may be used briefly (<6 hours) and extremity perfusion must be closely monitored during this period and while on support.
- Assess the patient and evaluate the cause of bleeding (over anticoagulation, coagulopathy vs surgical site bleeding).
    - Send labs evaluating for coagulopathy (CBC, PT, PTT, Fibrinogen, Rotem, Anti-Xa) and assess the need for blood transfusions during prolonged periods of bleeding and correct any deficiencies.
- Anticoagulation goals may need to be adjusted if there is ongoing bleeding or oozing and the pump itself is otherwise functioning well. Heparin may even need to be held for short periods of time (<6-12 hours) for clinically concerning bleeding.
    - If clinically indicated for clinically significant bleeding, per manufacturer recommendations, maximum duration of running the Impella pump without heparin is no longer than 24 hours.
- If bleeding continues, consider platelet dysfunction, low fibrinogen, HIT.
- Surgical intervention for bleeding should be considered if bleeding is difficult to control with medical therapies.

HEMOLYSIS

- Some degree of hemolysis may occur at higher P settings. It is typical to see some mild hemolysis in the first 24-48 hours of support. This should improve.
- The etiology of hemolysis can be due to the expected mild sheering from the device, from higher P-level settings, suction events, or malpositioning of the Impella device.
- To evaluate the etiology, consider ECHO to assess positioning of cannula, check fluid status, suction events, and P-level setting.
    - P-level setting may need to be adjusted if the setting is too high, as well as fluid administration if patient appears hypovolemic
- If P-level setting and fluid status are unchanged but hemolysis is noted, consider ECHO to assess positioning of cannula. If the Impella has moved further towards the LV apex, the outflow may be close to the aortic valve and cells may be lysed as they exit the outflow of the Impella and hit the aortic valve leaflets.
- Hemolysis is clinically seen as a constellation of findings depending on the degree.
  Mild hemolysis may be seen only with lab findings of elevated LDH or plasma Hb with a stable or slowly decreasing hemoglobin value. Moderate to severe hemolysis manifests with elevated LDH, plasma Hb, elevated bilirubin, AST, and red/tea colored urine with an acute drop in hemoglobin.
- Significant hemolysis can induce AKI, continue to monitor renal function.

DEVICE CLOT

- In the setting of subtherapeutic anticoagulation or periods of profound inflammation, the device is at risk of developing fibrin deposition or thrombus formation, resulting in device failure.
- There may be a rise in purge pressure and drop in purge flow, rise in motor current either acutely or gradually, or drop in device flow overall.
- Consider TPA administration to the device in consultation with Abiomed, or your institution's protocol.

- If the device stops, support the patient clinically as indicated, and consult interventional cardiology and CT surgery as soon as possible.

DEVICE FAILURE

- This is not a common occurrence with the Impella device, however, when used for prolonged periods, there may be a risk of device failure/stoppage.
- Close monitoring of motor current trends will help to assess the function of the motor.
- If the motor current is increasing and is nearing its upper threshold, the ICU team, and proceduralist should be notified, as this may be an early sign of the motor reaching end of life. Each type of Impella device, at each P setting, will have a different motor current upper limit. Discussion may be had with your Abiomed representative regarding recommended thresholds and potential device exchange.

INFECTION

- As with any foreign indwelling device, there is a risk of infection. Prophylactic antibiotics are not generally recommended for the duration of the device. However, for surgical prophylaxis, cefazolin or other antibiotic covering skin flora may be administered for 24 hours postoperatively.
- Monitor site and continue site care, as described above, continuously evaluating for infection.
- If an infection occurs related to the device, antibiotic regimen to be individualized based on your institution.

SUCTION

- Several factors may cause a Suction alarm, including inadequate left ventricular filling or preload, incorrect Impella position against the papillary muscle or the mitral valve, or right ventricular failure.
- Suction may occur if the blood volume available for the Impella catheter is inadequate or restricted.
- Suction limits the amount of support that the Impella can provide to the patient and results in a decrease in expected Impella flow, arterial pressure and cardiac output. It can damage blood cells, leading to hemolysis.
- If the Impella detects suction, it automatically reduces motor speed to lower the flow rate to resolve the suction and displays the “Impella Flow Reduced” advisory alarm. If the suction is cleared, the controller returns the flow rate to the desired setting. If suction is still detected at the lowest motor speed, the controller displays the “Suction” alarm.
- If a suction alarm occurs, reduce the Impella P-level by 1 or 2 levels, or more, if suction continues. Assess the patient’s volume status, assess hemodynamics and RV function, evaluate catheter position using the placement signal, motor current, and imaging. Reposition Impella if necessary. When the suction alarm is resolved, resume pre-alarm flow rate.

OTHER CLINICAL CHALLENGES

Ectopy and arrhythmias

- Periods of ectopy or arrhythmia might be experienced with the Impella device in place. As long as there is preload to the left ventricle, the patient should be adequately supported with the Impella providing continuous flow and perfusion pressure.
- Recurrent refractory ventricular arrhythmias warrant assessment of device parameters and alarms for suction events as well as device position, LV filling and RV function by echo.
- During periods of arrhythmia, the patient may lose synchronous intrinsic contractility and therefore pulsatility, however will have a non-pulsatile blood pressure instead, a mean arterial pressure (MAP). If the MAP range is appropriate during the periods of arrhythmia, the patient is well supported.
- If the patient doesn’t have adequate MAPs during periods of arrhythmia, assess RV function, volume status, antiarrhythmic agent and consider adjusting P-level if appropriate to better support the patient clinically while the arrhythmia is being medically managed.

EMERGENCY PROCEDURES

CARDIOPULMONARY ARREST

If your patient arrests and loses blood pressure and perfusion pressure, and CPR is required:

- Decrease Impella to P-2 and continue chest compression as usual
- Notify interventional cardiologist and/or surgeon ASAP

During CPR P-2 is utilized to minimize potential damage due to dislodgement of the device during resuscitation. Once hemodynamics have been restored, an echo should be done to re-confirm placement. Increase P-level by two levels at a time until desired P-level is achieved.

DEFIBRILLATION/CARDIOVERSION

If defibrillation and/or cardioversion is required:

- P-level does not need to be adjusted
- Defibrillate/cardiovert as usual
- Image after to confirm accurate device position

DEVICE ALARMS AND MAINTENANCE

ALARMS

The Impella controller will sound an alarm tone, and display both an alarm message and a resolution message on the display screen. Alarm severity is color coded and please refer to device manual for alarm indications:

- Advisory (White)
- Serious (Yellow)
- Critical (Red)

Mispositioning:

- Assess positioning of the Impella device. Consider obtaining x-ray for gross patient movement. Evaluate with echo at bedside for exact positioning.
- If repositioning is required, it should be done under direct TTE/TEE guidance.
- If the device is found to be outside of the LV, it should only be repositioned under fluoroscopic guidance.
- If the device is found to be deep in LV, it can be repositioned at bedside with cath and close TTE/TEE guidance.

Low flow on Impella:

- Flow is lower than expected for set performance level. Either due to suction, inadequate preload or due to high afterload. Assess positioning with echo, volume status and blood pressure.

No flow or Impella stops/acute device stoppage:

- Clinically support the patient. If CPR is needed, drop Impella P-level to 2 and perform CPR.
- To troubleshoot the device, check the electric outlet and ensure that the Impella is plugged in. If off, attempt to restart.
- Obtain STAT echo and Xray. Decrease P-level by 1-3 lower than what was set, not going below 2, and monitor for improvement of flow and function along with patient hemodynamics. If flow resumes at a lower P-level, evaluate the patient's intravascular volume status as well as RV function and positioning. Under these circumstances, catheter function is not reliable and the Impella may stop again.
- If flow does not resume at lower P-level or P2, assess the patient and make sure the patient is stable, call Abiomed, Interventional cardiology and CT surgery STAT for potentially removing and/or replacing malfunctioning Impella.

Suction alarms (see above in complications):

- Suction waveforms will differ based on which Impella catheter is being used. Note the ‘suction alarm’ alert.
  - Intermittent suction alarm: will alert ‘suction alarm’ and the Impella controller will reduce the motor speed to resolve the suction, then resume flow and will resolve itself. If this occurs, assess

positioning with echo, assess preload as suction events may be due to low intravascular volume state and underfilled ventricle and evaluate RV function.

- Continuous suction alarm is an event that does not resolve and continues to alarm and you will see lower flows delivered on the Impella console as well as lower systolic pressures. If you see a continuous suction alarm, lower your P-level and assess positioning of the catheter with echo, assess RV function and preload. Once troubleshooting is complete and flows resume, resume P-level to prior settings.

MAINTENANCE

Impella Connect System Setup

- Please see figure in appendix

Transfer from AIC to AIC:

- Please see device manual or manufacturer App for detailed instructions

Changing Impella Purge Solution:

- Please refer to Impella App and AIC directions

Changing the Impella Purge Cassette and Fluid Bag:

- Please refer to Impella App and AIC directions

De-airing the Purge System:

- Please refer to Impella App and AIC directions

DEVICE WEANING AND REMOVAL

- Length of use of the devices: please refer to FDA PMA indications on page 1.
- The length of Impella support is dependent on underlying myocardial disease and indications for its use. In setting of acute cardiogenic shock, the length of therapy tends to be short (<7days). In the setting of bridge to decision the length of therapy might be longer depending on the designated destination or recovery.
- In the setting of good hemodynamics and evidence of improved ventricular function, the Impella can be weaned gradually.
- If a patient shows clinical improvement and the care team feels Impella support may no longer be needed, a gradual decrease in P settings may be performed first with close monitoring of hemodynamic parameters.
- Impella 5.5 with Smart Assist allows for monitoring of LVEDP trends as long as the P level is 4 or greater.

Rapid weaning:

If the Impella has been used for temporary circulatory support (< 7 days or clinically showing early signs of hemodynamic improvement with ability to wean P-level), the device can be weaned rapidly over the course of 24-48 hours while closely watching hemodynamics and patient tolerance to weaning. While weaning, assess hemodynamics and echocardiograms to assess native heart recovery with decreasing pump flows. If the patient has been weaned successfully to P2, do not wean further until ready to remove the device. If the patient's hemodynamics remain stable, decrease the P-level to P-1, pull the catheter into the aorta, and stop the motor by decreasing the P-level to P-0.

Weaning on ECMO:

For patients supported with Impella on ECMO the sequence of transition includes weaning Impella to lowest level possible before deciding to wean off ECMO (not lower than P2). Typically, Impella support is maintained until the patient is liberalized from ECMO and then weaned off.

Slow weaning:

- If the patient has been supported by the Impella over a long period of time (> 7 days or clinically needing full Impella support and showing slow signs of clinical improvement on Impella support), the Impella should be weaned gradually. Wean the P level on the Impella 1 or 2 times a day, while closely watching

hemodynamics and clinical tolerance. While weaning, assess hemodynamics and echocardiograms to assess native heart recovery with decreasing pump flows. Wean Impella P-level until you've reached P2 and wean no further unless ready to remove the catheter.
    - On the Impella 5.5, the LVEDP and native cardiac output can be monitored while weaning.
- Monitoring the hemodynamics (blood pressure, perfusion, CVP) are very important at this time.
- Echo guidance during Impella support wean may also be beneficial to evaluate ventricular size and function.
- In the event the patient doesn't tolerate Impella support wean, the team must consider continuation of current therapy versus transition to a durable VAD.
- While weaning and once at P2, if the patient's hemodynamics remain stable and the team is ready to remove the device, decrease the P-level to P-1, pull the catheter into the aorta, and stop the motor by decreasing the P-level to P-0.

Specific instruction for removal of the device:

- Femoral access:
    - With the device in the descending aorta turn the device to P-0 and unplug the power cable from the AIC.
    - The catheter shaft is pulled until the motor housing reaches the repositioning sheath at which point the repositioning sheath and the catheter are removed. Apply pressure to the puncture site.
    - If pre-closure sutures have been previously placed, tie down the sutures and observe hemostasis.
    - This can be done in the cath lab or at the bedside for uncomplicated femoral arterial access.

- Axillary access:
    - If the Impella was placed via a chimney graft, device removal should be performed in the cath lab or operating room. The surgeons will assist with removal and control bleeding at the graft before tying off the graft and closing the incision.
    - If the Impella was placed percutaneously, it is advised to remove it in the cath lab. Access can be obtained in the femoral artery and a wire advanced into the axillary artery. This will allow for balloon tamponade of the subclavian to create a dry field for obtaining hemostasis.
    - The Impella pump is removed as described in the femoral access section. Hemostasis can be achieved by pressing the vessel against the second rib. If pre-closure sutures have been previously placed those can be tied down. Again, having another point of access and a compliant balloon in the subclavian artery can allow for tamponade to temporarily control bleeding if necessary.

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 01/22/2021)*

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IMPELLA PERCUTANEOUS TEMPORARY VAD
Abbreviated Points for Quick Reference

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

The use of mechanical circulatory support in children is restricted to a few devices, many of which have been adapted from the adult experience. The Impella, is one such example that offers temporary mechanical circulatory support in children. Due to limited pediatric experience with this device, it is essential to have a structured approach to patient selection, device deployment, post-implant monitoring and guided therapy de-escalation.

ACTION REVISED DATE: 08/03/2022

OBJECTIVES

This document provides an abbreviated bedside overview of the Impella® percutaneous heart pumps. Please reference "IMPELLA PERCUTANEOUS TEMPORARY VAD Bedside Pearls for the Pediatric Patient" for more details.

PROTOCOL

ICU MANAGEMENT

ANTICOAGULATION

- Obtain baseline coagulation labs
- Start anticoagulation via the purge fluid as soon as patient is in ICU, if not already started in the OR
- Purge flow rate is automatically adjusted by the controller
- If anticoagulation goals are not met with purge fluid alone (heparin 25 IU/mL in D5W typically), add systemic heparin infusion
- If patient is supra-therapeutic on purge heparin alone, decrease heparin concentration by half to 12.5 IU/mL, if still supra-therapeutic, go down to 6.25 IU/mL
- If HITT is suspected, call Abiomed representative for recommendations (e.g. sodium bicarbonate in D5W)
- Antiplatelet agents are not typically used for Impella pumps

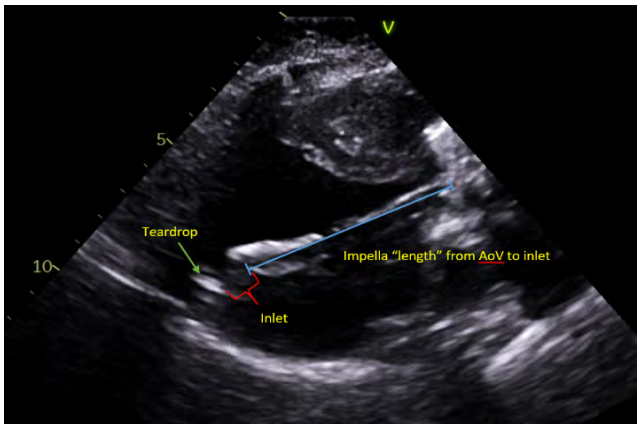
Monitoring of Anticoagulation

- Impella only (Anti-Xa or PTT per institutional preference)
  - Low risk of thrombosis, short term use or surgical bleeding – Anti-Xa 0.15-0.25 or PTT 50-60 sec
  - High risk of thrombosis or longer term use – Anti-Xa 0.2-0.3, PTT 60-70 sec
    * high PTT ranges with adequate or sub-therapeutic Xa goals, please consult with your local hematology or transfusion medicine team
- Impella + ECMO: Use ECMO anticoagulation goals (ACT, Anti-Xa, PTT per institutional protocol)

IMAGING TO MONITOR DEVICE POSITION

When to image:

- CXR daily x2-3 days, then space as able
- ECHO daily post placement x48 hours, measuring distance in ventricle - measure from the aortic valve to the inlet (lucent area prior to teardrop) in parasternal long-axis view
  - **Impella 5.5**: Distance 4.5cm below aortic valve
  - **Impella 2.5, CP, 5.0**: 3.5cm below aortic valve
- Repeat ECHO as needed if:
  - Having device alarms
  - >20% change in flows
  - Acute onset of hematuria or evidence of hemolysis
  - Suspected device movement
  - New or increasing ectopy or arrhythmia burden



DEVICE ALARMS

Malposition:

- Assess positioning of the Impella device with ECHO +/- CXR. If repositioning is required, notify interventional cardiology or surgical team and:
    - If deep in LV, pull back with ECHO guidance
    - If pulled out in aorta, should only be repositioned under fluoroscopic guidance

Low flow on Impella:

- Flow is lower than expected for set performance level. Either due to suction, inadequate preload, RV dysfunction, or due to high afterload. Assess position & function with echo, volume status and blood pressure.

No flow or Impella stops/acute device stoppage:

- Clinically support the patient. If CPR is needed, drop Impella P-level to 2 and perform CPR. See 'Emergency Procedures' section for proper procedure post ROSC.
- Check electric outlet and ensure that the Impella is plugged in. If off, attempt to restart.
- STAT ECHO and CXR. If device has power, decrease P-level by 1-3 lower than what was set (not below 2), and monitor for improvement of flow and function along with patient hemodynamics.
    - If flow resumes at a lower P-level, evaluate the patient's intravascular volume status as well as RV function and positioning. Under these circumstances, catheter function is not reliable and the Impella may stop again.
    - If flow does not resume at lower P-level, assess & clinically support the patient, call Abiomed, and STAT call to cath/surgery team for potential device explant or exchange.

Suction alarms:

- Intermittent alarm: alerts 'suction alarm,' and the controller will reduce the motor speed to resolve the suction, then resume flow and will resolve itself. Assess position with echo, assess preload, and evaluate RV function.
- Continuous alarm: an event does not resolve and continues to alarm, you will see lower flows and systolic pressures. Drop the P-level and assess positioning of the catheter, RV function and preload.

MANAGING COMPLICATIONS AND ADVERSE EVENTS

Potential adverse events include: hemolysis, bleeding, arrhythmias, thrombocytopenia, aortic valve or mitral apparatus injury, vascular injury, limb ischemia, device malfunction, site infections, cerebral vascular accident/stroke, or death.

HEMOLYSIS

- Can be due to the expected RBC shearing from the device, from higher P-level settings, suction events, or mal-positioning of the Impella device, especially in first 24-48 hours of support.
- Check fluid status, LDH, plasma free Hb, evaluate for suction events, and consider adjusting P-level setting, ECHO to assess positioning.
    - May need fluid administration vs drop in P-level settings vs device repositioning.

BLEEDING

- At access site or surgical sites – assess if coagulopathy vs surgical site issue:
    - Workup: Anticoagulation studies, platelet count/function, TEG
    - Evaluation of procedural sites by cath/surgical teams, consider hematology consult
    - Consider compression devices (safeguard or dressing for <6 hours), monitor extremity perfusion
- Anticoagulation goals may need to be adjusted if ongoing bleeding/oozing and the pump is otherwise working well. May need to hold heparin for up to 6-12 hours for clinically concerning bleeding.
    - Manufacturer recommendations: Max duration without heparin is no longer than 24 hours.
- If bleeding continues, consider platelet dysfunction, low fibrinogen, HITT, recheck labs, hematology consult.
- Surgical intervention should be considered if bleeding is difficult to control with medical therapies.

DEVICE CLOT

- If suboptimal anticoagulation or concerns for systemic inflammation, thrombus can form in the pump.
- May see a rise in purge pressure, drop in purge flow, rise in motor current, or drop in device flow overall.
- Consider tPA administration per Abiomed or your institution's protocol.
- Consider bivalirudin as thrombolytic therapy, if heparin is contraindicated or unable to achieve therapeutic levels (Abiomed does not recommend bivalirudin for routine use)

- If the device stops, provide clinical support and STAT call the cath/surgical team for replacement or explant.

DEVICE FAILURE

- Can be seen with prolonged use when device reaches end-of-life
- If the motor current trend is increasing and nearing its upper threshold, or there is an acute rise, the ICU team, and proceduralist should be notified, as this may be an early sign of the motor reaching end of life. Each type of Impella device, at each P setting, will have a different motor current upper limit. Discussion may be had with your Abiomed representative regarding recommended thresholds and potential device exchange.

INFECTION

- Prophylactic antibiotics not recommended but may consider cefazolin for 24 hours peri-operatively.
- If an infection occurs related to the device, antibiotic regimen to be based on your institution.

SUCTION

- Suction is manifested by material (myocardium, biofilm) being entrained into the inflow.
- Etiologies include inadequate LV filling or preload, incorrect Impella position, or RV failure.
- Suction results in a decrease in Impella flow, arterial pressure and cardiac output.
- It can damage blood cells, leading to hemolysis.
- If suction occurs, Impella automatically reduces motor speed to lower the flow rate to resolve the suction and displays the “Impella Flow Reduced” advisory alarm. If cleared, the controller returns the flow rate to the desired setting. If suction is still detected at the lowest motor speed, the controller displays the “Suction” alarm.
- If suction continues, reduce the P-level by 1 or 2 levels, and assess the volume status, hemodynamics, RV function, evaluate catheter position using the placement signal, motor current, and imaging. Reposition Impella if necessary. When the suction alarm is resolved, resume pre-alarm flow rate.

ARRHYTHMIAS

- If ectopy or arrhythmia occurs, as long as there is sufficient preload to the LV, the patient should be adequately supported with the Impella providing continuous flow and perfusion pressure.
- Recurrent refractory ventricular arrhythmias warrant assessment of device parameters and alarms for suction events as well as device position, LV filling and RV function by echo.
- May lose pulsatility during an arrhythmia, though should be able to measure a mean arterial pressure (MAP). If the MAP range is appropriate during the periods of arrhythmia, the patient is well supported.
- If the patient doesn’t have adequate MAPs during periods of arrhythmia, clinically support patient appropriately while assessing RV function, volume status, antiarrhythmic agent and consider adjusting P-level if appropriate to better support the patient clinically while the arrhythmia is being medically managed.

EMERGENCY PROCEDURES

CARDIOPULMONARY ARREST

If the patient arrests and loses blood pressure and perfusion pressure, and CPR is required:

- Notify interventional cardiologist and/or surgeon ASAP
- Decrease Impella to P-2 and continue chest compression as usual
    - During CPR, P-2 is utilized to minimize potential damage due to dislodgement of the device during resuscitation.
    - Once ROSC is achieved and hemodynamics have been restored, an echo should be done to re-confirm placement.
    - Increase P-level by two levels at a time, every 5-15 minutes depending on patient stability, until desired P-level is achieved.

DEFIBRILLATION/CARDIOVERSION

If defibrillation and/or cardioversion is required:

- P-level does not need to be adjusted
- Defibrillate/cardiovert as usual
- Image after to confirm accurate device position

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SECTION

Infection Prevention & Management

ANTIBIOTIC PROPHYLAXIS for Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Peri and postoperative infection continue to be challenging issues post VAD implant in pediatrics. Infection in patients include VAD-specific infections such as driveline infection, VAD pocket infection or cannula infections, in addition to VAD-related infections like blood stream infection and endocarditis. Not all of these are related to infection at the time of implant, but appropriate prophylaxis can likely prevent early infections as well as prevent colonization. There is currently not a published guideline for the antibiotic prophylaxis for pediatric VAD implant.

ACTION REVISED DATE: 01/31/2025

OBJECTIVES

Provide an example of standardized perioperative infection prophylaxis regimens at time of VAD implantation.

PROTOCOL

Pre-Operative

5-7 days prior to surgery or at first notification:

- Consider screening for MRSA colonization
- Antiseptic bath with an agent like chlorhexidine.
- Consider antibacterial ointment (mupirocin) to each nostril twice daily for 48-72 hrs., and up to 5 days if MRSA colonized
- Assess for extra thoracic infections and necessity of indwelling catheters/lines.

1 day prior to surgery:

- If no antiseptic bath with an agent like chlorhexidine has been initiated previously; an antiseptic bath should be done the evening prior to surgery.

Day of surgery:

- Antiseptic bath and rinse the morning prior to surgery.

Intraoperative

- First line, no risk factors:
  - Anti-staphylococcal therapy (i.e. cefazolin) IV 1 hour prior to sternotomy / re-dose for surgeries lasting > 4 hours or after 120 minutes on bypass.
- For patients with prolonged/complicated pre-op course or as warranted by local epi or patient factors:
  - Second or third generation cephalosporin 1 hour prior to sternotomy / re-dose for surgeries lasting > 4 hours or after 120 minutes on bypass.
- For patients with known MRSA colonization:
  - MRSA-directed therapy (i.e. vancomycin) IV 1 hour prior to sternotomy / re-dose for surgeries lasting > 4 hours or after 120 minutes on bypass
  - +/- Second or third generation cephalosporin 1 hour prior to sternotomy / re-dose for surgeries lasting > 4 hours or after 120 minutes on bypass
- Driveline dressing and immobilization to be applied in the OR

Post-Operative

- See intraoperative above for antibiotic choice.
- Antibiotics for 48-72 hours of therapy (adjust for renal dysfunction per pharmacy)
  - Extended durations may be considered for prolonged open chest
- Consider antifungal therapy for 48- 72 hours if patient has been on ECLS support for more than 5-7 days.

Note

Local epidemiologic antibiograms and alternatives for antibiotic allergies should prompt modification of antimicrobials.

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Care of Cannula Sites for Berlin Heart Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Ventricular assist device (VAD) dressing integrity is a critical factor for the prevention of device related infection. Inadequate dressing or dressing disruption is a major risk factor for bloodstream infections, device pocket infection and driveline site infections. Enhanced dressing adhesion promotes sterility and saves time as fewer dressing changes are needed.

ACTION REVISED DATE: 11/12/2024

OBJECTIVES

- Describe a detailed example of standardized VAD specific dressing change protocol for cannula sites
- Minimize risk of VAD related wound or device infection
- Promote VAD care and dressing techniques to optimize wound integrity and healing

PROTOCOL

In order to prevent infection of driveline sites, the dressing changes must be done in a sterile and consistent fashion. This is a 2-person activity. Consider a small group trained and competent (VAD dressing team) as consistency is key to optimize integrity and healing.

Dressing Frequency

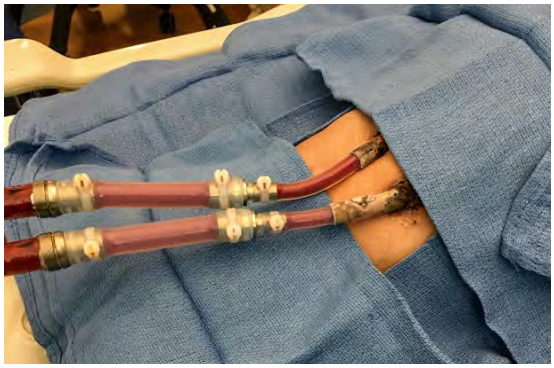
Weeks 0-1	Every day
Weeks 1-2	Every other day, (consider M/W/F to keep consistency in staff changing dressing)
Above Weeks 2	Discretion of the team, (consider twice weekly)

Steps for Dressing Change:

1. Perform hand hygiene and don clean gloves, hat, and mask. Mask patient if age appropriate.
2. Disinfect the table surface for sterile supplies
3. Assemble supplies for the procedure (This is an example, please see the end of the document for other options among the same supplies):
    - Masks, hats, clean gloves
    - Sterile gloves
    - Sterile gown
    - Sterile drapes/towel pack
    - Antiseptic solution
    - Sterile Water
    - 3 trays of sterile 4x4s
    - 4 individual 4x4s packages
    - Abdominal pad
    - Sterile scissors
    - Occlusive Sterile Dressing – One for each cannula
    - Border Dressing
    - Ace Wrap

4. Open sterile supplies onto table surface utilizing sterile technique
    - Set up 3 trays of sterile 4x4s
        - Antiseptic solution
        - Sterile water
        - Dry gauze

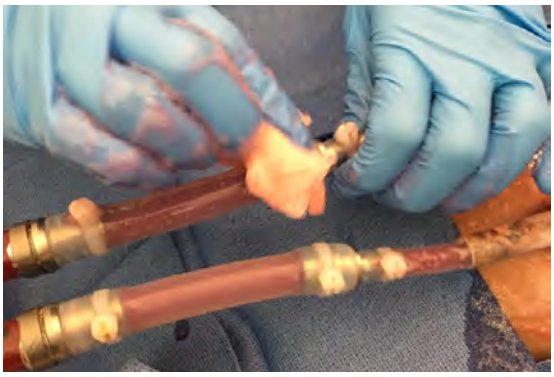
5. Remove patient's current cannula dressing and assess site. Ensure picture of wound site is uploaded into media section in EMR if available



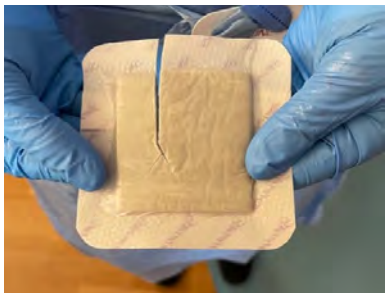
6. Doff clean gloves, clean hands, and don sterile gown and sterile gloves
7. Place sterile towels around patient to create sterile field
8. With antiseptic solution soaked 4x4 gauze, clean from insertion site outward using both a side to side and circular motion. Gently clean skin around 1st cannula. Discard gauze.

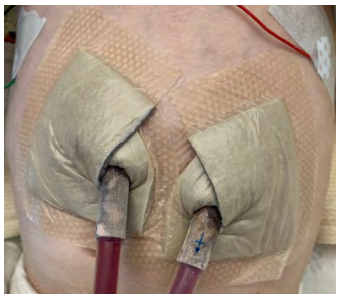
- **Repeat procedure for all subsequent cannula sites using an antiseptic solution-soaked gauze**

9. Clean each cannula on all sides using an antiseptic solution-soaked gauze. Thread the gauze around the cannula. Using a back-and-forth motion, shimmy the gauze up the cannula from the insertion site to where the Berlin pump attaches, ensuring you clean all sides of the cannula.
    - **Repeat procedure for all subsequent cannulas using an antiseptic solution-soaked gauze**



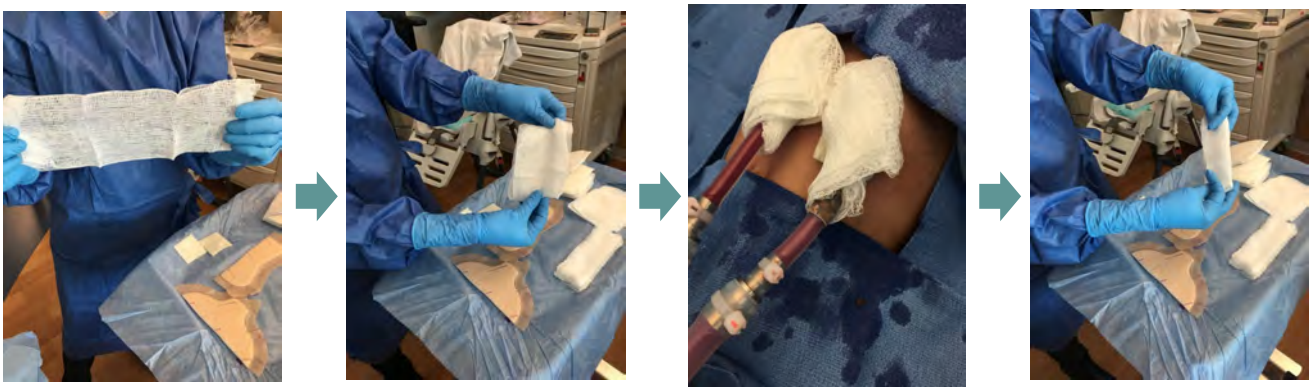
10. **Repeat #8 and #9 twice for each cannula site**
11. Rinse each site using a sterile water soaked 4x4 gauze
12. Dry each site using a dry 4x4 gauze
13. Prepare Dressings:
    - Cut dressing into squares big enough to fit around each cannula. Cut ½ way down the center and then make two smaller cuts to make a “Y” shape.



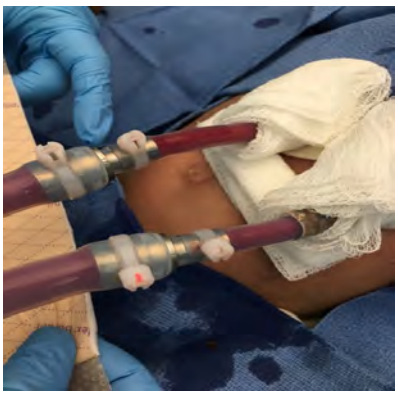


- Place cut square under cannula and chevron so that the ends of the gauze cross over each other on top of the cannula. Repeat on other cannula(s).

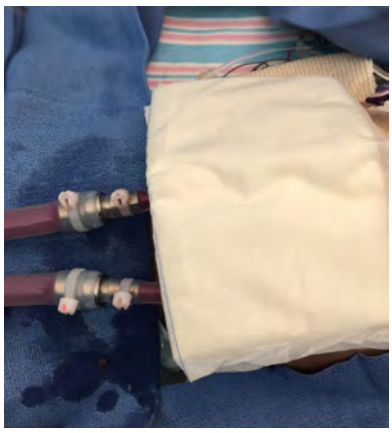
14. Take one dry 4x4 gauze. Unfold it. Fold in half lengthwise. Fold in half widthwise once and chevron around cannula. Repeat on other cannula(s).



15. Roll up a 4x4 and place one under both cannulas for padding



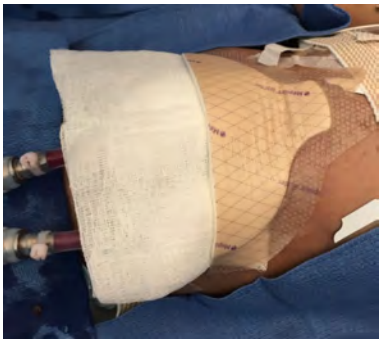
16. Place abdominal pad on top of dressing



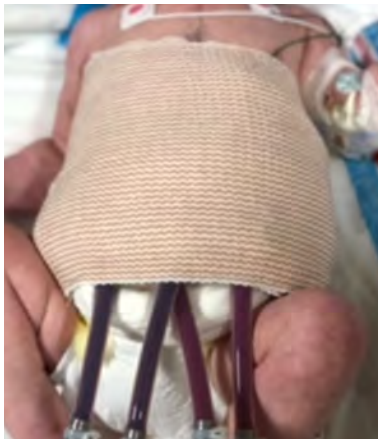
17. If using border dressing cut in half horizontally. Using the rounded edge, place at lower border of rolled 4x4's and secure to skin to create a barrier between dressing and diaper area. Place other half of border dressing on the top portion of the dressing PRN

- This is no longer part of the sterile dressing of the cannula sites, but rather an extra layer to prevent soiling of sterile dressing

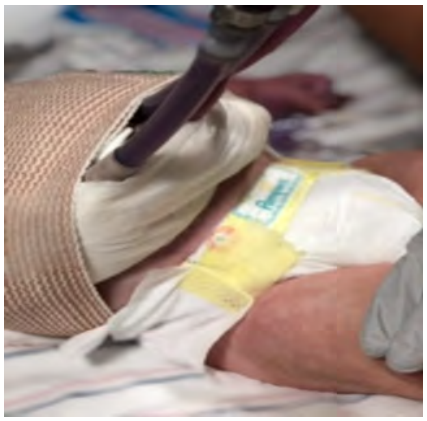




18. Dressing should be secured with elastic bandage, not too tight as to prevent cannulas from kinking.



19. Fold and tuck the top of the diaper downwards to help prevent the dressing from becoming soiled.



Product Considerations:

- Antiseptic solution
  - Hibiclens (more gentle for infants)

    - 2% ChloraPrep Swabstick
    - Chlorhexidine BD E-Z Scrub 4% CHG, sponge side only, bristle removed
    - Betadine (with confirmed CHG allergy)
- Occlusive VAD dressing
    - Mepilex AG
    - Aquacel AG and telfa tape
    - Gauze chevron followed by silverlon strips
    - Mepilex foam over silverlon strips
    - Telfa®
    - Mefix® 6 inch dressing tape (*since Mefix® is a silicone-based product that decreases epidermal stripping from tape
    - Covaderm
    - Primapore/Bordered Gauze
    - Silvercel and Hydrofilm
- Border dressing
    - Mepilex Sacral Border
- Securement device
    - Ace Wrap
    - Spandage Tubular Retainer Net
    - Abdominal binders
- Consider PHI compliant photo documentation in EMR of serial cannula site photos.

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4) J Heart Lung Transplant 2016; 35:108–14. April 2016 Volume 35, Issue 4, Supplement, Page S350 Site Management Strategies in Pediatric Ventricular Assist Device (VAD) Patients. M.V. Horn et al.

Care of DRIVELINE Exit Site for Implantable Continuous Flow Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Ventricular assist device (VAD) dressing integrity is a critical factor for the prevention of device related infection. Inadequate dressing or dressing disruption is a major risk factor for bloodstream infections, device pocket infection, and driveline site infections. Enhanced dressing adhesion promotes sterility and saves time as fewer dressing changes are needed.

ACTION REVISED DATE: 3/6/24

OBJECTIVES

- Describe detailed example of standardized VAD specific dressing change protocol
- Minimize risk of VAD related wound or device infection
- Promote VAD care and dressing techniques to optimize wound integrity and healing

PROTOCOL

In order to prevent infection of driveline sites, the dressing changes must be done in a sterile and consistent fashion. This is a 1-person activity or can include 2 persons. Consider a small group trained and competent (VAD dressing team) as consistency is key to optimize integrity and healing. If the patient or family prefer to change the dressing and have been deemed competent, this is acceptable with RN supervision.

Dressing Frequency

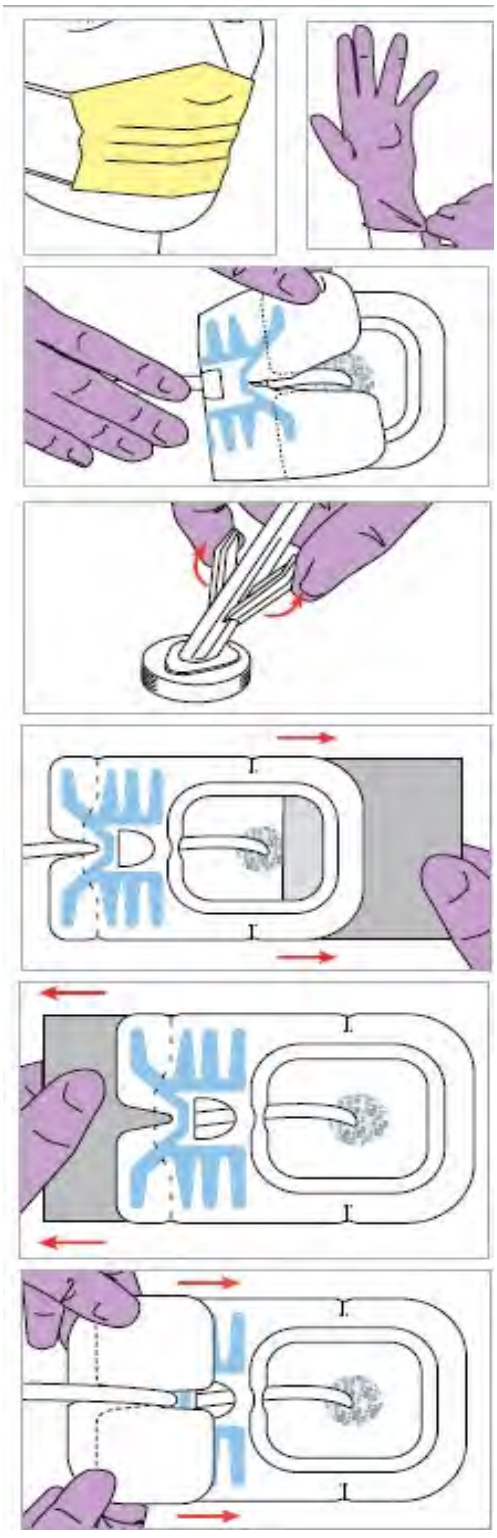
Weeks 0-1	Every day
Weeks 1-2	Every other day, (consider M/W/F to keep consistency in staff changing dressing)
Above Weeks 2	Discretion of the team, (consider once or twice weekly)

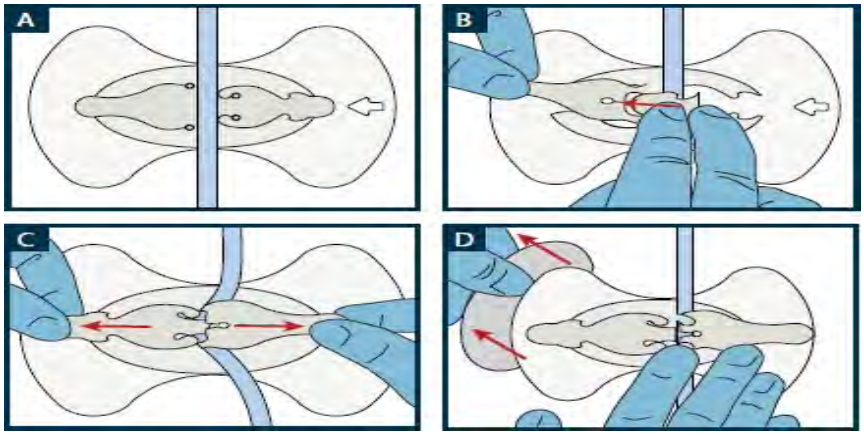
Planning & Supplies

- Sterile gloves
- Clean gloves
- Masks for people in room including patient
- Antiseptic swab or scrub (See end of document for specific product considerations)
- Occlusive VAD dressing (See end of document for specific product considerations)
- Antimicrobial disc (See end of document for specific product considerations)
- Sterile scissors
- Securement device (See end of document for specific product considerations)
- Camera to upload picture of exit site

Procedure

1. Clean and clear surface for driveline dressing supplies
2. Place masks over mouths (everyone in room and the patient).
3. Wash hands
4. Don clean gloves
5. Remove old dressing; ensure that the driveline does not tug when removing the dressing
6. Inspect the dressing site for signs of infection. Take photo of site and upload to EMR.
7. Remove gloves and wash hands properly again.
8. Open sterile gloves to create sterile field; drop dressing, scissors, antiseptic swab, and gauze onto sterile field.
9. Don sterile gloves.
10. The dominant hand should be “clean.” Use the “clean” hand to grasp antiseptic swab. Use the “dirty” hand to grasp the driveline using the sterile gauze to pick up and hold up the driveline for ease of cleaning.
11. Pinch the wings of antiseptic swab to release the antiseptic solution.
12. Use the antiseptic swab, starting at the exit site, then moving outwards and down the driveline. Use the “dirty” hand to lift the driveline as necessary to get around the site. Time and friction disinfects the site. Consider scrubbing site for at least site for 60 seconds.
13. Allow the area to completely air dry. At least 90 seconds.
    DO NOT BLOT, BLOW, OR WIPE AT THE CLEANED SITE
14. According to hospital’s protocol, consider applying antimicrobial disk over insertion site. *Avoid if skin breakdown or irritation is present
15. Use “clean” hand and apply occlusive dressing to the site**,** ensuring that the dressing is completely occluded on all 4 sides. Consider a split dressing approach and chevron ends over each other.
16. Re-Secure and stabilize the driveline with a driveline securement device with a small amount of slack. Apply new anchor if previous anchor has been on for 1 week or longer; or is not well secured





17. Waterproof barrier (Example: Press and Seal/AquaGuard) should be placed over driveline site prior to all showers. A dressing change should always be completed after a shower.

18. Document photo of dressing change and condition of exit site. Dressing should be assessed per hospital policy, and if it becomes saturated/unocclusive, consider dressing change sooner than determined routine frequency

Product Considerations:

- Antiseptic swab or scrub
    - ChloraPrep Swabstick
    - Hibiclens
    - Iodine (if CHG allergy)
- Occlusive VAD dressing
    - Sorbaview
    - Split gauze and tegaderm
    - Covaderm
    - Tegaderm plus
    - Primapore/Bordered Gauze
    - Silvercel and Hydrofilm
- Antimicrobial disc
    - Biopatch
    - Aegis
- Securement device
    - Foley anchor
    - Centurion anchor
    - K-loc

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Driveline and Cannula Site Infection Management for Pediatric VAD Patients

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Infection is one of the most common adverse events following VAD implantation. Infections remain one of the major contributors to morbidity, mortality, and hospital readmissions in VAD patients, especially driveline and cannula site infections.

ACTION REVISED DATE: 3/6/24

OBJECTIVES

To review the management of driveline and cannula site infections for pediatric VAD patients.

PROTOCOL

Close surveillance and monitoring of clinical symptoms and driveline/cannula site appearance.
Considerations for treatment of driveline and cannula site infections include:

Prevention:

- Perioperative Antibiotics (See ACTION Antibiotic Prophylaxis Protocol)
- Sterile Dressing Changes (See ACTION Care of Driveline and Cannula Site Protocols)
- Hand hygiene:
  - Strict hand hygiene by healthcare workers.
  - Patients and caregivers should receive continuing education on proper hand hygiene and dressing change routines.
- Immobilization of drivelines and cannulas:
  - Consider Foley anchor to prevent drivelines from pulling and tugging (see image).
  - Anchoring at the time of implant is beneficial.
  - Certain centers have found benefit in using retention sutures (for ~6-8 weeks), especially in obese patients.
- Barriers to prevent contamination of driveline/cannula site with bodily fluid:
  - If patient has a G-tube, consider placement of ostomy bag around G-tube to prevent gastric contents from leaking into the driveline/cannula site.
  - For incontinent or diapered patients, consider the use of Steri-Drape 3M barriers to prevent urine and feces from coming in contact with the driveline/cannula site.
- Showering:
  - Once showering is approved, consider taking showers on days driveline dressing is scheduled to be changed and change dressing immediately following the shower
  - Avoid contact of shower water (consider using Aquaguard as a border around site)
  - Keep driveline site as dry as possible during the shower
- Maintain good nutrition

Foley Anchor

Monitoring:

- Frequent monitoring of driveline or cannula sites
  - Recommendations for Dressing Frequency

        - Weeks 0-1: Every Day
        - Weeks 1-2: Every Other Day
        - Above 2 weeks: Consider twice weekly or at the discretion of the care team
- Any acute event related to driveline integrity such as trauma, tugging or pulling, should be assessed closely for breakdown around site.
    - Signs of driveline site disruption after a tugging/pulling event include bleeding, new discharge, and/or visualization of disruption of the driveline-skin barrier.
- Exposure of velour on driveline sites is a major risk factor for infections and should be monitored.

