VAD EXPLANT: HOW DO WE GET THERE?

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Huntington Beach, CA

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DISCLOSURES/OBJECTIVES

- No financial disclosures
- Describe the indications for VAD explant
- Describe the published experience in pediatric and adult patients undergoing VAD explant
- Case presentation of an unsuccessful VAD explant

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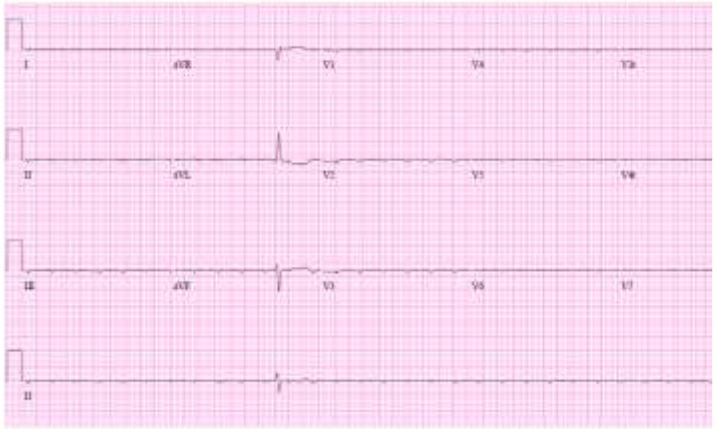
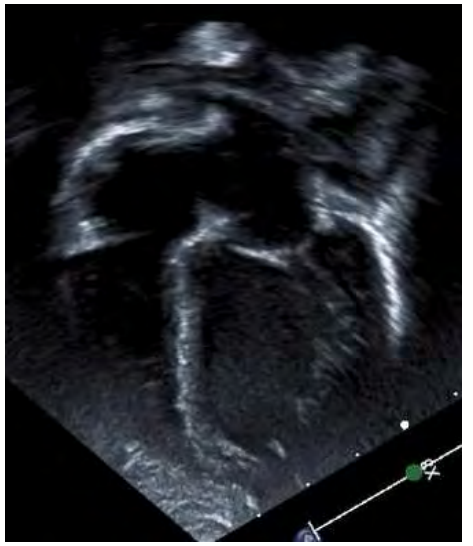
WHO MAY BE A CANDIDATE FOR VAD EXPLANT?

- No set criteria

- Patients with a reversible cause of cardiac dysfunction
  - Myocarditis
  - Arrhythmia-induced cardiomyopathy
  - Peripartum cardiomyopathy

- Patients in whom long-term recovery can be expected (? remission)
  - Idiopathic DCM
  - Familial DCM
  - Anthracycline cardiotoxicity





