WEANING and EXPLANT Protocol for Pediatric VADs

**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:** 2/9/2022

**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 support1
* 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)
	1. Incorporation of Reverse Remodeling Therapies

|  |  |  |
| --- | --- | --- |
| **Phase** | **Goals** | **Medications to Incorporate** |
| Post-op / Acute | Hemodynamic stabilityRelief of heart failure symptomsRecovery of end-organ injuryVAD RPM optimizationDecongestion | 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 optimizationIncorporation 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 toleratedDigoxin* 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
 |

* 1. Suggested Heart Failure Medication Target Dosing
		1. See ACTION Duchenne Muscular Dystrophy Therapy and Heart Failure Medication Optimization Harmonized Protocols for suggested incorporation / uptitration of oral remodeling therapies
		2. Individual patient regimens must be tailored to patient responses and tolerance
		3. Medication doses may need to be adjusted for renal dysfunction, blood pressure response, other side effects
	2. Surveillance for Remission from Heart Failure
		1. Echocardiograms
			1. Once per week for at least the first 2 weeks
				1. Assess decompression of LV on VAD support
				2. Aortic valve may continue to open
		2. Subsequently once every 2-4 weeks
			1. Assess for continued decompression
			2. See ACTION Echocardiography Protocol for full details of echo assessment of VAD
				1. 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)
		3. Laboratory (while inpatient)
			1. BNP or NT-proBNP – weekly
			2. End organ function every 1-2 weeks
		4. Functional assessments (continuous flow VADs)
			1. 6-minute walk test to establish baseline
				1. Weekly post-VAD until discharge, then at 1 month, 3 months, and 6 months post-implant
	3. LVAD Management
		1. Goal: Left-heart decompression
		2. Maintain higher LVAD RPM to limit myocardial wall stress, decongest left heart, provide BP support for incorporation of reverse-remodeling therapies
		3. However, LVAD RPM increases may be limited by right heart function, interventricular septal shift, worsening tricuspid regurgitation, etc
1. Loading / Evaluation Phase (>3 Months Post-Implant)
	1. Surveillance for Remission from Heart Failure
		1. Echocardiograms
			1. Continue monthly echocardiograms
			2. Should improvement in LV function be seen, consider RAMP study / RPM change echo (continuous flow VADs)
				1. Suggested schedule: Approximately every 1-3 months with outpatient clinic visits, especially when weaning of VAD flows is taking place
				2. Protocol: See ACTION LVAD RPM Optimization / RAMP TTE Protocol

Total decrease in RPM should be no more than 200 RPM for HeartWare (HVAD). Minimum RPM: 1800 RPM

Total decrease in RPM should be no more than 400 RPM for Heartmate 3 (HM3) devices. Minimum RPM: 4000 RPM

* + 1. Laboratory
			1. BNP or NT-proBNP – at least monthly
			2. End organ function – at least monthly
		2. Functional assessments (continuous flow VADs)
			1. 6-minute walk testing
				1. Suggested schedule: at 1 month, 3 months, and 6 months post-implant at time of outpatient clinic visits
				2. 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 guidelines2
	1. LVAD Management & Myocardial Loading
		1. 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 INR therapeutic at time of encounter
		2. LVAD RPM wean
			1. Consider weaning HVAD by 40-100 RPM per encounter (~monthly)
				1. 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
				1. Perform VS, echo
				2. Lower RPM and repeat VS, echocardiogram
				3. If no change in patient symptoms, VS, echo, consider leaving VAD at new lower RPM

Note: for HVAD patients, ensure trough on new RPM is >2 L/min given increased risk for thrombosis as troughs approach 0 L/min

As above, consider repeating 6-minute walk testing at clinic visit following a RPM change