Evaluation:

- Appearance of driveline or cannula site
    - Assess color, tenderness, swelling, drainage amount and consistency, foul odor, undermining (erosion at base) at the site, or tunneling (see Figure and pictures below)
- Consider Imaging if there are clinical concerns for infection
    - Sterile US of driveline site/cannula site to evaluate for pocket infections
        - Consider timing of dressing change to follow the US
    - CT scan or PET if concerns for deep driveline/cannula site infections
    - ECHO (Consider TEE if strong suspicion for endocarditis)
- Consider evaluation of systemic involvement if patient develops signs or symptoms of infection (fever, nausea, vomiting, diarrhea, fatigue, or hemodynamic changes)
    - Inflammatory and infectious markers (CBC, CRP, ESR, pro-calcitonin)
    - Blood cultures (if suspicion of systemic infection)

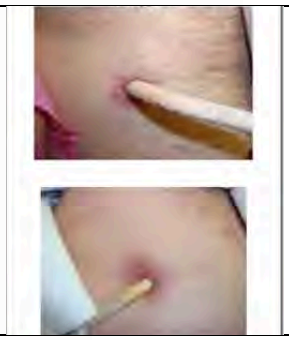
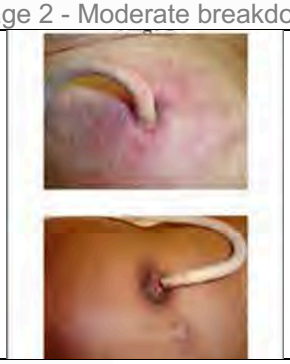
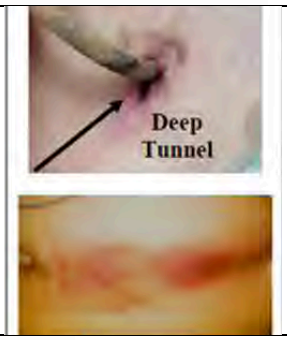
Stage 1 - Mild breakdown	Stage 2 - Moderate breakdown	Stage 3 – Severe breakdown
		
Appearance: - Pink, healthy tissue incorporating into the driveline - Little or no erythema - No tenderness - No drainage	Appearance: - Persistent disruption of skin at exit site - Some erythema - Mild tenderness - Possible local cellulitis - Small amount of drainage (note color, odor, amount) may be culture negative	Appearance: - Severe skin disruption (bleeding from granulation tissue, pulled away from the driveline, cellulitis, bleeding) - Erythema - Severe tenderness with infection tracking along driveline tract - Moderate to copious purulent drainage.

Figure 1: The classifications of driveline infection proposed by the Sharp Memorial group

Treatment:

- Review dressing change protocols to ensure compliance and close monitoring (See ACTION Care of Driveline and Cannula Site Protocols)
- Treatment should be based on the staging of the driveline/cannula site
- Consider increasing dressing change frequency
- Consider Wound Team Consult
- Degree of Breakdown/Infection

- Stage 1 – Mild Breakdown
  - Increase frequency of dressing changes and close monitoring
    - Consider changing dressing type to one with anti-microbial and absorbency properties such as Mepilex AG
    - Consider adding antimicrobial disc such as a Biopatch (also consider that the Biopatch could be the cause of this irritation and should be discontinued)
    - Consider adding products with silver (healing and microbial properties) such as Aquacel rope to site if erythema
    - Consider changing to less concentrated chlorhexidine such as dilute Hibiclens from CHG swab if site is erythematous
  - If a tugging or pulling event occurs, the driveline skin barrier may be disrupted, and additional prevention efforts should be started.
    - Increase frequency of dressing changes
    - There is no evidence to support the use of oral antibiotics when there is disruption of the driveline without any other signs of infection
    - Reverting to the management strategy at the time of VAD implant is a reasonable approach to prevent infection after disruption and avoid side effects of antibiotics such as antibiotic resistance, diarrhea, or GI discomfort
- Stage 2- Moderate Breakdown
  - Daily dressing changes and close monitoring
    - Consider using product with silver (healing and microbial properties)
    - Silver wound vac sponge
    - Silverlon instead of CHG Biopatch if site is erythematous
  - Consider CV Surgery evaluation for local debridement
  - Consult consultation with an infectious diseases specialist
  - Consider sterile culture from driveline/cannula site (bacterial and fungal) when there is evidence of purulent drainage
  - With superficial DLI without concerns for systemic illness, consider oral antibiotic therapy
    - For first line empiric antibiotic treatment, consider anti-staphylococcal coverage
      - patient may warrant broader coverage based on epidemiologic or patient factors
      - Local epidemiologic antibiograms and alternatives for antibiotics allergies should prompt modification of antimicrobials
- Stage 3 – Severe Breakdown
  - Daily Dressing Changes and Close Monitoring
  - Monitor for signs of systemic Infection (fever, or leukocytosis)
  - Consider Admission for IV Antibiotics
    - For first line empiric antibiotic treatment, patient may warrant broader coverage based systematic involvement
      - Local epidemiologic antibiograms and alternatives for antibiotics allergies should prompt modification of antimicrobials
    - Consider sterile culture from driveline/cannula site (bacterial and fungal) when there is evidence of purulent drainage
      - Culture and susceptibility can guide more targeted therapy if available
    - Duration of therapy should be based on clinical response and resolution of infectious signs/symptoms. Antimicrobial coverage may be required for duration of VAD support and decisions should be made with an infectious diseases specialist.
  - Consider CV Surgery evaluation and possible admission to OR for debridement/explant needs for invasive infections

        - Consideration of wound vac
        - Consideration of pump replacement
    - Anticoagulation Considerations due to systemic inflammatory response:
        - Consider close monitoring of inflammation and fibrin in pump
        - Consider frequent surveillance of PTT/DTT for patients on bivalirudin.
        - Antibiotic therapies can potentiate effects on INR. Additional surveillance of anticoagulation assays should be considered.
- Other Considerations
    - Re-occurring infections:
        - Chronic suppressive oral antibiotics may be considered
        - Consider re-tunneling of driveline/cannulas or replacement of pump
    - Avoid medihoney to driveline site as it has been associated with biofilm formation [2]
    - Consider other causes of chronic rash and drainage (forms of dermatitis). Dermatology consultation and biopsy may be helpful.
- Transplant Considerations
    - Early listing for transplant after infection related device complications to remove source of infection as long as patient is stable and effective antibiotics are available to treat the infection. Please consider that if there is a systemic infection, transplant and immunosuppression may pose more risk. Consider modification of induction therapy in a patient who is bacteremic.
    - Consult Transplant Infectious Diseases for guidance on timing for transplantation.
    - Active local infection is not an absolute contraindication to transplantation

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised 7/26/22)*

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APPENDIX

VAD Dressing Change Kits

Children's Hospital Colorado
We recently changed to the Medline EBSI Sensitive Skin VAD Kit with contents previously described. We have heard good feedback from families regarding ease of use and have had positive short-term experience with the Silverlon antimicrobial dressing.
https://www.medline.com/product/ERASE-BSI-Dressing-Change-Systems/Z05-PF153134
Medline, product number EBSI-1502

Morgan Stanley Children's Hospital of New York Presbyterian
For our driveline sites, we have kits that Centurion makes. Included is a sterile field, antiseptic applicator (Chloraprep), Silvercel dressing, 10-2x2 gauze, Hydrofilm dressing, face masks, clean and sterile gloves, and an anchor (we have 2 different kits--one with a smaller anchor and one with a larger anchor). Instructions regarding how to perform the dressing are also included. We do not have specific kits for our cannula dressings.

Texas Children's Hospital
We utilize Centurion Chronic driveline kit. You can customize.

Norton Children's Hospital
We use Wound Care Resources or Acelis. Our DLES kit has the silverlon disc, sterile gloves, mask, sterile water wipe, preventix stick, alcohol swab and clear dressing. We prefer to use the cath grip holder, not the Foley anchor and sometimes have to find other dressings, if the child is sensitive.

C.S. Mott Children's Hospital
We use centurion Kit. We have two one for daily dressing's and one for weekly dressings. Both include clean & sterile gloves, gown, mask's,hat and sterile field, 3-steril saline wipes, 2-chlorprep applicator's, 2-skin protectant (cavalon) sticks, Silverlon disk, sorbaview dressing and anchor. The weekly kits contains a sorbaview with clear window and 2 anchor's. The daily kit dressing sorbaview dressing does not have window, and has only 1 anchor. Both include step by step directions for dressing change.

Children's Healthcare of Atlanta
Right now, we gather the supplies individually and create our own on a sterile field, but I am working with a Medline rep to get a kit. They provide a standard kit for HM3 called EBSI sensitive skin VAD kit, which includes gloves, hand sanitizer, 2 hair bouffants, 2 masks, adhesive remover, sterile gloves, 4x4 split gauze, 1 chloraprep, 1 silverlon dressing, 1 saline wipe, sorbaview dressing, and anchor. They also offer custom kits, I am waiting on pricing. We are working on possibly creating a custom kit for the Berlin and PediMag, but Medline would want to be able to provide to other centers as well in order to make it cost-effective. I am happy to give you the contact info of the rep I have been working with if you reach out to me: margaret.ciarletta@choa.org.

Levine Children's Hospital
For our drivelines we have recently changed to using a custom kit from Centurion as well that the adult VAD team created. There are 4 different kits depending on patient needs or sensitivities. Two with chloraprep and two with Hibiclens. In the groups of two there are 1 with Silverlon dressing and one without for the patients that are further out postoperatively. Each kit has an anchor, 4x4 gauze, split 2x2 gauze, saline wipe(only in silverlon kits) Cavalon sticks, 4 pairs sterile gloves (2L and 2XL), 2 masks, sorbaview dressing, and tweezers (more for adult population if needed). The staff and patient families like the custom kits much better. For our cannula dressings we just gather all the supplies. Happy to give any information I can on the kit pricing and order numbers! Contact info: Stephanie.Rought@atriumhealth.org.

Children's Memorial Hermann Hospital
We use a custom kit through Medline for inpatient and also provided via DME for our outpatients. EBSI LVAD Multi- Day Mgmt Kit. Inside it has pockets for each step holding the supplies needed, and includes a picture and written step-by-step instructions. Outside of the kit contains gloves, masks x2 and freederm adhesive removal. Inside contains 2 chlorapreps, saline wipe and silverlon patch, Cavilon no-sting barrier, sorbaview, medium cathgrip anchor, and a sterile 2x2 gauze.

Children's Hospital of Pittsburgh

We also recently changed from a custom kit from Centurion to a new kit supplied by Medline which now includes the Silverlon dressing. This kit includes pictorial instructions, along with the following contents: gloves (2), hand sanitizer, mask (2), adhesive remover, 4x4 gauze sponge, saline wipes (2), Prevantics preps (2), Sureprep skin protectant, Silverlon dressing, foam dressing, SecureView dressing with closure piece, Cathgrip double anchor securement device, and drape. The weekly driveline tray kit code is EBI1526.

VAD Nutrition

Energy Intake, Fluids, and Micronutrients

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

For children with end-stage heart failure, VAD support aims to improve cardiac output, allowing for stabilization of end organ function and optimization of nutritional and functional status. Children with a VAD may experience early satiety, anorexia and nausea which potentially compromise their nutrition and recovery. Therefore, appropriate nutritional assessment and therapy may decrease risk for morbidity and mortality.

ACTION REVISED DATE: 05/29/24

OBJECTIVES

1. Establish a standardized nutritional approach to minimize nutritional deficits in patients with VAD.
2. Identify micronutrients requiring evaluation, supplementation, and management in patients with VAD.

PROTOCOL

I. Process:

a. New Implants
   i. Nutritional assessment as part of the inpatient or outpatient VAD evaluation in advance of surgery by RD
   ii. RD to reassess each VAD patient following VAD placement and during the remainder of hospital stay
   iii. RD may follow VAD patients after discharge on a consult basis and/or request from VAD team
   iv. If emergent implantation RD to conduct nutritional assessment post-operatively

b. VAD Readmissions
   i. Nutrition screening and care evaluation per each institution's nutrition policy
   ii. Assessment per institutional policy or at the request of the VAD team for patients determined to be at high nutrition risk, with reassessment and follow-up

II. Nutrition Assessment:

a. Growth history including current height and weight as well as nutrition-focused physical exam
b. Diet history including appetite, food habits, special diet adherence, food allergies, cultural, religious, and ethnic food preferences, intake history, eating problems, and social issues affecting food intake
c. Use of herbs and supplements, medication use, and identification of potential nutrient-drug interactions
d. Physical activity, physical limitations
e. Obtain baseline labs, if possible. NOTE: levels are impacted by critical illness
   i. Complete metabolic panel including serum albumin, magnesium, BUN and creatinine
   ii. Pre-albumin
   iii. Complete blood count with differential

iv. C-reactive protein
v. Reticulocyte count
vi. Zinc
vii. Vitamin A
viii. Vitamin C
ix. Vitamin D 25-OH, if levels very low consider checking parathyroid hormone
x. Selenium
xi. Iron studies (iron level, total iron binding capacity, ferritin, transferrin, transferrin saturation (if not included in other studies))
xii. Vitamin B levels if malnutrition is suspected and/or malabsorption under investigation

f. History of nutrition-related medical conditions (e.g., diabetes, hypertension, disorders of lipid metabolism)
g. Education needs for the acute care and outpatient (pre-admit and post-discharge) settings are identified. Educational needs address existing medical conditions, cultural and religious beliefs, physical and/or cognitive limitations, and barriers to communication.
h. Nutrition problems are identified (nutrition diagnoses) based on presenting signs and symptoms, according to the International Dietetics and Nutrition Terminology (IDNT) and causes or potential causes of these problems are determined.
i. The nutrition assessment is used to formulate a nutrition care plan, which is documented in the patient's medical record. The nutrition care plan includes:
    i. Prioritized short- and long-term goals
    ii. Nutrition prescription to include recommended diet order, enteral or parenteral nutrition order, and vitamin and mineral supplementation. It may be adjusted for concurrent medical issues. It will also include any needs for nutrition education or counseling, as well as incorporation of additional interdisciplinary team members such as OT, ST, and PT.
j. The RD contacts physicians and other healthcare team members to discuss the nutritional prescription. The RD attends rounds per institutional policy.

III. Nutritional reassessment

a. Indicators defined in the nutrition prescription to determine response to nutrition
    i. Intervention (i.e., weight gain, linear growth, etc.)
    ii. High risk inpatients are reassessed frequently at the discretion of the RD or RD or per the nutrition policy of each institution.
    iii. Reassessment includes:
        1. Updating of the subjective and objective data gathered during the prior nutrition assessment and identification of any changes
        2. Assessment of implemented interventions and recommendations
        3. Assessment of progress towards goals
        4. Revision of nutrition diagnoses, as needed
        5. Revision of goals and nutrition prescription as needed
        6. Timeframe for nutritional reassessment
b. The RD contacts physicians and other healthcare team members to discuss the nutritional prescription. The RD attends rounds per institutional policy.

IV. VAD Patient Population Nutrition Recommendations:

a. Protein
    i. Infants < 1 year old:
        1. Pre-term: 3.5-4 g/kg/day
        2. Term: 3 g/kg/day
    ii. Children ≥ 1 year old and Adolescents: 2 g/kg/day
    iii. Compromised renal function may affect protein prescription per RD
b. Energy
    i. Indirect calorimetry is the gold standard for determining energy requirements. It is a clinical tool that measures resting energy expenditure by analyzing the concentration of O2 and CO2 in respiratory gases. Resting energy expenditure can be used to determine total energy expenditure if physical activity levels are known. When this is unavailable or contraindicated, predictive equations can be used. If using predictive equations, note that VAD patients may have Total Energy Expenditure (TEE) that is 10-30% higher than healthy controls.
    ii. The RD should adjust nutrition prescription for individuals needs based on growth velocity and physical assessment throughout their entire VAD course.
    iii. In normal weight children and adolescents this is generally calculated via the patient's basal metabolic rate and multiplying this number by an activity and/or stress factor.
        1. In critically ill VAD patients, those in catabolic state, may need an activity or stress factor as high as 2.
        2. The clinical expertise of the RD can assist with determining individual energy requirements in pediatric patients.
    iv. If the patient is overweight or underweight, or malnutrition is suspected an alternative predictive equation may be used.
        1. The Pediatric Nutrition Care Manual provides calculators for appropriate equations, including the WHO Equations for REE's
    v. Early nutrition intervention is critical to support a positive nitrogen balance. Measuring Nitrogen balance while possible is labor intensive requiring 24-hour urine urea nitrogen (UUN) collection and not possible at times.
        1. Protein intake/6.25 - (UUN + 4*) = Nitrogen balance
        *To account for average loss via sweat and feces.
    vi. All goals may of course be impacted by patient status, infection, intubation, etc.

c. Fluid
    i. Fluid Intake: Patient specific fluid requirements determined upon review of serum sodium levels, underlying medical condition (i.e., heart failure, obesity) and a physical examination of fluid status by the provider
        1. In some cases, fluid restriction is needed, close collaboration with RD is recommended in these cases to ensure both nutrition and hydration needs are met.
    ii. Body weight < 10 kg: 100 ml/kg/day for maintenance
        1. Infants will often receive 140-150 ml/kg/day to support sufficient calories.
    iii. Body weight 11-20 kg: 1000 mL + 50 mL/kg >10 kg
    iv. Body weight >20 kg: 1500 mL + 20 mL/kg >20 kg
d. Enteral Nutrition (EN)
    i. Early EN delivery is recommended if oral diet cannot be initiated within 24-48 hours of admission to the ICU in the critically ill pre-or

post-operative VAD patient.

ii. Current intake is compared to calculated requirements and limits. Nutrition-related deficits and excesses (protein, calories/energy, vitamins, minerals, fluid, etc.) are identified.

1. For patients who are attempting to consume all their calories orally, a 3-day calorie count should be initiated with input from RD regarding best strategy to meet daily intake goals (can include oral supplements if needed).

V. Micronutrient Requirements:

a. Micronutrients such as trace elements, vitamins, and electrolytes are essential, and deficiencies may result in poor wound healing and/or clinical deterioration.

b. All VAD patients would benefit from baseline levels as defined in Section II.

c. See table below for goal levels, dosing recommendations and laboratory evaluation follow-up for patients receiving supplementation or replacement.

i. For patients in the lower end of the reference range consideration should be given to empiric supplementation at ½ the deficiency dose if enteral nutrition will be delayed and parental nutrition is not undertaken in the interim. The ½ deficiency dose is a strategy utilized at some institutions and reflected the table below to ensure adequate micronutrients for wound healing.

d. VAD patients without any micronutrient deficiencies should receive the following:

i. Daily multivitamin with iron.

1. Small, young and pre-term infants may need adjustments in consultation with RD and pharmacy based on their ability to metabolize specific nutrients.

2. Fish oil (omega-3 fatty acid) supplementation to reduce inflammatory response and platelet aggregation. Suggested dosing is to meet adequate intake (AI) for age. Dosing beyond this amount should be managed with physician guidance.

a. Allergy to fish is an absolute contraindication.

Nutrition Management of VAD Patients

RD to Complete Nutrition Assessment*

Nutrition Status
- Estimate nutritional needs
- Assess growth history and presence of malnutrition
- Determine nutrition diagnosis and set nutrition goals

Physical
- Obtain nutrition focused physical exam
- Obtain description of wound type, size and location (if applicable)

Diet History
- Assess adequacy of intake
- Assess best method of obtaining nutrition (PO, EN, TPN)
- Assess for GI symptoms

**Refer to Nutrition Care Guidelines for Pediatric VAD patients for additional information*

↓

Ensure Adequate Intake of Nutrients

Obtain Lab Values and Provide Supplementation
- Draw Vitamins A, C and D (25 OH Total), Zinc, Selenium and iron studies (iron level, TIBC, ferritin, transferrin).
- If concern for wound healing, start Vitamin C and Zinc empirically while awaiting labs, continue if a deficiency is confirmed.
- Check levels monthly.
- Check B Vitamins only if concern for deficiency / malnutrition (per RD recommendations).

Maximize Nutrition
- Oral nutrition supplements for those taking PO
- Work with RD/DTR to determine & obtain nutrient dense food & beverage items that patient will tolerate.
- Start MVI if not on PN/EN (<1 year: 1 ml Poly-vi-sol; >1year: 1 Children's Chewable Vitamin daily)
- If unable to take or meet estimated needs with PO, provide EN/PN. If taking partial PO, typically provide EN as overnight continuous feeds to promote daytime oral intake.

↓

Ongoing Assessment of Nutrient Intake Adequacy
- Growth velocity and growth chart z-scores
- PN/EN Nutrient Intake Analysis
- Complete intake/output and/or calorie counts
- Monitor adequacy and tolerance of protein per BUN, creatinine levels/ratio, and length growth (in infants)
- Check nutrition labs monthly
- Wound healing and physical assessment

Nutrient	Recommendation	Notes
Energy	Increased, based on RD's assessed needs	Adjust, based on growth velocity
Protein	1.5-2x RDA/age initially or per disease specific condition; if wound not healing, may increase 20-25% above current dose	Monitor renal labs; Do not increase if dose is maximized
Vitamin C†¥	Deficiency/empiric dose while awaiting lab: 5x RDA for age	Do not exceed upper limit for age. Renal dysfunction: no more than 2x RDA
Zinc†¥	Deficiency/empiric dose while awaiting lab: 2x RDA for age divided in 2 equal doses Parenteral <5 years: 100mcg/kg/d (max 5 mg/day) Parenteral >5 years: 2.5-5 mg/d	Do not exceed UL for age, as toxicity could cause copper deficiency and potentially impair wound healing; consider disease specific recommendations
Vitamin A†¥	Deficiency dose: 2x RDA for age	Do not exceed upper limit for age. Corticosteroids may increase need for Vit A.
Vitamin D†¥	If patient is receiving EBM, start 400 IU cholecalciferol If patient is on corticosteroids, start 400 IU cholecalciferol Deficiency dose (<30): 2000 IU cholecalciferol	Continue maintenance dosing after repletion. 0-12months: 400 IU/d >12 months: 600-1000 IU/d
Iron	Deficiency dose and/or with active VAD: 3-6 mg/kg/d	Provide IV iron if needed.
Selenium†	Deficiency dose: 2-5x RDA	Do not exceed UL for age.
B Vitamins†	Deficiency dose: 2-5x RDA (check only if concerned for deficiency)	Do not exceed UL for age.
Omega-3 FA	To reduce the risk of thrombosis, fish oil supplementation is initiated on all children with a VAD at ~1000mg/day.	Do not provide if fish oil is contraindicated.

†If lab value is in lower 20% of normal range, provide 1/2 deficiency dose

¥ Adapted from: *Nutrition Interventions to Optimize Pediatric Wound Healing: An Evidence-Based Clinical Pathway. Nutrition in Clinical Practice. August 2014; 29 (4): 473-482.*

Dietary Reference Intakes (DRIs): Recommended Dietary Allowances (RDA), Adequate Intakes (AI) and Tolerable Upper Intake Levels (UL) of Vitamins and Minerals

Age	Vitamin A (µg/d)	Vitamin C (mg/d)	Vitamin D (IU/d)	Zinc (mg/d)	Iron (mg/d)	Thiamin (B1) (mg/d)	Pyridoxine (B6) (mg/d)	Folate (B9) (µg/d)	Cobalamin (B12) (µg/d)	Selenium (µg/d)
Infants										
0-6 months	400*	40*	400*	2*	0.27*	0.2*	0.1*	65*	0.4*	15*
	600	ND	1000^	4	40	ND	ND	ND	ND	45
7-12 months	500*	50*	400*	**3**	**11**	0.3*	0.3*	80*	0.5*	20*
	600	ND	1500^	**5**	40	ND	ND	ND	ND	60
Children										
1-3 years	**300**	**15**	600*	**3**	**7**	**0.5**	**0.5**	**150**	**0.9**	20
	600	400	2500	7	40	ND	30	300	ND	90
4-8 years	**400**	**25**	600*	**5**	**10**	**0.6**	**0.6**	**200**	**1.2**	30
	900	650	3000	12	40	ND	40	400	ND	150
9-13 years	**600**	**45**	600*	**8**	**8**	**0.9**	**1**	**300**	**1.8**	40
	1700	1200	4000	23	40	ND	60	600	ND	280
Adolescent and Young Adult Males										
14-18 years	**900**	**75**	600*	**11**	**11**	**1.2**	**1.3**	**400**	**2.4**	55
	2800	1800	4000	34	45	ND	80	800	ND	400
19-30 years	**900**	**90**	600*	**11**	**8**	**1.2**	**1.3**	**400**	**2.4**	55
	3000	2000	4000	40	45	ND	100	1000	ND	400
Adolescent and Young Adult Females										
14-18 years	**700**	**65**	600*	**9**	**15**	**1**	**1.2**	**400**	**2.4**	55
	1800	1800	4000	34	45	ND	80	800	ND	400
19-30 years	**700**	**75**	600*	**8**	**18**	**1.1**	**1.3**	**400**	**2.4**	55
	3000	2000	4000	40	45	ND	100	1000	ND	400

This table (taken from the DRI reports, see www.nap.edu) presents Recommended Dietary Allowances (RDA) in **bold type** or Adequate Intakes (AI) in ordinary type followed by an asterisk (*). The numbers in red are tolerable upper intake limits (UL).

An RDA is the average daily dietary intake level sufficient to meet the nutrient requirements of nearly all (97–98 percent) healthy individuals in a group. It is calculated from an Estimated Average Requirement (EAR). If scientific evidence is insufficient to establish an EAR, and thus calculate an RDA, an AI is usually developed. For healthy breastfed infants, an AI is the mean intake. The AI for other life-stage and gender groups is believed to cover the needs of all healthy individuals in the groups, but lack of data or uncertainty in the data prevent being able to specify with confidence the percentage of individuals covered by this intake. The upper limit is derived from ***.

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Pediatric VAD Patient and Device Selection

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

There are limited data available to guide decision making related to pediatric VAD patient and device selection, and significant variation between centers related to timing of VAD placement for specific patient populations. This document is intended as a tool to assist in the creation of center-specific processes to promote consistent decision making regarding timing of VAD implantation and device selection.

ACTION REVISED DATE: 06/24/2024

OBJECTIVES

To provide a standardized approach to patient and device selection in a pediatric VAD program. While multiple factors may contribute to differences in medical decision making between pediatric VAD centers, this document aims to 1) promote a consistent and well-established decision making process within each center related to timing of VAD implantation and device selection 2) summarize available data regarding patient risk stratification, 3) and provide some insight into themes in medical decision making related to patient and device selection among Action member sites.

PROTOCOL

1. Patient and Device Selection – Decision making process
    a. The right time to implant a VAD in a pediatric patient is when the potential benefits of VAD support outweigh the potential risks. This seemingly simple rule is complicated in practice, with the risks associated with VAD placement influenced by both patient specific factors (age, size, anatomy, level of illness, etc), device specific factors, and center specific factors (center experience with a particular device, anticoagulation protocol, surgical technique, etc.). The “right time” for implantation will differ between patients and, even for the same theoretical patient, may differ between centers.
    b. The complexity described above and the lack of robust data related to optimal timing of VAD implantation for specific pediatric patient populations precludes the creation of set implantation criteria in pediatric patients [1].
    c. In the absence of universal criteria, the potential for inconsistent medical decision-making related to pediatric patient or device selection presents challenges both regarding optimizing patient outcomes and providing equitable care to all patients
    d. The development of center-specific standardized approaches to patient and device selection will allow pediatric VAD centers to provide more consistent care to pediatric patients with advanced heart failure. Recommended elements of a decision making process include:
        i. A consistent team tasked with decision making related to VAD patient and device selection. This team would likely include heart failure/VAD cardiologist, CT surgeon, intensivist, and VAD coordinator.
        ii. An established trigger to formulate a VAD plan (i.e. determine the threshold for VAD placement and the preferred device and

cannulation strategy) for a specific patient. Potential triggers could be referral for heart transplant evaluation, admission to CICU with advanced heart failure, etc.

iii. A mechanism to effectively disseminate a patient's VAD plan to the wider care team

2. Patient risk stratification:
    a. Any effort to identify risk factors for mortality in pediatric VAD patients is complicated by small patient numbers and the collinearity between multiple variables. VAD outcomes for infants < 5 kg have generally been inferior to larger patients, for instance[2]. Small infants are generally sicker at implant, more likely to have congenital heart disease, and more likely to be supported with paracorporeal devices than older children, however. Separating the relative risks imparted by the patients' age, size, level of illness, anatomy, and device type is not possible based upon the currently available data. Table 1 presents data from survival analyses that have attempted to identify independent risk factors for mortality in pediatric VAD patients, acknowledging that the interdependence of age, device type, and illness severity in the available data precludes truly understanding the contribution that these various factors make to overall risk.

Table 1. Factors Independently Associated with Mortality during VAD support

Risk Factors for General Pediatric VAD Population	
Risk Factor	**Hazard/Odds Ratio**
Percutaneous Device	HR 13.5 early hazard[3], HR 2.7 mortality[4]
Mechanical Ventilation at Implant	HR 4.3 constant hazard [3], HR 1.96 early hazard [5]
Paracorporeal Continuous Flow	HR 4.1 early hazard[3]
Paracorporeal Continuous vs PP	HR 1.86 early hazard [5]
BiVAD	HR 3.6 early hazard [3], HR 6.2 constant hazard [5]
Low Volume Center (<15)	HR 3.3 early hazard [3]
Pedimacs Profile 1	HR 2.6 early hazard [3], HR 1.6 mortality [4]
Elevated Bilirubin	HR 1.1 constant mortality hazard [3]
BUN (mg/dL, 10-unit increase)	HR 1.1 early hazard [5]
Ascites	HR 3.2 constant hazard [5]
Meld-XI score	HR 1.1 per unit rise [4]
Congenital heart disease	HR 2.9 mortality [6], HR 2.3 mortality [4], HR 3.1 early hazard [5]
ECMO during hospitalization	HR 2.3 constant hazard [5]
eGFR	HR 0.9 mortality[6]
Risk Factors for Patients Supported with Paracorporeal Pulsatile Devices	
Younger Age (natural log of age)	HR 0.7 early hazard [3], HR 0.59 mortality[7]
Dialysis	HR 23.2 early hazard [3], HR 2.6 early hazard [5]
Low Volume Center (<15)	HR 4.4 early hazard [3]
Weight < 10 kg + CHD	OR 4.8 mortality[8]
Weight < 10 kg + Bilirubin > 1.2	OR 5.3 mortality[8]
BiVAD	HR 4.6 mortality [7], HR 2.1 early hazard [5]
Congenital heart disease	HR 2.4 early hazard [5]
Risk Factors for Patients Supported with Paracorporeal Continuous Flow Devices	
Blood Type O	HR 4.0 early hazard [3]
Prior Valve Operation	HR 8.5 early hazard [3]
Severe RV dysfunction	HR 2.8 early hazard [3]
BiVAD	HR 2.0 early hazard [5]
Congenital heart disease	HR 2.7 early hazard [5]
BUN (mg/dL, 10-unit increase)	HR 1.2 early hazard [5]
Risk Factors for Patients Supported with Intracorporeal Continuous Flow Devices	

ECMO at Implant	HR 5.3 constant hazard [3]
ECMO during hospitalization	HR 3.9 constant hazard [5]
BiVAD	HR 5.7 constant hazard [5]

b. In order to help with risk assessment, ACTION has worked to develop prognostic tools to predict risk of mortality for pediatric VAD patients
   i. One tool available on the ACTION website - https://www.actionlearningnetwork.org/calculator/ - utilizes 11 variables (diagnosis, height, weight, device strategy, device type, dialysis, creatinine, ECMO, need for TPN, need for mechanical ventilation, need for chemical paralysis) to estimate a patient's risk of mortality with VAD support, with an AUC of 95.4% based upon data from 1314 patients in the ACTION registry [9]
   ii. A second simpler tool designed for bedside use utilizes 5 variables (diagnosis, weight, ECMO, mechanical ventilation, and VAD type) and showed modest ability to predict VAD mortality risk when validated in an external cohort of patients from the Pedimacs registry, with better predictive ability than Intermacs profile (ROC 0.78 vs ROC 0.42). (Reaney M, Boucek K, Lorts A et al., External validation of a risk score assessment for pediatric ventricular assist device mortality - Abstract presented at ISHLT meeting, Prague, 2024)

c. Given the limitations and complexity in the data presented above, it has not been possible to develop evidence based guidelines regarding optimal timing of VAD implant for specific pediatric patients. In such an environment, "consensus practice" can also be informative. Compiled results of 2 surveys of pediatric VAD providers regarding the impact various risk factors would have on clinical decision making at their center are presented in Table 2. Decision making among ACTION centers regarding illness threshold for VAD implant and device selection for specific patient populations is presented in Table 3.

Table 2.

Would Make Much More Reluctant to Implant a VAD	Would Make Slightly More Reluctant to Implant a VAD	Would Not Influence Timing of VAD Implantation
Weight < 5 kg (63%)*	Weight 5-15 kg (55%)*	Mild developmental delays/behavioral concerns (100%)**
Active malignancy/chemo (77%)* Active malignancy/uncertain prognosis (64% unlikely to implant)[2] Active malignancy/poor prognosis (89% unlikely to implant)**	Single Ventricle Heart Disease – Stage II Palliation (68%)*	Systemic RV physiology (59%)*
Blood stream infxn/abx (95%)*	Fontan with severe ventricular dysfnxn, low TPG, no PLE (50%)*	Pt/Family illiteracy (55%)*
Hemorrhagic stroke <1 mo (55%)*	Multiple prior thrombi, no documented hypercoagulable state (50%)*	Ischemic stroke >1 mo (54%)*
Single Ventricle Heart Disease – Stage I Palliation (50%)*	Hypercoagulable state (59%)*	>1 year post chemo/low recurrence (41%)* *Wide variation: 27% more reluctant; 32% more likely* Hx of cancer in remission 2-3 yrs (100% likely to implant)**
Ischemic stroke <1 mo (50%)*	History of poor compliance (57%)*	
Fontan with high TPG, PLE (41%)*	Dev delay with behavioral problems (77%)*/mod-severe behavioral concerns (54% unlikely to implant)**	

	Viral resp infxn (76%)*	Hx of cancer in remission <1 year (71% likely to implant)**
	Fever/Inflam markers (45%)*	BMI <15 (70% likely to implant)**
	Duchenne MD (45%)*	BMI >35 (74% likely to implant)**
	Non-Duchenne MD (55%)*	
	Hemorrhagic stroke >1 mo (41%)*	

*A plurality of respondents in survey of ACTION centers (n=22, % of respondents indicated in parentheses) indicated that this risk factor would make their center much less likely to implant a VAD (red column), slightly less likely to implant a VAD (yellow column), or have no impact on their decision to implant a VAD (green column) in a patient. In the surveys, the alternative to proceeding with VAD implant was continuing to attempt to optimize medical management.
**Joong et al. (2020), multi-center survey of VAD team members (n=65 respondents).

Table 3: Percentage of respondents likely to recommend VAD implant and type of device preferred for each scenario (ACTION Center Survey, n=22) [11]

3.5 kg Infant	**DCM**	**Device Selection**	**Single Ventricle, Stage I**	**Device Selection**
Milrinone, HFNC, GFR>90	5%	50% PC; 50% PP	5%	100% PC
Milrinone, HFNC, GFR 35	25%	43% PC; 57% PP	5%	100% PC
Milrinone, vent, GFR>90	68%	47% PC; 53% PP	23%	75% PC; 25% PP
Milrinone, vent, GFR 35	68%	44% PC; 56% PP	36%	73% PC; 27% PP
8 kg Toddler	**DCM**	**Device Selection**	**Single Ventricle, Stage II**	**Device**
Milrinone, HFNC, GFR>90	18%	83%PP; 17% PC	9%	67% PC; 33% PP
Milrinone, HFNC GFR 35	59%	86% PP; 14% PC	18%	38% PC; 62% PP
Milrinone, vent, GFR>90	86%	79% PP; 21% PC	36%	50% PC; 50% PP
Milrinone, vent, GFR 35	95%	76% PP; 23% PC	59%	64% PC; 36% PP
45 kg Teenager	**DCM**	**Device Selection**	**Single Ventricle, Stage III**	**Device**
Milrinone, HFNC, GFR>90	41%	100% IC	23%	100% IC
Milrinone, HFNC GFR 40	100%	100% IC	59%	100% IC
Milrinone, vent, GFR>90	100%	100% IC	90%	100% IC
Milrinone, vent, GFR 40	100%	100% IC	77%	100% IC

DCM= Dilated Cardiomyopathy, HFNC= High flow nasal cannula, GFR= estimated glomerular filtration rate, PP= Paracorporeal Pulsatile Flow; PC= Paracorporeal Continuous Flow; IC= Intracorporeal Continuous Flow

3. **Device selection:**
    a. Four broad classes of ventricular assist devices are available for pediatric patients: intracorporeal continuous flow (IC), paracorporeal continuous flow (PC), paracorporeal pulsatile flow (PP), and percutaneous devices). In general, the device selected for each patient will depend on their underlying diagnosis, anticipated duration of support and size. Below is an overview of potential devices that may be considered for the pediatric population, with special consideration given to patients in cardiogenic shock (Intermacs 1), and single ventricle patients.

i. It is important to note that device selection even amongst the same patient diagnosis and patient size will also vary depending on center specific practices (ie surgical preference, center expertise, etc).

b. **Acutely decompensating patients** (Intermacs 1)
   i. Multiple registry analyses have demonstrated that pediatric patients in cardiogenic shock (Intermacs Profile 1) prior to VAD implant have inferior survival outcomes [3, 12-14] . In contrast to adult data demonstrating that Intermacs Profile 2 patients also have decreased survival compared to less ill patients, the pediatric data have suggested that Profile 1 patients comprise a uniquely high-risk group.
      a. In light of these data, efforts to proceed with VAD implanation before a patient has deteriorated to Intermacs 1 status will likely improve outcomes.
      b. There are adult data suggesting that utilizing a "bridge to a bridge" approach, i.e. using short term support including VA-ECMO, intra-aortic balloon pump (IABP), or percutaneous VADs such as Impella to stabilize a patient in cardiogenic shock and improve end-organ function prior to proceeding to durable VAD may be associated with improved LVAD outcomes in Intermacs 1 patients [15, 16]. Whether this approach could improve outcomes for pediatric patients in cardiogenic shock is unclear.

c. **Long term support in patient with two ventricle physiology**
   i. Intracorporeal devices can only be implanted in children with sufficient space within the thorax to accommodate the device and thus are typically implanted in children with a BSA ^{3} 0.8 m^2.
   ii. IC devices have been associated with higher survival to transplant and lower morbidity than paracorporeal devices [3]. Contemporary pediatric outcomes with IC support are excellent [17, 18], and an IC device is generally the preferred option for long term support for children of adequate size.
   iii. Smaller children typically receive paracorporeal (continuous or pulsatile flow) devices. Paracorporeal continuous flow devices have been associated with higher risk of mortality compared to paracorporeal pulsatile flow devices [5], though as discussed above, this must be interpreted in the context of multiple interdependent risk factors.
   iv. Biventricular Support
      a. Depending on the patient's size, biventricular support can be accomplished with implantation of both right and left ventricular support. This is most commonly done with bilateral PC or PP devices in smaller children, or an IC LVAD and PC RVAD in larger patients, though numerous strategies, including the use of percutaneous devices, are possible. Biventricular support has been associated with inferior survival in children [5], but there is some evidence that this increased mortality risk may be attributable to the higher level of illness in patients receiving BiVAD support [19]. There remains significant practice variation among centers in identifying which LVAD patients will require RVAD support [20].
      b. The Syncardia TAH may be considered as a means of biventricular support in patients with a T10 to sternum measurement > 10 cm or in those whom accommodate the device as determined by an advanced imaging fit study

c. Potential clinical scenarios for which a TAH may be considered: biventricular failure, LV thrombus, aortic valve insufficiency, or graft rejection.

Table 4: Commonly used VADs in Children

Device	Device Type	Flow (lpm)	BSA limit (m^2)	Notes
Short-Term				
Rotaflow	PC	0-10	NA	
Pedimag	PC	0-1.5	NA	
Centrimag	PC	0-10	NA	
Impella	Perc	2.5-5.5	³0.9[21]	Available devices include CP, 5.5, RP Device fit determined by ventricular and peripheral vessel dimensions
Durable				
Berlin EXCOR	PP	Variable	³0.2	Mutiple pump sizes available
Pedimag	PC	0-1.5	NA	
Centrimag	PC	0-10	NA	
HeartMate 3	IC	Up to 10	³ 0.8[17]	
Syncardia TAH	IP	Up to 10	³ 1.2[23]	50 cc and 70 cc available T10 to sternum and/or fit study used to determine candidacy

PC= paracorporeal continuous; PP= paracorporeal pulsatile; IC= Intracorporeal continuous; Perc= Percutaneous

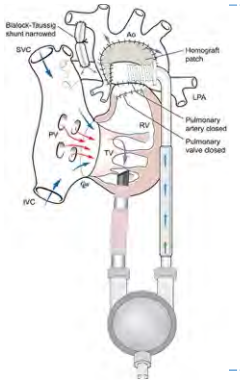
d. VAD support in patients with single ventricle physiology

i. While VAD implantation in single ventricle patients is increasing, experience is still limited and mortality is high particularly among stage 1 [24] and stage 2 (Rabinowitz EJ et al., *JHLT Open*, 2024) SV VAD recipients. There is no uniform accepted approach to this complex patient population and device strategy should be tailored to the patient's anatomy and physiology, and center-specific practices

ii. Type of SV failure is important to delineate, as patients with end-stage systolic failure with an elevated EDP can potentially benefit from SV VAD support. Evidence for benefit from SV VAD support is lacking for patients with plastic bronchitis, protein-losing enteropathy, or preserved ventricular function with isolated "right-sided" failure (e.g. elevated Glenn/Fontan pressures with normal EDP)

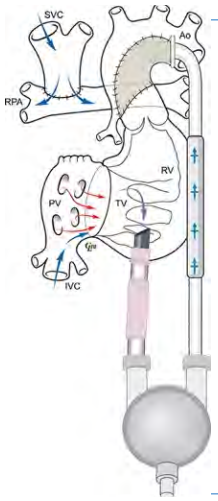
iii. The following are general approaches to VAD selection in SV patients based on experience in ACTION centers and reported literature (Figure 1)

Figure 1: Device Selection: Single Ventricle with Systolic Failure



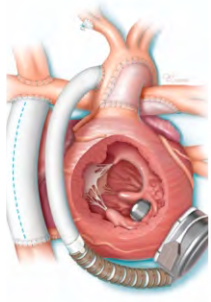
Stage 1

- Common approaches: PediMag/CentriMag or Rotaflow with Berlin cannulas, Berlin EXCOR (some start with continuous-flow first then convert to Berlin)
- Less common configurations: TAH configuration
- Clinical pearls/considerations:
  - Source of pulmonary blood flow? (e.g. Sano takedown and aortopulmonary shunt placement, PGE infusion, PDA stent)
  - Ventricular vs atrial cannulation
  - Aortic cannulation considerations: chimney graft vs neo-aorta/pulmonary artery cannulation
  - High CI typically required (~4-6 l/min/m2)



Stage 2

- BSA <0.8-1
  - PediMag/CentriMag or Rotaflow with Berlin cannulas, Berlin EXCOR (some start with continuous-flow first then convert to Berlin)
- BSA >0.8-1
  - HM3 or devices above
- Clinical pearls/considerations:
  - Dichotomous venous return - only IVC venous return is decompressed from VAD, pressure differential between SVC and IVC, potential for significant cyanosis and increased venovenous (VV) collateral development over time
  - Consider VV collateral coiling (OR vs Cath lab depending on location)
  - Take down to Stage 1/BTS? Keep as BDG? Fontan completion?
  - Ventricular vs atrial cannulation
  - High CI typically required (~4-6 l/min/m2)



Stage 3

- BSA <0.8-1
  - PediMag/CentriMag, Rotaflow, Berlin EXCOR
- BSA >0.8-1
  - HM3, or devices above
  - SynCardia (particularly if preserved systolic function)
- Clinical pearls/considerations:
  - Fenestration creation vs fenestration closure (some centers create fenestration to allow for greater unloading of systemic venous system, balance with potential increased cyanosis and theoretical risk of thromboembolism)
  - Consider coiling AP collaterals
  - Ventricular vs atrial cannulation
  - High CI typically required (~4-6 l/min/m2)

[6] [25-31]

*stage 1 image and stage 2 image Griselli et al; stage 3 image Adachi, Burki, Fraser

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 12/18/2020)*

PRE-IMPLANT Protocol for Pediatric Patients Evaluated for VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

VAD candidacy should be determined through a multi-disciplinary assessment of the patient's cardiovascular status, medical comorbidities, and psychosocial risk factors.

ACTION REVISED DATE: 03/20/2024

OBJECTIVES

To provide a standardized, thorough approach to pre-VAD implantation work-up and patient selection that also takes into account the need for center specific variables and preferences.

PROTOCOL

The decision to place a VAD in a pediatric patient is generally made by a multi-disciplinary team including CT Surgery, Cardiology (HF/VAD specialist), Cardiac Intensive Care (physician and nursing input), & VAD coordinator.

Consults to consider (all patients): Palliative Care, Nutrition, OT/PT, Social Work/Psychology.

Consults to consider (based upon clinical indication): Hematology, Infectious Disease, Pulmonology, Nephrology, GI, and Neurology.

Financial clearance/insurance authorization should be obtained prior to VAD placement.

Chemistry and Microbiology				
	☐	Comprehensive Metabolic Panel	☐	Brain Natriuretic Peptide or NT pro-BNP
	☐	Cystatin C	☐	MRSA screen
	• Screen for infection if clinically indicated (procalcitonin, CRP, ESR, cultures) • Additional testing as needed for patient specific concerns			
Hematology				
	☐	Type and Screen	☐	Fibrinogen
	☐	CBC w/ Differential	☐	Anti-Xa if on heparin
	☐	PT/INR, PTT	☐	
	• Consider additional thrombophilia or bleeding work up if concerning family history or clinical course: antiphospholipid antibodies, protein C and S, Factor V Leiden, prothrombin 20210, activated protein C resistance, cardiolipin IgG/IgM, warfarin pharmacogenomics, lupus anticoagulant if > 6 mo, MTHFR mutation, plasma homocysteine, TEG, von Willebrand panel, HIT assay (Anti-heparin PF4 Ab), Serotonin release assay if HIT+			
Ancillary Studies				
	☐	EKG	☐	Echocardiogram
	☐	Chest X-Ray	☐	
	• Consider Head CT if patient at high risk (i.e. ECMO) or unable to get reliable neurologic exam • Chest CT if needed for fit assessment • If needed/optional: 6 min walk test, cardiac catheterization, PFTs, EEG, abdominal US, vessel map, video swallow study, dental clearance, PEDSQOL/VADQOL			

Durable VAD Indications
Inability to separate from temporary MCS/ECMO
Symptomatic heart failure with intolerance of inotropes
Development of end organ compromise despite inotropic support. Examples of end organ compromise might include: a. Need for invasive or non-invasive positive pressure ventilation b. Renal dysfunction c. Feeding intolerance d. Hepatic dysfunction e. Mental status changes or need for sedation to prevent destabilization f. Inability to ambulate or participate in physical therapy

Potential Durable VAD Contraindications
Irreversible intrinsic lung, liver, or kidney disease. Relevant subspecialty service should be consulted for guidance on potential for end-organ recovery with improved cardiac output.
Risk for intracranial bleed and/or neurologic compromise due to acute stroke, congenital AVM, or Moya-Moya. Neurology and/or neurosurgery should be consulted.
Clotting disorders, such as underlying coagulopathy (factor VIII deficiency, DIC) or thrombotic disorders (Factor V Leiden). Hematology service should be consulted to aid with risk assessment.
Active systemic infection. Infectious disease service should be consulted.
Active malignancy or recent malignancy with high risk of recurrence. Oncology service should be consulted.
Anatomic variant or severe valvar disease incompatible with VAD implantation/support.
Pregnancy.
Social factors limiting ability to care for VAD or ongoing non-adherence.
While not a contraindication to MCS, severe obesity (BMI > 35 kg/m^2) is associated with increased morbidity in LVAD patients and should be considered in comprehensive risk assessment.