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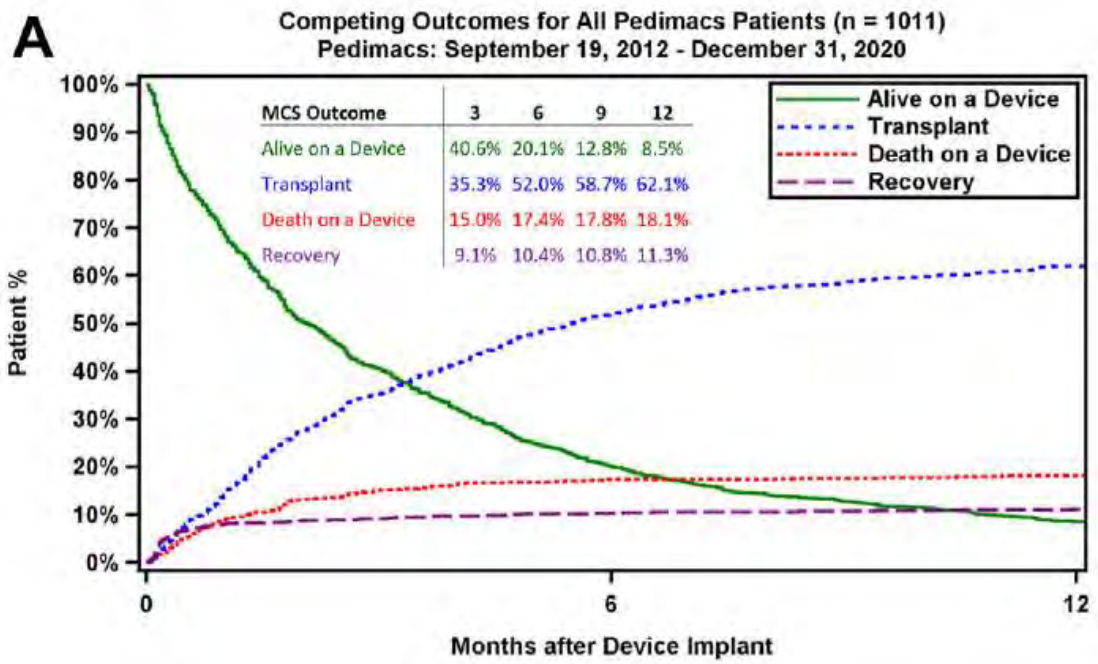
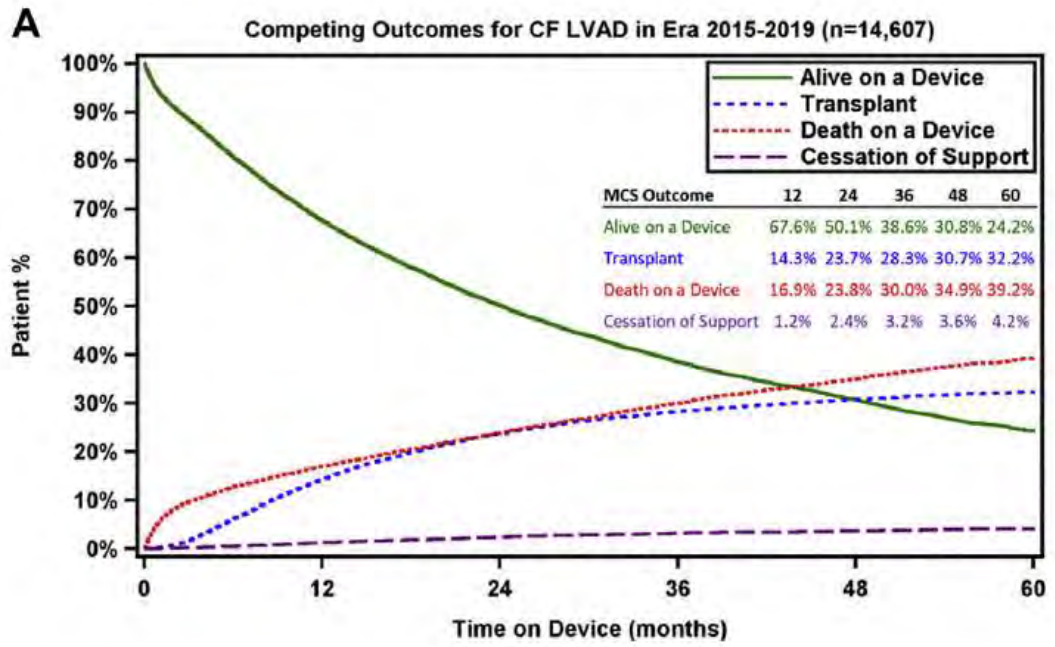
HOW COMMON IS VAD EXPLANT?

Pedimacs



Rossano, et al Ann Thorac Surg 2021

Intermacs



Molina, et al Ann Thorac Surg 2021

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BASIS FOR BRIDGE TO RECOVERY (BTR) STRATEGY