1. Interrogation Phase Pre-Explant: Myocardial Function & VAD RAMP Cath Study
	1. Suggested schedule
		1. First cath within the first 6 months of VAD placement
		2. Can consider serial hemodynamic assessments while loading and assessing potential for explant
	2. Pre-Cath Logistics / Planning:
		1. Establish indication for catheterization:
			1. VAD optimization (“RAMP” study)
			2. Assess for remission from heart failure (“off-pump” study)
		2. Any additional assessment or intervention required? Examples: coronary angiography, angiography for baffle leaks/obstruction, collateral assessment, etc
		3. 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)
		4. Review vascular access – may need vascular ultrasound prior to procedure
		5. Review anticoagulation – continue medication until day of procedure unless supra-therapeutic
		6. Determine mode of echo imaging: TEE vs TTE
		7. Notify all necessary teams that need to be available: Imaging, HF, VAD coordinator, CV surgery
		8. Check labs within 1 week of study
			1. Optimize hemoglobin if necessary
			2. Ensure anticoagulation within target range
	3. Day of Cath Logistics:
		1. Hold anti-hypertensives
		2. No warfarin or aspirin the morning of the procedure
		3. Routine VAD labs: serum chemistry, CBC, LDH, plasma free hemoglobin, BNP/NT-proBNP, INR
		4. 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
		5. 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
		6. Monitoring
			1. Blood Pressure and Heart Rate Monitoring:
				1. Discuss with Anesthesia regarding monitoring of BP and goal BP- arterial line versus Doppler MAP
				2. If obtaining arterial access, see if Doppler MAP correlates
				3. Unexplained sinus tachycardia, similar to pre-implant, may be a subtle sign any changes made during cath are not well-tolerated
			2. VAD Monitoring:
				1. VAD parameters including VAD waveform or PI should be monitored
				2. Obtain images of VAD monitor at various RPMs (pre and post at a minimum)
				3. For HVAD, avoid adjusting RPM to where trough is approaching 0 or suction present on waveform
			3. Additional Monitoring
				1. Near-infrared spectroscopy (NIRS) may additionally be used for monitoring tissue oxygen delivery throughout the procedure
	4. Imaging Assessment:
		1. Establish with imaging team regarding what parameters will be monitored throughout the case
		2. See supplemental tables at end of protocol for suggested echo data to be collected
	5. **Cath assessment –** **Continuous Flow VADs**
		1. Obtain baseline hemodynamics via right heart cath (see supplemental table at end of protocol for recording hemodynamics), record baseline echo parameters
		2. 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
		3. If acceptable baseline hemodynamics and patient anticoagulated, decrease RPM by 40-100 RPM
		4. Wait 10-15 minutes between RPM changes before reassessing hemodynamics and repeating imaging
		5. 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”
		6. 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)
	6. **Cath assessment –** **Pulsatile VADs**
		1. 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.
		2. 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
		3. In addition to suggested weaning protocol below, other Berlin weaning protocols have been published by Miera et al3 and Berlin Heart4 and may also serve as helpful guides
		4. 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
				1. Durations mentioned below are for 10 & 15 mL pumps
				2. For 25 & 30 mL pumps, the duration of pause is 10, 15, and 30 minutes for Day 2, 3, and 4/5, respectively4
				3. 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 for **3 minutes** **Important:** Pump has to be manually pumped to fill and eject every 10 seconds | * 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** * **Important:** Pump has to be manually pumped to fill and eject every 10 seconds
 | Same as Day 2 with hemodynamic measurements in catheterization (see supplemental table at end of protocol) |