Temporary VAD should be considered as a bridge to candidacy or to durable VAD support if:

1. Anticipated duration of support < 2 weeks
2. Patient is InterMACS profile 1 with evidence of end organ dysfunction

AUTHORS

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RIGHT HEART FAILURE
Management for Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND We do not have a great solution for long term RV MCS in biventricular circulation. Progressive RV dysfunction causes end-organ damage; often jeopardizing LVAD and transplant candidacy. RV failure in LVAD pediatric patients has an incidence of up to 50% and is associated with increased mortality on device. Prevention and/ or early identification of RV failure is of utmost importance.

ACTION REVISED DATE: 01/28/2025

OBJECTIVES

1. To define RV failure
2. To identify and understand risk factors and predictors of RV failure
3. Guidelines for monitoring and evaluation of RV failure
4. Medical and surgical management options and algorithms for treatment of RV failure when it develops

PROTOCOL

1. *Definition and grading of right heart failure after LVAD (From ACTION-ARC Adverse Event Definitions)*[1]

Right heart failure/dysfunction is defined as one finding from both the hemodynamics and imaging categories as follows, greater than 10 days after the index operation, without the presence of device malfunction or thrombus.

1.) Hemodynamics: right sided or systemic venous filling pressure elevated above 14 mm Hg for greater than 24 hours OR clinical evidence of high central venous pressure (eg, effusions, ascites, hepatomegaly) in the setting of inadequate delivery of preload
to the LVAD (calculated CO that is less than 50% expected, not responsive to pump parameter changes).

2.) Imaging: greater than moderate/severe tricuspid regurgitation, or greater than moderately/severely reduced right ventricular systolic function, documented in medical record.

Alternatively, criteria can be met by one of the following events at any time after the index procedure, in the absence of device malfunction or pump thrombus: transition to ECMO (for right-sided dysfunction) or implantation of an RVAD. These criteria are met any time after the index procedure, if RVAD or ECMO is needed. If only medical management is required, criteria can be met any time greater than 10 days after completing the index procedure. Each event will have an associated grade.

Grade 1-2: mild-moderate.

Grade 3: severe – defined as use of vasoactive infusions or need for new invasive management of effusions/ascites or unable to remove surgical drains due to the need to treat the manifestations of right heart dysfunction after 10 days from index procedure, determined by treating provider to be secondary to right heart dysfunction.

Grade 4: Life-threatening – defined as use of ECMO for right heart dysfunction or implantation of RVAD as separate procedure.

Grade 5: Fatal – defined as death resulting directly or primarily from right heart dysfunction.

2. *Predictors of right heart failure*

Patient selection and timing of implant appear to be key components to avoiding/preparing for RHF. However, no variables exist that can reliably predict right heart failure independently.

Data are limited in pediatrics. The largest, a Pedimacs analysis, identified the following factors associated with RHF: [14]

female gender
Intermacs profile 1
younger age
smaller BSA
chemical paralysis during first week post-LVAD
pulsatile flow devices.

The following associations are from adult RHF risk models that perform only modestly when applied to different adult cohorts and may not be directly applicable to the pediatric population.

- **Demographic/ clinical[10]**
  - Female gender
  - Prior cardiac surgery
  - Inotrope dependency or vasopressor use
  - Need for mechanical ventilation
  - Extremes of age, lower BSA
  - Pre-operative circulatory support
  - Advanced InterMACS profile

- **Biochemical (markers of end organ damage)**
  - Elevated serum creatinine (> 2 in adults) or elevated for age
  - Elevated BUN (> 39 in adults) or elevated for age
  - Elevated AST, INR and total bilirubin (>2.0)
  - Persistently elevated pro BNP post-implant

- **Echocardiographic[2, 3, 4, 5,6]**
  - Severe systolic RV dysfunction
  - Severe TR
  - RV fractional area change (RVFAC) measured in apical 4 chamber view using the formula RV end-diastolic area – RV end-systolic area)/ RV end-diastolic area. Impairment in RV function <30%.
  - RVS – peak longitudinal strain, speckle tracking measures RV contractile function. A peak strain cut off of -9.6% in adults predicts post LVAD RV failure with a specificity of 76% and a sensitivity of 68%. Age based norms exist in Pediatrics.
  - Tricuspid annular plane systolic excursion (TAPSE). Independent of ventricular geometry. Tricuspid valve annular motion < 7.5 mm in adults, or lower than normal age-related reference values.
  - Increased RV to LV end-diastolic diameter ratio- poor reproducibility

- **Hemodynamic[6,7]**
  - Elevated CVP/ RAP or CVP/ pulmonary capillary wedge pressure > 0.63
  - Low cardiac index
  - Lower mean PAP
  - Elevated PVR

  In adult sized patients can consider
  - Low RV stroke work index: (Mean PAP – mean RAP)/ stroke volume. < 300 mm/mL/m2. Preload dependent
  - Lower Pulmonary artery Pulsatility Index (PAPi) : systolic PAP – diastolic PAP)/ CVP in CF-VADs predicts need for RVAD[8]

- **Intra-operative events**
  - Ischemia from prolonged bypass, blood transfusions, bleeding and shock

- Disruption of bypass grafts or coronaries supplying RV
- Air embolism
- Sub-optimal ventilation, alveolar hypoxia, hyperinflation or atelectasis that increases PVR
- Acidosis causing ischemic injury

3. Evaluation for right heart failure

To make the diagnosis of right heart failure, the following patient domains must be carefully and frequently monitored and assessed.

Symptoms – GI complaints, poor feeding, exercise intolerance
Physical exam – Jugular venous distention, Tachypnea, Tachycardia, Holosystolic murmur (TR), Heave, Hepatomegaly, Edema, Ascites, Pleural effusions
Labs – transaminases (ALT may be more specific), total/direct bilirubin, BUN, creatinine, cystatin C, BNP or NT-proBNP
Echo – RV size, function (*see above* for specific measurements), dilated IVC
Hemodynamics – CVP, hypotension, *see above*
VAD – Evidence of decreased LVAD preload: decreased pulsatility/flows (CF device) or filling (pulsatile device)

4. Medical management of right heart failure

PREOPERATIVE

- Perform careful echocardiogram and consider right heart catheterization to assess RV function and for risk assessment. *See above for specifics.*
- Minimize preload – aim for lower CVP with diuresis, fluid restriction and even renal replacement therapies if needed.
- Maximize end organ function – timely/earlier referral for LVAD to avoid cardiogenic shock, consider temporary circulatory support for patients in shock to recover end organ function prior to durable LVAD implantation.

INTRAOPERATIVE

- Careful myocardial preservation techniques
- Complete deairing to avoid air embolism to the right coronary artery
- Aggressive intraoperative ultrafiltration while on bypass.
- Minimizing crossclamp time
- Minimize transfusions and excessive fluid
- Avoid acidosis, hypercapnia, hypoxemia
- Wean off of bypass on inotropic support, not hypervolemic, stable respiratory status with supplemental oxygen and many centers report to using iNO, especially in the setting of elevated PVR.
- Slow, careful uptitration of LVAD with transesophageal echocardiographic and hemodynamic guidance – keep interventricular septum midline/neutral and rounded if possible. Avoid excessive RPM and significant leftward shift of the septum.
- Consider concomitant tricuspid valvuloplasty in the setting of significant baseline tricuspid regurgitation

POSTOPERATIVE

Minimize preload

- Fluid restrict (to 1/3 to 2/3 maintenance rate as tolerated). Avoid unnecessary fluid boluses. Diurese aggressively. Aim for CVP <12 or lower as tolerated. Consider renal replacement therapies (ultrafiltration, dialysis) early if fluid overloaded and unresponsive to escalating, high dose diuretics.

Minimize RV afterload

- Adequate respiratory support to avoid hypoxemia and hypercapnia. Avoid excessive positive pressure and extubate as soon as clinically feasible.
- Continue/consider iNO. Transition from iNO to sildenafil for chronic therapy, especially in the setting of baseline elevated PVR. Consider additional selective pulmonary vasodilators in select patients with high baseline PVR.

Maximize RV contractility/output

- Centers will often use combination of milrinone (inotropy and pulmonary vasodilation) and another inotropic agent (dopamine, epinephrine, dobutamine) for RV support and systemic afterload reduction if needed.
- Wean support carefully while monitoring for symptoms, exam, hemodynamics and end organ function.
- Maintain sinus rhythm, treat arrhythmias, consider pacing for any relative bradycardia to improve RV output.
- Consider digoxin

Optimize VAD

- Evidence of decreased LVAD preload (decreased pulsatility in continuous flow devices or decreased filling in pulsatile devices) and decreased LVAD flows/output should raise concern for RV failure in the absence of bleeding/hypovolemia.
- Ensure appropriate VAD settings by echocardiogram: LV decompression while keeping interventricular septum midline/neutral and rounded if possible. Avoid significant leftward shift of the septum. Close attention to tricuspid regurgitation and RV size.
- Low threshold for catheterization, hemodynamic assessment and VAD ramp study to identify optimal settings.

LATE or CHRONIC RIGHT HEART FAILURE

- Consider other comorbidities and contributors including obesity, pulmonary stenosis, pulmonary embolism, obstructive sleep apnea, tamponade, device thrombosis, liver/renal dysfunction.
- Obtain hemodynamic catheterization and optimize device as above
- Acute management principles as above

5. Mechanical circulatory support for right heart failure

- In the setting of significant RV dysfunction, mechanical RV support should be considered (as early as in the OR) to avoid significant end organ dysfunction and to maximize possibility of RV recovery.
- Elective/planned/earlier RVAD is associated with better long-term survival than emergency RVAD implantation.
- Severe right heart failure despite optimal medical management should prompt consideration for MCS.
- Choice of RVAD device depends on patient size, center experience, device availability and anticipated duration of support. Most commonly used ‘temporary’ devices include paracorporeal CF (Centrimag, Rotaflow) and percutaneous (Impella RP Flex, Protek Duo). Dependent on patient size, potential durable, longer-term options include intrapericardial (Heartmate 3), paracorporeal (Berlin Heart, Centrimag) or Total Artificial Heart Syncardia.

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STEROIDS & INFLAMMATION in Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Systemic inflammation may result from chronic heart failure prior to implant or from the interaction of blood with the artificial surfaces of the VAD. Given that a pro-inflammatory state may predispose to hypercoagulability, some centers have elected to use a short course of systemic glucocorticoids. While there is limited published outcome data available about this approach, some centers have found corticosteroid therapy beneficial in maintaining adequate anticoagulation.

ACTION REVISED DATE: 03/20/2024

OBJECTIVES

To provide a standardized approach to the monitoring, evaluation, and treatment of systemic inflammation in children undergoing paracorporeal VAD support.

PROTOCOL

Monitoring:

- Obtain baseline inflammatory markers (CRP or high-sensitivity CRP, fibrinogen) following VAD implantation
- Recommend trending inflammatory markers daily for 7 days post-implant and then weekly thereafter or with any clinical concerns, such as new onset fever or difficulty maintaining adequate anticoagulation (including increased fibrin deposition). For smaller children - may modify frequency to minimize blood draws.

Evaluation:

May consider beginning glucocorticoid therapy if:

1) New onset fever with negative initial cultures and infectious work-up
2) Elevated inflammatory markers. Centers have used the following cut off values:
    - CRP > 15 mg/dL or unexplained increase from post-implant baseline
    - High-sensitivity CRP > 70 mg/dL or unexplained increase from post-implant baseline
    - Fibrinogen > 600 mg/dL or unexplained increase from post-implant baseline
3) Inadequate anticoagulation despite being within therapeutic range
4) Need for rapid escalation or decrease in anticoagulation with no other clear identified etiologies (i.e. stable renal/hepatic function, adequate medication delivery)

Treatment:

Initial Dose: Methylprednisolone 2 mg/kg IV (maximum dose: 60 mg/day)

Days 1-5: Methylprednisolone 1 mg/kg IV q 12 hrs (maximum daily dose: 60 mg/day)

- Duration may be increased if inadequate response
- Some centers have reported using up to 15 mg/kg pulse in unresponsive patients

Taper: If inflammatory markers have begun to normalize (CRP < 4 mg/dL, hs-CRP < 30 mg/dL, fibrinogen < 400 mg/dL) and adequate control of anticoagulation can begin to taper over 3-5 days. A longer taper may be necessary if patient required a greater duration of steroid therapy.

Additional considerations:
May consider omega-3 fatty acid supplementation to augment inflammatory response. There is limited data regarding dosing; however, centers have used 500 mg BID for all ages.

With glucocorticoid therapy, recommend monitoring for side effects such as hypertension, hyperglycemia, impaired wound healing, fluid retention, and alterations in INR.

Recommend concomitant H2 blocker or proton pump inhibitor prophylaxis therapy to minimize gastritis.

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Steps to Start a VAD Stroke Management Pathway

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HARMONIZED PROTOCOL

"An attempt to harmonize turned into a guide to strategize!"

ACTION REVISED DATE: *04/25/2024*

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

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- (Revised: 1/29/20)

Background

- Strokes continue to be a leading cause of morbidity and mortality in pediatric VAD patients with very little consensus on management strategies

- Stroke management in VAD patients is challenging due to the competing risks of neurological and cardiac complications surrounding anticoagulation management and intervention strategies as well as bringing teams together that do not routinely interface

- Prompt action is needed by these multidisciplinary teams to balance these competing risks in order to minimize morbidity surrounding these events

Objectives/Goals:

- To create a comprehensive guide for sites to design a stroke management pathway for the rapid detection, diagnosis, and management of ischemic and hemorrhagic strokes in pediatric VAD patients centric to their team and institution culture, resources, and philosophy

- Promote pre-emptive discussion and organization of institution-specific key players required for effective management of VAD strokes (Neurology, Neurosurgery, Neuroradiology, Cardiac anesthesia, cath lab, etc.)

VAD Stroke Example Pathways:

- I. Bedside Stroke Recognition Tool
- II. VAD Stroke Diagnosis
- III. VAD Ischemic Stroke Management
- IV. VAD Hemorrhagic Stroke Management
- V. VAD Subdural Hemorrhage Management
- VI. Appendix to Pathways/ICU Clinical Management

I. Bedside Stroke Recognition Tool

Placed at the bedside attached to the back of the stroke prevention checklist for appropriate and objective neuro assessment by nursing and other frontline providers

VAD Nursing Neurologic Exam (circle appropriate exam)
GOALS: Assess mental status and motor symmetry

Intubated Exam:
Option 1: (for children unable to follow commands)
Eye opening or moving to tactile stimulation
Pupil reactivity, fixing/tracking examiner if awake
Moves arms to light touch or nail bed pressure (assess for symmetry)
Moves legs to light touch or nail bed pressure (assess for symmetry)
Ankle clonus (bilaterally)

Option 2: (for children able to follow commands)
Following commands (bilaterally)
- thumbs up, show two fingers, give high 5
- wiggle toes

Proximal strength (bilaterally)
Pronator Drift
-pronator drift (see pic)
-leg drift (have patient hold leg 1 foot above bed for 5 seconds)
Distal strength (bilaterally)
-squeeze hands
-wiggle toes
Ankle Clonus (bilaterally)

Non-intubated exam:
Option 1: (for children unable to follow commands)
Eye opening or moving to tactile stimulation
Fixing and tracking examiner
Moves arms to light touch or nail bed pressure (assess for symmetry)
Moves legs to light touch or nail bed pressure (assess for symmetry)
Ankle clonus (bilaterally)

Option 2: (for children able to follow commands)
Answering questions
Identifying objects
Following commands (bilaterally)
- thumbs up, show two fingers, give high 5
- wiggle toes

Proximal strength (bilaterally)
-pronator drift
-leg drift (have patient hold leg 1 foot above bed for 5 seconds)
Distal strength (bilaterally)
-squeeze hands
-wiggle toes
Ankle Clonus (bilaterally)

Frequency of exam:
Q2 hr while awake, q4hr while sleeping
Q4 hr while awake, defer exam while sleeping
Qshift while awake

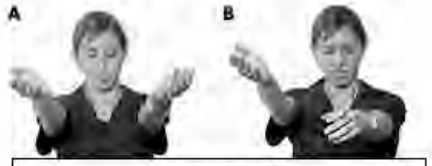
New onset headache?

Focal neurodeficit? (e.g. unilateral weakness/sensory change, vision loss, double vision, speech difficulty, dizziness, difficulty walking)

*If suspected stroke, activate Suspected Stroke Algorithm – see VADs page 4

RED FLAGS:

1. Acute Neuro-deficit: acute unilateral weakness. Inability to speak/understand. Gait instability. Vision loss. Altered mental status
2. Headache WITH: altered mental status, vomiting



Pronator Drift

Ask patient to hold arms up like they are holding a pizza box, have them close their eyes, look for drift in one arm

Ankle Clonus

Ann & Robert H. Lurie Children's Hospital of Chicago

HARMONIZED

I. Bedside Stroke Recognition Tool

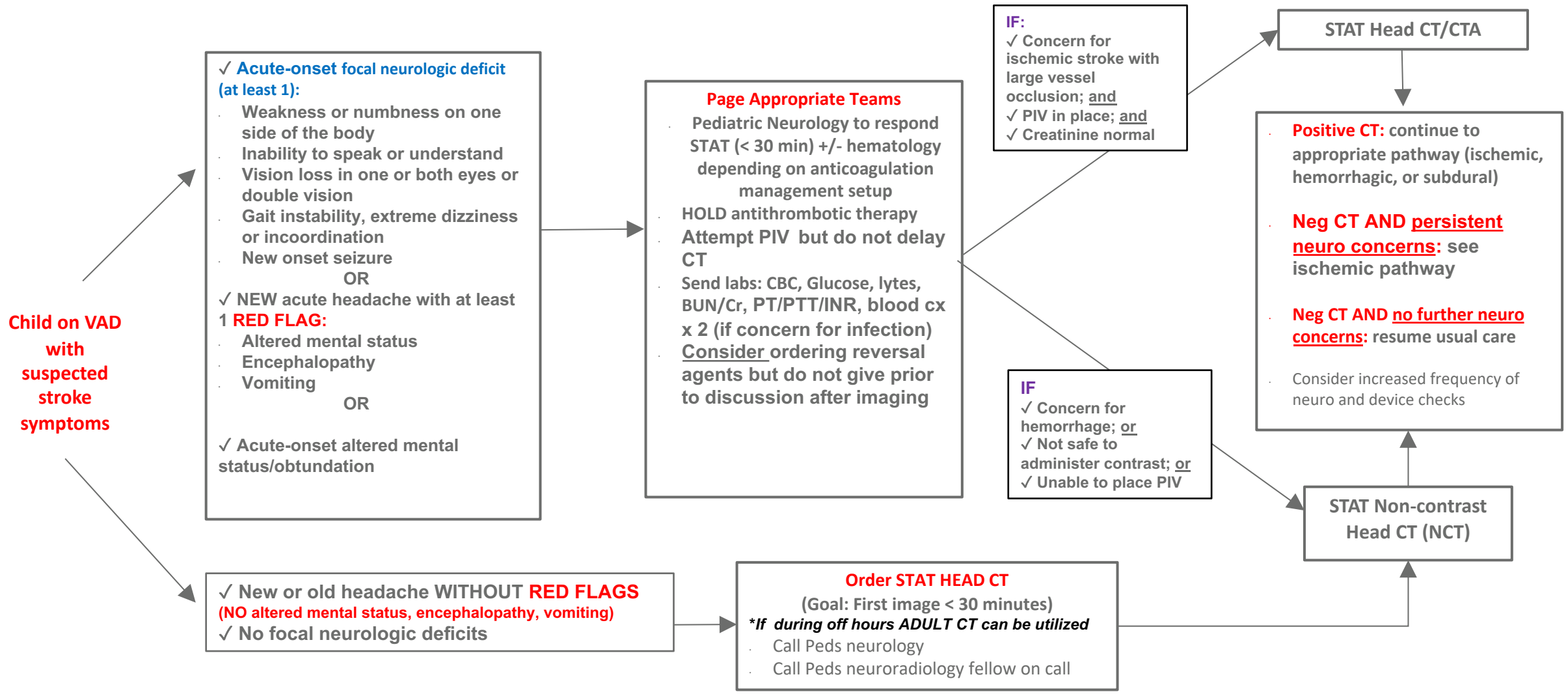
C.S. Mott Children's Hospital
University of Michigan

Placed at the bedside attached to the back of the stroke prevention checklist for appropriate and objective neuro assessment by nursing and other frontline providers

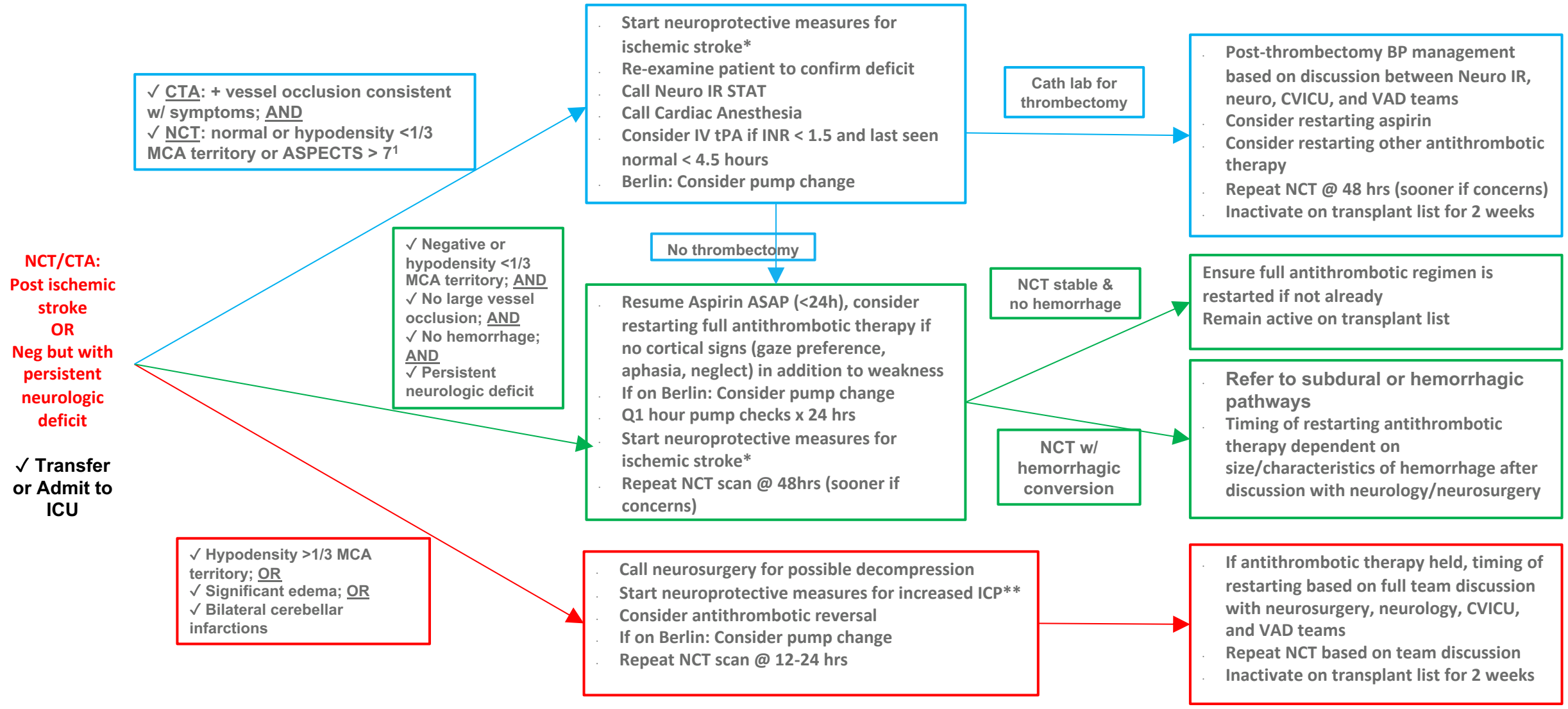
Signs & Symptoms	Description
Hemiparesis	Arm or leg weakness or paralysis, facial droop
Numbness	Loss of sensation on one side of the body or one limb, includes neglect of one side of the body
Aphasia	Difficulty finding words, garbled or nonsensical speech, loss of speech, difficulty understanding language
Vision deficit	Loss of vision in one half or quadrant of visual field, visual neglect of part of visual field, gaze preference
Dysarthria	Slurred speech
Ataxia/dysmetria	Unsteady gait, incoordination
Eye abnormalities	Misaligned eyes, eye movement paralysis, double vision, nystagmus
Nonspecific	Headache, nausea, vomiting, altered mental status, new focal seizure, increased irritability

HARMONIZED

II. Ventricular Assist Device (VAD) Stroke Diagnosis Pathway



III. VAD Ischemic Stroke Management Pathway



[1] ASPECT score = 10-pt score based on CT findings for MCA stroke

Refer to the Appendix for neuroprotective measures for ischemic stroke (*) or for increased ICP (**)

IV. VAD Hemorrhagic Stroke Management Pathway

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NCT: + acute hemorrhage (not subdural)

✓ Call neurosurgery

✓ Start neuroprotective measures for increased ICP & hemorrhagic stroke*****

✓ Transfer or admit to ICU

Meets 1 of following:
- Urgent neurosurgical intervention planned
- Mass effect with >5mm midline shift
- Infratentorial location (posterior fossa)
- Significant hydrocephalus
- Clinical signs of herniation
- Major neurologic deficit[2]
- Neuroimaging signs of active bleeding (CT black hole sign, CTA spot sign, fluid-fluid level)

YES

NO, and meets following:
Tiny/small bleed[1] AND no neurologic deficits

- Continue to hold antithrombotic therapy[3]
- Q1hr neurochecks (with pupillometer) x 24 hrs
- Repeat NCT @ 4-6 hrs

NCT stable

- Resume antithrombotic therapy at prior dose
- Remain active on transplant list

Bleed expansion

- Continue to hold antithrombotic therapy[3]
- Reverse heparin with protamine
- Reverse anticoagulation with 4F-PCC + Vit K for goal INR <=1.4
- Transfuse platelets
- Neurosurgical intervention if indicated
- Repeat NCT per NSG
- *Avoid factor VIIa (increased risk of thrombosis)*

- Hold antithrombotic therapy for 1-2 weeks[3], then resume at low dose
- Titrate to goal antithrombotic therapy over 1-2 weeks
- Repeat NCT 12hrs after resuming antithrombotic therapy and again at full therapy (sooner if clinically indicated)
- If unable to obtain neuro exam, repeat NCT prior to resuming antithrombotic therapy
- Inactivate on transplant list until repeat NCT at full antithrombotic therapy

Bleed expansion

NO, and meets 1 of following:
- Moderate-sized bleed[1]
- Minor focal neurologic deficit[2]

- Continue to hold antithrombotic therapy[3]
- Consider reversal of heparin with protamine
- Reverse anticoagulation with FFP + Vit K for goal INR <=1.4
- Transfuse platelets
- Q1h neurochecks (with pupillometer) x 24 hrs
- Repeat NCT @ 4-6 hrs
- *Avoid factor VIIa (increased risk of thrombosis)*

NCT stable

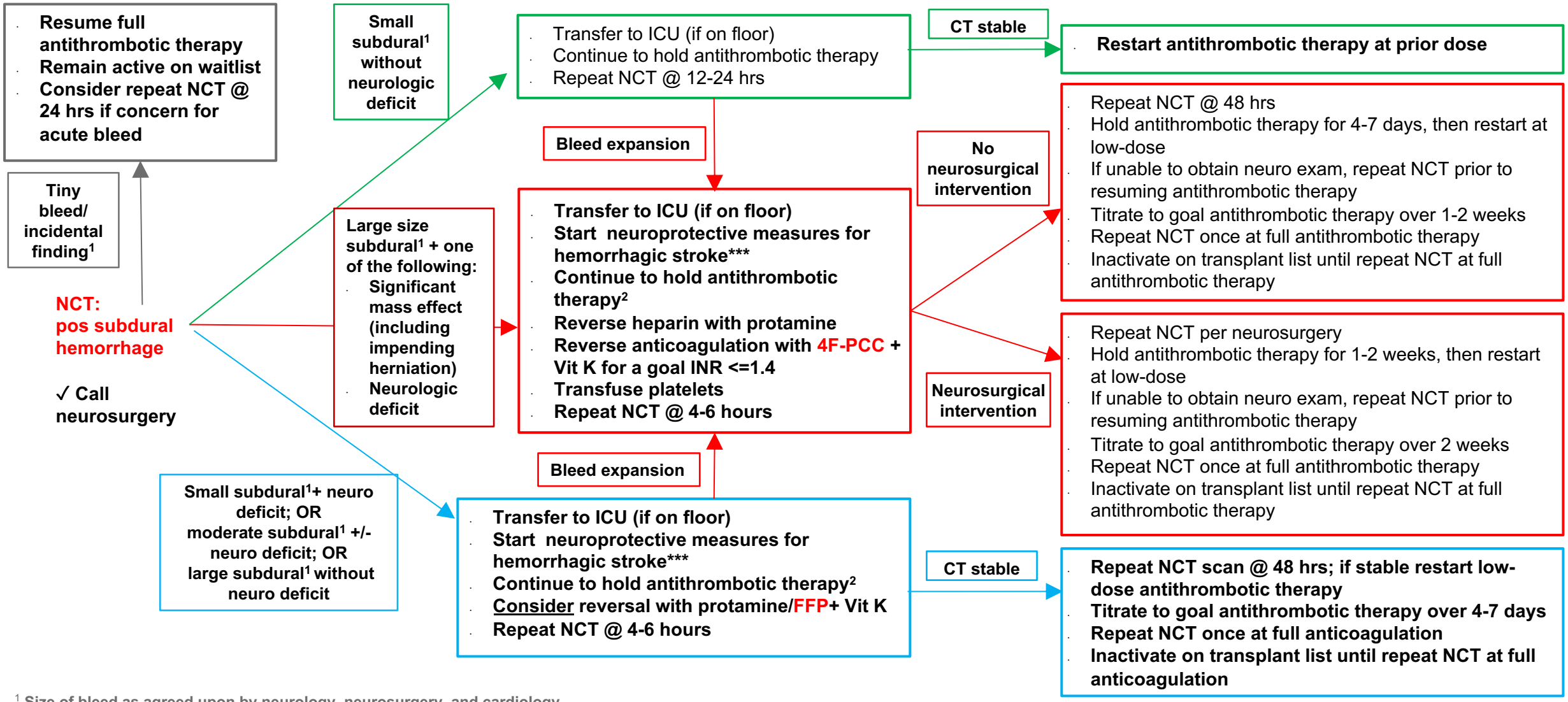
- Resume low dose antithrombotic therapy 24-48 hrs from initial scan and titrate to goal over 1-2 weeks
- If unable to obtain neuro exam, repeat NCT prior to resuming antithrombotic therapy
- Repeat NCT once at full anticoagulation
- Inactivate on transplant list until repeat NCT at full anticoagulation

[1] Size of bleed as agreed upon by neurology, neurosurgery, and cardiology
[2] Minor or major neurologic deficit as agreed upon by neurosurgical, neurology, and cardiology
[3] When holding antithrombotic therapy, monitor for pump thrombosis: Berlin – Q1hr pump checks; CF-VADs – daily LDH

Refer to the Appendix for neuroprotective measures for increased ICP (**) and hemorrhagic stroke (***)

HARMONIZED

V. VAD Subdural Hemorrhage Management Pathway



[1] Size of bleed as agreed upon by neurology, neurosurgery, and cardiology

For ***hemorrhagic neuroprotective measures, please refer to the Appendix

VI. Appendix to VAD Stroke Management Pathways

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*Neuroprotective measures for ischemic stroke

- Continuous cardiorespiratory monitoring
- NPO, **Head of bed FLAT**
- BP goals based on clinical scenario:
- If pulsatile pump, aim for systolic blood pressure 50-95%ile for age but can accept unsustained SBP 15% above 95%ile for age unless tPA candidate.
- If continuous-flow, Doppler pressures as high as tolerable (10mm Hg above baseline systolic Doppler goals, but no higher than 85)
- Target euvolemia and avoid hypovolemia: Isotonic fluids without dextrose unless hypoglycemic (0.9% NS at maintenance)
- Treat sustained severe hypertension with short acting, easily titratable agents (i.e. hydralazine, nicardipine, clevidipine; avoid nitroprusside and esmolol)
- Normoglycemia and Normothermia (Acetaminophen or cooling blanket for T>37.5; monitor for shivering)
- Seizure control with antiepileptic drugs if suspected seizure activity (i.e. 20mg/kg fosphenytoin or Keppra 40mg/kg unless contraindications)
- If intubated, maintain pCO2 > 40

**Neuroprotective measures for increased ICP

- Continuous cardiorespiratory monitoring
- NPO, Head of bed 30 degrees, midline
- BP goals based on clinical scenario:
- If pulsatile pump, aim for Systolic blood pressure 25-50%ile for age; avoid hypertension and hypotension
- If continuous-flow, aggressively maintain systemic Doppler pressure goal (hyper- and hypotension may both be detrimental)
- Target euvolemia (general CVP 5-8)
- Target higher sodium goals in discussion with neurology
- Treat hypertension with short acting, easily titratable agents (i.e. hydralazine, nicardipine, clevidipine; avoid nitroprusside and esmolol)
- Euglycemia; aggressively control hyperglycemia
- Euthermia: Acetaminophen or cooling blanket for T>37.5; monitor for shivering
- Seizure control with antiepileptic drugs if suspected seizure activity (i.e. 20mg/kg fosphenytoin or Keppra 40mg/kg unless contraindications)
- If intubated, maintain pCO2 > 40

***Neuroprotective measures for hemorrhagic/subdural stroke

- Continuous cardiorespiratory monitoring
- NPO, Head of bed 30 degrees, midline
- BP goals based on clinical scenario:
- If pulsatile pump, aim for systolic blood pressure 25-50%ile for age; avoid hypertension and hypotension
- If continuous-flow, aggressively maintain systemic Doppler pressure goal (hyper- and hypotension may both be detrimental)
- Target euvolemia (general CVP 5-8); hypotension and dehydration has potential to cause traction on bridging veins and expanding subdural bleed
- Target higher sodium goals in discussion with neurology
- Treat hypertension with short acting, easily titratable agents (i.e. hydralazine, nicardipine, clevidipine; avoid nitroprusside and esmolol)
- Euglycemia; aggressively control hyperglycemia and Euthermia (Acetaminophen or cooling blanket for T>37.5; monitor for shivering)
- Seizure control with antiepileptic drugs if suspected seizure activity (i.e. 20mg/kg fosphenytoin or Keppra unless contraindications)
- If intubated, maintain pCO2 > 40

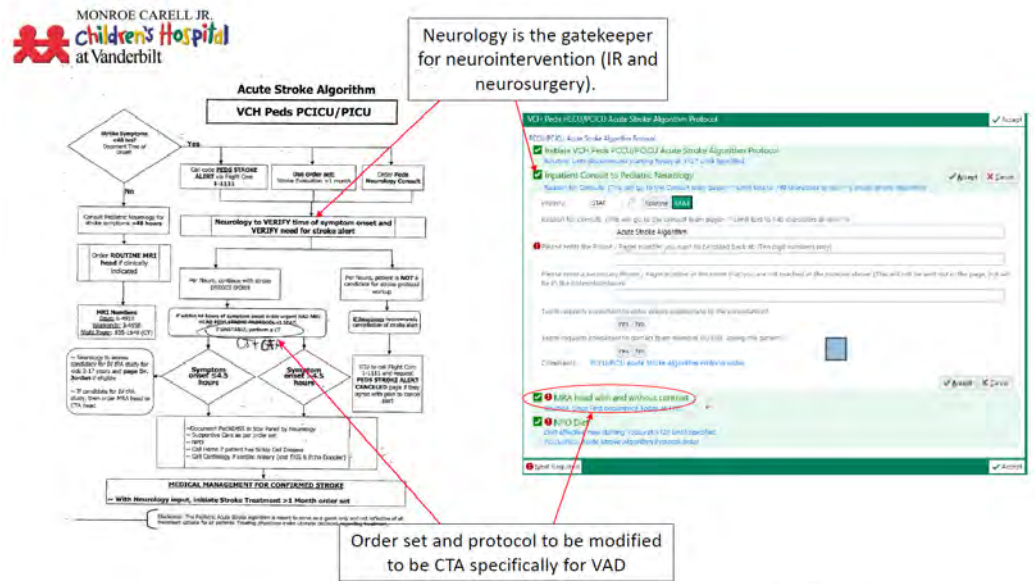
HARMONIZED

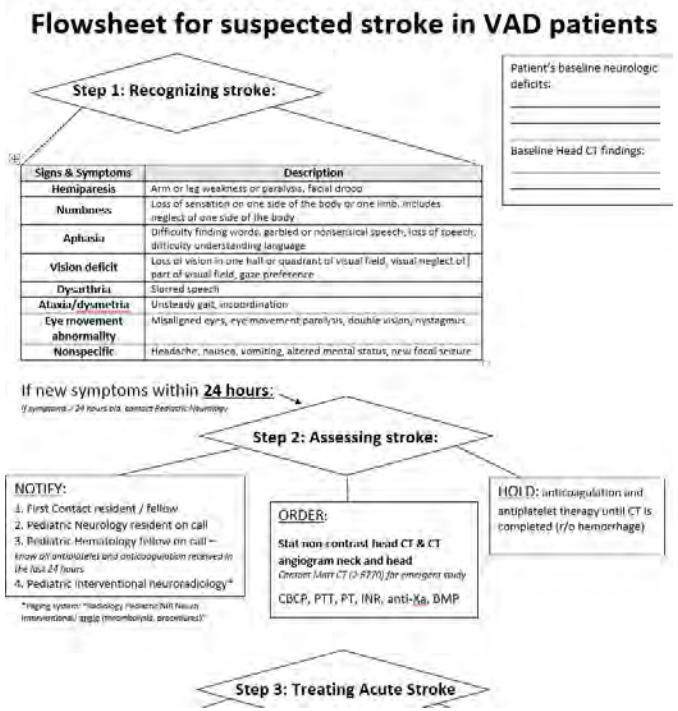
Word Formatted Pathway Examples

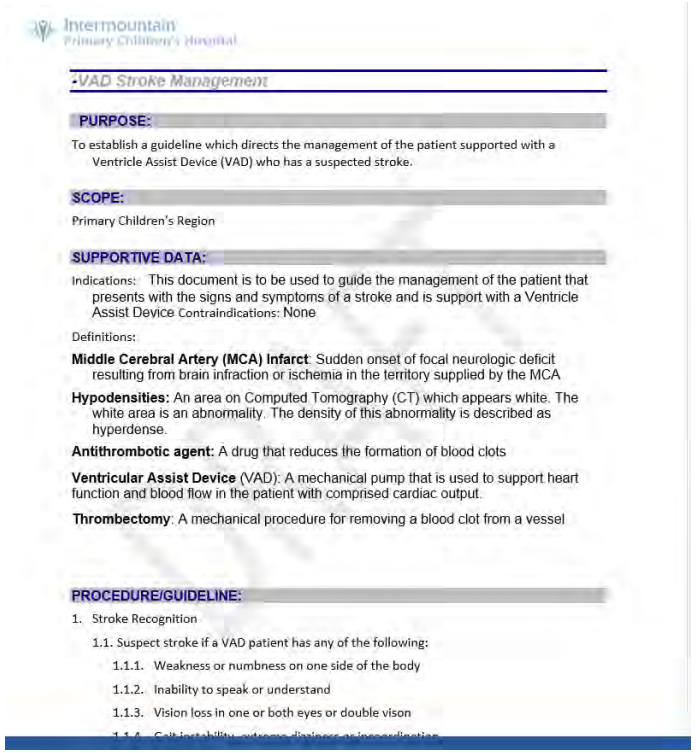
Refer to Basecamp folder for WORD templates (click links below):

1. University of Michigan – C.S. Mott Stroke Flowsheet
2. Primary Children's Hospital – VAD Stroke Guideline
3. Monroe Carell Jr. Children's Hospital at Vanderbilt – VAD Stroke Diagnosis & Treatment
4. Lurie Children's Hospital – VAD Nursing Neurologic Exam

Monroe Carell Jr. Children's Hospital at Vanderbilt, Primary Children's Hospital, & C.S. Mott Children's Hospital







HARMONIZED

ABC's of Stroke Management

High Points for Multidisciplinary Discussion

ANTICOAGULATION

- When/if to hold? For How long?
- When/if to reverse?
- Discuss competing risks that are important for both sides (cardiology and neurology/neurosurgery)
- When to restart? What will Neurosurgery intervene on?

BLOOD PRESSURE

- ICU management with neuroprotective measures - make sure both neuro and CVICU are clear and have been a part of discussion around goals

COMMUNICATION

- Communication between VAD team, CVICU, Neurology, and Neurosurgery is crucial and paramount to success of any pathway

High Points for Multidisciplinary Discussion

Key Points/Discussion Topics

- Clarify the path of your hospital's stroke code so all understand the timing and goals of the stroke code.
- If VAD team and transplant team are not the same people, make sure transplant is involved especially in discussions around deactivation and when to activate safely.
- How will the team socialize your pathway across all disciplines to make it successful and effective
- Discussions with neurosurgery about when they would like to be involved and indications for surgical intervention
- Discussions with neuro IR, what is their time frame for intervention and what is the smallest patient they will attempt an intervention
- Discussions with cardiac anesthesia regarding any interventional/surgical procedures
- Discussions regarding the number and frequency of follow-up CT scans being mindful of radiation exposure.

Conclusion/Take Aways:

- Rapid multidisciplinary management of strokes are required to minimize morbidity in Pediatric VAD patients

- The individual components of these multidisciplinary teams and resources may differ slightly at each institution, but clearly defined roles and responsibilities should be figured out prior to these events

- No one process will work at every site but applying various components of this document can help programs develop a center specific pathway that leverages institutional resources and culture

SynCardia Total Artificial Heart (STAH) Management

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

SynCardia Total Artificial Heart (STAH) offers opportunities for mechanical circulatory support in older children and young adults. Due to limited pediatric experience with this device, a structured approach to both patient selection, and patient management is essential followed by careful monitoring and guided therapy.

ACTION REVISED DATE: 8/21/2024

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OBJECTIVES

This document will provide an overview of the 50cc and 70cc STAH devices, patient selection, implantation techniques and management strategies.

DEVICE DESCRIPTION AND SPECIFICATIONS

The STAH is a pulsatile biventricular device that replaces the native ventricles and valves functioning as a total support device for both pulmonary and systemic circulation. There are currently two SynCardia TAH devices available (see figures below) for cardiac transplant-eligible patients. The device is rarely used for destination therapy in young patients due to the complex needs associated with outpatient care.

- 50cc TAH - Approved device for patients with BSA 1.2 m^2-1.85 m^2 (potentially smaller with FIT study)
- 70cc TAH - Approved device for patients with BSA ≥ 1.7 m2 T10 measurement of 10cm or greater.

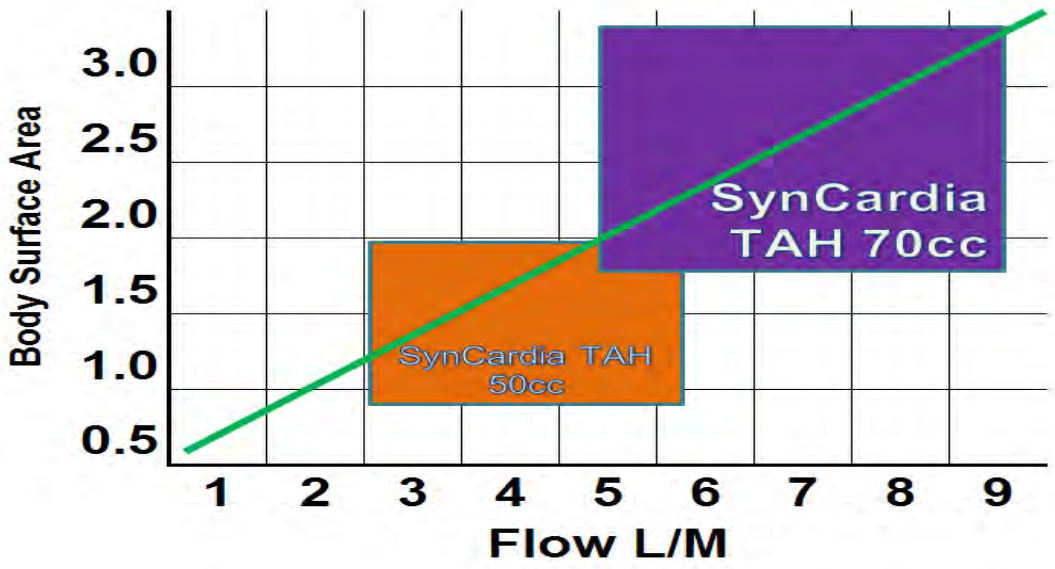


Figure 1: Flow vs body surface area for the 70cc and 50cc TAH.

	70cc TAH-t	50cc TAH-t
Stroke Volume	70 mL	50 mL
Displaced Volume	400 ml	270 ml
Inflow Valve Diameter	27 mm	25 mm
Outflow Valve Diameter	25 mm	23 mm
Diaphragms	four (4) flexible polyurethane	
Maximum Output	10.5 LPM	7.5 LPM

Figure 2: Dimensions of the 70cc and 50cc pump.

INDICATIONS FOR IMPLANTATION

As with many temporary and durable mechanical support devices, the success of support is dependent on careful patient selection. Current experience highlights 4 primary indications for biventricular support:

1. Severe Biventricular Failure
    a. Restrictive or hypertrophic cardiomyopathy
    b. Failed transplant cardiac graft
2. Significant ventricular thrombotic burden
    a. Clot burden unamendable to thrombectomy
3. Incessant Arrhythmias
4. Congenital Heart Disease
    a. Valvular disease and myocardial dysfunction
    b. Fontan circulatory failure

CONTRAINDICATIONS TO IMPLANTATION

The following conditions **may not be appropriate for implantation of the TAH-t:**

- Irreversible end-organ dysfunction
- Risk of inability to anticoagulated or significant bleeding disorders
- Active systemic infection
- Active malignancy
- Insufficient space to accommodate a TAH including thoracic cage deformities
- Poor transplant candidacy is a relative contraindication

PRE-IMPLANTATION EVALUATION AND ASSESSMENT

IMAGING

Optimal candidacy and device selection will depend on a comprehensive assessment which includes detailed cardiac and vascular imaging.

The following routine measurements should be performed:

- Chest CT – Distance from posterior sternum to anterior spine at T10
    - 70cc
        - Patients with a T10 measurement ≥ 10 cm. Patients supported by the 70cc TAH typically have a body surface area (BSA) ≥ 1.7 m^2.
    - 50cc
        - Patients with an adequate T10 measurement as determined by 3D imaging assessment or by other standard clinical assessments. The 50cc TAH is intended to support patients with a BSA ≤ 1.85 m^2.
- Fit study: Segmented chest CT with contrast is performed. Using a reconstructed model of the device and the CT scan results the imaging team can determine fit with virtual reality.