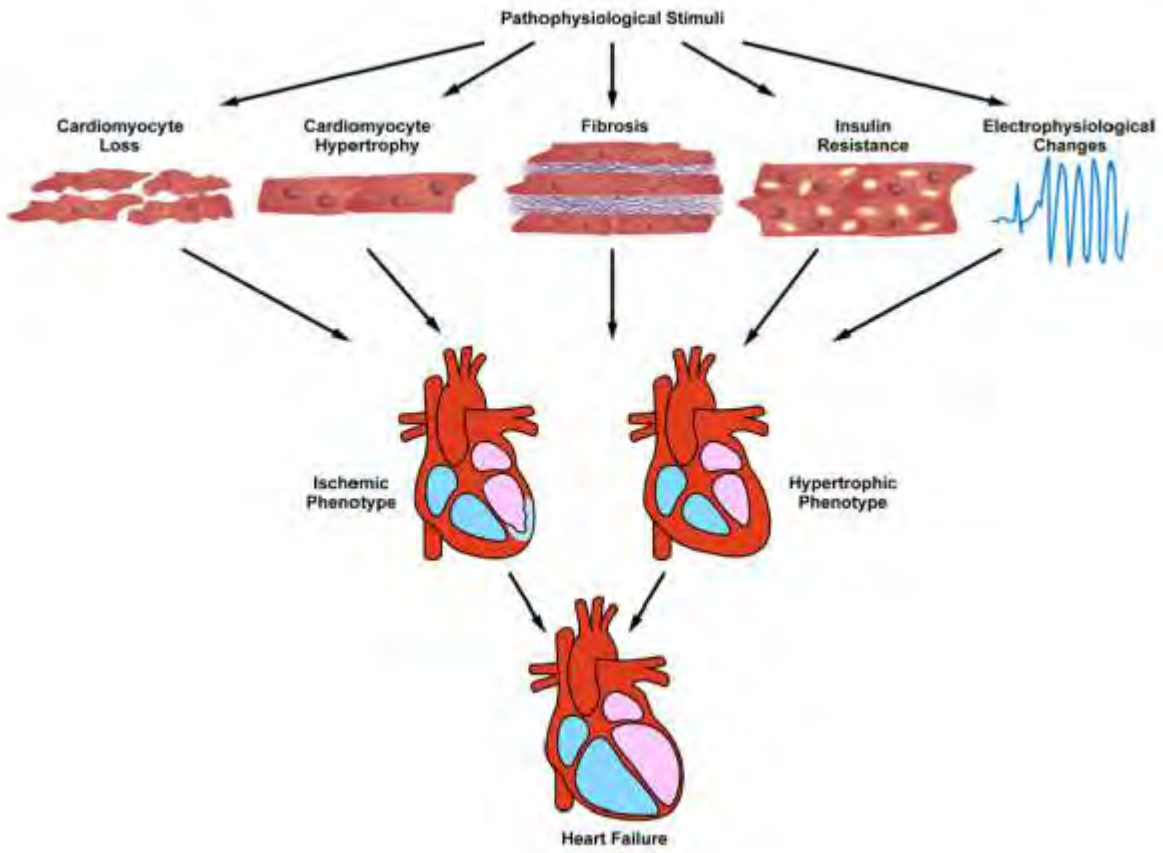

Table 1 Cardiac Reverse Remodeling Changes Following LVAD Support that have been Extensively Reviewed in Past Review Articles[55,73,74,149,150]

Hypertrophy regression	Regression of LV myocyte hypertrophy	5,7,9-11,14-18
T-tubules and cytoskeleton	Reversal of cytoskeletal genes by LVAD unloading	19-23
	No reversal on cytoskeletal proteins	24
Contractility and Calcium Signaling	Improved contractility	24,25
	Improved calcium signaling	26-28
	Normalization of Na/Ca exchanger, SERCA, RYR2 post LVAD support	27,28
	Upregulation of b-adrenergic receptor density	29-33
Cell death, apoptosis and autophagy	Decreased markers of autophagy post LVAD support	34
	Autophagy as an adaptive mechanism in the failing heart	35
	NOS, osteopontin, Hsp72 and FLIP	36-39
	Beclin-1, autophagy-related gene 5 (Atg5), and microtubule-associated protein-1 light chain-3	34
	MEK/Erks, Akt/GSK-3beta, Bcl-2	14,40,41
Cytokines and Neurohormones	TNF-a, IFN-γ	42-46
	TLR-4, IL-1b, IL-6, IL-8, FAS, FLICE	47-51
	MCP-1, IP-10, CRP	52
	ANP, BNP	53
	Aldosterone, renin	54