* + 1. Cath assessment – Alternative Timing
			1. A longer period of observation “off-pump” can be performed prior to explant
			2. Anticoagulation
				1. Heparin 50 units/kg or max dose of 5000 units should be given prior to first rate change
				2. Monitor ACT throughout case and maintain >250 with repeat heparin bolus if needed
			3. Recommended Timing
				1. Baseline hemodynamics (see supplemental table at end of protocol)
				2. If acceptable baseline hemodynamics and patient anticoagulated, decrease Berlin rate by 50% for 5 minutes
				3. If acceptable hemodynamics, pause Berlin and perform off-pump hemodynamics. **Important:** Pump has to be manually pumped to fill and eject every 10 seconds
				4. If stable, continue off-pump trial with data collection at 15, 30, 45 minutes. Trial can be extended to 60 minutes if additional data needed
1. Assessing Suitability for Explant
	1. Explant criteria to consider (adapted from adult studies - Dandel et al5, RESTAGE-HF trial6)
		1. 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)
		2. 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
		3. 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/m2
			3. Other hemodynamics acceptable during off-pump trial
		4. Right Ventricle
			1. No worsening of RV function following LVAD implant and during LVAD weans / off-pump trial(s)
		5. Rhythm
			1. Sinus or A-V synchronous rhythm
		6. Sustained decrease in BNP/NT-proBNP from initial level post-implant
2. Post-Explant Surveillance
	1. Post-explant pharmacologic therapies
		1. Continue all reverse remodeling therapies for at least 12 months after explant
		2. Unknown to what extent (if any) reverse remodeling therapies can be weaned without recurrence of heart failure
	2. Functional and Echo assessments: Suggested schedule: weekly for 2 weeks then biweekly for a month followed by monthly for six months
	3. 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.

**REFERENCES**

1. Wever-Pinzon O, Drakos SG, McKellar SH, et al. Cardiac recovery during long-term left ventricular assist device support. *J Am Coll Cardiol* 2016;68(14):1540-53.
2. http://www.nutritioncare.org/Guidelines\_and\_Clinical\_Resources/Malnutrition\_Solution\_Center/
3. Miera O, Germann M, Cho MY, et al. Bridge to recovery in children on ventricular assist devices—protocol, predictors of recovery, and long- term follow-up. *J Heart Lung Transplant* 2018;37(12):1459-1466.
4. EXCOR® Pediatric VAD: Ventricular Assist Device with Stationary Driving Unit Ikus Rev. 2.1 - Instructions for Use 1000721x09 Revision 8. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwid\_IHftcv1AhUnlmoFHb\_0BdcQFnoECAcQAQ&url=https%3A%2F%2Fwww.fda.gov%2Fdownloads%2FAdvisoryCommittees%2FCommitteesMeetingMaterials%2FPediatricAdvisoryCommittee%2FUCM537702.pdf&usg=AOvVaw3o2rYH6mxltxGdoHdS98en
5. Dandel M, Hetzer R. Myocardial recovery during mechanical circulatory support: weaning and explantation criteria. *Heart Lung Vessel* 2015;7(4):280-8.
6. Birks EJ, Drakos SG, Patel SR, et al. Prospective Multicenter Study of Myocardial Recovery Using Left Ventricular Assist Devices (RESTAGE-HF [Remission from Stage D Heart Failure]) Medium-Term and Primary End Point Results. *Circulation* 2020;142:2016-2028.

***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: 9/28/2021)*

**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 m2) |  |  |  |  |
| Mixed Venous / Systemic Sat (%) |  |  |  |  |
| CI (L/min/m2) |  |  |  |  |
| 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** |
| **VAD** | Rate (BPM) |  |  | 0 | 0 | 0 | 0 | 0 | 0 |
| Output (L/min/m2) |  |  | N/A | N/A | N/A | N/A | N/A | N/A |
| Time Off Pump (min) | N/A | N/A | 0 | 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 m2) |  |  |  |  |  |  |  |  |
| MV / Systemic Sat (%) |  |  |  |  |  |  |  |  |
| CI (L/min/m2) |  |  |  |  |  |  |  |  |
| Lactate |  |  |  |  |  |  |  |  |
| **Echo** | LVEDD (mm) |  |  |  |  |  |  |  |  |
| LV EF (%) |  |  |  |  |  |  |  |  |
| AoV/MV/TV regurg |  |  |  |  |  |  |  |  |
| TAPSE (mm) |  |  |  |  |  |  |  |  |
| RVEDD (mm) |  |  |  |  |  |  |  |  |
| RV function |  |  |  |  |  |  |  |  |