    - Contact for fit studies:
        - Elizabeth Oei RN, BS, MSN, FNP-BC
          203-807-0965
          eoei@syncardia.com

LABORATORY ASSESSMENT

Diagnostics blood tests recommended prior to device deployment

Chemistry and Microbiology				
	☐	Comprehensive Metabolic Panel	☐	Brain Natriuretic Peptide or NT pro-BNP
	☐	Cystatin C/GFR	☐	HLA/ PRA
	☐	CRP	☐	+/- MRSA screen (institutional preference)
Hematology				
	☐	Type and Screen	☐	Heparin Induced Antibody Testing
	☐	CBC w/ Differential	☐	LDH
	☐	PT/INR, PTT	☐	Anti-Xa if on heparin
	☐	Fibrinogen, D-dimer	☐	TEG or ROTEM (if available)
	● Consider additional thrombophilia or bleeding work up if concerning family history or clinical course (see Action Pre-Implant Protocol for details)			
Ancillary Studies*				
	☐	Head CT	☐	Ultrasound Doppler (arterial & venous) to establish vessel patency, information on access and line placement
	☐	Echocardiogram	☐	CT Scan with IV Contrast for T10 measurement and Fit study
	● Consider if abdominal/renal ultrasound			

***Institutional preference**

IMPLANTATION TECHNIQUES

ABBREVIATED SURGICAL TECHNIQUE (Courtesy of D. Morales)

Steps

1. Median sternotomy
2. Dissect out pericardial contents
3. Take down Left diaphragm
4. Pass the left and right devices about 3 cm below the costal margin
    a. Holes should be snug
5. Reverse the atrial cuffs and trim the left and right to 3 mm
6. Encircle aorta, pulmonary artery, SVC and IVC
7. Need to dissect entire heart (prior to CPB or as much as possible)
8. Bicaval cannulation and use Carotid cannula
    a. May consider using R Jugular as SVC cannula
9. Go on with IVC cannula and then remove R IJ and cannulate SVC
10. CPB to 32C

11. Cross clamp & CP
12. Start to excise heart
13. Cut across RVOT and identify TV and cut a few (3-4 mm) below annulus until septum
14. Cut apex off LV and incise LV towards MV (stopping 5-10 mm from annulus) then cut parallel to annulus towards lateral wall until septum
15. Transect MPA and excise RVOT
16. Place vent into PV with posterior stitch on ventricle
17. Transect aorta and open anterior LVOT
18. Cut septum leaving 3 mm on TV side which will leave slightly longer septum on MV side
19. Excise TV
20. Open RA at this point and over-sew the coronary sinus; unless can clearly see through TV
21. Start with left cuff placing in annulus and use MH 3-0 prolene (two needles) laterally thru cuff and get some valve tissue and annulus in stitch (full thickness bites) tie around LVOT
22. Do right cuff and start at inferior corner of septum and RV (forehand to a backhand) go clockwise first
    a. Septal bites will go thru both cuffs
23. Size of SynCardia cuff and tissue cuff depends on sizing and room available.
24. Invert both cuff
25. Check the cuffs for leaks by inserting the tester (larger one)
    a. Hard to place need to use needle holders at 10 and 2 and stretch cuff placing inferior part of tester in first while assistant pulls open the cuff
    b. With the LA test will need to place hand behind and occlude the PVs
    c. Then place PreviLeak if we have it again or Vista Seal
26. Usually cut PA graft to 6 cm and the aortic at 3 cm
27. Sew PA graft and then aortic graft
    a. Use strips of bovine pericardium
28. Check these grafts for leaks with the tester
    a. Will need to occlude MPA for PA test
29. Sew in Gortex membrane on left pericardium just above PVs and one in diaphragmatic surface (Interrupted to just tack)
30. Bring in the LV pump and do atrial connection with needle holder technique (10 and 2 o'clock)
31. Connect aortic graft
32. Bring RV and use same needle holder technique for atrial connect
33. Connect PA graft
34. Place active root vent and 18 gauge needle in graft (head down)
35. Place right Gortex membrane
36. Wean off CPB
    a. Need only vasodilators (i.e. nipride, nicardipine) and vasoconstrictors (vasopressin, norepinephrine, etc.)
37. LV pressure is 200 mmHg
38. RV pressure is 100 mmHg
39. Rate at 40 bmp then increase rate and de-air
40. Start with vacuum at 0 and slowly uptitrate as needed.
41. OFF CPB
42. TEE to R/O IVC and PVs okay (leave TEE until chest is closed)
43. While achieving Hemostat
    a. Repair Right Neck Vessels
    b. Close neck
    c. Close Pacemaker Pocket site
44. After Hemostasis achieved, place Esmark strips around SVC, IVC, MPA and aorta
45. Place anterior Gortex membrane (attach all membranes to each other with interrupted sutures

See Surgical Animation: https:/www.youtube.com/watch?v=-P3Z7rr8kzE%20

INTRA-OPERATIVE ECHOCARDIOGAM

- TEE should be used before and after chest closure. Close evaluation for the following should be considered:
    - IVC compression
    - SVC compression
    - Pulmonary vein compression

POST-OPERATIVE PATIENT AND DEVICE MANAGEMENT

ANTICOAGULATION

Anticoagulation is required to prevent clot formation, although considered lower risk due to high CO. Optimal anticoagulation is achieved through a combination of heparin/coumadin and aspirin.

- Anticoagulation to begin as soon as post-operative bleeding has resolved. Given higher risk of bleeding post-op and lower thrombosis risk, anticoagulation may be delayed more so than intracorporeal continuous flow VADs. Often anticoagulation is started 48-72 hours after implant.
    - If choosing heparin, target PTT 40-70 or UFH level 0.2-0.4 have been used. May also follow TEG or ROTEM to aid in optimizing anticoagulation.
    - If choosing bivalirudin, an initial PTT target of 40-50 target with escalation of PTT target 60-80 once there are no concerns for bleeding has been used. Although bivalirudin is not the approved medication for the TAH.
- Aspirin (typically 40.5-81 mg depending on kg) typically started POD 3-5 once post-operative bleeding has been controlled and no concerns for bleeding on heparin or bivalirudin infusion.
- If platelet count increases, consider increasing aspirin.
- In adult patients, a does may be as high as 650 mg.
- When patient is clinically ready, they can be bridged to warfarin per institutional practice. Recommend target INR 2.0-3.0.

Other agents

The decision to use agents other than Heparin should be based on institutional experience with monitoring of the listed agents and careful analysis of risk-benefit ratio based on clinical condition. Information presented in this section is based on institutional experience and adult experience from published case reports.

LABORATORY MONITORING

Post-implantation labs obtained should reflect baseline assessment of patient oxygen delivery, coagulation profile, hemolysis, hemoglobin and end organ function, as well as frequency which allows monitoring of the device and patient response to the device and anticoagulation.

Baseline labs post SynCardia placement: CBC; Chemistry with liver function; Hemolysis labs: plasma free Hb, LDH; Coagulation profile: PTT, PT/INR, Fibrinogen, D-dimer, anti-Xa, ACT (POCT), TEG or ROTEM may be used depending on hospital preference; blood gas with lactate and mixed venous oxygen saturation if available.

Recommended laboratory testing following device deployment

Laboratory Markers	24-48h post implantation	Chronic Monitoring
Hematology and Coagulation		
CBC	Q6-12H	Daily
LDH	Q24H	Daily until stable
PT INR	Q24H	Daily until stable
PTT and Anti-10a	Q12H or with every titration	Daily
TEG or ROTEM*	Q24H	Daily until stable
Chemistry and Microbiology		

CRP	Q24	Daily-Weekly
Cystatin C	Once	Weekly
Ancillary Studies		
CXR		Daily
Echocardiogram (TEE)	PRN	
PRA		Q 2 weeks*

***These are recommendations only and each center is encouraged to use center-based practice.**

Additional Labs to Consider:

- Renal panel to assess end organ function
- Hepatic panel to assess end organ function
- Due to high risk of pancreatitis in patients recovering after cardiogenic shock, a pancreatic enzyme panel should be performed and monitored accordingly.

IMAGING

If there is concern for decreased fills, imaging the liver and U/S of the SVC and IVC may be helpful. If unusual pulmonary edema, a TEE for pulmonary vein compression may be needed. CT scan with contrast may also be helpful. Catheterization and angiogram is **NOT** possible; wires in the TAH will cause the device to malfunction.

DEVICE MANAGEMENT

The goal is to have partial fill and full eject.

- 50-60 ml for the 70cc TAH-t
- 30-40 ml for the 50cc TAH-t

Pressure waveforms seen below:

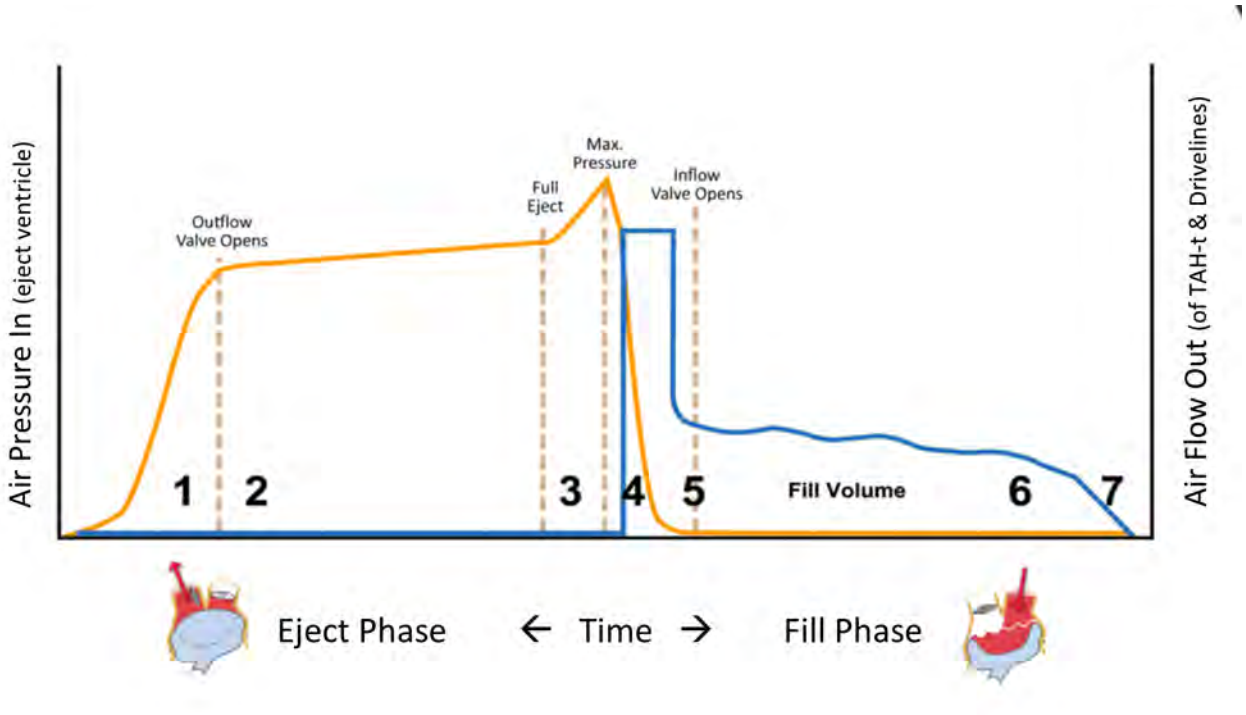


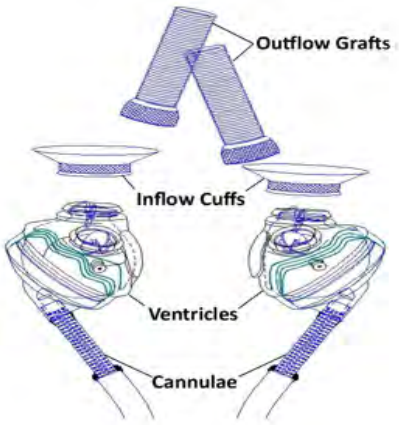
Figure 3: Pressure wave forms as related to cardiac cycle.

DEVICE SETTINGS

	70 cc	50 cc
Left and Right Fill	50-60	30-40
Heart rate	110-140	110-140
Systolic Duration	45-55%	45-55%
Left Drive Pressure	180-210	180-210
Right Drive Pressure	60-100	60-100
Vacuum Pressure	0 to -13	0 to -13

Figure 4: Normal ranges for device settings.

EQUIPMENT

<table>
<tr><th>Implantable TAH Pump Components</th><th>Companion 2 Driver System</th><th>Freedom Driver</th></tr>
<tr>
<td> 
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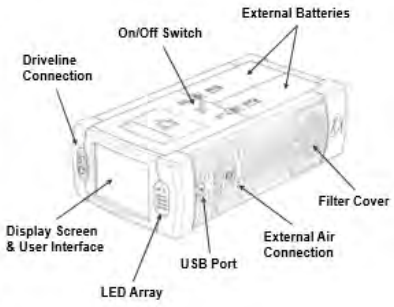
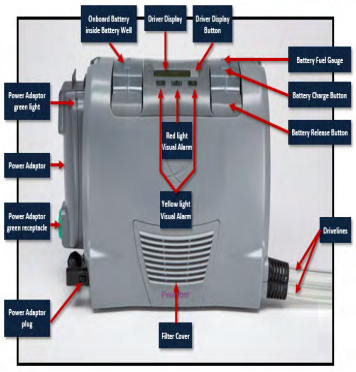


C2 Driver - powers the TAH and pneumatically drives air into the pump.</td>
<td> 

The Freedom Driver</td>
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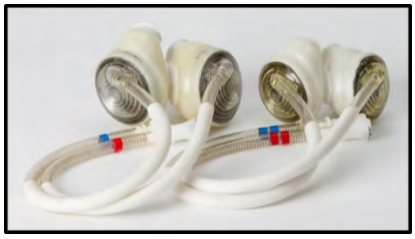
<td> 
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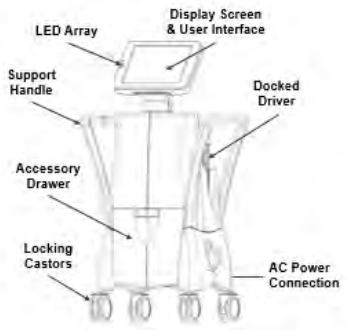

Hospital cart</td>
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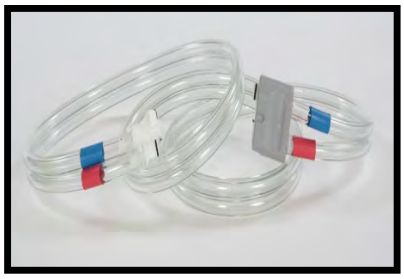
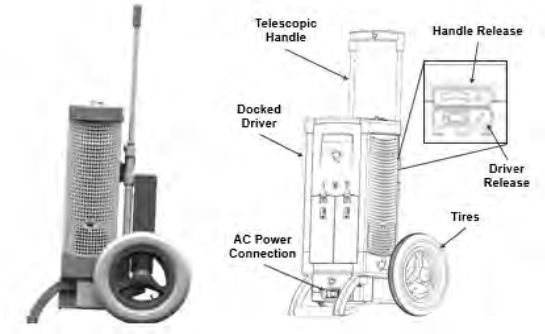


Drivelines



Caddy

Figure 5: See above for equipment components.

PATIENT MANAGEMENT

LINES AND TUBES

- Due to risk of entangling central or midline catheters in the TAH valves, all central line or midline catheters must be placed under fluoroscopy or direct visualization to ensure appropriate placement with their extremity at their side and also with their arm elevated over their head.
- **Tip should NOT be near the TAH.**
- Sutures and anchoring device placed after insertion. Dislodgement should prompt a stat chest x-ray to confirm line position.

ANTIBIOTICS

- Standard perioperative prophylaxis to be given unless concern pre-implant or development of concerning symptoms.
- If prolonged ICU course preoperatively consider fungal prophylaxis.
- Procalcitonin and/or CRP to be followed routinely and PRN if concerned.

HEMODYNAMIC MONITORING

- CVP is usually between 10-15 mmHg
- Running patient dry is preferable (Consider patients dry weight)
- Use device settings (especially vacuums) to augment cardiac output

ANEMIA MANAGEMENT

- **Patients on SynCardia will run a lower than normal hematocrit.**
- PRBC transfusions ordered by the VAD team if Hct <20, if hemodynamically indicated, or patient has clinical signs of hypovolemia with the anemia.

- LDH and plasma free hemoglobin to be monitored for red cell lysis (expect high LDH)

HYPERTENSION

- Target normotensive blood pressures
- In the immediate post-operative period, nipride/nicardipine and appropriate sedation may be used to optimize blood pressure control. Short term agent like hydralazine may be considered as adjunct.
- If chronic hypertension, can consider transitioning to enteral agents such as ACE inhibitor, calcium channel blocker or use of a clonidine patch.

Hypertensive Crisis Management

Note: When increased systemic vascular resistance (afterload) occurs, the TAH (especially the Freedom driver) is unable to deliver appropriate cardiac output and will begin alarming. It is imperative to lower blood pressure and set a specific goal for each patient.

Example Outpatient Hypertensive Urgency Plan for a 50 kg patient with goal BP >140 mmHg

Use	Medication	Directions
Elevated systolic blood pressure greater than 140 mmhg	**Nifedipine (Procardia) [10 mg cap]**	**Take 1 cap (10 mg) as directed for blood pressure greater than 140 for two consecutive measurements**
Elevated systolic blood pressure greater than 160 mmhg	**Nitroglycerin (Nitrostat) [0.4 mg sublingual tablet]** ***store in original container**	**Dissolve 1 tab (0.4 mg) under the tongue as directed for systolic blood pressure greater than 160** **Dissolve under the tongue. Do not chew, crush or swallow**
Elevated systolic blood pressure greater than 140 mmhg (and no response to other drugs)	**Hydralazine [10 mg tab]**	**Take 1 tab (10 mg) as directed**

OTHER

Diuresis

- Recommend IV diuresis immediately post-op to target a CVP ~10-15 see the chart to estimate the CVP in the appendix. (CVP is not always as low as you may expect).
- Use vacuums to improve fill when possible. Minimize fluid boluses.
- Transition to oral furosemide once hemodynamics stabilized.
    - If inadequate, additional agents may be added or ultra-filtration may be initiated.
- Dialysis possible with modification of settings during treatment.

GI Prophylaxis

- Recommend proton pump inhibitor (PPI) for post-operative GI prophylaxis and especially after initiation of ASA.
- Patients transition to oral PPI once on oral anticoagulation.

Nutrition

- Nutritional rehabilitation should be optimized. Recommend consulting dietician.
- Consider assessing for nutritional deficiencies and vitamin supplementation to optimize wound-healing.

Pain Management

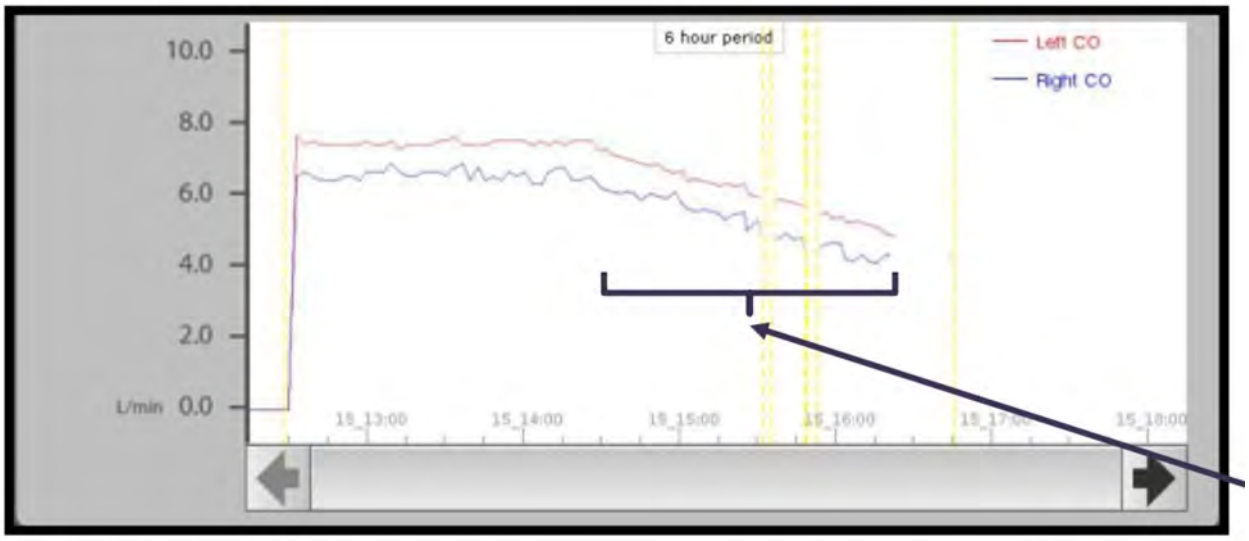
- Initially IV medications used post-operatively and then transitioned to oral once extubated and taking nutrition.
- Oral pain control may be needed long term.
- Consider noise cancelling headphones for sleep.
- NSAIDs such as Ibuprofen or Toradol should **NOT** be used; they inhibit the effect of aspirin.

MANAGING COMPLICATIONS AND ADVERSE EVENTS

Potential adverse events include, but are not limited to: bleeding, fluid overload/device overfill, cerebral vascular accident/stroke, hemolysis, infection, device malfunction and death.

BLEEDING

- Must watch closely for mediastinal bleeding leading to tamponade.
- Assess the patient and evaluate the cause of bleeding (over anticoagulation, coagulopathy vs surgical site bleeding).
    - Send labs evaluating for coagulopathy (CBC, PT, PTT, Fibrinogen, Rotem, Anti-Xa) and assess the need for blood transfusions during prolonged periods of bleeding and correct any deficiencies.
- Anticoagulation goals may need to be adjusted if there is ongoing bleeding or oozing and the pump itself is otherwise functioning well.
- If bleeding continues, consider need for surgical exploration.
- Surgical intervention for bleeding should be considered if bleeding is difficult to control or there is evidence of tamponade.
- Tamponade is usually caused by compression of IVC, SVC, PVs or obstruction of atrial flow. This compression may be due to clot compressing a vital structure.
- The waveform below is an example of cardiac tamponade with slow decrease in flows.



HEMOLYSIS

- Some degree of hemolysis will occur. LDH usually runs 2-3 x normal.
- Although rare, significant hemolysis can induce AKI, abdominal/GI issues and feeding difficulties, continue to monitor renal function.

DEVICE CLOT

- Although rare, in the setting of subtherapeutic anticoagulation or periods, low fill volumes or of profound inflammation, thrombus formation could occur, resulting in device failure.

DEVICE FAILURE

- This is not a common occurrence with the SynCardia device, however, if you are concerned a change in the driver should occur. A C2 backup should be available at all times.

INFECTION

- As with any foreign indwelling device, there is a risk of infection. Prophylactic antibiotics are not generally recommended for the duration of the device. However, for surgical prophylaxis, cefazolin or other antibiotic covering skin flora may be administered for 24 hours postoperatively.
- If the patient has been in the ICU for a prolonged time prior to implantation consider anti-fungal prophylaxis.

EMERGENCY PROCEDURES

Loss of consciousness

If your patient loses blood pressure and loses consciousness and perfusion pressure, CPR should **not** be performed. Defibrillation should **not** be performed. Code dose epinephrine will not help the patient. Consider hanging a sign on the bed about the patient's status and alerting your code team that the patient is not a standard resuscitation. Also consider a medical alert bracelet.

Emergency Switch off the SynCardia Freedom Driver:

- **Disconnect BLUE, Disconnect RED**
- **Reconnect RED, Reconnect BLUE**
- You don't want **BLUE** on without **RED** because of risk for development of pulmonary edema

Responding to cannula issue

- Apply silicone tape only to seal the hole. (aka rescue tape)
- Prophylactic application of rescue tape over zip ties securing the CPC connector in the cannula is recommended.
- Call VAD team for further instructions.

ECMO

- Patients can go on V-V ecmo for respiratory failures if needed. Contact SynCardia for further information about experience in the field.

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Waveforms

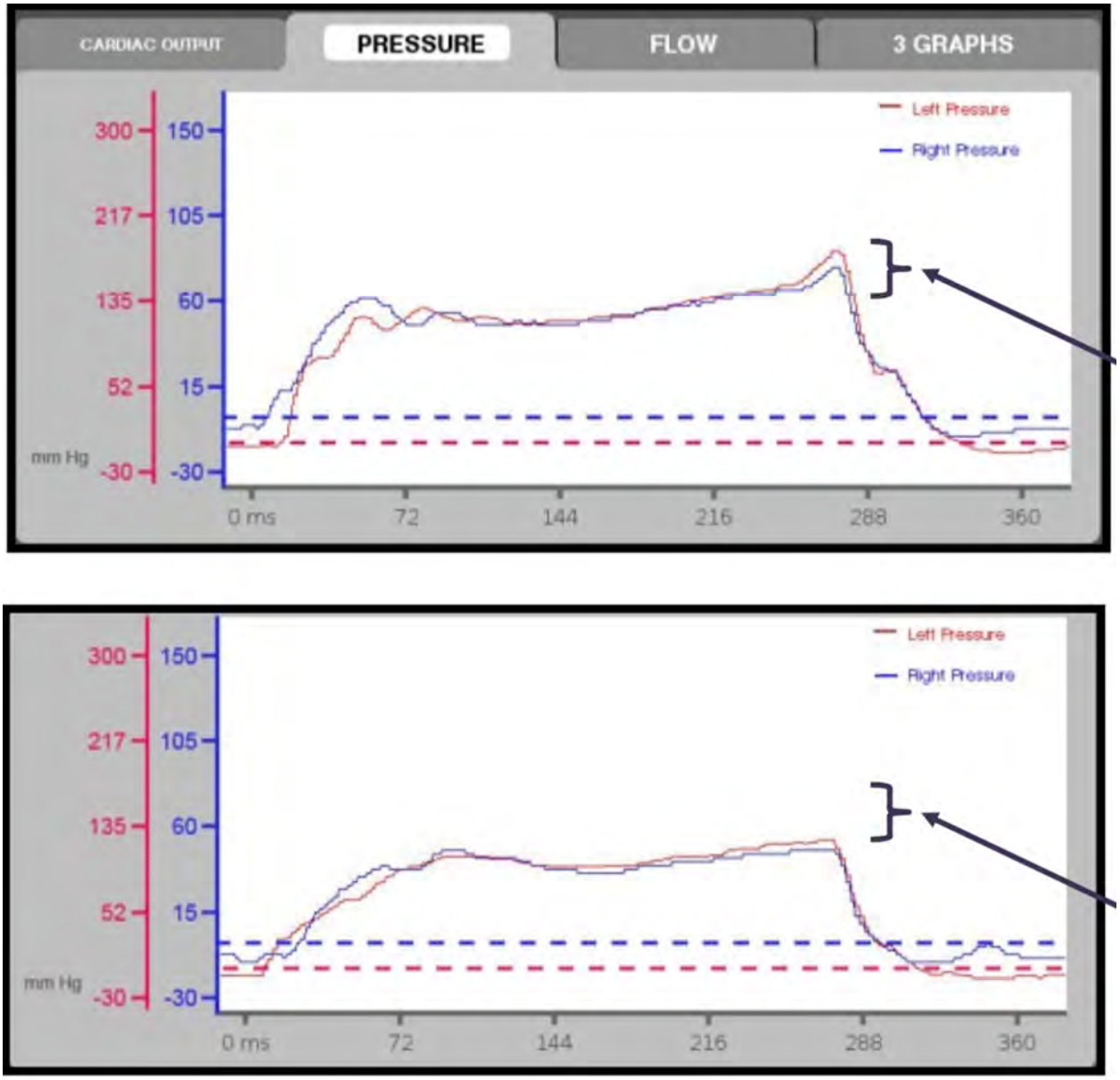

Figure 6: Top image shows full ejection with sharp eject flag or waveform. Bottom image shows a blunted flag or waveform of both right and left.

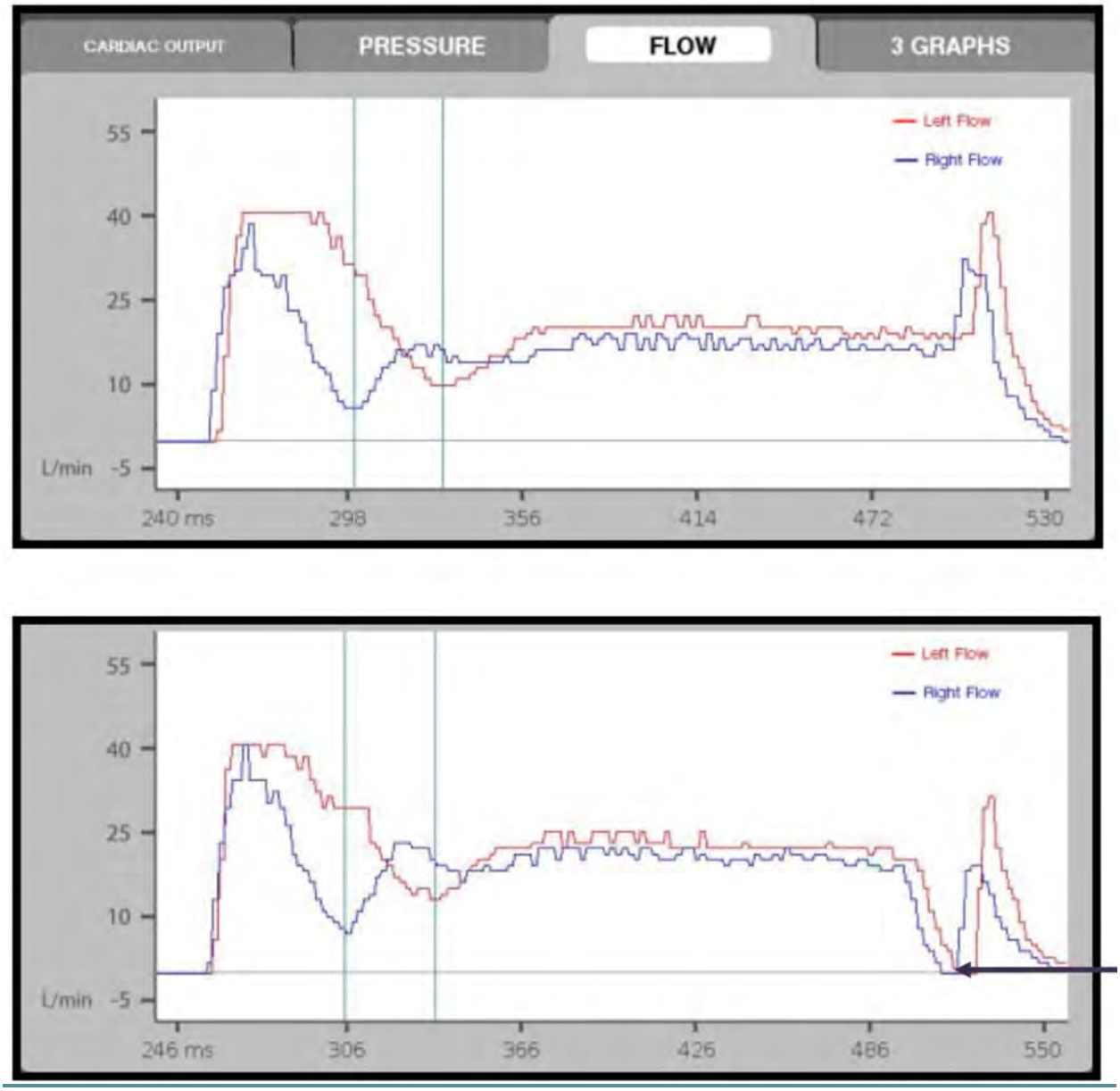

Figure 7: Top image shows partial fill and the bottom image shows full fill of both devices.

APPENDIX 1: NURSING BEDSIDE TEAM ASSESSMENT AND MONITORING

ASSESSMENT

The SynCardia TAH "acts" like a native heart in that it is:

- Fluid sensitive – With low circulating volume, there will be low cardiac output
- Partial fill, full eject – The ventricles will partially fill and fully eject to prevent hemostasis

Assessment focuses on assessing cardiac output:

- ADEQUATE Cardiac Output:

- ✓ Extremities are warm – pulses present: radial, femoral, DP/PT
- ✓ Cap refill is < 3 seconds
- ✓ No mottling or duskiness is present
- ✓ Partial Fills and Full Eject
- ✓ No evidence of tamponade on waveforms

HYPERTENSION MANAGEMENT

- **Target normal blood pressure**
  - **If hypertensive, pump will eventually fail to fully eject (**a fault alarm will intermittently sound) **or fail** (on the Freedom Driver a continuous fault alarm will sound). Treat patient with prn rescue meds as ordered for elevated SBP and call Heart Failure/VAD or ICU team.
- **Emergency meds should be kept with the patient at all times and there should be standing prn orders for when and how to treat hypertension**

Battery Life

- For C2 Driver, battery life is 1 hour (batteries trickle drain simultaneously)
- For Freedom Driver, battery life is approximately 2 hours (batteries trickle drain simultaneously)

SYSTEM CHECKS

Frequency determined by institutional policy

- Document the following system parameters. Note that Freedom Driver will only monitor HR (beats/min), left fill volume, left cardiac output)
  Example C2 Driver Parameters for 70 cc pump:
  - Left and Right Fill Volume
    - Goal is “partial fill”: 50-55 mls
  - Heart Rate
    - Typical range: 110-140 bpm
  - Systolic duration
    - Typical range: 45%-55%
  - Left and Right Drive Pressure
    - Left typical range: 180-210 mmHg default setting 200mmHg
    - Right typical range: 60-100 mmHg default setting 100mmHg
  - Left and Right Vacuum Pressure
    - Left typical range: 0 to -13 mmHg
    - Right typical range: 0 to -10 mmHg
  - Blood Pressure
  - Left and Right Cardiac Output
    - Typical range: 6-9 L/min
  - Drivelines OK (no kinks, etc.)
  - Air Leaks (Y/N)
  - AC Power Lamps on (x3)
  - Any Visible or Audible alarms (Y/N)

- C2 Driver: Monitor waveforms per institutional policy. Can consider every 1 hour in the ICU and every 4 hours when on the floor:
  - Partial fill
    - If flow waveform drops to “zero baseline” – this indicates **full fill** and needs to be investigated and resolved.
  - Full eject flag (waveform)
    - If “flag” missing on waveform – this indicates **partial eject** and needs to be investigated and resolved.

- Document the following Q shift:
    - Back-up Driver set/ready (Y/N)
    - Driveline Connectors Available (Y/N)
    - Battery Checks OK
        - If not on medical air, batteries will last for 1 ½ hrs.
        - Internal battery will last for 10 min.
    - Driver Key Location
    - Emergency equipment at bedside:
        - If on C2 Driver Only: Back-up C2 Driver, plugged in and emergency tool kit
        - If on Freedom: back-up Freedom Driver, batteries, power cord, emergency tool kit and C2 Driver

ACTIVITY

- After approved by care team:
    - Up ambulating at least TID, Up in Chair at least TID
    - Use of Incentive Spirometry/Cough Deep Breathing Exercises
    - OT/PT Consults
- Travel outside of the room should be approved by the care team at rounds. Patient must always have emergency back-up equipment with them.
- Patient **should be accompanied by appropriately trained staff per institutional policy and have appropriate back up equipment.**
- **If leaving the unit or floor for a procedure, ensure appropriately trained staff are available to accompany the patient and monitor the driver.**

FREEDOM DRIVER

- Review HR setting as per order (only parameters viewed: HR, FV and CO)
- Reminder…Battery Life for Freedom Driver=Fully Charged provides 1.5 ***hours*** of battery life
- Documentation/assessment every per institutional policy
- Patient may only leave the floor with a SynCardia trained individual, accessary bag with backup batteries, power-cord, SynCardia Freedom Driver and unit phone number.
- Three types of alarms
    - Battery – beeping tone with blinking yellow light
        - One or both batteries with <35% remaining charge - change one at a time
        - Alarm will continue until both batteries are charged above 35%
    - Temperature (“hot flash”) – beeping tone with blinking red light
        - Ensure filter and/or fan is not blocked
        - Move Freedom Driver to a different area
    - Fault – constant tone with solid red light
        - **Patient not getting the CO they need**
            - Check for disconnection, hypertension
            - Assess fluid status (elevate LEs, increase fluid intake)
            - One or both batteries with <30% remaining charge - change one at a time
    - **Call the Heart Failure/VAD Team on Call to notify of fault alarms and patient assessment.**

WHEN TO CALL THE MD

- **All issues/concerns: Call Heart Failure/VAD/ICU Team**
- **If patient is in distress-call Rapid Response/Code (based on clinical picture). If Rapid Response/Code called, the Heart Failure/VAD Team should be notified immediately.**

- **No Compressions/Defibrillation/ACLS & PALS Drugs**
- Heart Failure/VAD Team should be called for:
    - Fever/Signs of Infection
    - Concern for bleeding
    - Any changes in Anticoagulation Management
    - Changes in Neuro status
    - Concerning Hemodynamic changes
    - Hypertension
    - Any evidence of poor perfusion
    - Device alarms

APPENDIX 2: FREEDOM DRIVER MANAGEMENT

The Freedom Driver is a portable pneumatic device that provides additional mobility for stable TAH patients. Transition to the Freedom Driver is initiated at the discretion of the VAD team at the following criteria:

- **Closed Chest**
- **Prior stable mobility using C2 Driver**
- **Hemodynamic/Hypertension Stability (at least 5 days without rate change on C2)**

Procedure for switching between C2 Driver to Freedom Driver: (Please notify all care teams prior to switching drivers)

1. Ensure patient is in a seated/rested position and all necessary materials available
    a. Have back up freedom drive and hand pump available
        i. Will need 2 VAD trained personnel at bedside to complete switch
2. Insert two fully charged batteries to primary Freedom Driver
3. Connect the primary Freedom Driver into a red wall power outlet
4. Verify that the Freedom Driver starts (you should hear the motor and feel air pumping from the drivelines)
5. Prepare patient for switch. Coordinate switch with additional personnel. Perform steps 6 and 7 **simultaneously.**
6. Disconnect **BLUE** cannula from **BLUE** C2 driveline
    a. Press and hold metal release clip.
    b. Pull **BLUE** cannula from **BLUE** C2 driveline
    c. Immediately insert **BLUE** cannula to **BLUE** Freedom driveline until click is heard
    d. Lightly tug on connection to make sure it is secure
7. Disconnect **RED** cannula from **RED** C2 driveline
    a. Press and hold metal release clip.
    b. Pull **RED** cannula from **RED** C2 driveline
    c. Immediately insert **RED** cannula to **RED** Freedom driveline until click is heard
    d. Lightly tug on connection to make sure it is secure
8. **NOTE**: **Disconnect BLUE, Disconnect RED**
    a. Reconnect RED, Reconnect BLUE
        i. You don't want **BLUE** on without **RED** because of risk for development of pulmonary edema

Note: Freedom Driver support can vary from C2 driver. If patient becomes unstable, immediately switch back to C2 and manage patient's condition.

Emergency Department Hypertensive Urgency Management

1. Obtain IV access and call the VAD/ICU Team
    a. While obtaining access, give Nitroglycerin 0.4 mg tablet by sublingual route
2. IV therapy available in ED STS Pyxis:
    a. Hydralazine

i. Initial Dose: 10-20 mg/dose, may increase to 40 mg/dose. Do not dilute. Use 20 mg/mL concentration.
ii. Administration: IV over 1-2 minutes; Do not exceed 0.2 mg/kg/min
iii. Frequency: May repeat in 2 hours

b. Labetalol
i. Initial Dose: 20 mg; may administer 40-80 mg, up to 300 mg total cumulative dose. Do not dilute. Use 5 mg/mL concentration.
ii. Administration: IV over 2-3 minutes; do not exceed 2 mg/minute
iii. Frequency: May need to administer every 10 minutes

3. Order Nipride continuous infusion to bedside to start at 1mcg/kg/min (if needed, consult with VAD Attending)

4. Change from Freedom Driver to C2 Driver.

Flashing Yellow Alarm: BATTERY ALARM

On the Freedom Driver, the battery alarm indicator will be flashing yellow and you will hear an intermittent "beep" that is 3 beeps in a row.

This means that the battery on that side is either: (1) below 35% power [most likely in the ED], (2) missing or (3) installed incorrectly. You must follow these steps:

Call VAD coordinator, have ESR page CICU attending and VAD attending – (ALWAYS 1st STEP)

Assess and manage patient for medical/cardiac illness

What if TAH stops?
If the SynCardia TAH stops pumping there will be no flow to either lungs or systemic circulation. Need to immediately switch patient to BACKUP Driver unit. Remember as noted below, epinephrine, chest compressions defibrillation will NOT fix this problem.

Is TAH functioning?
Auscultate left lower chest to evaluate:
(1) opening and closing of mechanical valves
(2) sound of the driver moving air
If TAH not functioning, you will hear NOTHING!

YES

NO

Back-up equipment arrived to STS (Would be brought by VAD coordinator or CICU doc)

Patient stable?

Flashing Red Alarm (with high pitched intermittent screeching alarm)
OR
Solid Red Alarm (with continuous loud alarm)

If that battery has power, then:
(1) exchange it for a fully charged battery (see picture guide), or
(2) connect to external power (see picture guide)
If that battery has no power, then:
(1) reinsert battery until locked into place, or
(2) if that does not fix problem, then either exchange battery or connect to external power

YES

NO

YES

Check whether the battery on that side has any indicator lights on showing power

Treat per ACLS protocol, except: **No chest compressions, defibrillation, cardioversion, pacing or epinephrine**[1]

Treat for cardiogenic shock

Move to that algorithm

Discuss further management and disposition with CICU/VAD attending

[1]The SynCardia total artificial heart has replaced the native ventricles and most of the atrium of each side. Therefore, there is no indication for chest compressions, defibrillation, cardioversion, pacing or epinephrine. Medications will NOT change heart rate or augment contractility. However, fluids for preload and medications for afterload/systemic blood pressure may be indicated. Remember, systemic blood pressure that is too high will prevent cardiac output. Maintain SBP < 140 mmHg.

Flashing Red Alarm: TEMPERATURE ALARM

On the Freedom Driver, the red visual alarm indicator will be flashing read and you will hear an intermittent screeching audio alarm.

This means that either: (1) the internal temperature of the Driver is too hot or (2) the temperature of the onboard batteries is too hot or cold. You must follow these steps:

Call VAD coordinator, have ESR page CICU attending and VAD attending – (ALWAYS 1st STEP)

Assess and manage patient for medical/cardiac illness

What if TAH stops?
If the SynCardia TAH stops pumping there will be no flow to either lungs or systemic circulation. Need to immediately switch patient to BACKUP Driver unit. Remember, as noted below, epinephrine, chest compressions, defibrillation will NOT fix this problem.

Is TAH functioning?
Auscultate left lower chest to evaluate:
(1) opening and closing of mechanical valves
(2) sound of the driver moving air
If TAH not functioning, you will hear NOTHING!

YES

Patient stable?

YES

Remove any objects that are blocking the Filter Cover and/or Fan

If no improvement, then:
(1) Remove and change filter (see picture guide)

If still no improvement, then:
(1) Move Freedom Driver to a cooler or warmer area

Discuss further management and disposition with CICU/VAD attending

NO

Treat per ACLS protocol, except: **No chest compressions, defibrillation, cardioversion, pacing or epinephrine**[1]

Treat for cardiogenic shock

NO

Flashing Yellow Alarm (with intermittent 3-beep alarm)
OR
Solid Red Alarm (with continuous loud alarm)

YES

Move to that algorithm

Back-up equipment arrived to STS (Would be brought by VAD coordinator or CICU doc)

[1]The SynCardia total artificial heart has replaced the native ventricles and most of the atrium of each side. Therefore, there is no indication for chest compressions, defibrillation, cardioversion, pacing or epinephrine. Medications will NOT change heart rate or augment contractility. However, fluids for preload and medications for afterload/systemic blood pressure may be indicated. Remember, systemic blood pressure that is too high will prevent cardiac output. Maintain SBP < 140 mmHg.

Solid RED Alarm: FAULT ALARM

On the Freedom Driver, the red visual alarm indicator will be solid red and you will hear a continuous screeching audible alarm.

This means that there a problem with the: (1) patient, (2) drivelines or (3) Freedom Driver. Driver problems include malfunction of driver, battery(s) with less than 30% charge, or external power connected without at least one correctly inserted onboard battery. You must follow these steps:

Call VAD coordinator, have ESR page CICU attending and VAD attending – (ALWAYS 1st STEP)

What if TAH stops? If the SynCardia TAH stops pumping there will be no flow to either lungs or systemic circulation. Need to immediately switch patient to BACKUP Driver unit. Remember, as noted below, epinephrine, chest compressions, defibrillation will NOT fix this problem.

Assess and manage patient for medical/cardiac illness

Is TAH functioning?
Auscultate left lower chest to evaluate:
(1) opening and closing of mechanical valves
(2) sound of the driver moving air
If TAH not functioning, you will hear NOTHING!

YES

NO

Back-up equipment arrived to STS (Would be brought by VAD coordinator or CICU doc)

Patient stable?

Correctly install batteries and external power supply (see picture guide)

NO

Does Driver have 2 power supplies?

(2 charged batteries –or– 1 charged battery and external power supply)

YES

NO

YES

If BP is low and CO is low, then:
(1) Have patient relax/interrupt Valsalva maneuver
(2) Check for kinks or disconnects in drivelines and fix if applicable
(3) NS bolus

If BP is high and CO is low, then:
(1) Manage systemic HTN in coordination with VAD team

Check patient BP and CO reading on Driver

Treat per ACLS protocol, except: **No chest compressions, defibrillation, cardioversion, pacing or epinephrine**[1]

Treat for cardiogenic shock

Malfunction of Driver

Switch to Backup Freedom Driver
(see picture guide AND *discuss with VAD team by phone if not present*)

Discuss further management and disposition with CICU/VAD attending

[1]The SynCardia total artificial heart has replaced the native ventricles and most of the atrium of each side. Therefore, there is no indication for chest compressions, defibrillation, cardioversion, pacing or epinephrine. Medications will NOT change heart rate or augment contractility. However, fluids for preload and medications for afterload/systemic blood pressure may be indicated. Remember, systemic blood pressure that is too high will prevent cardiac output. Maintain SBP < 140 mmHg.

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Transfusion Rationalization on Pediatric Ventricular Assist Devices

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Iron deficiency and anemia are extremely common comorbidities in patients with heart and/or kidney failure and inflammatory states, as well as childhood growth and blood loss. These factors are common denominators in children supported with ventricular assist devices (VADs). Clinically, despite already known effects on oxygen carrying capacity, iron depletion can reduce exercise capacity and quality of life and should be treated, even in absence of anemia. Iron deficiency and anemia in hospitalized children are further affected by poor nutritional balance and blood loss. For example, frequent phlebotomy for laboratory sampling can significantly impact neonates and infants' hemoglobin levels. Studies suggest that children can tolerate $0.25ml \cdot kg^{-1} \cdot day^{-1}$ of blood sampling without a fall in hematocrit, hence sampling should be tailored to child needs balancing the net result of multiple samples and blood wasted daily.