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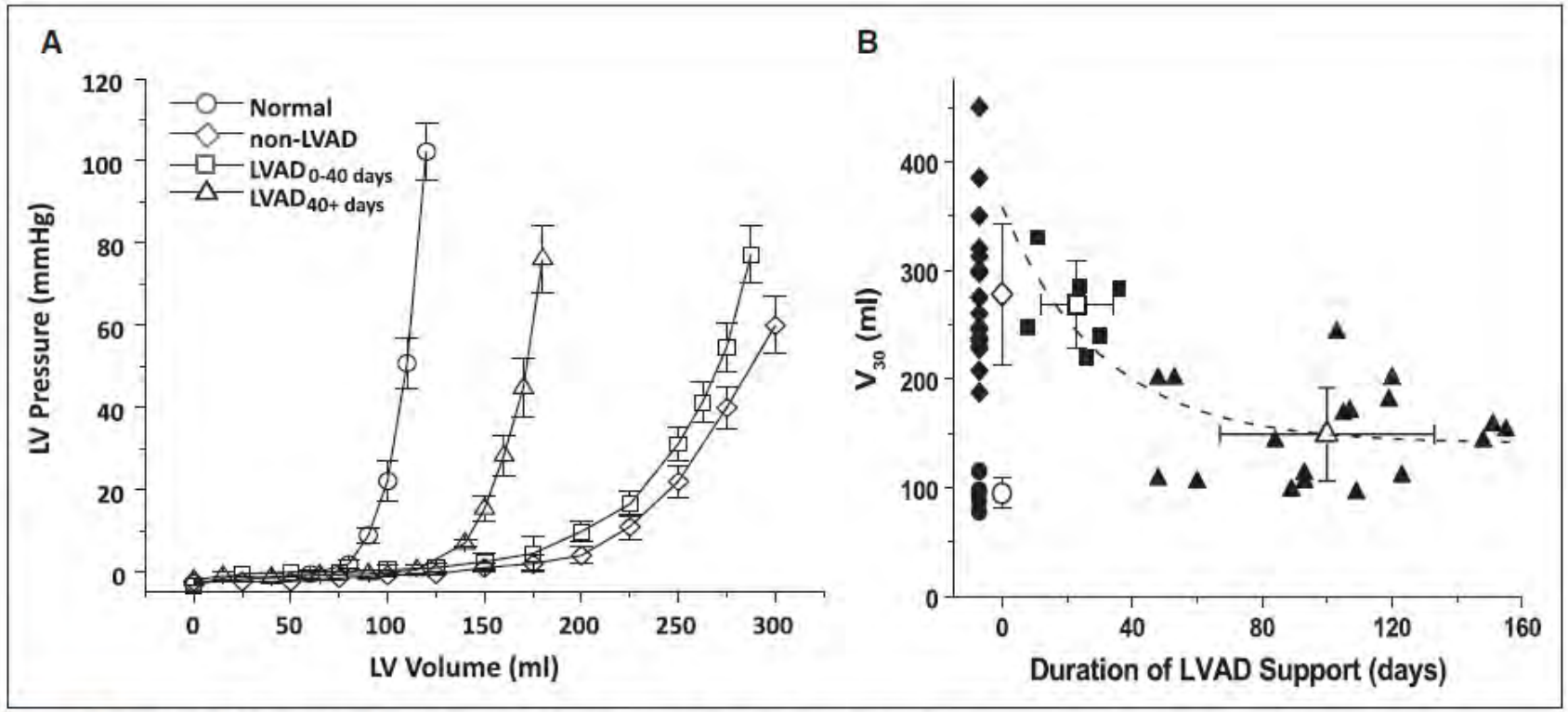

Figure 2. Effect of Mechanical Unloading on LV Pressure-Volume Relationship.
A, Time-dependent left ventricular assist device (LVAD)–associated reverse structural remodeling as indexed by leftward shifts toward normal of the end-diastolic pressure-volume relationship. **B**, Volume at a filling pressure of 30 mm Hg (V_{30}) as a function of duration of support in comparison to normal (open circles) and hearts that did not undergo LVAD support (diamonds); squares and triangles are data from patients supported by LVAD for 0 to 40 d and >40 d, respectively.[19] LV indicates left ventricle.

Burkhoff, et al Circ Res 2021

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HOW DO WE KNOW WHO MAY BE A CANDIDATE FOR RECOVERY?

- Predictors of recovery (adults)
  - Short heart failure duration (<5 years)
  - Nonischemic cardiomyopathy
  - Age <50
  - Cr <1.2 mg/dL
  - LVEDD <6.5 cm

50% of these patients can be explanted

Of these, 80% will be free from transplant/redo VAD

Table 2 Intermacs Cardiac Recovery Score (I-CARS)

Clinical Characteristic	Incidence Rate of Recovery v pts without characteristic (events/100-pts-yrs)	OR (95% CI)	Score
Nonischemic Cardiomyopathy	1.6 vs 0.3	4.7 (3.1-7.1)	3
Implanted ICD	2.9 vs 0.5	3.7 (2.6-5.2)	2
Age <50 years	2.2 vs 0.5	1.9 (1.4-2.7)	1
Time from Diagnosis <2 years	2.7 vs 0.5	2.2 (1.5-3.1)	1
Creatinine ≤1.2 mg/dl	1.4 vs 0.5	2.0 (1.4-2.7)	1
LVEDD <6.5 cm	1.6 vs 0.7	1.8 (1.3-2.5)	1
Total Score Range			0-9

Abbreviations: ICD, Implantable Cardioverter Defibrillator; LVEDD, left ventricular end diastolic diameter.
Low probability group (0-3 points), an intermediate probability group (4-6), and a high probability group (7-9).

Kanwar, et al JHLT 2022

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PATHWAY FOR RECOVERY: RESTAGE-HF

METHODS: Forty patients with chronic advanced heart failure from nonischemic cardiomyopathy receiving the Heartmate II LVAD were enrolled from 6 centers. LVAD speed was optimized with an aggressive pharmacological regimen, and regular echocardiograms were performed at reduced LVAD speed (6000 rpm, no net flow) to test underlying myocardial function. The primary end point was the proportion of patients with sufficient improvement of myocardial function to reach criteria for explantation within 18 months with sustained remission from heart failure (freedom from transplant/ventricular assist device/death) at 12 months.

RESULTS: Before LVAD, age was 35.1±10.8 years, 67.5% were men, heart failure mean duration was 20.8±20.6 months, 95% required inotropic and 20% temporary mechanical support, left ventricular ejection fraction was 14.5±5.3%, end-diastolic diameter was 7.33±0.89 cm, end-systolic diameter was 6.74±0.88 cm, pulmonary artery saturations were 46.7±9.2%, and pulmonary capillary wedge pressure was 26.2±7.6 mm Hg. Four enrolled patients did not undergo the protocol because of medical complications unrelated to the study procedures. Overall, 40% of all enrolled (16/40) patients achieved the primary end point, $P<0.0001$, with 50% (18/36) of patients receiving the protocol being explanted within 18 months (pre-explant left ventricular ejection fraction, 57±8%; end-diastolic diameter, 4.81±0.58 cm; end-systolic diameter, 3.53±0.51 cm; pulmonary capillary wedge pressure, 8.1±3.1 mm Hg; pulmonary artery saturations 63.6±6.8% at 6000 rpm). Overall, 19 patients were explanted (19/36, 52.3% of those receiving the protocol). The 15 ongoing explanted patients are now 2.26±0.97 years after explant. After explantation survival free from LVAD or transplantation was 90% at 1-year and 77% at 2 and 3 years.

Birks EJ, et al Circ 2020

Highlights

- Nonischemic cardiomyopathy
- HMII LVAD
- Younger age (35 y)
- Intensive medical regimen
- 40% explanted after mean 1.1 years on device
- 90% 1-year event free survival

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PATHWAY FOR RECOVERY: RESTAGE-HF

Pump Optimization

- Increase pump speed until LVEDD and MR are minimized
- Goal LVEDD < 6 cm
- MR < moderate

Pharmacologic Management

- Started immediately after weaning of inotropic support:
  - Lisinopril 20 mg BID
  - Carvedilol 50 mg BID
  - Spironolactone 25 mg daily
  - Digoxin 125 mcg daily
  - Losartan 150 mg daily