Transfusion thresholds and the impact of excessive blood transfusions are becoming a more frequent topic of debate. Data is lacking on optimal transfusion thresholds, as are strategies for blood sparing in children with VADs, where viscosity and shear stress can affect pump function and risk of thrombosis. Patient blood management programs and early establishment of transfusion thresholds, although well recognized and appreciated in the adult setting, are yet to become a standard of care in the pediatric patient population.

ACTION REVISED DATE: 10/28/24

OBJECTIVES

To review strategies for minimizing blood loss, while optimizing transfusion thresholds in pediatric patients supported with VADs in a broad, yet individualized approach.

PROTOCOL

1. Establish lower thresholds for transfusion (first 1-2 weeks post implant):

If patients' clinical markers of oxygen delivery and extraction are preserved in the context of adequate hemostasis, hematocrit is targeted based on patients' individual needs, using laboratory and clinical context such as: mixed venous saturation with an appropriate extraction ratio obtained from an upper extremity central venous line (if feasible), near-infrared spectroscopy (NIRS), arterial saturation and oxygen requirements, adequate end-organ function, or signs of exacerbated heart failure.

a. Biventricular physiology: Hematocrit of 25 or greater (suggested)
b. Univentricular physiology: Hematocrit of 30 or greater (suggested)
c. Multidisciplinary approach to establish transfusion thresholds for other blood products in the context of individual needs and according to hemostasis management algorithm used.

2. Micro-nutrient supplementation (1-2 weeks post implant, if not yet initiated):

a. Iron, reticulocytes, and hemoglobin studies:
    i. If iron stores are inadequate, it is suggested to start iron supplementation at 6 mg/kg/day of **elemental** iron. Iron absorption is best in the acidic gastric environment and, although iron can cause gastrointestinal discomfort, administration of antacids, milk and calcium can impair its absorption and should be (ideally),withheld until 1 hour before or 2 hours after an iron dose. Some pediatric formulas contain iron and vitamin supplementation, and additional supplemental iron dosing should be adjusted to the total daily dose target. Careful attention should be given to iron storage tests in the setting of hemolysis, as iron supplementation can lead to iron overload and hepatic dysfunction. In severe cases

of iron deficiency and GI intolerance, iron infusions can be administered according to patient needs.

ii. Intravenous Iron:
Contraindications: Significant active infection, history of anaphylaxis with IV iron.

- Results are superior when used with lower baseline ferritin and with concurrent use of erythropoietins as marrow stimulating agents (ESA).

$$\text{Total replacement dose (mg of iron)} = 0.6 * Wt\ (kg)\left(100 - \frac{Hg\ (actual)}{Hg\ (ideal, e.g. 12)} * 100\right)$$

- Usual preparations include Venofer™ (iron sucrose) and Injectafer™ 9 (Ferric carboxymaltose). Institution-specific formulations can be considered. Most studies report maximum doses of IV iron as 200mg per infusion of iron sucrose and 1000mg per infusion of ferric carboxymaltose.
- Routine pre-medication is not required (consider pre-medication if atopic history). Slower infusion rates decrease adverse event risk.

Monitoring: HR, BP, O2 Sat every 15 minutes. Less than 1/200,000 infusions will result in serious adverse event. Common issues with administration include: *muscle cramps, nausea/vomiting, headache, dyspnea, extravasation, fever, blood pressure changes*. Risk of anaphylaxis is low.
Follow CBC, reticulocyte count, ferritin, iron panel pre-dose and at a minimum of 1 and 4 weeks after administration, and then monthly.

b. Folic acid level, B12, and B6 levels: Folic acid is essential for DNA synthesis and erythrocyte membrane stability. It is sometimes supplemented to facilitate erythropoiesis. Folic acid and Vitamin B12 also aid in the treatment and balance of hyperhomocysteinemia together with other B vitamins.
c. Other vitamin levels, along with an assessment of micronutrient status, can aid in absorption of iron (example Vitamin C).

3. Erythropoietin (EPO) supplementation (1-2 weeks post implant):

Erythropoietin is produced by the kidney and can be affected by renal dysfunction/injury, inflammatory states and other medications (especially chemotherapy and theophylline). Consider starting in accompaniment with iron and folic acid supplementation and, ideally, after ensuring iron storage levels adequate. Studies have shown a potential increase for thrombotic events in adult population thought to be secondary to increased viscosity and non-specific thrombopoietin effect sometimes causing an increase in platelet count. Studies in pediatric patients are limited and report conflicting results.

A retrospective single-center study (Hughes et al., 2022) found no clear association between epoetin alfa use and increased thrombotic risk, though variability in clinical practice was noted, underscoring the need for further prospective evaluation. Similarly, a multicenter analysis (Dillon et al., 2024) found that erythropoietin use was associated with reduced transfusion requirements but remained independently associated with an increased risk of stroke during VAD hospitalization.

Anecdotally, several pediatric VAD centers have implemented regular use of erythropoietin stimulating agents (ESA) without clear evidence of increased thromboembolic events. More data is needed to analyze the effect of blood product sparing and thromboembolic episodes in relationship to use of ESAs.

Some centers measure erythropoietin level prior to supplementation. This can be done in conjunction with the hematology team. If hemoglobin is low, then supplementation is started. Other centers start

ESAs empirically based on the assumption of ongoing baseline hemolysis and need for transfusions. Once ESA started, one should carefully verify ESA dose-response, potentially using rate of hemoglobin (Hgb) increase over time. If rapid increase in Hgb (ex: greater than 1g/dL in any 2-week period), consider decreasing ESA dosing by 40-50%.
Suggested ESAs and dosing:

a. Epogen 50-100 Units/kg IV two to three times per week (MWF)
b. Darbepoetin 0.45-0.8 mcg/kg/dose IV weekly

Caution: Please monitor for thrombosis in the context of ESA supplementation when platelet counts increase over 450,000. Consider stopping ESA and resume once platelet counts below 300,000. Monitor for hemolysis throughout. Would also be cautious if on the ASA-sparing ACTION protocol for HeartMate3.

4. Hemolysis tests: CBC, direct and indirect bilirubin, LDH, plasma free hemoglobin:

These tests can be done periodically to monitor for hemolysis. Most patient hemolyze down to a nadir and then stop, which is usually in the range of a hematocrit of 25-35. Anecdotally, hemolysis complications have been more significant with single ventricle physiology patients. Interventions may include:

a. Decrease diuresis and prevent hemoconcentration
b. Check for possibility of transfusion reaction
c. Check for immune mediated or cold-agglutin-mediated hemolysis due to medications or infections
d. Rule out pump thrombosis
e. Trial of pulse steroids in inflammatory states and treat suspected clots (please refer to ACTION steroids harmonization document)
f. Ensure adequate afterload reduction to minimize turbulent flow and shear stress
g. If paracorporeal support: exchange pump to a larger pulsatile device, maintaining cardiac index with a lower ejection rate
h. Change to a continuous flow VAD
i. Review cannulation technique and site. Consider checking grafts with CT scan if appropriate.

5. Judicious laboratory frequency (2 weeks post implant):

When patient is stable, laboratory frequency can be adjusted to minimize blood loss by phlebotomy.

a. Cohort blood sampling to once or twice weekly, if possible, to minimize blood draws, with exception of your chosen method of anticoagulation (at discretion of institutional preference), such as monitoring for bivalirudin, heparin, or enoxaparin effect.
b. Blood sampling techniques: if feasible, minimize waste of blood sampling by considering revising techniques, such as waste-free “push and pull” technique or point-of-care tests with nursing leadership.
c. Explore using pediatric minimum sample volumes per institutional practice and batch sampling to optimize sample usage
d. In case of “out of range” anticoagulation goal test results, institute a practice guideline with your local team (for example: early warning of established “out of range” results, repeat sample with adequate technique, prevention of sampling contamination, STAT laboratory test execution) in the context of clinical assessment of the patient at bedside (ex: addition of hepzyme test to verify aPTT contamination by heparinized lines, reminders of timely testing for bivalirudin aPTT samples).

6. Surveillance and treatment of bleeding:

Please refer to *ACTION Bleeding protocol*.
If significant or major bleeding, consider investigation for innate or acquired factor related deficiencies and conditions, such as Factor V, Factor VII, von-Willebrand family, angiodysplasia, or arterio-venous malformations.

Tests: consider more frequent surveillance of diagnostic studies and adequate anticoagulation accordingly. TEG or ROTEM could be a valuable surveillance tools for propensity of bleeding (TEG: R>20 or 25 min and MA<40 mm; ROTEM INTEM CT >300, HEPTEM CT >210 sec, EXTEM A10 <35 mm, FIBTEM A10 <9 mm) and should be correlated in the context of other tests of heparin or bivalirudin effect and other clinical scenarios (example sepsis and DIC).
As per previous published literature TEG platelet mapping (TEG/PM) is not recommended to be used to guide antiplatelet therapy. Baseline TEG is only used to assess baseline values such as R and MA to give a more general guidance for anticoagulation and initiation of antiplatelet use. Once initiated antiplatelet are increased by protocol.

Treatment: consider revisiting anticoagulation goals and anti-platelets. Establish temporary transfusion thresholds during bleeding events according to severity.

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WEANING and EXPLANT Protocol for Pediatric VADs

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Reverse remodeling and remission from heart failure are possible on VAD support, and explantation of VADs due to improvement in myocardial function can be achieved. Optimization of heart failure therapies to facilitate reverse remodeling, surveillance for improvement in myocardial function, and assessment of response to decreases in VAD support are essential to identify children who may be candidates for VAD explant.

ACTION REVISED DATE: 6/21/2024

OBJECTIVES

- Describe a systematic approach to screening pediatric LVAD recipients for evidence of remission from heart failure
- Characterize a regimen for weaning & optimization of LVAD support for both pulsatile and continuous flow pediatric LVADs
- Describe off-pump testing protocols that can safely provide information about myocardial performance off VAD support
- List objective criteria that may help identify patients in whom a VAD explant may prove successful

PHILOSOPHY

- Remission from heart failure definition: Freedom from the symptoms of heart failure (e.g. normalization of breathing, feeding, activity tolerance) and normalization of end-organ function attributable to recovery of ventricular function.
- All patients with VAD should be considered candidates for remission from heart failure and possible VAD explant by default, until clinical trajectory is properly characterized
    - *A priori* designation of a patient as a "remission candidate" leads to a higher incidence of remission from heart failure on VAD support[1]
- Timing of Listing for Transplant
    - Consider delaying listing or making Status 7 for transplant for 3 months after intracorporeal continuous flow VAD placement to allow time to evaluate for potential remission from heart failure
    - For patients on paracorporeal pulsatile VAD support, consider surveillance evaluations below while patient is listed & awaiting transplant to assess for possible remission from heart failure
    - Signs of possible remission: increasing LV ejection fraction (LVEF), decreasing LV end-diastolic dimension (LVEDD), decreasing LV end-diastolic volume (LVEDV)
    - Remission seen – continue without listing or as Status 7 in discussion with patient, VAD & transplant team while sustainability of remission is explored
    - Remission not seen – proceed to 1A listing in discussion with patient, VAD & transplant team

PROTOCOL

1. Resuscitation / Recovery Phase (Implant – ~3 Months Post-Implant)
    a. Incorporation of Reverse Remodeling Therapies

Phase	Goals	Medications to Incorporate
Post-op / Acute	Hemodynamic stability Relief of heart failure symptoms Recovery of end-organ injury VAD RPM optimization Decongestion	Diuretics as needed for decongestion • Aim for absence of congestive symptoms (tachypnea, abdominal pain/nausea/splanchnic congestion, extremity edema) • Pulsatile VADs filling no less than 80-90% ACE-I / ARB / ARNI • Once off inotropes, start and begin slow uptitration
Convalescent / Pre-discharge	Continued VAD optimization Incorporation of additional goal-directed therapies	ACE-I / ARB / ARNI • Titrate to maximum tolerated dose for goal blood pressure according to age and goal established by medical team β-Blocker • Initiate and uptitrate to goal HR according to age and goal established by medical team Spironolactone / Eplerenone • Initiate and uptitrate for K < 5 Nutritional Optimization • Check and replete iron stores • Supplement Vitamin D levels if inadequate • For additional nutritional optimization recommendations, refer to ACTION VAD Nutrition Harmonized Protocol
Maintenance / Home therapies	Optimization of reverse-remodeling therapies towards goal	Optimization of ACE-I/ARB/ARNI, β-blocker, spironolactone/eplerenone to goal doses as tolerated Dapagliflozin – consider initiating per center protocol if using Digoxin • Can consider digoxin. Initiate at 5-10 mcg/kg/day • Monitor every 4-6 weeks for toxicity or more frequently if potassium derangements and / or signs suggestive of toxicity

    b. Suggested Heart Failure Medication Target Dosing
        i. See ACTION Duchenne Muscular Dystrophy Therapy and Heart Failure Medication Optimization Harmonized Protocols for suggested incorporation / uptitration of oral remodeling therapies
        ii. Individual patient regimens must be tailored to patient responses and tolerance
        iii. Medication doses may need to be adjusted for renal dysfunction, blood pressure response, other side effects
    c. Surveillance for Remission from Heart Failure
        i. Echocardiograms
            1. Once per week for at least the first 2 weeks
                a. Assess decompression of LV on VAD support

b. Aortic valve may continue to open

ii. Subsequently once every 2-4 weeks
1. Assess for continued decompression
2. See ACTION Echocardiography Protocol for full details of echo assessment of VAD
a. Minimum assessment requires LV EF (or at least qualitative description of LV systolic function if unable to quantify ejection fraction), RV function, LVEDD and Z-score, LVEDV, native valve function / insufficiency (especially aortic valve)

iii. Laboratory (while inpatient)
1. BNP or NT-proBNP – weekly
2. End-organ function every 1-2 weeks

iv. Functional assessments (continuous flow VADs)
1. 6-minute walk test to establish baseline
a. Weekly post-VAD until discharge, then at 1 month, 3 months, and 6 months post-implant

d. LVAD Management
i. Goal: Left-heart decompression
ii. Maintain higher LVAD RPM to limit myocardial wall stress, decongest left heart, provide BP support for incorporation of reverse-remodeling therapies
iii. However, LVAD RPM increases may be limited by right heart function, interventricular septal shift, worsening tricuspid regurgitation, etc

2. Loading / Evaluation Phase (>3 Months Post-Implant)

a. Surveillance for Remission from Heart Failure
i. Echocardiograms
1. Continue monthly echocardiograms
2. Should improvement in LV function be seen, consider RAMP study / RPM change echo (continuous flow VADs)
a. Suggested schedule: Approximately every 1-3 months with outpatient clinic visits, especially when weaning of VAD flows is taking place
b. Protocol: See ACTION LVAD RPM Optimization / RAMP TTE Protocol
i. Total decrease in RPM should be no more than 200 RPM for HeartWare (HVAD). Minimum RPM: 1800 RPM
ii. Total decrease in RPM should be no more than 400 RPM for Heartmate 3 (HM3) devices. Minimum RPM: 4000 RPM

ii. Laboratory
1. BNP or NT-proBNP – at least monthly
2. End organ function – at least monthly

iii. Functional assessments (continuous flow VADs)
1. 6-minute walk testing
a. Suggested schedule: at 1 month, 3 months, and 6 months post-implant at time of outpatient clinic visits
b. After VAD RPM change, would also repeat 6-minute walk test at next clinic visit to assess functional response to RPM change
2. No more than mild malnutrition by ASPEN guidelines[2]

b. LVAD Management & Myocardial Loading
i. If following criteria met, consider weaning LVAD RPM
1. Resolution of heart failure symptoms
2. Demonstration of increasing LV EF, decreasing LVEDD/LVEDV, no more than mild mitral insufficiency on serial echocardiograms
3. Stable or normal right heart function
4. Downtrending or normalized BNP / NT-proBNP

5. Patient anticoagulation therapeutic at time of encounter

ii. LVAD RPM wean
   1. Consider weaning HVAD by 40-100 RPM per encounter (~monthly)
      a. Note: for HVAD patients, ensure trough on new RPM is >2 L/min given increased risk for thrombosis as troughs approach 0 L/min
   2. Consider weaning HM3 by 100-200 RPM per encounter (~monthly)
   3. Testing at new RPM
      a. Perform VS, echo
      b. Lower RPM and repeat VS, echocardiogram
      c. If no change in patient symptoms, VS, echo, consider leaving VAD at new lower RPM
         i. Note: for HVAD patients, ensure trough on new RPM is >2 L/min given increased risk for thrombosis as troughs approach 0 L/min
         ii. As above, consider repeating 6-minute walk testing at clinic visit following a RPM change

3. Interrogation Phase Pre-Explant: Myocardial Function & VAD RAMP Cath Study

a. Suggested schedule
   i. First cath within the first 6 months of VAD placement (option if no signs on recovery)
   ii. Can consider serial hemodynamic assessments while loading and assessing potential for explant

b. Pre-Cath Logistics / Planning:
   i. Establish indication for catheterization:
      1. VAD optimization (“RAMP” study)
      2. Assess for remission from heart failure (“off-pump” study)
   ii. Any additional assessment or intervention required? Examples: coronary angiography, angiography for baffle leaks/obstruction, collateral assessment, etc
   iii. If anticipated intervention, have they had recent dental exam within 3-6 months? (poor dental health may place patient at increased risk of infection of any prosthetic material)
   iv. Review vascular access – may need vascular ultrasound prior to procedure
   v. Review anticoagulation – continue medication until day of procedure unless supra-therapeutic
   vi. Determine mode of echo imaging: TEE vs TTE
   vii. Notify all necessary teams that need to be available: Imaging, HF, VAD coordinator, CV surgery
   viii. Check labs within 1 week of study
      1. Optimize hemoglobin if necessary
      2. Ensure anticoagulation within target range

c. Day of Cath Logistics:
   i. Hold anti-hypertensives
   ii. Consider holding warfarin and aspirin the morning of the procedure depending on VAD type
   iii. Routine VAD labs: serum chemistry, CBC, LDH, plasma free hemoglobin, BNP/NT-proBNP, INR
   iv. Planning: Cath team
      1. Communicate with cath team regarding anticipated RPM changes and what hemodynamic measurements should be recorded during case
      2. Leaving a Swan-Ganz catheter in place during the cath (as opposed to using a balloon-wedge) significantly aids in obtaining hemodynamic data quickly
   v. Anesthesia plan
      1. Discuss with anesthesia whether general anesthesia vs conscious sedation is planned. Significant vasodilation during the case could make interpretation of

hemodynamics difficult. Ideally catheterization would be performed with patient sedated but breathing spontaneously to mimic as closely as possible the physiology in the awake state

2. Discuss with Anesthesia regarding importance of communicating initiation of vasoactive agents during case as this will affect interpretation of data

vi. Monitoring

1. Blood Pressure and Heart Rate Monitoring:
    a. Discuss with Anesthesia regarding monitoring of BP and goal BP- arterial line versus Doppler MAP
    b. If obtaining arterial access, see if Doppler MAP correlates
    c. Unexplained sinus tachycardia, similar to pre-implant, may be a subtle sign any changes made during cath are not well-tolerated
    d. Ensure rhythm is the same throughout case, as different rhythms at different times could affect interpretation of hemodynamics
2. VAD Monitoring:
    a. VAD parameters including VAD waveform or PI should be monitored
    b. Obtain images of VAD monitor at various RPMs (pre and post at a minimum)
    c. For HVAD, avoid adjusting RPM to where trough is approaching 0 or suction present on waveform
3. Additional Monitoring
    a. Near-infrared spectroscopy (NIRS) may additionally be used for monitoring tissue oxygen delivery throughout the procedure

d. Imaging Assessment:

i. Establish with imaging team regarding what parameters will be monitored throughout the case

ii. See supplemental tables at end of protocol for suggested echo data to be collected

e. **Cath assessment – Continuous Flow VADs**

i. Obtain baseline hemodynamics via right heart cath (see supplemental table at end of protocol for recording hemodynamics), record baseline echo parameters

ii. Heparin 50 units/kg or max dose of 5000 units should be given prior to first RPM change

1. Monitor ACT throughout case and maintain >250 with repeat heparin bolus if needed

iii. If acceptable baseline hemodynamics and patient anticoagulated, decrease RPM by 40 RPM (HVAD) / 100 RPM (HM3)

iv. Wait 10-15 minutes between RPM changes before reassessing hemodynamics and repeating imaging

v. Can repeat steps iii & iv to incrementally decrease LVAD RPM (during VAD optimization study). If performing “off-pump study”, VAD RPM should be gradually decreased to 1800 RPM (HVAD) / 4000 RPM (HM3) – net “zero” flow through VAD to assess myocardial performance “off-pump”

vi. At end of case, VAD RPMs should be set to the optimum RPM identified during cath (RAMP study) or back to baseline (off-pump study)

f. **Cath assessment – Pulsatile VADs**

i. Caution: It is important to recognize that prolonged pump stoppage and operation of the device at lower beat rates are not recommended because of the risks of blood stagnation and thrombus formation.

ii. Suggested trial steps below can be done over several days, with non-invasive assessments on days 1-4 and cath on day 5

1. Heparin 50 units/kg or max dose of 5000 units should be given prior to any rate change

2. If acceptable baseline hemodynamics and patient anticoagulated, decrease Berlin rate

iii. In addition to suggested weaning protocol below, other Berlin weaning protocols have been published by Miera et al[3] and Berlin Heart[4] and may also serve as helpful guides

iv. Cath assessment (Day 5 of protocol below)
   1. Heparin 50 units/kg or max dose of 5000 units should be given prior to first rate change
   2. If acceptable baseline hemodynamics and patient anticoagulated, decrease Berlin rate
   3. Monitor ACT throughout case and maintain >250 with repeat heparin bolus if needed
   4. Duration of VAD pause
      a. Durations mentioned below are for 10 & 15 mL pumps
      b. For 25 & 30 mL pumps, the duration of pause is 10, 15, and 30 minutes for Day 2, 3, and 4/5, respectively[4]
      c. A longer period of observation "off-pump" can be performed prior to explant – see "Alternative Timing" section below

Day of wean	VAD action	Parameters Monitored
Day 1	LVAD rate decreased by 50% for 30 minutes	• Vital Signs every 3 minutes • Continuous NIRS • Mental status • SvO2 measurement every 10 minutes • Echocardiogram every 10 minutes (suggested data to be collected in supplemental table at end of protocol)
Day 2	LVAD rate decreased by 75% or to 35 bpm (whichever was higher) for 30 minutes; following this, LVAD completely paused or a rate of 10 bpm for **3 minutes** **Important:** Pump has to be manually pumped to fill and eject every 10 seconds if paused.	• Same as Day 1 • SvO2 measurement q10 minutes and **at the end of pause.** • Echocardiogram every 10 minutes **and at the end of the pause**
Day 3	LVAD rate decreased by 75% or to 35 bpm (whichever was higher) for 30 minutes; following this, LVAD completely paused for **6 minutes** **Important:** Pump has to be manually pumped to fill and eject every 10 seconds	Same as Day 2
Day 4	LVAD rate decreased by 75% or to 35 bpm (whichever was higher) for 30 minutes; following this, LVAD completely paused for **10 minutes** **Important:** Pump has to be manually pumped to fill and eject every 10 seconds	Same as Day 2
Day 5- Right heart catheterization	LVAD rate decreased by 75% or to 35 bpm (whichever was higher) for 30 minutes; following this, LVAD completely paused for **10 minutes**	Same as Day 2 with hemodynamic measurements in catheterization (see supplemental table at end of protocol)

	• **Important:** Pump has to be manually pumped to fill and eject every 10 seconds	

v. Cath assessment – Alternative Timing
   1. A longer period of observation "off-pump" can be performed prior to explant
   2. Anticoagulation
      a. Heparin 50 units/kg or max dose of 5000 units should be given prior to first rate change
      b. Monitor ACT throughout case and maintain >250 with repeat heparin bolus if needed
      c. Thorough inspection of Berlin at baseline and every 15 minutes while pump stopped to assess for development of any clot / fibrin, which would be an indication to stop test
   3. Recommended Timing
      a. Baseline hemodynamics (see supplemental table at end of protocol)
      b. If acceptable baseline hemodynamics and patient anticoagulated, decrease Berlin rate by 50% for 5 minutes
      c. If acceptable hemodynamics, pause Berlin and perform off-pump hemodynamics. **Important:** Pump has to be manually pumped to fill and eject every 10 seconds
      d. If stable, continue off-pump trial with data collection at 15 and 30 minutes. Trial can be extended to 45 or 60 minutes if additional data needed

4. Assessing Suitability for Explant
   a. Explant criteria to consider (adapted from adult studies - Dandel et al[5], RESTAGE-HF trial[6])
      i. Functional status
         1. Resolution of failure to thrive and other signs of chronic heart failure
         2. Max VO2 > 16mL/kg/min on cardiopulmonary exercise testing (if performing)
      ii. Echo with VAD at lowest RPM for at least 15 minutes
         1. LV end-diastolic dimension Z-score <+2 standard deviations, or <60mm (adult-size patients)
         2. LV end-systolic dimension Z-score <+2 standard deviations, or < 50mm (adult-size patients)
         3. LVEF ≥45%
         4. No more than mild aortic or mitral insufficiency
      iii. Cath with VAD at lowest RPM for 15 minutes (1800 RPM HVAD, 4000 RPM HM3)
         1. LVEDP / PCWP < 15mmHg
         2. CI ≥2.4 L/min/m^2
         3. Other hemodynamics acceptable during off-pump trial
      iv. Right Ventricle
         1. No worsening of RV function following LVAD implant and during LVAD weans / off-pump trial(s). Also, take note of tricuspid regurgitation.
      v. Rhythm
         1. Sinus or A-V synchronous rhythm
      vi. Sustained decrease in BNP/NT-proBNP from initial level post-implant

5. Post-Explant Surveillance
   a. Post-explant pharmacologic therapies
      i. Continue all reverse remodeling therapies for at least 12 months after explant, most data supports GDMT indefinitely.
   b. Functional and Echo assessments: Suggested schedule: weekly for 2 weeks then biweekly for a month followed by monthly for six months

c. Consider cardiac catheterization at 3-6 months post-explant if function has not normalized, or sooner if function has declined or there is return of heart failure symptoms / end-organ dysfunction

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NOTE

This protocol represents consensus recommendations based on industry and institutional protocols, as well as literature from adult clinical practice. Any treatment plan must be individualized and made taking into account a patient's unique characteristics, clinical data, and institutional expertise.

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VAD RAMP Hemodynamics – CF VAD

Name: Date: BSA:

Assumed VO2: Hemoglobin:

		Baseline	RPM	RPM	RPM
VAD	Speed (RPM)				
	Flow (L/min)				
	Power (W)				
	Amplitude (HVAD) PI (HM3)				
Hemodynamics	MAP (mmHg)				
	CVP (mmHg)				
	RVEDP (mmHg)				
	PA (S/D/M) (mmHg)				
	PAPi				
	Wedge (mmHg)				
	TPG (mmHg)				
	PVR (WU x m^2)				
	Mixed Venous / Systemic Sat (%)				
	CI (L/min/m^2)				
	Lactate				
Echo	AoV Opening?				
	Septum Position				
	LVEDD (mm)				
	LV EF (%)				
	AoV/MV/TV regurg				
	TAPSE (mm)				
	RVEDD (mm)				
	RV function				

VAD RAMP Hemodynamics – Berlin

Name: Date: Assumed VO2: Hemoglobin: BSA:

		Baseline	½ Support	Off Pump	Off Pump	Off Pump	Off Pump	Off Pump	Off Pump
Support (vasoactives, O_2, iNO, etc)									
VAD	Rate (BPM)			0	0	0	0	0	0
	Output (L/min/m^2)			N/A	N/A	N/A	N/A	N/A	N/A
	Time Off Pump (min)	N/A	N/A	5	15	30	45*	60*	
Hemodynamics	Heart Rate (BPM)								
	SPB/DPB/MAP (mmHg)								
	CVP (mmHg)								
	RVEDP (mmHg)								
	PA (S/D/M) (mmHg)								
	PAPi								
	Wedge (mmHg)								
	TPG (mmHg)								
	PVR (WU x m^2)								
	MV / Systemic Sat (%)								
	CI (L/min/m^2)								
	Lactate								
Echo	LVEDD (mm)		X		X				
	LV EF (%)		X		X				
	AoV/MV/TV regurg		X		X				
	TAPSE (mm)		X		X				
	RVEDD (mm)		X		X				
	RV function		X		X				
Gas	pH		X						
	pCO_2		X						
	pO_2		X						

*If using these timepoints

PART TWO

Heart Failure

SECTION

CardioMEMS™

CardioMEMS™ Protocol

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Decompensated heart failure in pediatric and adult patients leads to an increase in hospital admissions. Recent technologic advances have led to an implantable wireless device, CardioMEMS™, that allows frequent filling pressure monitoring and subsequent medication titration. This has now become a tool to direct heart failure management.

ACTION REVISED DATE: 08/21/24

OBJECTIVES

To provide an overview of CardioMEMS™ implantation and management.

PROTOCOL

PATIENT SELECTION

All heart failure patients, including those with ACHD, may be considered for CardioMEMS™ implantation.

Patient selection criteria:

Diagnoses:

- Patients with DCM with systolic dysfunction and symptomatic heart failure
- Patients with HCM or RCM and symptomatic heart failure
- Congenital heart disease with symptomatic failing physiology
- Heart transplant graft vasculopathy with symptomatic restrictive physiology

Indications based on 2022 FDA expanded use:

- Patients with at least NYHA Functional Class II heart failure
- At least one heart failure hospitalization in the past 12 months and/*or* elevated natriuretic peptide level
- Fluid status difficult to manage, as determined by care provider

The following patients may not be appropriate for implantation of the CardioMEMS™ system:

- Distal branch PA diameter <7mm or >10 mm at the target implantation site
- Chest asymmetry (pectus, scoliosis)
- GFR ≤25 ml/min/1.73m2
- BMI >35 kg/m^2 or chest circumference >165 cm
- History of non-adherence
- Known coagulation disorder or inability to tolerate dual antiplatelet or anticoagulation therapy
- Patients with implantable loop recorder on the same side as the target vessel
- History of recurrent (>1) pulmonary embolism or deep vein thrombosis
- Consider if appropriate if there is a PT stent.

PRE-IMPLANTATION

Assess that there is adequate program staffing to support close, frequent follow-up with patient and data review.

Education consult with CardioMEMS™ Healthcare Provider:

- Discussion of CardioMEMS™ procedure, device, and pillow
- Discuss anticoagulation and medications to hold prior to procedure

- Provide CardioMEMS™ infographic and brochure
- Provide myCardioMEMS™ smartphone app

Diagnostic studies prior to CardioMEMS™ implantation:

- Consider CT angiogram or MRI of chest to assess branch PA size in patients <18 years of age or those with CHD
- CBC, Renal Function, Brain Natriuretic Peptide (BNP), chest x-ray within 30 days of implantation
- If HF team not involved already, consider consulting the HF team prior to implantation.

Scheduling and prior authorization:

- CardioMEMS™ team to submit cardiac catheterization request and notify Abbott representative.
- Complete Abbott CardioMEMS™ prior authorization form including patient demographics, insurance, and clinical justification. (See the prior authorization approval form attached) Of note, some insurance companies do not cover this sensor implant regardless of clinical history or lab values.
- Some centers may use the Abbott Patient Therapy Access Program to help with insurance approval. The Abbott Hotline is (855) 569-6430 ptahotline@sjm.com.
- Ensure insurance approval prior to implantation. If a patient is admitted to the hospital, approval for the procedure may be covered under the existing inpatient prior authorization.
- Notify Abbott representative of implantation date once insurance approval obtained.

IMPLANTATION (see implant procedure accessories product guide at end of document)

- Diagnostic Studies: CBC, Renal, BNP, INR (typically < 1.5 or at discretion of catheterization lab staff based on individual patient considerations).
- Obtain an accurate weight the day of procedure.
- Please see manufacturer IFU for official recommended implantation procedure and electronic system setup.
- Steps for implantation:
    1. Obtain venous vascular access (femoral or internal jugular) with a 12-French introducer sheath (or 11-French Terumo Pinnacle sheath).
    2. Perform a right heart catheterization (and left heart catheterization, if indicated) with complete hemodynamic assessment.
    3. Perform a pulmonary artery angiogram in order to evaluate vessel course and diameter.
        a. A target vessel that is located posteriorly, within a lower lobe of either lung, and with a diameter of 7-10mm is optimal.
    4. Either the existing vascular sheath or a 12-French long sheath (such as a Cook Flexor sheath) can be utilized to introduce the device. A long sheath can be helpful in tortuous anatomy, such as that of patients with an atrial switch operation, or following concomitant pulmonary artery stent implantation, but is not necessary in all cases.
    5. A 0.018-inch wire should be anchored in the target vessel. An Abbott Steelcore wire can be used.
    6. Agitate the device in saline for 60 seconds.
    7. Advance the delivery catheter through the sheath and over the wire into the target branch.
    8. If a long sheath is utilized for delivery, additional angiograms can be performed to confirm device position.
    9. Release the device by unscrewing the cap on the delivery catheter, and then by retracting and removing the wires from the catheter.
    10. Calibrate the device using the Hospital Electronics System (HES) placed under the patient's back, while performing a directly measured pulmonary artery pressure within the same vessel with an end-hold catheter. While patients with Fontan physiology have non-pulsatile flow, the system still calibrates using the equivalent of systolic and diastolic values (as opposed to atrial A and V waves). The system calibrates using a 10-second average leading up to data

input. If patient is intubated, consider a breath hold to limit effects of respiratory variation during calibration.

POTENTIAL ADVERSE EVENTS

- General cardiac catheterization complications, i.e. bleeding, bruising, hematoma formation, infection
- Device migration
- Heart failure exacerbation related intra-procedure fluid administration
- Arrhythmias
- Device-related thrombosis

EARLY POST-IMPLANTATION

- Ensure post-catheterization documentation includes hemodynamic pressure; pulmonary capillary wedge pressure, pulmonary artery systolic, diastolic, and mean pressures, and CVP/RA pressure.
- CardioMEMS™ post-procedure handout provided to patient.
- Place baseline wedge pressure in Merlin.net (note any discordance).
- Add patient to CardioMEMS™ care team.
- Medication prescriptions/adjustments provided to patient
    - Clopidogrel and Aspirin PO daily x 30 days then will remain on Aspirin therapy (certain patients, i.e. Fontan, may require full anticoagulation with warfarin or alternatives)
    - May need adjustments to diuretic therapy.
- Consider longer observation course for pediatric patients.
- Chest x-ray the day following implantation to assess position or prior to discharge if discharged on the day of implantation

POST-IMPLANTATION FOLLOW UP

- Follow up phone call within one day of implantation.
- Inform patient to transmit daily CardioMEMS™ readings for 30 days.
- Daily weights to be recorded.

POST-IMPLANTATION CLINIC AND MONITORING

- 1-week post-procedure clinic visit.
    - Laboratory studies: Renal Profile, BNP
    - Assessment of catheterization site.
    - Set thresholds (typically 10mmHg increments).
    - Set up myCardioMEMS™ smartphone app (requires PA sensor serial number).
- Daily CardioMEMS™ readings for 30 days. Reassess established thresholds following 30 days of management. **Please see Post-Implantation Management algorithm.**
- Repeat labs (Renal, Profile, BNP) 30 days post-implantation and consider a 30-day appointment if frequent medication changes are being made.
- Close ongoing follow up; frequency to be dictated by clinical status.

BILLING: Remote Monitoring

- CPT 93264-Remote Monitoring Code
    - Weekly review for 30 days by physician or health care provider
    - Can only bill every 30 days – do not bill if not monitored for 30 days
    - Template for billing (Name, monitoring period, optimal PA pressures) attach the direct trend viewer
      SUMMARY: I utilized the remote monitoring platform (Merlin.net™ PCN) to set optimal targets for pulmonary artery pressure thresholds as part of acute and chronic management of patient's heart failure. During the period indicated above, I monitored the patient's pulmonary artery pressures weekly via trend analysis and notification reports which provide alerts when patient's PA

pressures were outside of range to prompt immediate action in medication changes and communications. The weekly reports are archived in the Merlin.net PCN system which serve as a parallel record to document weekly PA pressures, medication changes, and clinical notes. Included are the patient's transmission and trend analysis reports to support weekly management of pressures within optimal range.

- Educational clinic based visit pre implant
  - Acceptable templates for billing
    - I have spent 30 minutes face- to- face with Ms. X and her family, all of which was in counseling and coordination of care. We discussed…….
    - I have spent 30 minutes face to face with this patient and greater than 50% of this time was spent in counseling and coordination of care regarding……

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 04/28/2020)*

Implant procedure accessories

Procedure Accessory/F7	Options		Product Code
PA Catheter	7 Fr x 110 cm Swan-Ganz™ (SG) with (TD)	If thermodilution (TD) needs to be performed and use one catheter for access and all RHC measurements.	Edwards 131F7
	7 Fr x 110 cm Pulmonary Wedge Catheter	More steerable than SG and better angiogram. Pressures and Modified Fick CO can be measured – No TD.	Arrow AI-07127
			Medtronic 150075
Introducer Sheath	SJM Fast-Cath™, 12 Fr		406128
	SJM Ultimum™ EV, 12 Fr		407655
	Terumo Pinnacle™, 11 Fr		RSS101
	We encourage the use of .018" exchange length Hydrophilic Nitinol wires for the use of CMEMS implantation such as the CardioMEMS Guidewire.		
Delivery Guidewire Options	SJM, CardioMEMS™ Guidewire, 0.018" x 260 cm (Stiff Nitinol)		CM2010
	Covidien/EV3™, Nitrex™, 0.018"x300 cm (Stiff Nitinol)		N183002
	Cook Roadrunner™ 0.018" x 300 cm (Stiff Nitinol)		G07584

Swan-Ganz™ catheter is a trademark of Edwards Lifesciences Corporation.

Considerations for Advanced Heart Failure Consultation in Congenital Heart Disease (CHD) Patients: *Guidance for primary cardiologists*

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

To aid in and standardize decision-making on timing of referral of CHD patients for advanced heart failure consultation with the aim of harmonizing referral practices, improving timely referral and facilitating collaborative care to enhance patient outcomes.

Patient population: Two ventricle CHD patients

CONSIDERATIONS FOR REFERRAL[1,2]

Symptoms

1) NYHA Class 3-4 symptoms attributable to heart disease (pulmonary or systemic ventricle) despite optimal medical or surgical therapy

AND/OR

Clinical Events

1) > 2 admissions for heart failure in a 6-month period without a reversible cause
2) Any admission for heart failure that requires continuous inotropic therapy (even if only transiently required)
3) Life-threatening arrhythmias refractory to medical or surgical therapy

AND/OR

Evidence of end-organ dysfunction attributable to heart disease defined as:

1) Progressive liver disease attributable heart disease-related congestion despite optimal therapy
2) Patients with pulmonary hypertension with a potential risk of developing fixed elevation in pulmonary vascular resistance which might preclude future heart transplantation[3]
3) Adult patients with progressive cachexia or pediatric patients with refractory growth failure attributable to heart disease despite optimal therapy
4) Patients with progressive cardiorenal syndrome or with refractory hyponatremia (<130mmol/L) attributable to heart failure despite optimal therapy

[1] In adult patients, referral should be to a combined program including both ACHD and advanced heart failure providers

[2] In patients with a high probability of prolonged waiting list time such as those with high levels of allosensitization earlier referral should be considered.

[3] Particular monitoring of patients with a systemic morphologic RV

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Disclaimer: *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This referral guideline was developed as a consensus tool for general cardiologists. The information in the guideline is based on center practices, individual opinions, experiences, and, where available, published literature. Providers & centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that this is meant as a guideline and not as standard of care. (Revised: 02/06/2020)*

Fitness Assessment and Promotion in Pediatric Heart Failure: Stable Post-VAD and Heart Failure

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

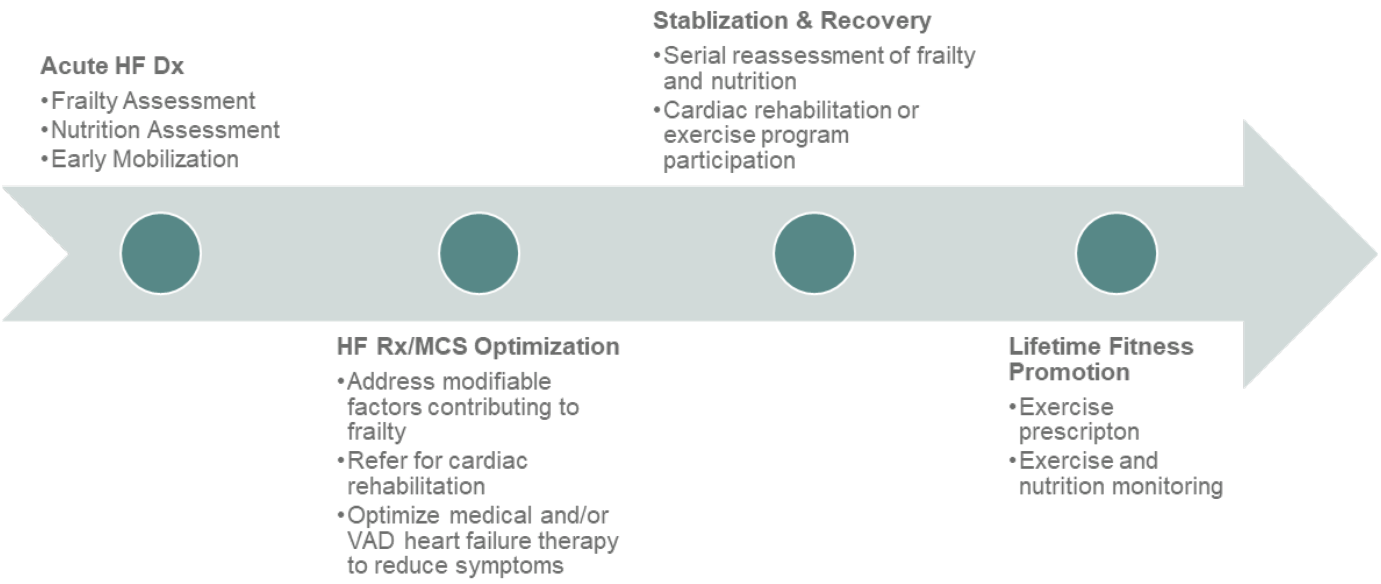
Due to disease severity in children and young adults with heart failure, patients are at risk for deconditioning and associated morbidity and mortality. Assessing the severity of deconditioning or frailty in children and young adults can be difficult due to lack of standardized assessment tools or guidelines. How to safely encourage and manage rehabilitation and exercise in these patients with heart failure, including VAD, is also challenging.

ACTION REVISED DATE: 03/06/2024

OBJECTIVES

Standardize physical fitness assessment and promotion in children and young adults with heart failure and stable ventricular assist device (VAD) support to maintain or improve functional fitness.

PROTOCOL



Section 1: Frailty Assessment

Frailty refers to the multisystem physiologic reserve and vulnerability to stressors and poor health outcomes. Frailty and poor fitness may compromise the success of advanced heart failure therapies.[1] Frailty consists of multiple components, and we present the following suggested framework (including suggested metrics that each have normative values in the pediatric population) recognizing the need for further validation in pediatric heart failure patients*:

1. Muscle Mass Assessment
    a. Mid-upper arm circumference (cm)
    b. Lean body mass (kg) per dual X-ray absorptiometry (DXA) or bioelectric impedance analysis (BIA)

2. Strength Assessment
    a. Hand grip strength (kg) per hand grip dynamometer
        -Recommended for ages ≥ 6 years old using published reference values (see table)

3. Speed and Sub-maximal Aerobic Capacity Assessment
    a. Six-minute walk test distance (m)
    b. Two-minute walk test distance (m) (if cannot complete 6MWT)
        -Can be performed as 3 years old with published reference values (see table)
    c. Aerobic capacity assessment (CPET)
        -For older patients (typically ≥7) with ability to perform more strenuous exercise assessment (described in Section 2)

4. Fatigue
    a. Patient and parent reported per questionnaires
        -PedsQL Fatigue Scale (includes pediatric and adult versions)
            -Parent report available as young as 2 years old
            -Patient report available as young as 5 years old

5. Functional Status
    a. Patient-reported per questionnaire: Pediatric Physical Activity Questionnaire (PAQ)
        i. PAQ-A Scale (age 14-20 years old)
        ii. PAQ-C Scale (age 8-14 years old)
    b. Device based assessments per accelerometry (either validated, research-grade accelerometer or commercially available devices such as Apple Watch or FitBit)
    c. Provider-assigned
        i. 5-15 years: Lansky Play-Performance Scale
        ii. >15 years: Karnofsky Performance Scale (KPS)
    d. Early mobility assessment tool (Boston AmPAC) – gauges independence with basic mobility skills in the early stages of a VAD and identify when a patient is now ‘functional’ to return to more vigorous exercise.

*Assessment of each Frailty component as being normal or abnormal should include use of normative z-score values when appropriate (with abnormal being outside ± 2 z-scores) or published normative cut-offs for questionnaires and scales.

Specific Frailty Metric Instructions

Mid-upper arm circumference (MUAC) can easily be measured and normalized using z-score tape One such tape is manufactured by Abbott with instructions shown below.

Abbott

Children's Mercy KANSAS CITY

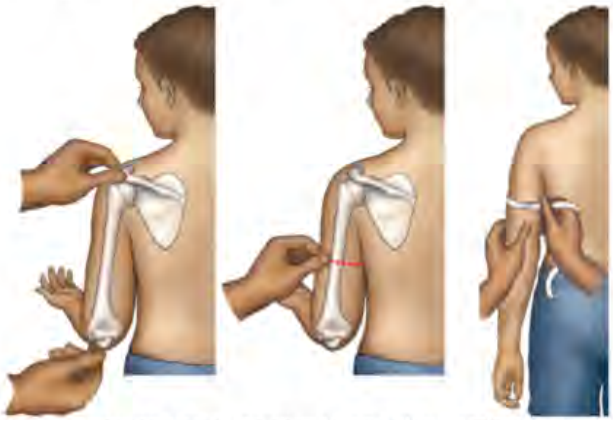
MUAC *Z*-Score Tape

INSTRUCTIONS FOR USE

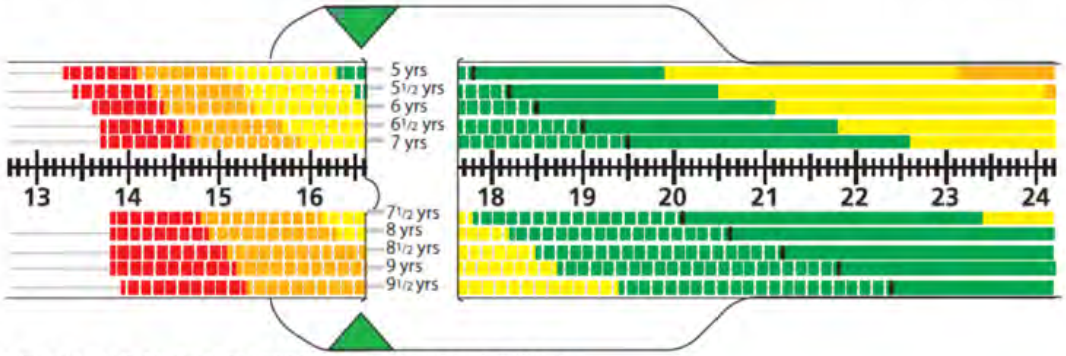
1. Your Mid-Upper Arm Circumference (MUAC) *z*-score tapes may arrive individually or in sets containing one 2-sided infant tool and one 2-sided child tool. If it comes as a set, you will want to separate the individual tapes.