Explant Criteria

- At zero net flow:
  - LVEDD < 6 cm
  - LVESD < 5 cm
  - LVEF > 45%
  - LVEDP/LPCW < 15 mm Hg
  - CI > 2.4 L/min/m^2
  - VO_2 max >16 mL/kg/min

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PEDIATRIC VAD RECOVERY EXPERIENCE

- Limited published experience, small numbers, heterogenous diagnoses, etc

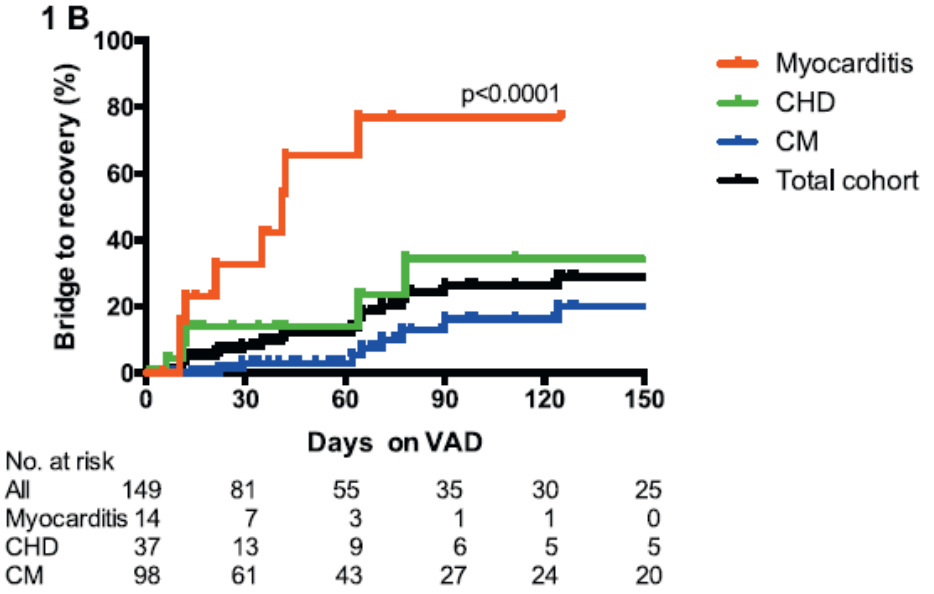
BACKGROUND: The majority of children supported with ventricular assist devices (VADs) are bridged to heart transplantation. Although bridge to recovery has been reported, low recovery patient numbers has precluded systematic analysis. The aim of this study was to delineate recovery rates and predictors of recovery and to report on long-term follow-up after VAD explantation in children.

METHODS: Children bridged to recovery at our institution from January 1990 to May 2016 were compared with a non-recovery cohort. Clinical and echocardiographic data before and at pump stoppages and after VAD explantation were analyzed. Kaplan–Meier estimates of event-free survival, defined as freedom from death or transplantation after VAD removal, were determined.

RESULTS: One hundred forty-nine children (median age 5.8 years) were identified. Of these, 65.2% had cardiomyopathy, 9.4% had myocarditis, and 24.8% had congenital heart disease. The overall recovery rate was 14.2%, and was 7.1% in patients with dilated cardiomyopathy. Predictors of recovery were age <2 years (recovery rate 27.8%, odds ratio [OR] 5.64, 95% confidence interval [CI] 2.0 to 16.6) and diagnosis of myocarditis (rate 57.1%; OR 17.56, 95% CI 4.6 to 67.4). After a median follow-up of 10.8 years, 15 patients (83.3%) were in Functional Class I and 3 (16.7%) in were in Class II. Mean left ventricular ejection fraction was 53% (range 28% to 64%). Ten- and 15-year event-free survival rates were both 84.1 ± 8.4%.

CONCLUSIONS: Children <2 years of age and those diagnosed with myocarditis have the highest probability of recovery. Long-term survival after weaning from the VAD was better than after heart transplantation, as demonstrated in the excellent long-term stability of ejection fraction and functional class.