2. Familiarize yourself with the key that orients you to the age group, the colors and the markings. Note that the 2 green arrow heads represent the zero-end of the tape measure, and this is where you read the patient's MUAC measurement and *z*-score. To measure, slide the tail end of the tape into slit "A" and back out through slit "B" to create a loop.

3. Identify the midpoint of the upper arm between the acromion and the olecranon process (between the shoulder cap and elbow) and slide the loop of the device up to the midpoint (the ruler on the tape can be used to assist with this process). You should make sure that the elbow is fully extended (in other words, that the arm is straight and hanging down at side) before measuring. Pull the tail end of the tape until it is snug but does not compress the skin to read the MUAC measure and *z*-score.



4. Identify the color band corresponding to the specific age of the patient. In the example below, the MUAC is 16.6 cm. This measure correlates the age-based MUAC in centimeters with nutrition risk categories based on the *z*-score, visually represented by color coded lines.



Example of MUAC *z*-score ranges when measured at 16.6 cm:

Age (yrs.)	MUAC *z*-score range	Risk classification
5	0 to -1	Normal
7	-1 to -2	Mild undernutrition
9	-2 to -3	Moderate undernutrition

Note: Your MUAC *z*-score tapes are for multi-use. Discontinue use if degradation occurs.

Reference table for *z*-score ranges on tape:

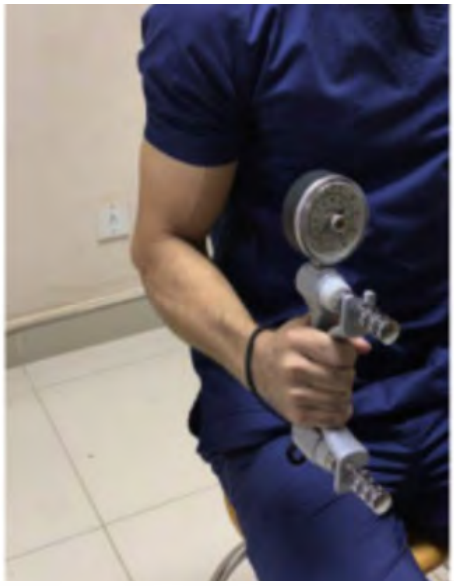
Color/Pattern Key	MUAC *z*-score range	Risk classification
Solid orange	2 to 3	Moderate overnutrition
Solid yellow	1 to 2	Mild overnutrition
Solid green	0 to 1	Normal
Hashed green	-1 to 0	Normal
Hashed yellow	-2 to -1	Mild undernutrition
Hashed orange	-3 to -2	Moderate undernutrition
Hashed red	-4 to -3	Severe undernutrition

There are tapes for age ranges 2-23 months, 24-59 months, 5-9 years, and 10 to 18 years.

Link to instructional video by Abbott Nutrition Health Institute:
https://anhi.org/resources/podcasts-and-videos/muac

Website to auto-calculate MUAC z-score: https://peditools.org/cdcmuac/

Hand grip strength can be easily measured with use of a handgrip dynamometer. A medical grade digital or hydraulic dynamometer (e.g., Jamar) set at the second position is used. The dominant hand is ascertained (i.e., right-handed vs. left-handed). As initially recommended by the American Society of Hand Therapy and later described in the NIH Toolbox, the patient is instructed to sit in an upright position with shoulders adducted, elbow flexed at 90° and forearms in neutral position[2,3] as illustrated below.



The patient is encouraged to give their best effort in isometric grip strength, with one repetition for each hand. The test is then repeated for 2 successive trials, alternating between each hand (3 total trials per hand). The average value of the dominant hand is compared to published normative values for children (6-19 years)[4] and adults.[5] Because weak and frail patients can fatigue easily on this test, it is reasonable to use the maximum value of the dominant hand. Ideally, a center should be consistent in whether the average value or maximum value of the dominant hand is used.

Table 2
Average Performance of Normal Subjects on Grip Strength (lb)

		Males			Females		
Age	Hand	Mean	*SD*	Range	Mean	*SD*	Range
6–7	R	32.5	4.8	21–42	28.6	4.4	20–39
	L	30.7	5.4	18–38	27.1	4.4	16–36
8–9	R	41.9	7.4	27–61	35.3	8.3	18–55
	L	39.0	9.3	19–63	33.0	6.9	16–49
10–11	R	53.9	9.7	35–79	49.7	8.1	37–82
	L	48.4	10.8	26–73	45.2	6.8	32–59
12–13	R	58.7	15.5	33–98	56.8	10.6	39–79
	L	55.4	16.9	22–107	50.9	11.9	25–76
14–15	R	77.3	15.4	49–108	58.1	12.3	30–93
	L	64.4	14.9	41–94	49.3	11.9	26–73
16–17	R	94–0	19.4	64–149	67.3	16.5	23–126
	L	78.5	19.1	41–123	56.9	14.0	23–87
18–19	R	108.0	24.6	64–172	71.6	12.3	46–90
	L	93.0	27.8	53–149	61.7	12.5	41–86

Note: The mean scores for individuals, aged 14 to 19 years, may be slightly low (0–10 lb lower than they should be) due to instrument error detected after the study.

Table 2: Performance of All Subjects an Grip Strength (pounds)

		Men					Women				
	Hand	Mean	SID	SE	Low	mm	Mean	SID	SE	Low	High
20-24	R	121.0	20.6	3.8	91	167	70.4	14.5	2.8	46	95
	L	104.5	21.8	4.0	71	150	61.0	13.1	2.6	33	88
25-29	R	120.8	23.0	4.4	78	158	74.5	13.9	2.7	48	97
	L	110.5	16.2	3.1	77	139	63.5	12.2	2.4	48	97
30-34	R	121.8	22.4	4.3	70	170	78.7	19.2	3.8	46	137
	L	110.4	21.7	4.2	64	145	68.0	17.7	3.5	36	115

The six-minute walk test (6MWT) is a feasible and standardized measure of gait speed and endurance that has been classically part of the Frailty assessment in adults and can be performed in most children. The distance covered in meters is compared to published normative values (Klepper et al).

TABLE 2

Subject Characteristics (Mean ± SD) for the Full Sample and by Age Group

Age (y)	Height (m)		Weight (kg)		Leg Length (cm)		BMI (kg/m^2)		6MWD (m)	
	N	Mean ± SD	N	Mean ± SD or Median (IQR)[a]	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
7-8	20 T	1.32 ± 0.08	20 T	31.52 ± 8.99	20 T	70.79 ± 4.89	20 T	18.15 ± 4.02	28 T	527.09 ± 64.2
	14 F	1.30 ± 0.07	14 F	29.77 (10.9)[a]	14 F	70.61 ± 4.9	14 F	17.48 (5.23)[a]	14 F	519.64 ± 69.31
	6 M	1.31 ± 0.08	6 M	29.24 ± 4.7	6 M	71.21 ± 5.28	6 M	16.65 ± 1.48	14 M	534.54 ± 60.3
9	20 T	1.35 ± 0.06	19 T	34.14 ± 8.5	18 T	72.45 ± 4.41	19 T	18.73 ± 3.86	27 T	531.66 ± 80.27
	12 F	1.35 ± 0.07	11 F	30.91 (15.30)[a]	11 F	72.32 ± 4.77	11 F	18.2 ± 3.6	16 F	542.54 ± 80.25
	8 M	1.36 ± 0.05	8 M	35.94 ± 9.24	7 M	72.66 ± 4.14	8 M	19.39 ± 4.35	11 M	515.83 ± 81.4
10	32 T	1.44 ± 0.08	32 T	45.1 ± 9.88	31 T	78.12 ± 5.17	32 T	21.6 ± 3.5	35 T	497.15 ± 66.81
	21 F	1.44 ± 0.07	21 F	42.91 ± 8.97	21 F	77.2 (5.83)[a]	21 F	20.92 ± 3.28	22 F	496.69 ± 63.98
	11 M	1.45 ± 0.10	11 M	50 (23.48)[a]	10 M	78.8 ± 6.9	11 M	22.52 ± 3.93	13 M	497.94 ± 74.03
11	8 T	1.50 ± 0.03	8 T	42.1 ± 7.46	8 T	81.06 ± 2.61	8 T	18.81 ± 3.45	8 T	533.63 ± 85.42
	4 F	1.50 ± 0.04	4 F	43.24 ± 10.52	4 F	81.1 ± 1.4	4 F	19.16 ± 4.9	4 F	532.33 ± 92.25
	4 M	1.50 ± 0.03	4 M	40.97 ± 3.95	4 M	81.01 ± 3.73	4 M	18.46 ± 1.84	4 M	534.93 ± 88.90
All	80 T	1.39 ± 0.09	79 T	35.23 (15.67)[a]	77 T	75.19 ± 5.95	79 T	18.52 (6.50)[a]	100 T	518.50 ± 72.56
	51 F	1.38 ± 0.09	50 F	34.77 (15.95)[a]	50 F	74.84 ± 5.7	50 F	19.56 ± 3.92	57 F	518.32 ± 73.16
	29 M	1.40 ± 0.10	29 M	39.84 ± 11.33	27 M	75.85 ± 6.5	29 M	18.65 (6.82)[a]	43 M	518.73 ± 72.61

Abbreviations: 6MWD, 6-minute walk distance; IQR, interquartile range.

[a]Skewed data is presented as the median (Interquartile range); T = total sample; F = Female; M = Male.

The two-minute walk test (2MWT) is a feasible and standardized measure of gait speed and endurance. For younger patients, the 2MWT distance is highly correlated to the classic six-minute walk test and has the advantage of a higher completion rate. For these reasons, the 2MWT is preferred by the NIH as the standard motor function tool for gait and may an option for younger patients (3-8 years old) or patients who cannot perform the 6MWT. Instructions for standardized 2MWT execution are included in the NIH Toolbox[6] (https://www.youtube.com/watch?v=8ysD6YdhNjY). The distance covered in meters is compared to published normative values for children[7] and adults (>17 years).[8]

Table 1. Summary of demographic variables and 2-minute walk distances for boys and girls 3–17 years of age.

Age	Sex (*n*)	Height (m) Mean (SD)	Body mass (kg) Mean (SD)	Distance (m)	
				Mean (SD)	95% CI
3	Boys (63)	1.00 (0.09)	16.3 (2.8)	122.9 (26.6)	116.2, 129.6
	Girls (54)	1.02 (0.08)	15.9 (2.2)	125.9 (24.9)	119.1, 132.7
4	Boys (70)	1.09 (0.10)	18.5 (3.6)	137.7 (23.6)	132.1, 143.3
	Girls (88)	1.08 (0.09)	17.5 (3.1)	143.3 (23.4)	138.3, 148.3
5	Boys (72)	1.14 (0.12)	20.7 (4.2)	155.1 (25.2)	149.2, 161.1
	Girls (80)	1.12 (0.09)	20.6 (4.9)	155.4 (22.9)	150.4, 160.5
6	Boys (68)	1.23 (0.10)	24.2 (5.4)	171.4 (20.6)	166.5, 176.4
	Girls (84)	1.12 (0.11)	24.1 (5.3)	174.1 (22.7)	169.1, 179.0
7	Boys (99)	1.27 (0.11)	27.5 (6.6)	184.0 (29.8)	178.1, 189.9
	Girls (89)	1.26 (0.12)	28.1 (6.7)	182.2 (24.3)	177.0, 187.3
8	Boys (81)	1.32 (0.12)	29.9 (7.4)	193.3 (25.5)	187.0, 199.6
	Girls (81)	1.33 (0.11)	31.2 (7.8)	187.1 (26.6)	181.2, 193.0
9	Boys (80)	1.37 (0.10)	33.8 (7.4)	196.9 (27.4)	190.8, 203.0
	Girls (75)	1.38 (0.08)	31.9 (6.0)	199.8 (23.0)	194.5, 205.1
10	Boys (91)	1.41 (0.09)	40.1 (11.2)	195.4 (26.3)	189.9, 200.9
	Girls (97)	1.43 (0.10)	38.9 (9.0)	194.4 (23.1)	189.7, 199.0
11	Boys (92)	1.50 (0.09)	47.0 (11.3)	200.9 (26.7)	195.4, 206.5
	Girls (93)	1.52 (0.10)	48.1 (12.2)	197.5 (25.2)	192.3, 202.7
12	Boys (86)	1.56 (0.09)	52.0 (13.9)	202.6 (29.4)	196.3, 208.9
	Girls (102)	1.56 (0.09)	50.6 (12.5)	198.8 (25.1)	193.8, 203.7
13	Boys (104)	1.62 (0.10)	57.4 (15.7)	201.1 (28.9)	195.5, 206.7
	Girls (89)	1.60 (0.07)	55.1 (12.4)	197.0 (23.7)	192.1, 202.0
14	Boys (101)	1.70 (0.09)	65.7 (17.8)	201.8 (29.9)	195.9, 207.7
	Girls (110)	1.63 (0.07)	59.3 (14.3)	192.3 (25.0)	187.6, 197.0
15	Boys (87)	1.72 (0.09)	68.2 (15.8)	202.9 (26.6)	197.3, 208.6
	Girls (99)	1.63 (0.07)	60.9 (14.5)	193.4 (24.3)	188.5, 198.2
16	Boys (97)	1.77 (0.09)	73.8 (19.6)	209.0 (29.4)	203.1, 214.9
	Girls (97)	1.62 (0.06)	61.1 (14.3)	194.1 (24.9)	189.1, 199.1
17	Boys (99)	1.78 (0.07)	80.0 (18.2)	204.2 (29.2)	198.3, 210.0
	Girls (103)	1.62 (0.07)	62.7 (17.3)	192.8 (27.2)	187.5, 198.1

Table 4 Norms for the 2MWT distance

Participants by Sex and Age Category, y (n)	Distance, m (mean [95% CI])	Distance, m/BMI (mean [95% CI])
Women		
18–54 (539)	183.0 (180.8–185.3)	6.82±0.09 (6.64–6.99)
55–59 (30)	176.4 (168.1–184.8)	6.41±0.35 (5.71–7.11)
60–64 (48)	166.4 (158.2–174.5)	6.26±0.26 (5.74–6.79)
65–69 (22)	155.2 (140.6–169.8)	5.48±0.45 (4.55–6.41)
70–74 (33)	145.9 (136.9–154.9)	5.01±0.31 (4.38–5.65)
75–79 (14)	140.9 (121.8–159.9)	5.58±0.54 (4.41–6.76)
80–85 (34)	134.3 (125.7–142.9)	5.01±0.19 (4.63–5.39)
Men		
18–54 (260)	200.9 (197.2–204.6)	7.40±0.13 (7.15–7.66)
55–59 (23)	191.0 (176.8–205.2)	6.92±0.38 (6.13–7.71)
60–64 (29)	179.1 (165.4–192.8)	6.43±0.33 (5.75–7.11)
65–69 (22)	184.2 (170.7–197.8)	7.08±0.35 (6.36–7.80)
70–74 (32)	172.4 (163.8–180.9)	6.50±0.26 (6.00–6.56)
75–79 (19)	157.6 (140.3–174.9)	5.78±0.44 (4.85–6.70)
80–85 (32)	144.1 (132.6–155.6)	5.74±0.30 (5.14–6.34)

Abbreviations: distance, mean 2MWT distance; distance/BMI, mean 2MWT distance normalized by BMI.

Distance SD = 32.8 m for Men, and 30.1 m for Women

Functional status can be measured with a validated scale commonly used in pediatric chronic disease. The Lansky Play Performance Scale (LPPS)[9] and the analogous Karnofsky Performance Scale (KPS)[10] for older adolescents and adults have been used for decades in various studies and registries including the UNOS database. The scale is summarized in the table below.

Table 1. Karnofsky/Lansky Scale

Karnofsky Scale (recipient age ≥ 16 years)		Lansky Scale (recipient age <16 years)	
Able to carry on normal activity; no special care is needed		**Able to carry on normal activity; no special care is needed**	
100	Normal, no complaints, no evidence of disease	100	Fully active
90	Able to carry on normal activity	90	Minor restriction in physically strenuous play
80	Normal activity with effort	80	Restricted in strenuous play, tires more easily, otherwise active
Unable to work, able to live at home cares for most personal needs, a varying amount of assistance is needed		**Mild to moderate restriction**	
70	Cares for self, unable to carry on normal activity or to do active work	70	Both greater restrictions of, and less time spent in active play
60	Requires occasional assistance but is able to care for most needs	60	Ambulatory up to 50% of time, limited active play with assistance/supervision
50	Requires considerable assistance and frequent medical care	50	Considerable assistance required for any active play, fully able to engage in quiet play
Unable to care for self, requires equivalent of institutional or hospital care, disease may be progressing rapidly		**Moderate to severe restriction**	
40	Disabled, requires special care and assistance	40	Able to initiate quite activities
30	Severely disabled, hospitalization indicated, although death not imminent	30	Needs considerable assistance for quiet activity
20	Very sick, hospitalization necessary	20	Limited to very passive activity initiated by others (e.g., TV)
10	Moribund, fatal process progressing rapidly	10	Completely disabled, not even passive play

For fitness scoring in this domain, a suggested system is to assign 0 points if the value is 80-100 (not significantly limited), 1 if 50-70 (mild to moderate restriction), or 2 points if 10-40 (moderate to severe restriction).

Section 2: Exercise Training

VAD Implant

Early Mobilization

Initial Exercise Training

Stable VAD/Heart Failure Phase

Serial Functional Assessements

Individualized Exercise Training

Refer to "Exercise Training for Early Post-VAD Pediatric Patients" Document:

1. Early mobilization post-VAD
2. Readiness Checklist for Exercise Training after VAD implant in children
3. Approach to Individualized Exercise Training in Early Pediatric VAD Recipients
4. VAD Exercise Training Tips to Avoid Adverse Events

Assessment Components	Assessment Tools
Aerobic capacity	Cardiopulmonary Exercise Test (CPET)[1] Six Minute Walk Test
Musculoskeletal strength	Maximal voluntary contraction 30 second chair rise Hand grip dynamometry
Composite	BOT Short Form Frailty score (future project)

Functional assessment occurs at regular intervals every 4-8 weeks

Individualized Exercise Training[2]

1. Exercise rehabilitation should occur 2-3x/week at minimum with goal ≥3x/week
2. Can occur either inpatient, outpatient, remotely (telemedicine or independent home training)
3. Can be performed by exercise physiologist or physical therapist
4. Can train with intracorporeal or paracorporeal VADs
5. CPET can provide guidance for identifying target heart rate (based on heart rate at anaerobic threshold) or perceived exertion

VAD Exercise Training Tips to Avoid Adverse Events

1. Individualized exercise assessment and prescription
2. Pre-screening with risk stratification
3. Prolonged graduated warm-up and cool-down
4. Low-to-moderate intensity exercise training
5. Avoid breath hold and Valsalva maneuver
6. Avoid trauma
7. Adapt for co-morbidities
8. Monitor training by exercise physiologist or physical therapist familiar with VAD
9. Keep the feet moving during active recovery
10. Monitor patients for 15 minutes post-exercise initially
11. Make sure VAD driveline is secured
12. Follow sternal precautions

Cardiopulmonary Exercise Testing

To determine functional capacity for individualized exercise training prescriptions, maximal cardiopulmonary exercise testing (CPET) should be considered. If feasible, cycle ergometry should used instead of treadmill due to safety and stability of a stationary bicycle, quantification of external work, and minimization of motion artifact, although treadmill can be considered with close supervision for fall risk. Patients may wear an abdominal binder and must have their driveline secured per center protocol to prevent driveline motion and irritation. Initial CPETs are performed after VAD implant based on clinical readiness as determined by the primary care team (protocol minimum 14 days post-implant). A follow-up CPET is performed following completion of the dedicated exercise training and rehabilitation program (individualized exercise training protocols developed based on baseline CPET as described below).

The CPET includes continuous heart rate and rhythm monitoring. VAD parameters are also continuously monitored throughout exercise and recovery. Metabolic and ventilatory data are assessed on a breath-by-breath basis using a metabolic cart. Parameters collected (Table) are measured at maximal exercise and at the ventilatory anaerobic threshold (VAT), including minute oxygen consumption (VO2), minute carbon dioxide production (VCO2), minute ventilation (VE), work rate (Watts) and the respiratory exchange ratio (RER). Methods for calculating the VAT are based on the V-slope and the ventilatory equivalents methods. Maximal tests are defined based on RER > 1.10, among other measures including heart rate response and subjective assessment of exertion (rate of perceived exertion, RPE) by the patient via a Borg scale. Normative values for the primary outcome variables have been published.[11] Doppler blood pressure and VAD monitor can be monitored at rest and peak exercise.

Table. Primary outcome variables during symptom-limited CPET for VAD recipients

	Rest	Anaerobic Threshold	Maximal Exercise
Heart Rate (bpm)	X	X	X
VAD Flow (L/min)	X	X	X
Work Rate (watt)		X	X
Indexed VO2 (mL/kg/min) Unindexed VO2 (L/min)		X	X
Pulsatility Index	X	X	X
Oxygen Saturation*	X	X	X
Doppler MAP	X		Optional

*oxygen saturation via pulse oximeter may have inconsistent measurement on continuous-flow devices

Target Heart Rate (HR)

The target HR range during exercise depends on the individual patient's physiology, including health of the conduction system and prescribed chronotropic medications, which is summarized as the heart rate reserve (HRR), as well as the desired training intensity. The HRR is calculated by subtracting the resting HR from the maximal HR during the baseline CPET. The target HR ranges can then be calculated as such:

Target HR Range for Light Intensity Aerobic Exercise = (Maximal HR – Resting HR) x 0.5 to 0.6 + Resting HR

Target HR Range for Moderate Intensity Aerobic Exercise = (Maximal HR – Resting HR) x 0.6 to 0.75 + Resting HR

Target HR Range for High Intensity Aerobic Exercise = (Maximal HR – Resting HR) x 0.75 to 0.9 + Resting HR

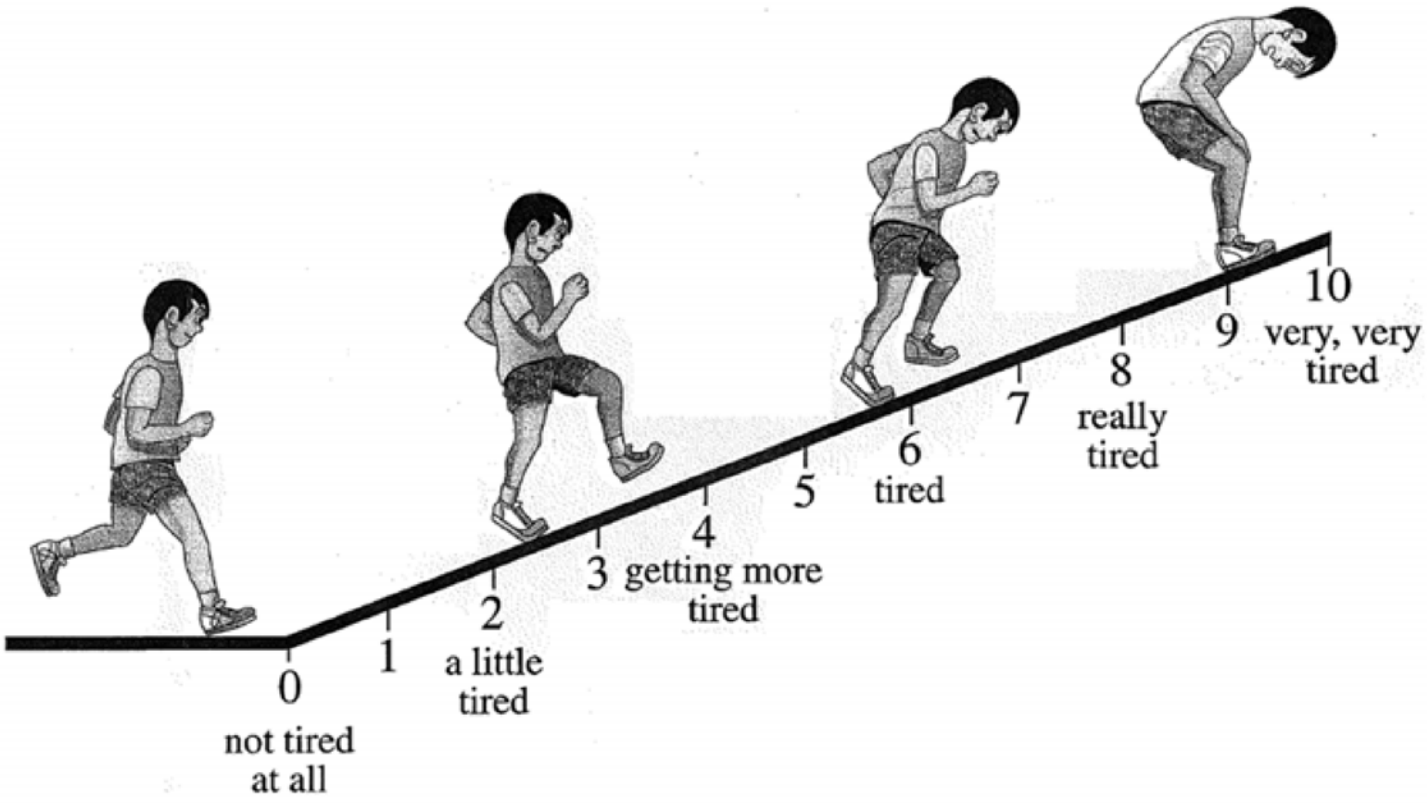
For example, a patient with a resting HR of 60 and maximal of HR 160 bpm would have a moderate intensity target HR range of 120 to 135 bpm based on this calculation:
(160-60) x 0.6 + 60 = 120 bpm
(160-60) x 0.75 + 60 = 135 bpm

Rate of Perceived Exertion (RPE)

The Borg scale is an example of an RPE scale. Such scales are useful when the target HR ranges are not known. Then can also be used to empower the patient to better assess their own exercise performance. In the example below, green indicates low intensity, yellow indicates moderate, and orange indicates high intensity exertion.

Borg RPE Scale			
6		How you feel when lying in bed or sitting in a chair relaxed	
7	Very, very light		
8		Little to no effort	Able to sing
9	Very light		
10			
11	Fairly light		Easily talk and can exercise for a long time at this pace
12		How you should feel with exercise or activity	
13	Somewhat hard		
14			You start to hear your breathing, but you are not gasping for air
15	Hard		Can talk but us one- or two-word answers
16			
17	Very Hard	How you felt with the hardest work you have ever done	
18			Breathing very hard, cannot talk
19	Very, very hard		
20	Maximal exertion	Don't work this hard!	

The OMNI scale is another useful RPE scale. An example is shown below.



Individualized Exercise Training Late after VAD Implant or Stable Heart Failure

Prescribed exercise therapy can be supervised by a PT or exercise physiologist depending on center resource availability and setting. When developing individualized exercise training (ET) recommendations for children with VADs, the baseline CPET provides valuable guidance by assessing for evidence of exercise-induced symptoms, arrhythmia, ischemia, or abnormal hemodynamic response, and to establish a baseline level of fitness. Furthermore, target heart rate during ET is based on submaximal and maximal CPET parameters. Specifically, the target heart rate range for moderate intensity exercise is calculated from the heart rate at the VAT or the desired perceived exertion.

ET can occur during inpatient, outpatient or home-based sessions (after initial stabilization and demonstration of adequate knowledge on how to safely perform exercises). ET should aim to incorporate developmentally appropriate play-based activities as much as possible to maintain patient engagement. ET consists of two to three sessions per week, lasting from 30-60 minutes. Sessions include aerobic and musculoskeletal conditioning and are performed under the guidance of a pediatric cardiac exercise physiologist. Each session begins with a 10- to 15-minute warm-up period using either cycle ergometry or treadmill walking. Level of exertion is maintained at the heart rate at VAT determined during baseline CPET.

After the warm-up, patients perform musculoskeletal conditioning consisting of play-based therapy or circuit training of resistance exercises depending on the developmental level of the patient for a period of 15 minutes. Resistance exercises concentrate on either upper extremity and torso strengthening (biceps, triceps, shoulder, back and abdominal muscles) or lower extremities (quadriceps, hamstring, and calf muscles). For older children, musculoskeletal training intensity is maintained at 60% of pre-training one repetition maximal voluntary contraction. Patients are instructed to perform one repetition every 3 to 4 seconds, with a goal of 15 repetitions performed in one minute. Patients are instructed regarding the correct lifting and breathing technique to avoid the Valsalva maneuver. Sessions end with a 10- to 15-minute cool-down period, again using either cycle ergometry or treadmill walking while maintaining heart rate at VAT.

Example exercise videos can be accesses via: Hep2go.com

-Users can set up free account and search exercises for video examples

Exercise Rehabilitation Example (Inpatient or Outpatient)

Weekly Schedule:

	Monday	**Tuesday**	**Wednesday**	**Thursday**	**Friday**
Aerobic Training	Treadmill or Cycle		Treadmill or Cycle		Treadmill or Cycle
Musculoskeletal Training	Upper body		Lower body		Both

TREADMILL WORKOUT:

5 minutes @ 2.5-3.0 mph followed by 10 minutes @ 3.5 mph

- Do not let your heart rate go over you target heart rate based on your baseline functional assessment.
- Use the RPE scale to judge your intensity (example Borg scale target: 13 out of 20)
- Take a break if you need to but finish the 15 minutes
- Drink water, stay hydrated!

STRENGTH:

- What you need: Light weights, towel, water
- Try to move through each exercise without taking a break, but if you need a minute for a quick water break that would be fine.
- Do as many as you can using correct form, comfortable weights (no more than 15 lbs.) and BREATHE!!.....blow out of your mouth when you move the weight.
- If you struggle with any given weight, put it down, pick up lighter weights and finish the set.
- Stretch arms out again

UPPER BODY

Warm-up

Neck rolls (3 each side holding for 5 seconds each)
Shoulder rolls (10 forward, 10 backward)
Cross hands over in front, put palms together and roll shoulders forward – Hold for 10 sec
Hands clasped together behind back, push hands down to stretch chest
Cross hands over in front, put palms together and roll shoulders forward – Hold for 10 sec
Hands clasped together behind back, push hands down to stretch chest
Small arm circles with palms out, fingers up (15 each direction)
Small arm circles with palms in, fingers down (15 each direction)
Shake arms out

Pick 6 exercises of those listed below (may need modification based on sternal precautions)

Alternate shoulder press: 12-15 reps
Start with weight at shoulder height. Raise weight straight up over head alternating hands.

Standard arm curls: 12-15 reps
Start with arms fully extended down at waist. Raise both weights up to shoulder level keeping elbows in next to chest.

Triceps kick back: 12-15 reps
Start with one foot in front of the other. Bend over at the waist with head up and back flat. Raise weights to side of the chest at the shoulder. Extend weights backward above the level of the back. Pause at the extension and try not to swing the weights.

Two arm shoulder press: 12-15 reps
Same as alternating shoulder press but raising both arms at the same time.

Cross over curls: 12-15 reps
Alternate arms curls but lift weight to opposite shoulder crossing over the chest.

Triceps press: 12-15 reps
Use one arm at a time. Raise weight straight up over head. Then bend at elbow and lower the weight behind your head. Raise weight back up to overhead position keeping elbow pointing straight up.

Upright rows: 12-15 reps
Hold weights down near your waist with straight arms. Raise weights together upward to just below chin. Make sure your elbows are above your hands as you raise the weights to your chin.

Static arm curls: 12-15 reps
Alternate weights in each hand. Perform 4 regular arm curls with one hand while the other hand is holding its weight halfway up. At the 4th rep switch hands with the same technique.

Chair Dips: 12-15 reps
Use a chair with no arms, a bench, or a step. With hands facing forward next to your side, raise yourself up (if using the chair) or dip yourself off the step, then raise yourself upward.

Front and lateral arm raises: 12-15 reps
With a straight arm raise weight up to shoulder level. Lower weight then raise weight directly to each side.

Curls: 24 reps
8 curls halfway up, 8 curls halfway down, 8 full curls

Lawnmower:12 reps each arm
One foot forward and bent at the knee, the other foot back and fairly straight. Using one weight in one hand and the opposite forearm resting on your front bent thigh. Start with the weight on the floor and raise it upward toward your armpit keeping your elbow in along the side of your body. The switch hands and legs... this looks like you are starting a lawnmower.

Elbow Out Lawnmower: 12 each arm
Same thing as the regular lawnmower but turn weight in the starting position so your knuckles are facing forward. When you raise the weight you elbow should go outward.

Reverse Grip Bent Over Row: 12 reps
One foot in front of the other with knees slightly bent, head up, and flat back. Hold a dumbbell in each hand with palms facing forward. Raise the weights from close to the floor upward to the side of your chest keeping your elbows in.

Seated Bent Over Fly: 12 reps
Sit at edge of bench, bend over, raise weights pulling back and pinching your scapula bones together.

LOWER BODY: Perform all 6 exercises listed below

Regular squat: 10 reps
Feet shoulder width apart. Bend at knees to almost a knee angle of 90 degree while keeping head up and back flat. Do not bend at waist…. bend at the knees to lower yourself.

Runner stance squat: 10 reps
Start with right foot in front and left back on the ball of your foot (heel up). Bend using front knee the same as a regular squat. After 30 seconds, switch legs and repeat.

3-Part Squat: 10 each position
These are squats in 3 positions: first with feet together, then with feet shoulder width apart, then a little wider but with toes pointed at 45 degree angle (make sure your knees bend outward over your toes).

Squat reach: 10 reps
Regular squat but when you stand back up raise arms to reach up toward the ceiling and go up on your toes (Balls of your feet like calf raises)

Calf raises (3 types, 20 each)
Stand with feet pointed out like a duck. Raise yourself up using the balls of your feet and pause at the top for 2 seconds. Perform 10 slow, then 10 fast calf raises. Repeat this using feet pointed straight, then pointed inward slightly like a pigeon. (60 total reps)

Tip-Toe Squats: 10 reps
Perform these on the balls of your feet (like a calf raise) without touching your heel to the ground.

Home-Based Rehabilitation Adaptation

Exercise interventions and rehabilitation programs can either be facility/hospital-based, home-based, or a hybrid of both. Facility-based programs can often be impractical or inaccessible for patients and their families, with significant associated time and financial costs. This is particularly true for pediatric cardiac centers providing regionalized care to geographically disperse regions. Home-based programs may present a more practical and attractive alternative in many circumstances, promote improved involvement and adherence, and lead to more equitable care. Traditional home-based programs, however, sacrifice the ability for real-time supervision of safety, technique, and compliance. Telemedicine-equipped programs with remote physiologic monitoring allow for live supervision, providing many of the advantages of a facility-based program while still allowing for the convenience and accessibility permitted by home-based programs. **It is recommended that patients be able to demonstrate appropriate and safe exercise participation under supervision of a trained exercise therapist before transitioning to a home-based exercise-training program.**

Home-based protocol
If a fully home-based protocol is intended, the following exercise regimen should be completed three times per week:

The protocol described above can be modified at the discretion of the clinical team and the pediatric cardiac exercise physiologist. If the necessary equipment is available, aerobic exercise can include the “Treadmill Workout” described above or walking/stairs or cycling if a stationary ergometer is available for the designated period, ensuring to not exceed a moderate intensity (“able to speak in full sentences”).

Following the aerobic warm-up a resistance training program can be designed to include upper and lower body exercises, with a total of 6 exercises listed above. The exercises can vary from day-to-day to introduce variability.

Requirements
In order for a home-based program to be effectively and safely administered, the following requirements should be in place:

- Clearance from the clinical team/cardiologist primarily caring for the patient
- Baseline maximal cardiopulmonary exercise test (CPET)
- Prior enrolment (at least 4 weeks) in an inpatient or outpatient hospital-based supervised rehabilitation program at equal or greater intensity without significant adverse events directly attributable to the program
- Parent/guardian available to be on site and supervising as needed
- Adequate knowledge on how to safely execute the exercises
- Access to a phone for reasonable urgent communication as needed

The following items would enhance the program but are not mandatory

- Supervision by pediatric cardiac exercise physiologist or clinician via telemedicine
- Remote physiologic monitoring, including but not limited to oximetry, ECG, and heart rate monitoring
- Objective assessment of outcome measures, including physical activity, weight, lean muscle mass, etc.

How to get exercise testing and cardiac rehabilitation services reimbursed

Medicare and most private insurers have historically covered cardiac rehabilitation services for conditions that are modeled after adult-acquired heart disease such as myocardial infarction or coronary bypass surgery. Pediatric cardiac rehabilitation reimbursement by payors has steadily gained traction, especially in HF, cardiomyopathy, and complex cyanotic CHD. There are two primary CPT codes: 93797 (cardiac rehabilitation without telemetry) and 93798 (cardiac rehabilitation with telemetry). Below is additional information on billing codes.

- Standard Exercise Test Codes
  - CPT 94618 - 6 Minute Walk Testing
  - CPT 94621 - Cardiopulmonary Exercise Test
  - CPT 93017 - Cardiovascular Exercise Test

- Standard Cardiac Rehabilitation CPT Codes (93797, 93798)
  - Established coverage for inpatients and outpatients meeting below criteria
    - CMS Coverage Criteria (January 1, 2010, Medicare Part B)
      - Heart attack within last 12 months
      - Coronary artery bypass surgery
      - Current stable angina
      - Heart valve repair or replacement
      - Coronary angioplasty or coronary stenting
      - Heart or lung transplant
      - Stable chronic heart failure defined as an EF of 35% or less and NYHA class II to IV symptoms despite optimal heart failure therapies for a minimum of 6 weeks
      - Other conditions as specified through a national coverage determination

- Standard Pulmonary Rehabilitation CPT Codes (G0237, G0239, G0424)
  - Does not include specifications for diagnosis coverage criteria or PFT guidelines (G0237, G0239)
    - Typically covers patients with chronic lung disease who have persistent symptoms despite medical therapy, functional limitations related to disease symptoms and impaired quality of life
  - CMS coverage criteria for outpatient services (January 1, 2010 Medicare Part B)
    - Moderate to very severe COPD (G0424) with GOLD classification
      - Stage 2 - Moderate COPD, FEV1 between 50-80% of predicted
      - Stage 3 - Severe, FEV1 30-50% of predicted
      - Stage 4 - Very severe to end stage COPD, FEV1 29% or lower or low blood oxygen levels and stage 3 FEV1

- Exercise Consultation Services Codes – Defined as, “education and training for patient self-management by a qualified, non-physician health care professional using a standardized curriculum, each 30 minutes”
  - CPT 98960 - Individual session
  - CPT 98961 - Group session
- Telehealth-based Exercise Therapy Sessions
  - CPT 98960 (95 modifier) - Individual session
  - CPT 98961 (95 modifier) - Group session

- Insurance Coverage
  - Coverage is not guaranteed but is more likely if linked diagnoses include heart failure (e.g., “Heart failure due to congenital heart disease” = ICD-10 codes 150.9, Q24.9), heart or lung transplant, or heart valve repair or replacement
  - Work with your center’s financial team to standardize a prior authorization process
  - Be prepared and willing to send supportive documentation and make a phone call

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ACTION/PHTS COVID-19 PMIS-T/MIS-C PEDIATRIC ANTITHROMBOSIS GUIDELINE OF CARE

Pediatric Heart Transplant Society

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Antithrombotic decisions should be driven by the primary care team, in consultation with anticoagulation specialists. This document is based on combined clinical experience and opinions of ACTION/PHTN members. Treatment should be individualized and based on the clinical condition of each patient.

ACTION REVISED DATE: 06/26/2020

PROTOCOL

Coronavirus disease (COVID-19), caused by a novel Coronavirus (SARS-CoV-2) virus is expanding in the pediatric population with ever growing array of clinical presentations. Its highly heterogenous clinical manifestation in adults has been well documented with a spectrum courses ranging from asymptomatic to multi-organ failure and death. Similar to adults, there are children who present with mild or no symptoms, however unique hyper-inflammatory syndrome(s) has emerged in children that appears temporally related to COVID-19 infection. Sometimes referred to as pediatric multisystem inflammatory syndrome- temporally associated with SARS-Cov2 (PMIS-T) or multisystem inflammatory syndrome in children (MIS-C), the constellations of symptoms have included one or more of a combination of the following: persistent fever, elevated inflammatory markers, evidence of cytokine storm, anemia, neutrophilia, lymphopenia, coagulopathy, vasodilatory shock with normal or depressed ventricular function, cardiogenic shock with moderate to severely depressed ventricular function, and/or Kawasaki disease (KD) features.

A significant morbidity identified in the COVID-19 population has been heightened risk of thrombotic complications secondary to pro-inflammatory state, multi-organ vasculitis, and immobilization. The estimated burden of thrombotic complications in children is still emerging as the disease presentation continues to be characterized and defined. Herein, we summarize and harmonize current antithrombosis practices in hospitalized pediatric suspected/confirmed COVID patients focusing on those with cardiac involvement and/or PMIS-T.

MIS-COVID Case Definition

1. One of the following: SARS-CoV-2 PCR positive test; negative test with COVID exposure in past month; or SARS-CoV-2 antibody test positive

AND

2. Criteria A, B, and C:

A. Fever > 38.5C

B. Laboratory markers of inflammation, including: increased CRP together with at least one or more of the following: neutrophilia, lymphopenia, elevated fibrinogen, elevated D-dimers, elevated ferritin, or hypoalbuminemia.

C. Clinical evidence of severe hospitalized illness including single or multi-organ dysfunction based on clinical judgment from record review, discharge diagnosis, laboratory, or diagnostic tests:

a. Cardiac (e.g. shock, elevated troponin, BNP, abnormal echocardiogram, arrhythmia)
b. Respiratory (e.g. pneumonia, ARDS, pulmonary embolism)
c. Renal (e.g. acute kidney injury or renal failure)
d. Liver (e.g. elevated bilirubin or elevated liver enzymes)
e. Neurologic, (e.g. CVA, aseptic meningitis)
f. Coagulopathy (e.g. elevated D-dimers, thrombophilia, or thrombocytopenia)
g. Gastrointestinal (severe abdominal pain, vomiting, diarrhea colitis)

HARMONIZED

Approach to Coagulation Testing

All patients admitted with confirmed/suspected COVID-19 infection should have the following coagulation labs obtained – (i) on admission; (ii) with any change in clinical status or level of care and (iii) at discharge

- CBC with differential (including nucleated RBC if available)
- BUN/Cr
- Fibrinogen
- **D-dimer**
- PT/INR
- aPTT from non-heparinized line (or with heparin neutralization if heparin-exposed line is utilized)
- LDH
- Ferritin
- History of remote or recent thrombotic events
- History of acquired or inherited thrombophilia
- Family history of any inherited thrombophilia

Optional labs that have been shown to provide some utility in assessing hypercoagubility include:

- VonWillibrand Factor antigen (generally elevated)
- Thromboelastography (TEG) or ROTEM - specifically looking for elevated clot strength/MA suggestive of hypercoagulability (MA>75mm)

Thromboprophylaxis Treatment Options

If on antiplatelet and/or anticoagulation for pre-existing condition (thromboprophylaxis or treatment)

- **Do not interrupt antiplatelet or anticoagulation therapy unless otherwise specified by your clinical care team**

1. Screen all patients at time of admission and daily for any of the following:
   - Documented thrombosis
   - Moderate to severe ventricular dysfunction
   - Increasing vasoactive infusion requirement
   - Sedated and/or paralyzed
   - Coronary dilation/aneurysm
   - D-dimer >3mcg/mL (or up-trending D-dimer)
   - Any rhythm abnormalities: heart block, etc.
   - TEG clot strength >80

   If any of the above, then consider the following:

   - Low molecular weight heparin (LMWH) titrated to treatment goals (LMWH level=0.5-1 units/ml)
   - If hemodynamically unstable (concern for need of mechanical circulatory support), and/or concern for risk of bleeding, and/or severe renal dysfunction:

- Unfractionated heparin (UFH) titrated to institutional goals for treatment (~aPTT 60-80s, 70-90s or anti-Xa/HAL of 0.35-0.7units/mL)
    - Bivalirudin as alternative option to UFH if unable to achieve therapeutic and/or stable levels with UFH (bivalirudin goal 1.5-2.5x baseline PTT or direct thrombin inhibitor (DTI) assay of 60-90s)

2. **For all other PMIS-T/MIS-C patients who do not have any of the above features at time of assessment then consider the following treatment:**
    - Low molecular weight heparin (LMWH) titrated to institutional prophylactic goals (generally 0.2-0.4units/ml)
3. With initiation of anticoagulation consider additional use of aspirin therapy (5mg/kg/day with a maximum of 81mg daily) in the following PMIS-T/MIS-C patients:
    - Kawasaki disease (if fulfills criteria for KD, then follow AHA recommendations for antiplatelet and anticoagulation therapy)
    - KD features with coronary dilation
    - Elevated clot strength (MA>75mm) in the setting of anticoagulation
    - Elevation in troponins
    - Change in ECG QRS with ST segment elevation
        - Consider one-time dose of 10 mg/kg/dose (max=325mg) followed by 5 mg/kg/day (max=81mg/day)
    - Consider TEG with platelet mapping and/or VerifyNow aspirin assay to ensure adequate platelet inhibition (AA inhibition >70% on TEG or ARU<550 on VerifyNow)
    - Aspirin non-responders based on AA inhibition or VerifyNow may use clopidogrel (Plavix); however, there isn't data available to support the use of this medication in PMIS-T / MIS-C. Usual dose is 0.2-0.5mg/kg/day (max=75mg/day). Efficacy may be assessed with VerifyNow P2Y12 assay (goal PRU<300).
4. For all PMIS-T/MIS-C patients ready for discharge with any remaining elevation of D-dimer, LDH, ferritin and/or CRP
    - Low-molecular weight heparin (LMWH) prophylactic dosing
    - Apixaban prophylactic dosing (0.05 mg/kg/dose BID rounded to nearest 0.625mg, 1.25mg, 2.5mg, 3.125mg, 5 mg)
    - And/or ASA 5 mg/kg/day (max=81mg/daily)

Recommend follow up via virtual visit or in clinic within 1 week of discharge with the following:

- Repeat ECHO if any abnormality documented at any time during admission
- Repeat ECG if any conduction or rhythm abnormality documented at any time during admission
- Repeat D-dimer, LDH, ferritin, CRP, CBC+diff, (BUN/Cr if discharged on LMWH), liver function tests (if discharged on apixaban), and TEG with platelet mapping or VerifyNow if discharged on aspirin with or without anticoagulation.

PMIS-T or MIS-C Antithrombosis Management Guide for Inpatients

Antithrombosis decisions may change over clinical course and are based on:

-Trends in D-dimer, aPTT, PT, fibrinogen, CBC/diff, LDH, ferritin, and TEG with PM

-Serial ECHOs (focus on coronary ectasia)

Screen all PMIS-T/MIS-C for any one of the following features:

- Documented thrombosis
- Moderate to severe ventricular dysfunction
- Increasing vasoactive infusion requirement
- Sedated and/or paralyzed
- Coronary dilation/aneurysm
- D-dimer >3mcg/dL (or up-trending D-dimer)
- Any rhythm abnormalities: heart block, etc.
- TEG clot strength >80mm

Reassess daily based on available data

YES

LMWH treatment (goal anti-Xa 0.5-1units/mL)

-NOTE: If unstable, risk of bleeding, or severe renal dysfunction, then therapeutic UFH (goal anti-Xa=0.3-0.7units/mL) or bivalirudin (1.5-2.5x baseline PTT or DTI=60-90s)

None of the above features?

All other PMIS-T / MIS-C patients

-LMWH prophylaxis (goal anti-Xa=0.2-0.4units/mL)

- Renal failure: IV/SubQ UFH or apixaban at prophylactic dosing

CONSIDER ADDITION OF ASA FOR:

-KD (follow AHA antiplatelet and anticoagulation recommendations)
-Coronary dilation
-TEG with PM showing high clot strength despite treatment anticoagulation
-ST segment changes
-Elevated troponins

- Low dose ASA 5 mg/kg/day (max =81 mg) for most patients
- Consider TEG + PM or VerifyNow AA to assess efficacy. (AA>75 or ARU<550)

* If any ST segment changes or elevated troponins, consider single dose of 10 mg/kg (max=325 mg) followed by maintenance low-dose ASA daily

At Discharge:

- If thrombosis, then continue treatment dosing anticoagulation for a total of 6-12 weeks or longer if indicated.
- For all other PMIS-T/MIS-C patients with cardiac involvement: continue prophylactic anticoagulation (LMWH or apixaban) and reassess with labs listed above at 1-2 weeks. Continue therapy until inflammatory markers normalize.
-For all PMIS-T/MIS-C pts started on ASA: continue ASA and reassess labs listed above and ECHO at 1-2 wks. Continue until ongoing cardiac abnormalities normalize. Reassess labs and ECHO every 4-6 weeks.

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SODIUM-GLUCOSE COSTRANSPORTER-2 INHIBITORS (SGLT2i)

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

There are no significant data on the benefit of SGLT2i in pediatric patients with heart failure (HF), although growing literature strongly supports the use of SGLT2i in adults with HF with either reduced or preserved ejection fraction.[1,2] The joint ACA/ACC/HFSA guidelines on management of HF includes the use of SGLT2i in adults with HFrEF as a class I recommendation.[3] The ESC has a class I recommendation for use of SGLT2i in adults with HFmEF and HFpEF as well.[4] The safety of SGLT2i in pediatric patients with HF is not fully established, but early reports demonstrate general safety and tolerability.[5]

ACTION REVISED DATE: 05/23/2024

OBJECTIVES

- Provide background and resources regarding use and dosing of SGLT-2 inhibitors (SGLT2i) in children with heart failure
- Provide guidance regarding considerations and precautions for use of SGLT2i in children with heart failure

PROTOCOL

For those considering the use of SGLT2i in pediatric patients:

- Timing and indications for SGLT2i initiation are not clear in pediatric heart failure.
- SGLT2i can be considered in the setting of systolic or diastolic HF and in the setting of Fontan circulatory insuffciency. This document provides guidance for usage of SGLT2i but does not address indications for use.
- SGLT2i can be considered in conjunction with other medications used to treat HF or alone. They may be started after other medications have been maximized or may be started sooner due to relatively limited side effect profile and benefit in those with impaired diastolic function.
- Goal Target Dose is based on major guidelines for therapy in adult patients with HF with reduced ejection fraction (HFrEF). See table for recommendations in patients >50kg. Dosing for patients <50kg has not yet been clarified.
- Dosing of pediatric patients with smaller doses of dapagliflozin has been reported with titration upwards if glucosuria is not found on lower doses.

Additional consideration/precautions:

The frequency of urinary tract infections and genital infections is increased in patients receiving an SGLT2i. An individualized discussion of the the risks and benefits based on a patient's dermatologic and urologic history is encouraged. Concomitant use of immunosuppressive medications should also be taken into consideration.

- Relative dehydration and natriuresis may be possible, and pre-emptive reduction in diuretics can be considered.
- eGFR may initially decline with initiation of SGLT2i due to tubuloglomerular feedback. Among adult patients, SGLT2i use is associated with preservation of kidney function and is now recommended for adults with chronic kidney disease.

SGLT2i associated ketoacidosis and Endocrine Related Considerations

- Euglycemic diabetic ketoacidosis (EuDKA) has been reported in adults on SGLT2i; it should be considered when a patient has an anion gap metabolic acidosis and/or elevated ketones, even when blood glucose < 200, or lactic acidosis of unclear etiology.[6] Consider checking ketones regardless of blood glucose levels if EuDKA is suspected.
- The recommendation from the FDA is to consider **holding SGLT2i 3-4 days before scheduled surgery**.[7]
- During times of fasting, dextrose-containing fluids + insulin can be considered. When DKA is supected, insulin should be started.[8]
- If a patient is already on insulin or other glucose-lowering medication, consider consultation with an endocrinologist prior to SGLT2i initiation.

Dosing Considerations:

Medication of Choice		Initial Dose	Titration Amount	Goal Dose Minimum	Dose Maximum
< 50 kg	Dapagliflozin	0.1 mg/kg/dose daily	0.1 mg/kg/dose daily	0.1 mg/kg/dose daily	0.2 mg/kg/dose daily
≥ 50 kg	Dapagliflozin	5-10 mg daily	5 mg daily	5 mg daily	10 mg daily
	Empagliflozin	5-10 mg daily	--	10 mg daily	10 mg daily

Therapeutic monitoring:

- Baseline renal function and Glucose
    - Check renal panel, HgbA1c, and glucose prior to initiation. Timing based on patient age and clinical status but generally should be within 7 to 14 days of initiation.
    - Repeat assessment should be performed within 2 weeks to 6 weeks or earlier if clinically indicated to assess hydration and renal function.
- Urinalysis for glucosuria
    - For smaller patients on smaller doses of dapagliflozin, repeat urinalysis within 1-3 weeks is reasonable to assess for presence of glucosuria. If glucosuria is not present, it is reasonable to increase to the higher dose if tolerated.

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PART THREE

Fontan

Considerations for Advanced Heart Failure Consultation in Fontan Patients:

Guidance for primary cardiologists

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

To aid in decision-making on timing of referral of Fontan patients for advanced heart failure consultation with the aim of improving timely referral and facilitating collaborative care to enhance patient outcomes.

Patient population: Fontan patients

Considerations for referral by type of clinical Fontan dysfunction

(recognizing overlap exists between categories)

Cardiac/Systemic Ventricular Dysfunction

1) Severe[1] systolic dysfunction by echocardiogram, MRI, or cardiac catheterization.
2) Moderately depressed (by qualitative assessment) systolic function on imaging when accompanied by ≥moderate systemic AV valve regurgitation.
3) Significant growth derangement or failure to thrive including cachexia or linear growth failure
4) Decreasing exercise tolerance by patient report or as measured on sequential formal exercise testing or 6-minute walk
5) Significant electrophysiologic abnormalities, including recurrent arrhythmias despite therapy, implantation of a cardiac pacemaker, or aborted sudden cardiac death event

Fontan Pathway Dysfunction

1) Symptomatic, chronic fluid overload persisting despite new or increasing diuretic therapy
2) Occurrence of chronic pleural effusions or ascites, chylous or nonchylous, refractory to therapy and occurring outside the initial Fontan post-operative period
3) Major hemodynamic disturbance *resulting in symptoms* despite therapy including: low systemic cardiac output, diastolic ventricular failure, significantly elevated Fontan pressure, or symptomatic cyanosis

Lymphatic Dysfunction

1) Protein-losing enteropathy that has failed medical therapy and requires multiple hospital admissions in a 12-month period or PLE requiring repeated albumin infusions to treat symptoms despite standard PLE medical therapy
2) Plastic bronchitis requiring chronic therapy

Extra-cardiac Dysfunction

1) Hemoptysis requiring evaluation that is unrelated to an infection and persists after standard intervention
2) Liver disease with impaired synthetic function/abnormal liver function testing or undergoing evaluation for liver transplantation
3) Chronic kidney disease – Stage 3 or greater[2]

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[1] Severe systolic dysfunction in a single ventricle can be graded by a qualitative assessment or by using calculated ejection fractions as follows: < 35% by echocardiogram or MR for a single LV; < 30% by MR for a single RV.

[2] Stage 3 CKD is an eGFR between 30 and 60 mL/min per 1.73 m^2

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Evaluation and Management of Protein Losing Enteropathy in Fontan Patients

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

The common endpoint of staged surgical palliation for patients with single ventricle physiology is the Fontan procedure. Approximately 5-12% of Fontan patients will develop protein-losing enteropathy (PLE), characterized by the abnormal intestinal loss of serum proteins. It is a potentially devastating disease with 5-year mortality reported as high as 50% after diagnosis. Although the exact cause of PLE is incompletely understood, abnormal mesenteric resistance, chronic systemic and enteral inflammation, derangement of the lymphatic circulation, and abnormal enterocyte basal membranes all likely play a role in PLE's development and progression. The role of abnormal lymphatic anatomy and function is increasingly appreciated. Regardless of underlying pathophysiology, PLE leads to significant morbidity in Fontan patients. Treatment strategies have evolved over time and have variable reported efficacy, contributing to the challenges in management of these complex patients.

ACTION REVISED DATE: 12/12/2024

OBJECTIVES

To offer standardized guidance for evaluation and management of Fontan patients during initial and recurrent episodes of PLE.

PROTOCOL

1. **Clinical definition of PLE in Fontan patients**
   Concurrent with the enteric loss of protein, patients with PLE present with a history of edema, abdominal distension (ascites), diarrhea, and/or effusions. Patients may also have reduced linear growth velocity with reduced bone density in chronic cases due to disruption in calcium regulation as well as consequence of steroid therapy. PLE patients may have increased susceptibility to infection due to stool immunoglobulin loss and lymphopenia. Laboratory derangements include hypoalbuminemia and hypoproteinemia. Coagulation abnormalities may also be present due to dysregulation of clotting factors which places patients at additional risk of thromboembolic events. PLE is often a chronic disease with a relapsing and remitting clinical course over time.

Hallmarks of PLE Presentation:

low serum albumin
–
positive stool alpha-1-antitrypsin
–
edema, effusions, ascites, GI symptoms, diarrhea

2. Initial evaluation of PLE

Laboratory evaluation			Diagnostics		Invasive imaging and intervention considerations (patient specific)
Blood			Echocardiogram	Holter monitor	Cardiac catheterization
Albumin	CBC w/diff	LFT	Electrocardiogram	Cardiac MRI	Lymphangiogram
Total protein	BMP w/Mg	+/- ATIII	CXR (AP & Lat)	+/-Venous US	MRI Interventional radiology
IgG level	INR, PTT	Vitamin D	Abdominal US		
Urinalysis	Stool alpha-1-antitrypsin				

**PLE specific lab work and diagnostic testing should be performed with new diagnosis PLE and then as indicated with recurrence of PLE. Invasive imaging and intervention should be performed on a patient-by-patient basis after initial evaluation.*

a. Physical Exam
- height, weight, BMI
- peripheral edema and/or ascites
- muscle wasting
- abdominal distension, hepatomegaly
- pulmonary exam changes consistent with pleural effusion

b. Laboratory Evaluation
- Serum albumin
- Serum total protein
- Stool alpha-1 antitrypsin level
  - Ideally collected via 24-hour stool collection (gold standard) but consider spot level in patients in whom 24 collection not possible.
- Complete metabolic profile (CMP) (including serum electrolytes, BUN, creatinine, calcium and magnesium) with inclusion of liver function tests
- Complete blood count with cell differential (CBC w/diff)
  - Assess for anemia and lymphopenia.
  - Coagulation studies, including INR and partial thromboplastin time (PTT)
  - Serum immunoglobulin G level
  - Serum vitamin D level
  - Pre-albumin level
  - Consider urinalysis, including protein, and urine creatinine
  - Consider anti-thrombin III level with history of thrombosis

c. Diagnostic studies
- Echocardiogram to assess current function and structures with particular attention to fenestration status, Fontan flow characteristics, pulmonary vein patency, atrial septum restriction, atrio-ventricular valve regurgitation, ventricular function, and ventricular outflow obstruction.
- Electrocardiogram (ECG) to assess baseline rhythm and serial changes
- Chest X-ray (CXR) with AP and lateral views to assess for pleural effusion and/or pulmonary edema

- Abdominal ultrasound (US) with Doppler to assess for ascites, liver size/architecture/vessel flow, spleen, and evidence of portal hypertension
- Holter monitor to assess baseline rhythm, sinus node dysfunction, occult arrhythmia
- Consider cardiac magnetic resonance imaging (MRI) to further assess function, Fontan circuit, valve function, potential anatomical obstruction, and collateral burden
- Consider venous US of upper and lower extremity veins to assess for patency and presence of new narrowing or obstruction

d. Invasive imaging and interventions
   - Cardiac catheterization
     - Measure Fontan pressures, cardiac output, ventricular end-diastolic pressure, and pulmonary vascular resistance, which will help to guide the medical management.
     - Evaluate and possibly treat any anatomic abnormalities that increase pressure in the Fontan pathway, such as baffle obstruction, pulmonary artery stenosis, and aortopulmonary collaterals
   - Consider lymphangiogram
     - MRI lymphangiogram
     - Interventional radiology

e. Lymphatic Intervention
   Patients with PLE recalcitrant to medical interventions may be considered for targeted lymphatic system interventions.

   The Fontan circulation, with its obligate increase in central venous pressure, is accompanied by increased hepatic lymphatic fluid production. This increased lymphatic volume drains via lymphatic channels that connect to the intestinal lumen, usually the duodenum. In addition, increased hepatic lymphatic fluid production may be accompanied by ascites. Both of these mechanisms may be partly responsible for the development of PLE. Hepato-duodenal lymphatic connections can be visualized by intra-hepatic or intra-mesenteric dynamic contrast MR lymphangiography using gadolinium. The presence of such connections can also be proven by intrahepatic lymphatic injection of iosulfan blue, with confirmation of iosulfan blue entering the duodenal lumen via concurrent endoscopy. These connections can then be embolized using glue injected via a transabdominal approach into the hepatic lymphatic channels; improvement or resolution of PLE has been reported in some patients undergoing this procedure.

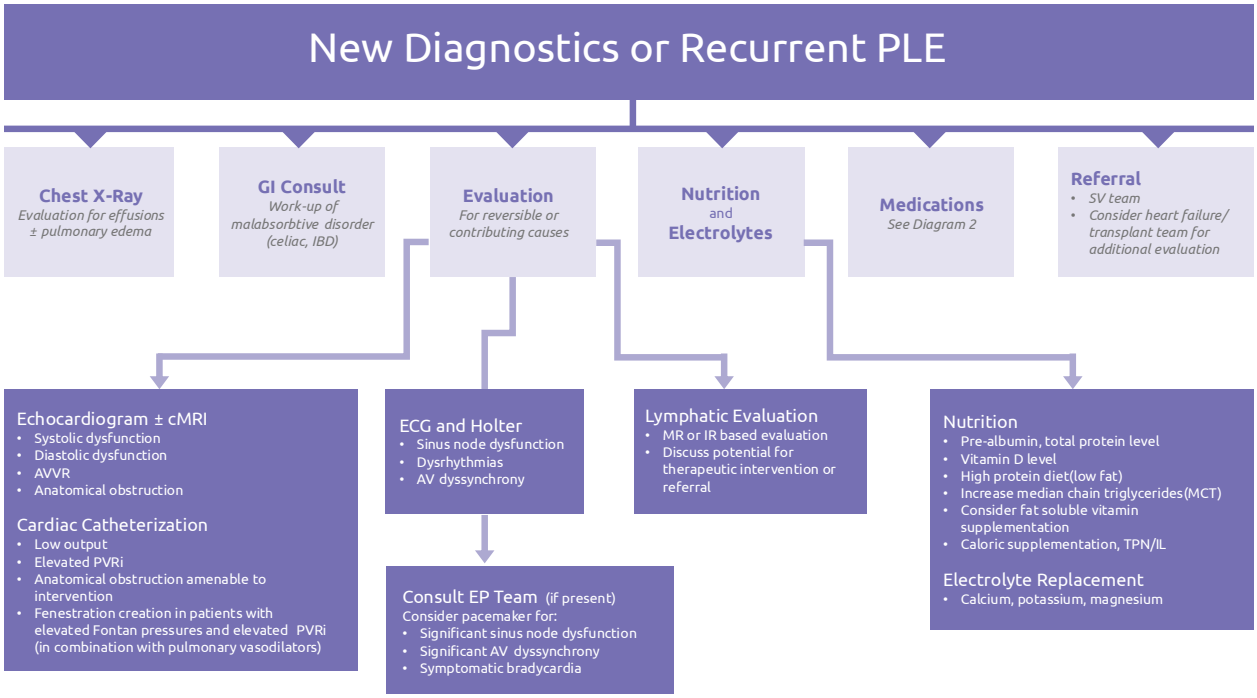
   “Rerouting” of the innominate vein (which receives thoracic duct effluent) to a lower-pressure cardiac chamber has also been performed in some patients with severe PLE. In such interventions, the innominate vein drainage is diverted to the left atrium, either via direct surgical anastomosis or by transcatheter means using a covered stent. This approach appears to be most effective for patients with high transpulmonary gradients. In practice, this approach is not commonly utilized.

   There are no absolute contraindications to lymphatic intervention. These procedures are not widely available at all centers but can play an important role for some patients who have failed all other therapies and may not be ideal candidates for heart transplantation. The following are relative contraindications or patients in whom lymphatic intervention may be less effective:
   - Presence of a permanent pacemaker, which may preclude the ability to perform MR lymphangiography. Direct intranodal lymphangiography using iodinated contrast can be performed as an alternative, but is cumbersome
   - Inability to hold anticoagulation for several days post-procedure due to severe thrombotic disease (due to requirement for transabdominal puncture for glue administration)
   - Pre-existing pancreatic or biliary disease (also due to requirement for transabdominal puncture)

- Patients who have undergone previous thoracic duct embolization or ligation
-

Lymphatic procedures are not without reported risks. Reported potential complications include transient abdominal pain, hemoperitoneum, transaminase elevation, bile duct spasm/obstruction, radiation-induced skin burns, pulmonary emboli of embolic material (potentially leading to edema or infarct), leg edema, pneumoperitoneum, stroke from embolic material, and uncommonly pancreatitis and/or biliary peritonitis.

f. Expert consultation
   - Dietician to help with initiation of high-protein diet and supplements
   - Hepatology/Gastroenterology with expertise in Fontan population and PLE
   - Electrophysiology (EP) for patient with concern for contributing sinus node dysfunction, arrhythmia and/or significant atrioventricular desynchrony
   - Consider Heart failure/transplant team referral as per ACTION document *"Considerations for Advanced Heart Failure Consultation in Fontan Patients"*



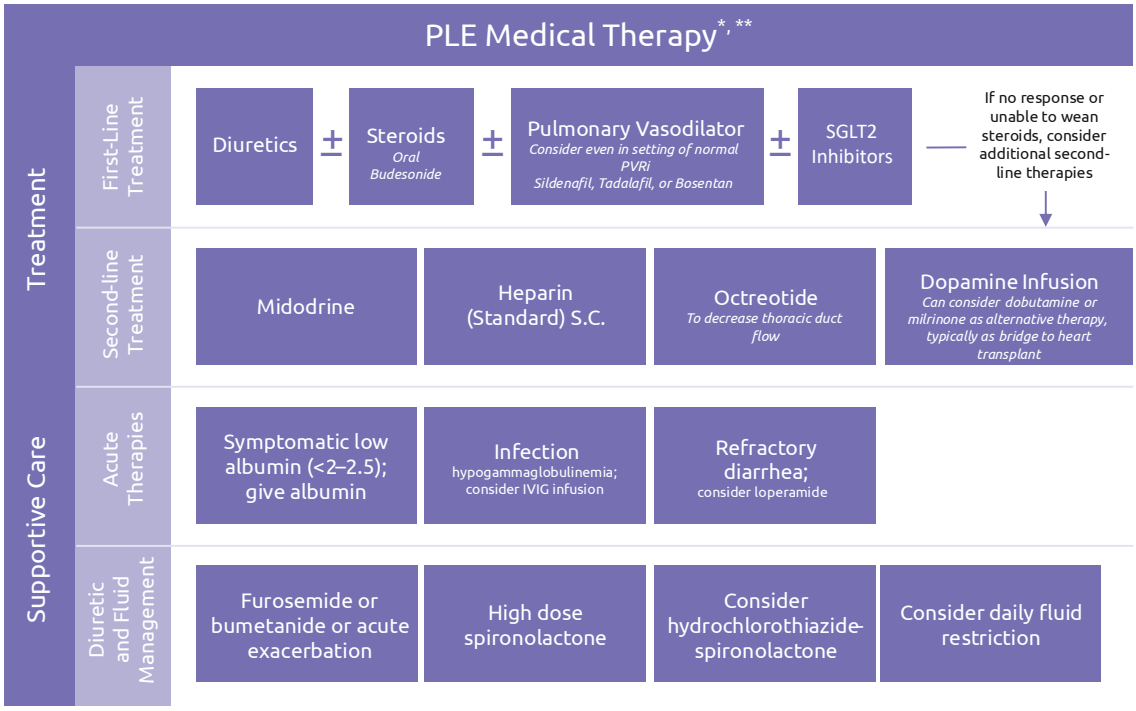
3. Management of PLE

Management of PLE includes evaluation for cardiac issues that may be amendable to intervention to optimize Fontan physiology and titration of medical therapy to treat related symptoms. Patients should be evaluated for anatomical lesions that can be treated via cardiac catheterization, dilation/stent of obstruction or embolization of significant collaterals. Patients should also be evaluated for potential venothrombosis given increased risk, particularly in patients with prior history or low ATIII levels. Some patients with identified lymphatic abnormalities may be candidates for lymphatic based interventions. Any rhythm disturbances, such as tachyarrhythmias or bradycardia, should prompt discussion with EP regarding possible anti-arrhythmic or pacing therapy. Medical management focuses on reducing volume overload, improving nutrition, and reduce recurrence. Risk and benefits of potential diagnostic evaluations and treatments presented in this guideline should be discussed in a multi-disciplinary fashion with involvement of the patient and family.

Depending on severity of symptoms and PLE at presentation, patients may require hospital admission for medical therapy, particularly in patients requiring intravenous therapy.

a. Dietary interventions (in consultation with experience dietician)
   - High-protein diet appropriate for age
   - Consider low long chain triglyceride (LCT) diet supplemented with medium chain triglycerides (MCT) may be beneficial if lymphatic abnormalities are contributing to PLE pathophysiology. Decreasing LCT intake theoretically decreases lymphatic flow and pressure which is thought to contribute to decreased losses via gastrointestinal tract. When this therapy is followed, it is crucial to provide adequate LCT, 2-4% of total calories, to prevent essential fatty acid deficiency. A serum triene-to-tetraene ratio can be obtained to assess for essential fatty acid deficiency.
   - Consider supplementation of fat-soluble vitamins in water-soluble forms to account for increased losses via the gastrointestinal tract.
   - In severe refractory cases, may require period of bowel rest and concurrent total parental nutrition (TPN) support
   - Discuss with team (including cardiac catheterization and interventional radiologist) referral for lymphatic intervention

b. Medications



**See suggested dosing in table below. If patient does not respond to first line therapy, discuss second-line therapy treatment strategy with advanced heart function support team.*

***Anticoagulation note: Warfarin levels may be affected by albumin infusions given changes in protein bound drug amounts. Caution should be applied in adjusting warfarin dosing in patients on warfarin receiving intermittent albumin infusions.*

Medication	Dosing Recommendations	Implications of therapy/clinical pearls
Albumin[1]	1-4g/kg/d divided every 4-6 hours with a goal of increasing serum albumin to ≥3 g/dL.	• Use 25% product • Follow albumin infusion with administration of diuretic such as loop diuretic • Central access not required
Aspirin	Daily 81mg po dosing	• Due to increased thrombosis risk • If thrombosis, consider change to SQ LMWH or warfarin
Budesonide	Oral delayed release capsule: - Children less than 7 years: starting dose 6 mg once daily[2,3] - Children greater than or equal to 7 years: starting dose 9 mg once daily or 3 mg Q8H[4,5]	• Consider "pulse" steroid course of 3-5 days with first or mild PLE episode (some patients may require longer term therapy with taper) • If prolonged therapy: after clinical improvement and albumin greater than 3 g/dL for at least 1-3 months, then consider wean over several weeks to 3 mg once daily or every other day with goal albumin greater than 2.5 g/dL. Consider completely tapering off in patients after augmenting other therapies and/or with significant side effects. • Prolonged therapy increases risk of acquired adrenal insufficiency.
Dapagliflozin (or Empagliflozin)	<50kg: Dapa 0.1mg/kg/dose daily ≥50Kg: Dapa 5-10mg (max 10mg) daily Empa 5-10mg (max 10mg) daily	• Mixed report of efficacy for PLE but widely used as first line clinically • Possible side effects of UTI and/or peritoneal infections • SGLT2i must be held at least 24-72 hours prior to planned NPO to avoid risk of ketoacidosis
Dopamine[6]	IV: 3-5 mcg/kg/min starting dose	• May provide benefit outside of improving cardiac function, chronotropy and/or mesenteric blood flow
Dobutamine	IV: 0.5-1 mcg/kg/min starting dose	• Often used as bridge to heart transplant
Furosemide	- IV: 0.5-2mg/kg/dose children, 20-40mg adolescents starting dose - PO: 0.2-2mg/kg/dose children, 20-40mg adolescents - Q6-24 hour dosing - 2 mg/kg/day reported in PLE (route unspecified)[7]	• Titrate dose and frequency to effect. Gradually decrease frequency and dose to minimal effect dose.
Heparin (UFH)[8,9,10]	SQ: 5000 units/m2/day divided BID	• Long term administration (greater than 6 months) can cause bone loss/softening due to a reduction in bone mineral density • Discontinue therapy if no response after trial of 2-3 months • If titrating higher than recommended dosing, consider obtaining UFH level 6 hours after dose given • LMWH does not appear to have the same efficacy/benefit that UFH does for these patients • Contraindicated in patients with recent significant bleeding
IVIG[11]	IV: 1g/kg/dose every 4 weeks *consider higher doses and/or more frequent administration in patients with very low IgG levels	• Consider dose adjustment for obesity (Ideal or adjusted body weight) • Some patients experience infusion site discomfort with peripheral infusion
Loperamide	- Use in children less than2 years generally not recommended - Use age and weight specific dosing	• One case report of use in an adult patient[12] • Use lowest effective dose for shortest duration • Use for PLE beyond 1 month has not been described
Midodrine	Children: starting dose ~0.2 mg/kg/day PO divided TID[13] Adolescent/adult: starting dose 2.5 mg PO two to three times daily[13] Maximum dose: 10 mg PO TID	• CHCO non-formulary medication • Monitor for supine hypertension and bradycardia
Milrinone	IV: 0.25-0.5 mcg/kg/min starting dose	• Caution/adjust dose for renal impairment • Often used as bridge to heart transplant
Octreotide	- continuous IV: 1-2 mcg/kg/hour - IM LAR depot: 10-20 mg monthly reported[14] - IM immediate release: 50 mcg TID reported[14]	• After continuous IV initiation, may convert to subcutaneous injections • May cause hyperglycemia, hypoglycemia, hypothyroidism, cholelithiasis • Cardiac side effects: bradycardia, QT prolongation • Caution/dose adjustment in patients with hepatic impairment
Sildenafil	Infants and children:	• Titrate to goal dose over several days • If no improvement within 3+ months, wean off

	- Starting dose: 0.5 mg/kg/dose PO every 6 hours reported[15] - Maximum dose: 1.5 mg/kg/dose PO every 6 hours reported[15] - Maximum total daily dose: 60 mg PO Adolescents and adults greater than 45 kg: - Starting dose: 10 mg PO every 8 hours	
Spironolactone[16,17,18]	PO/NG/G-tube: 4-6 mg/kg/day divided BID	• Consider transition to eplerenone if gynecomastia develops • Periodic serum potassium checks necessary
Tadalafil	0.5-1 mg/kg/dose once daily. Maximum dose is 40 mg (if tolerated)	• Consider as alternative for sildenafil with once daily dosing in older patients

4. Chronic PLE management

PLE in Fontan patients is often punctuated by exacerbation episodes with or without chronic symptoms. These patients require close monitoring for early intervention and medical optimization. PLE also places Fontan patients at increased risk for non-cardiac sequela which treating providers must be aware of. In some patients, severity and frequency of symptoms prompts referral for heart transplantation. In general, early referral to the heart transplant team is preferred.

a. Clinic visits
   - Every 6 months for patients with quiescent PLE
   - More frequently for patients with active PLE with consideration of escalation of treatment at each visit

b. Laboratory evaluation
   - Every 3-6 months early after diagnosis and then at least annually: BMP, Magnesium, LFTs, CBC, albumin, total protein

c. Diagnostic testing (in addition to routine cardiac testing for Fontan population
   - Consider DEXA-bone scan bi-annually in patients at high risk for or with prior h/o osteopenia

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Fontan VAD Management Protocol

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

In select cases of failing Fontan physiology, VAD has been demonstrated to be effective as a form of circulatory support. Physiologic optimization of VAD parameters in this unique population is likely to require individualization. There is limited published literature on VAD support of Fontan patients and we propose these recommendations based on collective clinical experience.

ACTION REVISED DATE: 10/28/2024

OBJECTIVES

1. Optimize physiologic support in post-VAD Fontan patients to include minimization of central venous pressures (CVP) and maximization of effective (non-aortopulmonary collateral) cardiac output.
2. Better define circulatory physiology in post-VAD Fontan patients.

PROTOCOL

PRE-OPERATIVE CONSIDERATIONS

1. Indications.
    a. VAD support can be considered for Fontan patients with:
        i. Signs and symptoms of heart failure or other signs of Fontan failure not responsive to medical management, *and at least one of the following*
            1. Poor systemic ventricular systolic function
            2. Poor systemic ventricular diastolic function
            3. Atrioventricular valve regurgitation
    b. The role of VAD support in individuals with isolated PVR elevation is unclear
2. Pre-VAD Assessment
    a. Cath:
        i. Consider pre-VAD cardiac catheterization to assess pressures, PVR, Fontan obstruction and presence/severity of shunts (ie Aorto-pulmonary (AP) collaterals)
        ii. In some cases, transcatheter closure of AP collaterals may be considered and any significant anatomic obstructions should be addressed, recognizing that gradients may be underestimated in the setting of low flow states and poor cardiac output
        iii. Perform PVR reactivity testing if concern for PVR elevation, to help inform pulmonary vasodilatory use
    b. Imaging:
        i. Ventricular function and distal anatomy may be incompletely characterized by echocardiography
        ii. Consider cardiac MRI to quantify systolic function, volumes, obstruction, flow differential, and collateral burden as well as anatomic data to inform device placement
        iii. In patients who cannot have a CMR, ECG gated CT angiography provides anatomical and some functional data

iv. MRI or CT can be used for 3D modeling and virtual fit

3. Multi-organ system assessment:
    a. Liver disease is not a contraindication to VAD support but extent of liver disease should be thoroughly assessed, including cross-sectional imaging (CT or MRI), assessments for varices and porto-systemic shunts, and evaluation for HCC. If available, obtaining a baseline elastography (ultrasound or MRI) allows for serial evaluations post-VAD with potential prognostic implications
    b. Renal disease may be underestimated by creatinine alone, and other methods for evaluation of renal function are recommended (such as Cystatin C, timed urine collection, or nuclear GFR)
    c. Consider pre-VAD head imaging and detailed neurologic exam.
    d. In patients who are able, consider obtaining baseline functional assessment with cardiopulmonary exercise testing or 6-minute walk
    e. In patients who are able, consider conducting a frailty assessment either using Fried criteria or the Essential Frailty Toolset
    f. Consider obtaining a formal nutritional evaluation
    g. Consider hematology consultation in patients with history of prior thromboembolic events

SURGICAL CONSIDERATIONS

1.) In some centers, a fenestration is created at the time of VAD placement.

Refer to separate *ACTION Harmonized Protocol on Patient and Device Selection*

POST-OPERATIVE CONSIDERATIONS

1. Post-op monitoring
    a. Lines: Optimizing blood flow through the Fontan circuit is critical, and requires in the first 3-5 days post-op:
        i. A reliable CVP catheter, *and either a* pulmonary arterial (PA) Swan-Ganz catheter, *or* an atrial line
        ii. CVP line alone can be considered, especially if low concern for PVR issues.
    b. Monitor NIRS, UOP, and lactate closely in the first 24-48h post-op
    c. Trend mixed venous saturations
    d. If a CardioMems was previously implanted, it can be used to help guide postoperative management
2. Hemodynamic targets
    a. Cardiac index (CI): Recommend initial target of 3.5-4.5 L/min/m^2 including both VAD and native output, to be titrated as needed to the filling pressures and hemodynamic requirements of the individual patient
        i. Patients' native cardiac output will contribute a part of the total CI
        ii. Higher CI may be needed, especially in the presence of significant AP collaterals
        iii. Target A-VO_2 gradient <30%
    b. Blood pressure: May require higher target than other heart diseases post-VAD, as there may be detrimental physiologic changes which occur with excessive vasodilation. Depending on CVP (which typically is >10 mmHg with a Fontan circulation) doppler or mean arterial pressure targets of as high as 100-120 mmHg for continuous flow devices have been reported to be necessary to achieve adequate end-organ perfusion pressure (PP = MAP – CVP).

c. CVP: Target CVP is based on a balance of decreasing systemic venous congestion while maintaining adequate VAD filling. Consider pulmonary vasodilators such as iNO in immediate post-operative period and sildenafil to help lower CVP.

3. Trouble-shooting: In cases of low cardiac output, consider the following:
    a. Inadequate preload
        Causes:
        i. Volume status or bleeding
            1. Signs: Low CVP, low cardiac output, suction events, low flow alarm
            2. Treatment: Volume, hemostasis
        ii. Elevated PVR
            1. Signs: Elevated CVP with low PCWP, hepatic congestion
            2. Treatment: consider pulmonary vasodilator therapy, fenestration creation, optimize ventilation strategy
        iii. Obstruction of pulmonary venous return
            1. Signs: Increased PCWP, increased pulmonary edema on CXR
                a. More frequently encountered with atrial cannulation/smaller patients
            2. Treatment: Surgical revision
    b. Tamponade
        Causes:
        i. Pericardial effusion, tissue edema, oversized intracorporeal VAD
            1. Signs: Increased CVP, increased PCWP, decreased cardiac output
            2. Treatment: Volume resuscitation, opening chest. (Note: because TTE/TEE often inadequate for imaging, treatment of tamponade often requires proceeding with surgical intervention due to high index of suspicion without confirmatory imaging)
    c. Increased afterload
        Causes:
        i. ↑SVR
            1. Signs: Decreased VAD flows, decreased power consumption, increased systemic blood pressure, increased pulsatility
            2. Treatment: Systemic vasodilator
        ii. Thrombus: in either the inflow or outflow, obstructing flow into/out of the device
            1. Signs: uptrending power consumption and evidence of hemolysis
            2. Treatment: increase anticoagulation, thrombolytic therapy, or device change
    d. Ineffective Cardiac output
        Causes:
        i. Excessive aortopulmonary collateral flow
            1. Signs: low Fick cardiac output or low mixed venous oxygen saturations (MVO2) with high VAD flows
            2. Treatment: cardiac catheterization for coiling, increase VAD speed
        ii. Neo/Aortic Insufficiency

1. Signs: low Fick cardiac output or low mixed venous oxygen saturations (MVO2) with high VAD flows
2. TTE for assessment
3. Treatment: Increase VAD flows typically will not overcome valve insufficiency; strongly consider surgical repair/replacement or catheter-based interventions (if thought amenable)

iii. Excessive Vasodilation
1. Signs: end-organ hypoperfusion in the setting of elevated VAD-assessed cardiac output matched by Fick cardiac output. Consider milrinone accumulation (esp if impaired renal function), infection, vasoplegia
2. Treatment: treat underlying etiology (ie, infection), vasopressin, methylene blue

4. Studies:
   a. Echocardiogram:
      i. Used to assess aortic valve opening, aortic and atrioventricular valve regurgitation, ventricular decompression, clots, and fenestration (if present) gradient
      ii. Consider TTE in first 1-3 days post-op and weekly while on vasoactive or respiratory support
   b. Ramp Study (see attached worksheet): Using a ramp study to optimize VAD support can be considered. If performed, recommend using both hemodynamic (cath) and imaging (echo) assessments while VAD settings are titrated
      i. Indications for Ramp Study:
         1. Optimization recommended within 2 weeks post-op, 2-3 months postop or prior to discharge, and 6-12 months post-op
         2. Evidence of heart failure/elevated Fontan pressures, persistent symptoms, or any clinical deterioration
         3. Suspicion for device thrombus
         4. If Swan-Ganz catheter,atrial or CVP line in place, Ramp Study (with echo) recommended early post-op and with any change in clinical status or support
      ii. Goals of Ramp Study:
         1. Decompression of ventricle and common atrium
         2. Minimize atrioventricular valve regurgitation (AVVR)
         3. No more than trivial aortic insufficiency
         4. Intermittent opening of the aortic valve
         5. Optimize Fontan pressures and PCWP
         6. Optimize AVO_2 difference
      iii. Safety:
         1. Ensure the patient is on therapeutic anticoagulation
         2. Ensure the ventricle and aortic root are free from thrombus
            a. Risk of thromboembolism with reduction in pump speed
         3. Allow ≥ 2 minute stabilization between speed changes
            a. When decreasing RPMs: monitor for increasing AVVR, increasing aortic valve opening (AoV), increases in Fontan pressures and PCWP, cyanosis (if fenestration) and any symptoms

b. When increasing RPMs: monitor for impendence of flow into inflow cannula, changes in Fontan pressures and PCWP, cyanosis (if fenestration), AoV not opening, increase in AI, suction events, and any symptoms

4. Test endpoints: completion of test/desired outcome attained, suction event, hypotension, hypertension, increased cyanosis, symptoms

iv. Echocardiography during Ramp Study, suggested views (adapted from *ACTION Harmonized Protocol on Echocardiography for CF-VADs*, refer to this protocol for images):

1. PLAX (2D, 3 beats): Ventricle internal diameter in diastole x3 beats
2. PLAX of PSX (M-mode, 10 beats): Aortic valve opening (out of 10 beats)
3. PLAX (Color, 3 beats): degree of AI
4. PLAX or A4C (Color, 3 beats): degree of AVVR
5. PSAX (2D, 3 beats): function
6. A4C (2D, 3 beats): function
7. PLAX, PSAX or A4C (Color, 3 beats): degree of AVVR
8. A4C or PLAX (2D, Color, PW, CW): inflow cannula
9. A4C or best view of fenestration if present (2D, PW): fenestration gradient

c. Cardiac catheterizations:

i. Recommended as part of Ramp Study as above (at 2 weeks post-op, 2-3 months post-op or prior to discharge, and 6-12 months post-op).

ii. Consider assessing for and addressing AP collaterals, especially if elevated wedge/end-diastolic pressures with evidence of organ hypoperfusion and high VAD output due to AP collaterals based on above assessment.

iii. Consider placement of an implantable pulmonary arterial pressure monitoring device to guide diuretic and VAD management based on findings during in-house RAMP studies.

PARA-CORPOREAL DEVICE CONSIDERATIONS

The above guidelines generally refer to patients with intracorporeal CF devices, though many of the same principles apply to smaller Fontan patients with a para-corporeal device.

1. Fontan patients typically have high CI needs and larger Berlin pumps are required than in patients with biventricular physiology
2. Some centers report starting with a CentriMag (with Berlin cannulas) to determine cardiac output needs and then converting to a Berlin pump
3. Berlin Heart: Blood flow through the Fontan is continuous and if supported with a pulsatile pump, there is no flow into the pump during pump systole. Therefore, to ensure adequate unloading and to minimize atrial/pulmonary venous hypertension, consider targeting ~75% fill and shortening the percent of time in pump systole.

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Ramp Study for Fontan VAD Patients on HW/HM3

Patient Name:_____ Patient MRN:_____

	VAD Settings				Hemodynamics					Echo		
	Speed (RPM)	Flow (LPM)	HW: Pulsatility HM3: PI	Power (Watts)	MAP (mmHg)	Fontan Pressure (mmHg)	PCWP (mmHg)	Ao/O2 sat	MVO2	AoV opening (%)	AI	AVVR
Baseline:												

Final Setting:	

Comments:

MAP should be recorded from arterial line or from doppler BP if no arterial access

2 minute stabilization period between speeds (minimum)

AoV opening: % aortic valve opening assessed using M-mode of AoV in parasternal long axis view, at least 10 consecutive cardiac cycles reviewed

AI/AVVR: graded 0 to 6; 0=none, 1=trace, 2=mild, 3= mild-mod; 4=mod; 5=mod-sev; 6=severe

Study Comments:

PART FOUR

Muscular Dystrophy

Dystrophinopathy Ambulatory Electrophysiologic Monitoring Harmonization

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Sudden death and aborted sudden death have been described in dystrophinopathy. The exact frequency of arrhythmia death has been difficult to assess given the frequency of unwitnessed mortality and potential contributions of respiratory failure. In addition, heart rate, heart rate variability, and arrhythmias have also been described in dystrophinopathy and are thought to be driven by fibrofatty infiltration of the myocardium.[1-3] Based on the risk and substrate, ambulatory monitoring is common, although highly variable in terms of frequency and method of screening.[4] This document is not meant to supersede recommendations such as the HRS consensus statement, but to provide specific guidance in relation to dystrophinopathy and to help harmonize clinical practice within the network. In particular consensus was sought regarding periodicity and duration of monitoring which are not specifically addressed in the existing guidelines or consensus statements.

ACTION REVISED DATE: 04/08/2024

OBJECTIVES

To harmonize clinical practice of ambulatory rhythm monitoring in dystrophinopathy based on expert consensus. There is no sufficient data at this time to specifically recommend a specific method, duration, or indication for initiation.

PROTOCOL

Duchenne muscular dystrophy (DMD)

Indication for Initiation for Monitoring

- Atrial and ventricular ectopy have been described in DMD. The frequency and severity of each generally correlates with the severity of cardiomyopathy, although individual cases of symptomatic arrhythmia including sudden cardiac death have been reported early in the disease process.[1, 2, 5] The substrate is generally thought to be areas of fibrofatty replacement of the myocardium, although the long term risk of arrhythmias in men with DMD and with preserved or relatively preserved systolic function is not well delineated. Using this as the paradigm, we propose the following:
    - Ambulatory rhythm monitoring is not recommended in asymptomatic young patients ≤ 18 years, without evidence of cardiomyopathy (LGE, systolic dysfunction, or left ventricular [LV] dilation), and who do not require night time respiratory support.
        - Yearly ambulatory monitoring is reasonable in adults (>18 years) and those who require night time respiratory support given the minimal data in these subgroups.
    - It is reasonable to obtain yearly ambulatory rhythm monitoring for patients with evidence of cardiomyopathy (LGE, systolic dysfunction, or LV dilation).
    - Yearly ambulatory rhythm monitoring is recommended in patients with systolic dysfunction.

Duration of Monitoring

- Longer duration, continuous, monitoring can increase the frequency of arrhythmia detection in relation to 24 hour Holter or event based monitoring systems.[6] This holds potential value in understanding the frequency of ectopy and arrhythmias, disease progression, and outcomes. However, further study is needed to demonstrate this clinical value and to understand the impact of this approach on resource utilization. The value and cost of the longer term monitoring strategies is likely center and insurance specific and these should be investigated accordingly when discussing risks and benefits with patients/families. With these factors in mind, we propose the following:

    - 24 hour Holter monitors are recommended for ambulatory monitoring of arrhythmias in dystrophinopathy patients with evidence of cardiomyopathy

    - Use of longer duration non-implantable monitors (e.g. Zio Patch) are reasonable for ambulatory monitoring of arrhythmias in dystrophinopathy patients with evidence of cardiomyopathy.

Implantable cardiac monitoring

- As noted above, longer duration, continuous, monitoring can increase the frequency of arrhythmia detection.[6] There is limited data on the risks or benefits of implantable loop recorders (ILR) in DMD. There is an ongoing study specifically addressing this topic. As we await these data, we propose the following:

    - Use of ILRs is reasonable in symptomatic patients where other methods of monitoring are not feasible or non-diagnostic (e.g. patients with developmental delay unable to tolerate external monitors, skin sensitivity, etc).

Specific considerations in Becker muscular dystrophy (BMD) and carriers

- There is limited data describing the utility of ambulatory monitoring in persons with BMD and carriers (both symptomatic and non-symptomatic). With this in mind, we propose the following;

    - Yearly ambulatory rhythm monitoring is recommended in patients with BMD and with evidence of cardiomyopathy (LGE, systolic dysfunction, or LV dilation).

    - Yearly ambulatory monitoring is recommended in carriers with evidence of cardiomyopathy (LGE, systolic dysfunction, or LV dilation).

    - Yearly ambulatory monitoring is reasonable in adults (>18 years) with BMD and those who require night time respiratory support in the absence of cardiomyopathy given the limited data in these subgroups.

    - Yearly ambulatory monitoring is reasonable in symptomatic carriers who require night time respiratory support in the absence of cardiomyopathy given the limited data in this subgroup.

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Dystrophinopathy Gene Therapy Diagnostic Harmonization

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Gene therapy trials to date have largely focused cardiac evaluation on safety endpoints, although we eventually hope to understand the potential impact of these therapies on cardiac disease. Safety data are also limited by patient number, variable gene delivery methods, transgene, post-gene delivery medical therapy, and duration of follow-up. Given these limitations, this document will attempt to harmonize clinical monitoring based on expert recommendation.

A team-based approach to gene therapy delivery is necessary, including providers from multiple disciplines seeking to treat patients as well as mitigate and appropriately monitor side effects. These include representatives from Gene Therapy prescribers (currently, largely Neurology), Pharmacy, Cardiology, Hematology, Gastroenterology, and discussion with other services that may be involved on a case-by-case basis. **We strongly expect these recommendations to evolve as further data becomes available. The below approach is a general recommendation, that we hope will serve as a basis for discussion and generation of institution specific guidelines.**

ACTION REVISED DATE: 10.5.23

OBJECTIVES

To harmonize clinical practice of diagnostic cardiac evaluation in DMD patients who have received gene therapy based on expert consensus.

BACKGROUND & POTENTIAL IMPACT OF GENE THERAPY

Troponin leak and clinical myocarditis have been documented in multiple gene therapy trials to date. The severity of injury has been highly variable, up to and including mortality that has been attributed to cardiac dysfunction. The short- and long-term risk of clinical dysfunction and arrhythmia remains unclear. As long-term cardiac dysfunction and arrhythmia have been shown in other myocardial inflammation syndromes (e.g. viral myocarditis, immune checkpoint inhibitor myocarditis/pericarditis, etc) similar sequelae with DMD gene therapy is possible.

Myocarditis after gene therapy may occur due to multiple reasons:

1) Immediate viral vector associated myocarditis
2) Humoral/cellular response to vector leading to generalized inflammation with cardiac involvement
3) Humoral response to protein product expressed in cardiac tissue

The immunologic responses that may lead to myocarditis can be seen both immediately post-administration, as well as in the weeks and months post-administration depending on the cause.

While there are many unknowns, cases of mortality after gene therapy are known in the dystrophinopathy community. Furthermore, further data is needed to understand the risks of myocarditis across the phenotype, genotype, and product spectrum. Our understanding is likely to evolve over time as we move toward additional patients receiving the first approved products. Towards the goal of maximizing safety, we strongly advocate for the following guiding principles:

- A **team-based approach** is strongly recommended, with prespecified involvement from Gene Therapy prescribers (often, but not exclusively Neurology), and additional major stakeholders including at least Pharmacy, Cardiology, Hematology, Gastroenterology/Hepatology, and team members well-versed in immunomodulation (some sites use Immunology, Rheumatology, or others). Other teams have included

Pulmonology, Nephrology and Infectious Disease. At a bare minimum, we encourage identifying the Cardiology team members to review labs and clinical questions.

- Our guidance for cardiac assessments is based on the initial, limited data. We encourage working with other team members to minimize extra blood draws over time. We anticipate multiple versions of this guidance as data evolves. Overtime minimizing the burden of care including diagnostic evaluation of all types will be an important step.
- **Informed consent detailing the possible cardiac complications is necessary.**

ASSESSMENTS

Troponin

Historically, troponin-I leak can be a sensitive and specific finding in myocarditis, when judged against the gold standard of endomyocardial biopsy.[13] However, use of troponin-I to imply clinical course of myocarditis remains difficult.[14] The association of elevated troponin in many patients with dystrophinopathies, as well as spontaneous episodes of elevation in troponin levels without infectious cause, makes the diagnosis of gene-therapy associated myocarditis more challenging.[8] Of note, there is no current recommendation for use of standard troponin-I vs high-sensitivity assays, but the same platform should be used for comparison. **Troponin assessment prior to gene therapy, and serially at pre-specified timepoints, is prudent for detection of myocarditis.**

Other Biomarkers

Other biomarkers, such as markers of inflammation, white cell counts, platelet counts, BNP are not typically part of the myocarditis diagnosis, have not been predictive of outcomes of classical myocarditis, and there is not yet enough publicly available data regarding gene therapy-associated myocarditis to fully assess their importance or timeline of change. **Thus other biomarkers would be exploratory, and are not advocated for or against at this time, but may help understand the totality of the myocarditis risk.**

Arrhythmia

Atrial and ventricular ectopy have been described in DMD, including in patients across the spectrum of cardiomyopathy (including prior to onset of systolic dysfunction). The frequency and severity of each generally correlates with the severity of cardiomyopathy, although individual cases of symptomatic arrhythmia including sudden cardiac death have been reported early in the disease process.[1-3] The substrate is generally thought to be areas of myocardial inflammation due to cell injury or fibrofatty replacement of the myocardium.

ECG findings can be non-specific in myocarditis, but classical changes in assessment of myocarditis should still be present, and should be considered as part of myocarditis screening. Sub-clinical myocarditis could also be missed early on, and secondarily, arrhythmia burden may be further increased. **This could be detected on later ambulatory rhythm monitor which should be undertaken within the first 6 months post-gene therapy.**

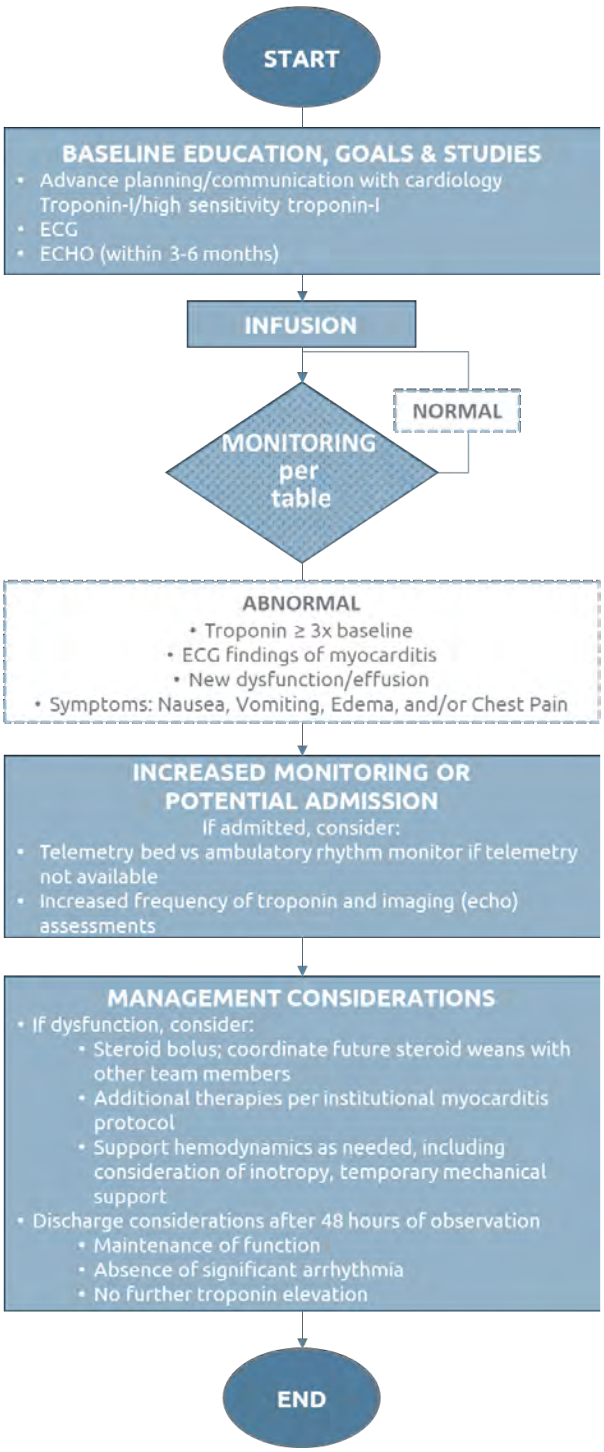
Imaging

Cardiac magnetic resonance (CMR) is the gold standard for assessment of ventricular function and has become a critical tool in the diagnosis of acute myocarditis. CMR studies suggest that the progression of DMD systolic dysfunction typically begins after the development of late gadolinium enhancement (LGE).[5] DMD patients have a classic pattern of LGE that begins in the subepicardium of the free wall at the base/mid-LV;[6, 7] of note, this pattern is identical to that seen in patients with acute myocarditis. In addition, data suggest that there can be patches of elevated T2 times in “healthy” DMD patients (i.e. asymptomatic patients at routine clinic visits), supporting the hypothesis that inflammation is part of the pathway of cardiomyopathy progression. Further complicating the picture, there have been multiple descriptions of dystrophinitis, a myocarditis-like picture that can develop in DMD patients and leads to classic findings of myocarditis including elevated troponin and CMR findings supportive of myocarditis based on the modified Lake-Louise Criteria.[8-10] While CMR is also the gold standard imaging method for the diagnosis of myocarditis and is currently an integral part of diagnostic criteria published by the CDC,[12] it may also be overly sensitive for the diagnosis of myocarditis.[13] There are also not insignificant risk for younger children requiring sedation for a diagnostic study, typically required in those less than 8 years of age at many institutions. **Based on these considerations and the current younger age group of 4-to 6-year-olds FDA approved to receive DMD Gene Therapy (Elevidys), we do not recommend CMRI for baseline or post-infusion screening at this time.**

As echocardiography has the advantage of availability, lower cost, and shorter duration without need for sedation, **We do recommend that echocardiography be undertaken at baseline and at pre-specified**

timepoints. Although DMD echocardiographic images are suboptimal compared with CMR, echocardiography is generally adequate for assessment of clinical changes, and images are generally better at the younger ages.[11] **Echocardiographic assessment would include function, effusion, and valvar regurgitation.**

PROTOCOL



	Baseline	3 Days post	1 Week post	2 Weeks post	3 Weeks post	4 Weeks post	2 Months post	3 Months post
Troponin	X	X	X	X	X	X	X	X
ECG	X		X	X	X	X	X	X
Echocardiogram	X		X	X	X	X	X	X
Ambulatory monitor								X

Light grey = recommendation

Dark grey = at provider discretion, pending other studies

Baseline Communication and Studies

We encourage pre-gene therapy discussions with families as related to goals of care, including willingness to receive inotropic medications and temporary mechanical circulatory support in case of serious hemodynamic complications. Gene Therapy providers (or primary neurologists) are likely most appropriate to have this conversation with patients/families, although with some aid from Cardiologists as needed. Similarly, we encourage communication by Cardiology team members with Cardiac ICU / Surgery teams of the (low) potential of these patients to require advanced cardiac therapies and to assess emergent care strategies preemptively.

We recommend **baseline troponin, ECG and echocardiogram within 3-6 months prior to gene therapy** infusion. At this age, these studies are likely to be normal, although troponin elevation in an asymptomatic DMD patient may be found, and thus serve as a baseline.

Post Gene Therapy Minimum Assessments

- Clinical assessment of any patient with nausea, vomiting, chest pain, palpitations, abdominal pain, severe fatigue, rapid breathing should always be obtained in person by gene therapy team with cardiology consultation as needed for clinical concerns. (GI symptoms are common post gene therapy infusion)
- Assessment of **troponin at 3 days post-infusion** is recommended to capture early virally-mediated cardiac inflammation
- At **one week** post-infusion, an assessment of **troponin, ECG and echocardiogram** is recommended.
- **Further troponin checks are to be undertaken at 2 weeks and 3 weeks post infusion.**
- If all normal studies, next assessment would be at **1 month** post-infusion with repeat troponin, ECG and echocardiogram.
- If all normal studies, next assessment would be at **3 months** post-infusion with repeat troponin, ECG, echocardiogram, and an ambulatory rhythm monitor

Abnormal findings

- An increased **troponin value of > 3 times that of the baseline warrants further investigation, at a minimum a follow-up troponin and ECG within the following day**, and may include imaging, physical exam, and cardiology consultation.
- **Troponin elevation > 3 times baseline paired with significant clinical symptoms or ECG changes, warrants an echocardiogram and hospital admission**
- **Any decrement in function on echocardiogram warrants an admission**
- **Troponin elevation > 10x baseline warrants admission for observation**
- **In patients with abnormalities to minimum screening studies not meeting above thresholds, it is reasonable to consider more frequent assessments**, including ECG or echo alongside the troponin at 2 weeks and 3 weeks post-infusion, or an extra troponin, ECG, and/or echo at 2 months post-infusion, or other interval at the discretion of the treating Cardiologists.

ADMISSION WITH CLINICAL CONCERN FOR MYOCARDITIS

Acute myocarditis of any etiology has a highly variable course without standardized clinical care protocols across institutions. We recommend continuing your institutional practices with some other considerations:

- If patients are admitted for monitoring, telemetry to assess for arrhythmias and frequent repeat troponins is appropriate. **If patient troponins do not increase, function remains normal, and no arrhythmias are seen after 48 hours of close observation, it may be reasonable to discharge without further therapies.**
- **Increased steroids to help attenuate the inflammatory response are often part of the treatment of gene therapy associated liver injury and may be helpful for gene therapy associated myocarditis.** Steroid bolus and tapers should be prescribed in collaboration with Neuromuscular/Gastroenterology/Hepatology colleagues in whom there may be other considerations.
- Later onset of myocarditis may indicate a humoral response, and discussion with Immunology/Rheumatology colleagues may be helpful.
- Preventing acute decompensation and supporting hemodynamics is always the goal which may require inotropes and temporary mechanical support. **Anticipatory discussions with patient, family, and critical care providers are important for best outcomes.**

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Duchenne Muscular Dystrophy (DMD) Medical Therapy Harmonization

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

Skeletal muscle weakness in DMD patients makes the assessment and attribution of common signs and symptoms of heart failure difficult, as activity intolerance, respiratory symptoms, edema, & poor appetite may be ascribed to other DMD processes. Given this, echocardiography and cardiac MRI (cMRI) take on an added importance in helping define cardiac risk through the assessment of ventricular dilation, function, and myocardial fibrofatty replacement in patients with DMD. The 2021 Universal Definition and Classification of Heart Failure also has underscored the potential value of assessing natriuretic peptide elevation in that document's proposed classification schema. This document is not meant to supersede the major heart guidelines, but rather to help harmonize clinical practice especially early in disease where there is significant variability in practice. This document will also address the use of angiotensin receptor-neprilysin inhibitor (ARNI) and sodium-glucose costransporter-2 inhibitors (SGLT2i).

ACTION REVISED DATE: 9/12/2022

OBJECTIVES

With limited data to guide patient care, significant phenotypic variability, and multiple treating physician teams, the medical management of these patients is difficult. The following document seeks to integrate the major recommendations with the Duchenne muscular dystrophy (DMD) Care Considerations, American Heart Association (AHA) Management of Cardiac Involvement Associated with Neuromuscular Diseases, and the 2022 AHA/American College of Cardiology (ACC)/Heart Failure Society of American (HFSA) Guideline for the Management of Heart failure, along with the clinical practice of the many institutions involved in the care of these patients. The recommendations and guidance provided herein is meant to provide a set of potential best practices and tools that should not supersede the clinical judgement of the treating team. Suggested doses, titration, monitoring, order of medication initiation and titration, and laboratory/vital parameters requiring dose reduction or maintenance should continue to be fully determined by the treating team according to standard practice and clinical judgement.

PROGRESSION OF MEDICAL THERAPIES

The following is a recommended progression of medical therapies, directed to defined therapeutic targets based on the degree of cardiac dysfunction or presence of fibrosis (Table 1). Specific recommendations and considerations for each drug class follow.

Table 1. Commonly used drug classes in Duchenne muscular dystrophy (DMD) cardiomyopathy and proposed therapeutic targets based on the degree of systolic dysfunction.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; ARNI, angiotensin receptor-neprilysin inhibitor; SGLT2i, sodium-glucose costransporter-2 inhibitor
* Indications for initiation of MRA therapy include both systolic dysfunction and evidence of cardiac fibrosis (see relevant section for specifics)

	Prophylactic	Mildly reduced EF (41-54%)	Reduced EF (31-40%)
ACEi/ARB	Prophylactic target	HFrEF target	HFrEF target

MRA*	Prophylactic target	HFrEF target*	HFrEF target
BB	--	--	HFrEF target
ARNI	--	--	Consider transition from ACEi/ARB
SGLT2i	--	--	Consider addition

ACE INHIBITORS (ACEI) and ANGIOTENSIN RECEPTOR BLOCKERS (ARB)

Indication for Initiation of Therapy

- ACE-inhibitor therapy is considered first line therapy for patients with DMD. Existing guidelines/scientific statements recommend initiation of therapy at 10 years of age or at least consideration of initiating therapy by age 10 in the absence of systolic dysfunction.[1, 2] The major care guidelines are consistent with the recommendation of the initiation of therapy at the onset of systolic dysfunction.

- Since the publication of Care Considerations and Management of Cardiac Involvement Associated with Neuromuscular Diseases, data has emerged suggesting initiation of therapy in patients with normal function with presence of late gadolinium enhancement (LGE) may slow the progression of disease.[3] Prophylactic initation of therapy also appears to delay/slow the development of heart failure.[4] Based on these data and the existing recommendations we propose the following indications for initiating therapy (Table 2):

    - The use of an ACEi (or ARB) is recommended in DMD by age 10 years given prophylactic initiation of therapy appears to delay/slow the development of heart failure and ~15-20% of patients will have LGE prior to age 10.[4, 5]

    - The use of an ACEi (or ARB) is recommended for patients with DMD and evidence of LGE on cardiac MRI or with systolic dysfunction (left ventricular ejection fraction [LVEF] < 55% and/or shortening fraction [SF] 28%).

    - It is reasonable to consider therapy ACEi (or ARB) prior to age 10 if there is evidence of ventricular dilation (z-score >2) prior to the onset of systolic dysfunction or onset of LGE.

    - The use of an ACEi (or ARB) is recommended for patients with evidence of cardiac fibrosis.

        - While typically seen on cMRI as the presence of LGE, some ECG findings may also be suggestive of fibrosis (e.g. deep and wide q-waves in lateral limb or precordial leads)

Medication dosing

- Optimal dosing prior to onset of LVEF <40% has not yet been established. The 2022 AHA/ACC/HFSA Guideline gives a 2b recommendation for initiation of typical Guideline-Directed Medical Therapy (GDMT) for patients with heart failure and mildly reduced ejection fraction (HFmrEF, 41%-49%). Recommendations described herein are based on expert consensus at the time of the current harmonization/reconciliation document. Goal Target Dose is based on major guidelines for therapy in patients with heart failure with reduced ejection fraction (HFrEF) noting that higher doses may be appropriate in a given patient.

Table 2.					
	Weight range	Initial Dose	Prophylactic Target	Reduced EF Target†	Uptitration Amount[#]
ACE INHIBITORS (ACEI)					
Enalapril	< 50kg	0.05-0.1 mg/kg BID	0.1 mg/kg BID	0.2 mg/kg BID	0.05-0.1mg/kg/dose
	≥ 50 kg	2.5 mg BID	5mg BID	10mg BID	2.5 mg/dose
Lisinopril	< 50 kg	0.1 mg/kg daily	0.1 mg/kg daily	0.4 mg/kg daily	0.1 mg/kg/dose
	≥ 50kg	5 mg daily	10mg daily	20mg daily	5mg/dose
Perindopril	≥ 50 kg	2 mg daily	4 mg daily	8 mg daily	2 mg/dose
ANGIOTENSIN RECEPTOR BLOCKERS (ARB)					
Valsartan	≥ 50 kg	40 mg BID	80 mg BID	160 mg BID	40 mg/dose
Losartan	≥ 50 kg	25 mg daily	50 mg daily	150 mg daily	25 mg/dose
# Doses are generally titrated every 2-3 weeks prior to HFrEF and may be uptitrated in 1-2 week increments in patients with HFrEF with appropriate monitoring or every few days in closely monitored (inpatient). † Routine use of combined high dose MRA and ACEI/ARB may be harmful. Close monitoring of potassium with uptitration or initiation/titration of other medications that may cause hyperkalemia is warranted.					

Therapeutic monitoring

- Baseline Cystatin C and basic metabolic panel should be considered in all patients, especially those with higher risk of renal disease.
    - It is reasonable to start lower dose, prophylactic target medications without baseline labs if no other concerns for renal disease, and not initiating concomitant MRA.
    - Repeating labs with significant dose titrations should be strongly considered
    - For younger patients on stable dosing repeat labs every 12-24 months; recommend checking every 12 months in older patients, or in patients currently taking medications known to cause hyperkalemia, or with clinical deterioration
- Blood pressure (BP)
    - Medications should continue to be uptitrated if BP remains at least > 90/50[6] mmHg unless patients are symptomatic;
        - BP goals should be adjusted based on age and weight derived normative blood pressure tables[7]
        - Older patients with DMD may tolerate blood pressures < 90/50 mmHg and goals may be titrated on an individual basis at the discretion of the cardiologist with appropriate monitoring
    - A home blood pressure cuff can be a useful adjunct for uptitration, `though it is not required

BETA-BLOCKERS (BB)

Indication for Initiation of Therapy

- Beta-blocker therapy is recommended for patients with systolic dysfunction in the Care Considerations and AHA guidelines.[1, 2] While the data are not yet definitive, this would also be consistent with evolving data in adults with HFmrEF, especially those with a downward trajectory in systolic function.[8] The 2022 AHA/ACC/HFSA Guideline also gives a 2b recommendation for BB for patients HFmrEF. Based on these data and the existing recommendations we propose the following indications for initiating therapy (Table 3):
    - Beta-blocker therapy is recommended for patients with DMD and with evidence systolic dysfunction (LVEF < 55% and/or SF < 28%)
- Patients with DMD commonly have sinus tachycardia prior to onset of systolic dysfunction and this may be a predictor of risk for disease progression.[9, 10] While tachycardia and autonomic dysfunction are well described, it remains unclear if therapy modifies this risk or disease trajectory.
    - It is reasonable to consider the initiation of BB therapy in patients with persistent sinus tachycardia or patients with symptomatic sinus tachycardia as defined by published, age specific values.[11, 12]

Medication dosing

- Optimal dosing prior to onset of LVEF <40% has not yet been established. Recommendations described herein are based on expert consensus at the time of the current harmonization/reconciliation document. Goal Target Dose is based on major guidelines for therapy in patients with HFrEF noting that higher doses may be appropriate in a given patient.
- For patients in whom beta-blocker therapy is initiated for sinus tachycardia dosing should be goal directed using age based norms.[11, 12]

Table 3.

	Weight range	Initial Dose	Initial Target Dose prior to Reduced EF	Reduced EF Target	Uptitration Amount[#]
Beta-blockers					
Carvedilol	< 50 kg	0.05-0.1 mg/kg BID	0.25 mg/kg BID	0.5 mg/kg BID	0.05-0.1 mg/dose
	≥ 50 kg	3.125 mg BID	12.5 mg BID	25 mg BID	3.125-6.25 mg/dose
Metoprolol succinate	< 50 kg	0.25-0.5 mg/kg/day	1 mg/kg daily	2 mg/kg/day	12.5 mg
	≥ 50 kg	25 mg daily	100 mg daily	200 mg daily	25 mg/dose

Doses are generally titrated every 2-3 weeks prior to HfrEF and may be uptitrated in 1-2 week increments in patients with HfrEF with appropriate monitoring or every few days in closely monitored patients (inpatient)

MINERALOCORTICOID RECEPTOR ANTAGONISTS (MRA)

Indication for Initiation of Therapy

- Preliminary evidence suggests MRA therapy is associated with a decrease in the decline of strain in patients with DMD.[13] Further studies are needed to assess the long term implications of these early changes, though reduced strain abnormalities have recently been shown to predict those at risk for developing systolic dysfunction.[14] Based on these data the Care Considerations has noted MRA therapy may be a useful adjunct therapy, but that long term investigations are needed.[1] The AHA guidelines have suggested that it is reasonable to consider the use of MRA therapy in the presence of systolic dysfunction and that it may be considered in the setting of LGE on cMRI.[2] For patients unable to tolerate cMRI or where regular cMRI screening is limited, it is reasonable to initiate MRA therapy at age 12 given the average age of first LGE detection.[5, 15] The 2022 AHA/ACC/HFSA Guideline gives a 2b recommendation for initiating MRA therapy for patients HFmrEF. Based on these data and the existing recommendations we propose the following indications for initiating therapy (Table 4).
    - It is reasonable to consider the initiation of MRA therapy in patients with LGE on CMR or if there are ECG findings suggestive of fibrosis (e.g. deep and wide q-waves in lateral limb or precordial leads)
    - It is reasonable to initiate MRA therapy in DMD by age 12 if CMR is unavailable or patients are unable to tolerate MRI without sedation/anesthesia
    - It is reasonable to initiate MRA therapy in DMD in the presence of systolic dysfunction at any age
    - MRA therapy is recommended for patients with DMD in the presence of systolic dysfunction (LVEF < 55% and/or SF < 28%) AND elevated natriuretic peptides

Medication dosing

- There appears to be no significant difference in the agent used, when assessing the change in strain.[16] While there has not been a direction comparison of 25 mg vs 50 mg dosing within a single trial cohort, there may be benefit for targeting the higher dose when considering the preservation of strain as an endpoint.

Table 4.

	Weight Range	Initial Dose	Prophylactic Target	Reduced EF or + LGE Target*†	Uptitration Amount#
MRA					
Eplerenone	≥ 50 kg	25 mg daily	25 mg daily	50 mg daily	25 mg/dose
Spironolactone	< 50 kg	0.25-0.5 mg/kg daily	0.5-1 mg/kg daily	0.5-1 mg/kg daily	0.5-1 mg/kg/dose
	≥ 50 kg	12.5 mg daily	12.5 mg daily	25-50 mg daily	12.5-25 mg/dose

*Weight based adjustments are reasonable based on patient size for patients < 50 kg.
Doses are generally titrated every 4 weeks with associated monitoring of potassium with uptitration or initiation/titration of other medications that may cause hyperkalemia.

†Routine use of combined high dose MRA and ACEI/ARB may be harmful. Close monitoring of potassium is warranted.

Therapeutic monitoring

- Baseline Cystatin C and basic metabolic panel should be considered in all patients, especially those with higher risk of renal disease or those on multiple therapies which can lead to hyperkalemia.
    - It is reasonable to start low dose, prophylactic target medications without baseline labs if no other concerns for renal disease and no other therapies which can lead to hyperkalemia
    - Repeating labs with significant dose titrations should be strongly considered
    - For younger patients on stable dosing repeat every 12-24 months; recommend checking every 12 months in older patients, in patients currently taking medications known to cause renal injury, medications which can lead to hyperkalemia, or with clinical deterioration

ANGIOTENSIN RECEPTOR-NEPRILYSIN INHIBITOR (ARNI)

Indication for Initiation of Therapy

- There is no significant data on sacubitril/valsartan in patients with DMD, and its use is not specifically addressed in in the Care Considerations or the Management of Cardiac Involvement Associated with Neuromuscular Diseases guidelines. Given this, the recommendations described are based on existing results from the non-DMD adult heart failure trials and the AHA and ESC chronic heart failure treatment guidelines.[17, 18] The 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment notes that ARNI is preferred to ACEI/ARB, while the European Society of Cardiology 2021 Guidelines for the Diagnosis and the Treatment of Acute and Chronic Heart Failure suggests that an ARNI may be considered as first-line therapy instead of an ACEI or with persistent symptoms despite ACEI/beta-blocker/MRA therapy. It also remains unclear if any statement of preference should apply to DMD in particular. Thus, while acknowledging the lack of date for ARNIs in DMD specifically, we propose the following indications for initiating therapy (Table 5):
    - The use of an ARNI can be considered in place of ACEI/ARB therapy for DMD patients with an LVEF ≤40% in the setting of a background of guideline directed medical therapy (GDMT).

Medication dosing

- Goal Target Dose is based on major guidelines for therapy in patients with heart failure with reduced ejection fraction (HFrEF) noting that higher doses may be appropriate in a given patient. See table for recommendations in patients >50kg. Dosing for patients <50kg should be weight-based. There are also tables for converting doses for patients on a stable ACEi/ARB that may be beneficial and avoid a decrease in dose. Anecdotal experience suggest achieving target doses may be especially challenging in frail, non-ambulatory DMD patients. This experience is consistent with the higher frequency of symptomatic hypotension in adult heart failure trials, combined with concerns for renal dysfunction and hyperkalemia in this population.

Table 5.

	Weight Range	Initial Dose	Reduced EF Target*†	Uptitration Amount#
Angiotensin Receptor-Neprilysin Inhibitor (ARNI)				
Sacubitril/valsartan	< 50 kg	0.8 mg/kg BID	3.1 mg/kg BID	0.7-0.8 mg/kg/dose
	≥ 50 kg	24/26 mg BID	97/103 mg BID	24/26 mg/dose

*Weight based adjustments are reasonable based on patient size for patients < 50 kg
Doses are generally uptitrated in 1-2 week increments in patients with HFrEF with appropriate monitoring or every few days in closely monitored (inpatient).
† Routine use of combined high dose MRA and ARNI may be harmful. Close monitoring of potassium with uptitration or initiation/titration of other medications that may cause hyperkalemia is warranted.

Therapeutic monitoring

- Baseline Cystatin C and basic metabolic panel
    - Repeat with each dose increase
    - For patients on stable dosing repeat every 6-12 months, with addition of medications known to cause hyperkalemia, or clinical deterioration

- Blood pressure (BP)
    - Medications should continue to be uptitrated if BP remains at least > 90/50[6] mmHg unless patients are symptomatic;
        - BP goals should be adjusted based on age and weight derived normative blood pressure tables[7]
        - Older patients with DMD may tolerate blood pressures < 90/50 mmHg and goals may be titrated on an individual basis at the discretion of the cardiologist with appropriate monitoring
    - A home blood pressure cuff can be a useful adjunct for uptitration, though it is not required

SODIUM-GLUCOSE COSTRANSPORTER-2 INHIBITORS (SGLT2i)

Indication for Initiation of Therapy

- There is no significant data on the use SGLT2i in patients with DMD, and its use is not specifically addressed in in the Care Considerations or the Management of Cardiac Involvement Associated with Neuromuscular Diseases guidelines. Given this, the recommendations described are based on existing results from the non-DMD adult heart failure trials and the AHA and ESC chronic heart failure treatment guidelines as well as expert consensus.[17, 18] Thus, while acknowledging the lack of data for SGLT2is in DMD specifically, we propose the following indications for initiating therapy (Table 6):
    - The use of an SGLT2i should be strongly considered in DMD patients with an LVEF ≤40% in the setting of a background of guideline directed medical therapy (GDMT) and without an additional contraindication.
    - SGLT2i therapy can be considered for patients with DMD in the presence of systolic dysfunction (LVEF < 55% and/or SF < 28%) AND elevated natriuretic peptides

Medication dosing

- Goal Target Dose is based on major guidelines for therapy in patients with heart failure with reduced ejection fraction (HFrEF). See table for recommendations in patients >50kg. Dosing for patients <50kg has not yet been clarified. Anecdotal experience suggest an initial 5 mg dosing regimen of dapagliflozin may be utilized in smaller patients with borderline or low blood pressure and challenges with liquid intake, while acknowledging this dose is not consistent with guideline recommended dosing.

Additional consideration/precautions

- The frequency of urinary tract infections and genital infections is increased in patients on SGLT2i. Patients with DMD are at risk for each of these infections and these can be severe independent of SGLT2i therapy. A individualized discussion of the the risks and benefits based on a patient's dermatologic and urologic history is recommended.

Table 5.

	Initial Dose	Goal Target Dose*†	Uptitration Amount#
SODIUM-GLUCOSE COSTRANSPORTER-2 INHIBITORS (SGLT2I)			
Dapagliflozin	10 mg daily	10 mg daily	n/a
Empagliflozin	10 mg daily	10 mg daily	n/a
*Weight based adjustments are reasonable based on patient size for patients < 50 kg. # Doses are generally uptitrated in 1-2 week increments in patients with HFrEF with appropriate monitoring or every few days in closely monitored (inpatient).			

Therapeutic monitoring

- Baseline Cystatin C and basic metabolic panel
    - Repeat with each dose increase
    - For patients on stable dosing repeat every 6-12 months
- Blood pressure (BP)

- Medications should be continued if BP remains at least > 90/50[6] mmHg unless patients are symptomatic;
    - Older patients with DMD may tolerate blood pressures < 90/50 mmHg and individualized BP goals should be developed at the discretion of the cardiologist with appropriate monitoring
- A home blood pressure cuff can be a useful adjunct for patients with borderline BP or history of symptomatic hypotension.

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Disclaimer: The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a

consensus tool for DMD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care.

VAD and Heart Transplantation in Duchenne Muscular Dystrophy: Guidance for Providers

ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

ACTION REVISED DATE: 11/17/2025

INTRODUCTION

Evolving Outcomes in DMD

The care of patients with Duchenne Muscular Dystrophy (DMD) is evolving rapidly, with advances in survival due to improved respiratory care measures, use of steroids to reduce inflammatory injury to skeletal muscle, and rapid introduction of gene targeting therapies to help preserve muscle function in a wide variety of means. Given this revolution in care and outcomes, it is appropriate to review the role of advanced cardiac therapies for this population, to ensure that use of VAD and access to heart transplantation is consistent with current medical realities.

This document is intended to provide shared knowledge and guidance for internal use by programs that wish to launch programs offering advanced cardiac care options to patients with DMD, or to enhance existing programs.

Heart Failure Phases in DMD

Prophylactic Care
Prophylactic therapy for early intervention, aims to preserve cardiac muscle function and delay the onset of cardiomyopathy. Guidance for this phase of care is provided elsewhere and addresses time to initiate heart failure medications as well as the need for systematic monitoring.

Asymptomatic LV Dysfunction
As DMD cardiomyopathy progresses and signs of cardiac dysfunction begin to appear, the pharmacologic approach intensifies. Combination heart failure therapy should be provided as tolerated, including Angiotensin blockade (e.g. ACE inhibitor, ARB or Sacubitril/Valsartan), beta blockade, aldosterone antagonist and perhaps SGLT2 inhibitor.

In this phase, the goal is to maintain stability in cardiac imaging and biomarkers, and to identify when heart failure symptoms develop.

Symptomatic Heart Failure
In the symptomatic phase of HF, the treatment focus shifts to the active management of HF symptoms. Symptoms may manifest as fatigue, diminished exercise capacity, impaired respiratory status not thought to be due to skeletal muscle dysfunction, or fluid overload. Diuretics play an increasing role in care, and the clinical course may evolve rapidly due to complications such as arrhythmias.

Current Experience with HF and VAD

A small number of case reports demonstrate feasibility of VAD support for DMD patients with outcomes limited primarily by the progression of DMD, and adverse events occurring at rates comparable to other populations treated with VAD. Literature includes a multi-center series of 18 muscular dystrophy patients treated with VAD, with 8 having DMD. Notably, 95% of the total cohort survived to hospital discharge. This series highlights the feasibility of VAD therapy for certain DMD patients while leaving most questions of selection and outcome unresolved.

With respect to heart transplantation, there are scattered case reports showing successful use of heart transplantation to treat advanced heart failure in patients with DMD. Additionally, a multi-center publication from the Cardiac Transplant Research Database identified 3 individuals with the diagnosis of DMD in that database, which spanned 1990-2005 and included 7,820 adult heart transplant recipients. Muscular dystrophy patients in this cohort had outcomes broadly comparable to the overall cohort. Similar to the situation with VAD, the use of heart transplantation in the DMD population has been uncommon, but appears feasible in selected candidates.

PRIOR TO INITIAL REFERRAL

Barriers to Referral

Awareness of the options of VAD and heart transplantation for DMD remains limited among patients, caregivers, and medical teams. Many individuals with DMD receive care at multidisciplinary clinics that have considerable DMD expertise but lack the capability to place and manage VADs or perform heart transplants. Partnerships between DMD care teams and advanced cardiac care centers can optimize not only access but also health outcomes for DMD patients.

Neuromuscular and cardiology providers should begin conversations about the potential of advanced therapies with patients and caregivers early in the care of DMD, well before any acute needs arise. These discussions could be integrated into system-based checklists used to manage care by many neuromuscular centers or "bright future" style anticipatory guidance during routine visits. Key topics for this approach include:

Table 1: Anticipatory Cardiac Guidance for DMD Care

- *Framing VAD placement and/or heart transplant as potentially viable, (though optional) treatments for some DMD patients with heart failure*
- *Building a general understanding of pre-, peri-, and post-operative management for these interventions*
- *Contextualizing advanced cardiac therapy within broader DMD care (e.g., nocturnal ventilation, heart failure management)*
- *Making patients and caregivers aware of additional resources available through partnering centers, advocacy organizations, and other reputable sources.*

Advanced cardiac centers may also consider offering adjunctive group or telehealth visits in the pre-referral period or after a referral. These visits would provide patients and caregivers an opportunity to meet care team members, ask nuanced questions specific to each treatment site, and help patients make informed care decisions.

For patients with DMD, routine cardiology care is recommended with a cardiologist experienced in managing DMD. It is important for DMD patients to establish a connection to a program that offers advanced cardiac therapies before significant heart failure symptoms develop as the clinical course subsequent to onset of symptoms is difficult to predict and may progress rapidly. Additionally, prolonged debilitation from heart failure may preclude eligibility for advanced cardiac therapies.

Optimizing Longitudinal Care

The consideration of advanced cardiac therapies may directly impact the management choices in certain DMD patients. Optimizing aspects of DMD care may increase a patient's eligibility for VAD placement or heart transplant later, particularly when specific factors for a poor surgical outcome are identified and proactively managed. By mitigating these potential vulnerabilities, patients may face fewer risks and have improved outcomes when they become candidates for VAD or transplant. Areas that should be targeted include:

Table 2: Optimizing Longitudinal Care

Area of Risk	Potential Interventions
Scoliosis	*Comfortable seating, reduced risk of pressure ulceration, improved pulmonary biomechanics*
Nutritional Health	*Gastrostomy tube to preserve nutritional status, leading to reduced risk of pressure ulceration, improved wound healing and more robust tissue integrity*
Osteopenia	*Support of bone health with directed therapeutics and appropriate steroid regimen can minimize risk of stress fracture and compression fractures, and improve post-operative mobilization*
Sarcopenia	*Pre-treatment activity regimens with stretching and strength building can improve pulmonary function and skeletal muscle strength, leading to earlier extubation and mobilization*
Weight management	*Avoidance of obesity and cachexia can reduce surgical risk, facilitate earlier extubation and mobilization, and reduce risk of pressure ulceration*
Pacemaker/ICD utilization	*Prevention of arrhythmia complications including cardiac arrest*
Respiratory Insufficiency	*Airway clearance and non-invasive respiratory support including positive pressure*

Indications and Timing of Referral

Traditional tools such as cardio-pulmonary exercise testing and NYHA heart failure classifications often prove inadequate to assess HF severity in DMD due to the neuromuscular limitations of DMD patients, especially for those who are non-ambulatory.

Referral for advanced cardiac therapy evaluation should be strongly considered if any of the following are present:

Table 3: Indications for Referral for Advanced Cardiac Therapy Evaluation

- *LVEF < 40%*
- *End-organ dysfunction (renal or liver dysfunction) due at least in part to heart failure*
- *Persistently elevated NT-proBNP*
- *Persistent fluid overload or increasing diuretic requirement*
- *Recurrent defibrillator shock*
- *Heart failure hospitalization*
- *Need to reduce/discontinue standard HF medications due to side effects*

These criteria should not be considered an absolute indication for advanced therapy, but rather an opportunity to engage relevant providers and families in the discussions regarding goals of therapy, indications for advanced therapy, and potential barriers to consideration for advanced therapies. Referral for advanced cardiac therapy evaluation should not necessarily entail a transfer of care to centers offering advanced cardiac therapies. Shared cared between the longitudinal care center and heart failure specialist is strongly encouraged.

PRE-SURGICAL EVALUATION

VAD vs Heart Transplant

In broad terms, VAD or heart transplant may be considered when medical therapy alone no longer proves effective, either by unacceptable heart failure symptoms, or the expectation of limited survival due to cardiac disease. VADs may serve as either a bridge to transplant (BTT) or destination therapy (DT).

Ambulatory status is not a primary determinant in this decision; however, if a patient does not have access to a 24/7 caregiver, hand function and proximal arm strength become essential considerations for managing VAD equipment independently.

Given the limited experience with both VAD and heart transplantation in this population, a comparison between these options should be informed by discussion with the patient and family regarding goals of care and priorities.

Assessment for Candidacy

For both VAD and heart transplantation candidacy, a comprehensive evaluation is indicated and should typically address the following considerations:

Table 4: Components of Pre-VAD and Transplant Evaluation

- *Pulmonary Function Testing (PFT): Collect baseline and trend data to inform perioperative planning and long-term management strategies.*
- *Neuromuscular Assessment: Comprehensive evaluation of strength and flexibility. Assessment of upper extremity function is particularly important for patients without full-time caregiving support, to determine capacity to manage VAD equipment.*
- *Nutritional Assessment: Ensure the patient's nutritional status is optimized prior to surgery to enhance recovery and support long-term health.*
- *Swallow Evaluation: Assess patient's ability to swallow prior to implant given the potential for sternotomy to affect vocal cord mobility and swallowing dynamics independent of neuromuscular status.*
- *Pediatric Surgery Planning: Coordinate with pediatric surgery for G-tube placement when indicated and discussion regarding VAD driveline placement.*
- *Psychosocial and Palliative Care Support: Involve palliative care early to address quality-of-life issues and establish realistic expectations for post-operative outcomes.*
- *Assessment of Caregiver Capacity: For patients reliant on caregivers, assess caregiver support to confirm adequate resources and abilities for post-VAD care.*
- *Assessment of Patient Capacity: Assess the patient's cognitive function and tailor education, assent/consent based on their capacity.*
- *Physical Therapy and Occupational Therapy (PT/OT) Assessment: Tailor PT/OT support to address specific rehabilitation needs, potential challenges following sternotomy (e.g. lifting and transfers), and maximize the patient's functional independence post-surgery.*
- *Orthopedic and Bone Health Evaluation: Evaluate scoliosis, chest wall stability, contractures, and bone health due to the long-term impact of steroid therapy, which can affect surgical and post-operative care.*
- *Venous Access Mapping: Plan venous access carefully, as DMD patients on long-term steroids may have calcified veins, increasing the risk of access challenges*

The patient with DMD who is referred for heart transplantation evaluation should undergo a comprehensive evaluation following the applicable institutional practice. This should be performed within the existing transplant selection process.

For patients accepted for transplant and placed on a waitlist, the dynamic nature of the underlying skeletal muscle and pulmonary disease should be kept in mind during a potentially long waiting interval. At the time of donor acceptance, the candidate should have recent pulmonary function testing (PFTs) and assessments of respiratory muscle strength (MIP/MEP, cough peak flow), ideally within the last 6 months.

SURGICAL AND PERIOPERATIVE CONSIDERATIONS

Preparation for Surgery

Ideally, assessments and interventions in key areas for longitudinal care discussed above should already be performed, but this should be reviewed and confirmed. Additionally, skin integrity should be regularly assessed and any ulcerations promptly treated. Need for post-operative gastrostomy tube should be anticipated and locations of both gastrostomy tube and VAD drivelines should be physically mapped out with respect to wheelchair restraining belts. A scoliosis evaluation should be performed. In addition, respiratory function should be fully characterized. Loss of 25-30% of FVC should be anticipated following thoracotomy.

Table 5: Respiratory Evaluation and Preparation

- *Pulmonary function testing with FVC, and FEF 25-75 to identify lung capacity and any restrictive or obstructive concerns*
- *Assessment of respiratory muscle strength with Max Inspiratory Pressure, Max Expiratory Pressure and Cough Peak Flow*
- *Assessment of end-tidal capnometry to serve as baseline value*
- *Polysomnography to understand need for positive airway pressure pre-operatively*
- *Tracheostomy teaching should be performed to prepare the family and patient*
- *Training with respiratory equipment such as CPAP, IPPB*

Surgical Technique

Use of TRAP door implantation technique may be considered in LVAD implantation to expand the pericardial space and minimize diaphragmatic disruption. Wheelchair bound patients are at high risk for driveline infections so careful attention should be paid to driveline position, enhanced by additional padding to reduce pressure.

Anesthetic Considerations

Table 6: Key Anesthetic Considerations

- *Airway management may be complicated by contractures, scoliosis or macroglossia*
- *Secretion management may require nebulizers, airway clearance and humidification during surgery*
- *Small tidal volume ventilation during CPB may mitigate small airway collapse*
- *Due to risk of rhabdomyolysis and malignant hyperthermia-like reactions, volatile anesthetics and succinylcholine should be avoided.*
- *Anesthesia machine should be flushed to remove traces of inhalational agents*
- *Monitoring of neuromuscular blockade should be performed to prevent residual blockade and facilitate early extubation*
- *ACE inhibitors/ARNi and SGLT2 inhibitors should be managed per institutional practice*
- *Perioperative steroids may be required to prevent emergence of adrenal insufficiency, depending upon prior therapy*
- *Vasoplegia management protocol should be in place per institutional practice*

Hemostasis and Thrombosis

There is increased risk of bleeding in DMD patients due to enhanced fibrinolysis and platelet dysfunction. Viscoelastic testing can support appropriate use of goal-directed intra-operative hemostasis, including reversal of anticoagulation in

VAD implantation. Meticulous hemostasis should be a priority for the surgical team. In the post-operative period, thrombotic complications may occur due to impaired venous drainage, and thromboprophylaxis should be employed including use of compression stockings.

Airway Management

Early extubation, ideally within 6 hours if hemodynamics are stable, is a key goal of post-operative management, with multiple ramifications. This requires an integrated approach to mechanical ventilation and pain management that maintains lung recruitment, supports gas exchange and minimizes splinting.

Table 7: Key Tenets of Airway and Ventilator Care

- *Focus on early extubation, preferably within 6 hours*
- *Full respiratory support during intubation*
- *Careful titration of opiate medications to avoid blunting respiratory drive*
- *Extubate from full support to full non-invasive support (usually to bilevel support)*
- *Avoidance of spontaneous breathing trials*
- *Airway clearance initially q2-3h*
- *Post extubation monitoring for hypercapnia*

Tracheostomy should be strongly considered if extubation has not been achieved in 5-7 days, to facilitate physical rehabilitation and clinical progression. Patients should be counselled about risk of tracheostomy in advance of surgery.

Preservation of Functional Status

Careful attention to wound care, liberal use of wound vacs and meticulous attention to early signs of pressure injuries are important to minimize the risk of such injury, particularly for patients on steroid therapy. Early mobilization can also be helpful for this, as well as for preservation of muscle strength and flexibility. Incorporation of rehabilitation teams into post-operative care planning is essential.

LONGITUDINAL CARE

VAD

In general terms, VAD management in a patient with DMD will follow the same treatment goals and principles as VAD care for other adolescents and young adults. Anticoagulation protocols may need to be tailored to individual circumstances given increased risks of both thrombosis and bleeding.

Heart Transplantation

A structured document ("flight plan") may be helpful in organizing peri-operative and post-operative care planning. This can be reviewed in a pre-transplant huddle of care providers. Post-transplant induction and maintenance immunosuppression should follow institutional practice. Vamorolone should not be regarded as an equivalent substitute for prednisone in anti-rejection properties given the lack of efficacy data, and consideration should be given to conversion to prednisone or deflazacort in the first 6 months in preference to vamorolone. For rejection surveillance, endomyocardial biopsies should be minimized given the increased procedural risk related to pulmonary and skeletal muscle function. Consider non-invasive surveillance including cell-free DNA and gene expression profiling in patients over age 15 years, combined with ECG, echocardiography, NT-proBNP and troponin as screening tools. Monitoring of renal function should be performed using Cystatin C rather than creatinine, given the reduced muscle mass in DMD patients. DMD patients are not believed to be at unusual risk of opportunistic infections when compared to typical heart transplant recipients. Ongoing management of bone health should follow institutional practice, and may include radiographic assessment of spine fractures, use of Dexa scans and consideration of bisphosphonate therapy. Rehabilitation should be directed by a team familiar with DMD patients and their care needs.

Repatriation for ongoing DMD Care
After discharge, the patient's local cardiologist may oversee routine VAD management or post-transplant care as per institutional protocols, coordinating closely with the advanced cardiac center to co-manage any complications. The handoff between the advanced cardiac center and local providers is critical. To support local providers and minimize the risk of delays in addressing complications, advanced centers may consider creating detailed care protocols or formal case management systems. These should include clear instructions on when to escalate care and ensure that local providers have ongoing telehealth support and 24/7 consultation access to advanced cardiac centers as needed.

Families should receive written care plans with escalation pathways and delineation of responsibilities between the local team and the referral center. Details will vary depending upon local center and family resources, but should be jointly established with both centers.

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Disclaimer: The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 3/6/2024)

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