J Heart Lung Transplant 2018;37:1459–1466



Medical therapy: ACEi, beta-blocker, MRA

Miera, et al JHLT 2018

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EXCOR WEANING PROTOCOL

Weaning of the EXCOR may be considered in subjects who meet the following eligibility criteria:

- LVEDD within normal limits (<98th percentile, or Z-score of +2)
- EF = 45% (i.e. no less than mild dysfunction)
- Lactate <3 mmol/L
- No clinical evidence of thromboembolism or bleeding
- Anticoagulation markers within target parameters

The weaning protocol can be divided into 5 steps and generally takes one week to complete.

- Day 0 (and throughout the weaning process). Confirmation of eligibility criteria for weaning.
- Day 0. Acute weaning challenge
- Day 1-4. Graduated weaning challenge with non-invasive assessment (echo).
- Day 5. Pump stoppage with invasive hemodynamic assessment with afterload challenge.
- Day 6. Pump stoppage with invasive hemodynamic assessment in OR (full anticoagulation).

This size-based weaning protocol accounts for physiologic differences in heart rate and stroke volume observed in children of varying ages.

In the operating room, explantation should be considered if the following criteria are met with the pump stopped for 20 minutes (after anticoagulation has been established in the target range for cardiopulmonary bypass):

- LVEDD less than 98th percentile (Z-score less than +2)
- EF≥ 45 % (i.e. no more than mild ventricular dysfunction)
- Normotensive on only Milrinone (no other inotropes)
- Lactate <3 mmol/L
- LVEDP < 12 mmHg
- Resting CI of > 2.8 L/min/m^2

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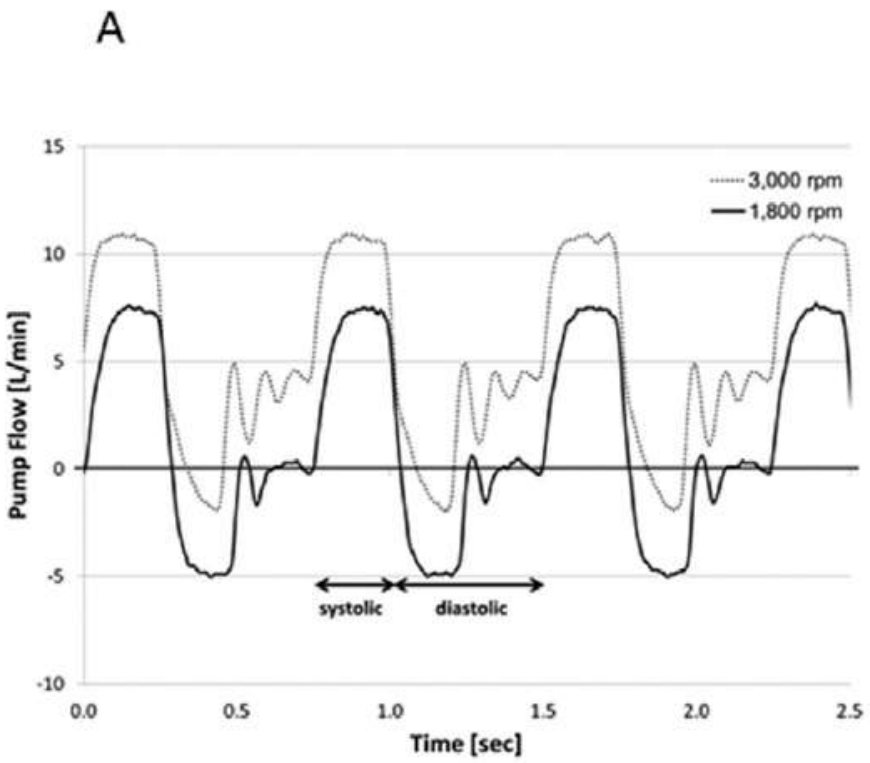
WHAT ABOUT WEANING CONTINUOUS-FLOW VADS?

- It is not feasible/safe to completely stop a cfVAD
  - Retrograde flow into LV
  - Increase LVEDd
  - Reduce afterload, may overestimate native LV systolic function
- Rather, the pump RPM are gradually decreased to a state where there is zero net flow
- Echo, cath, exercise data can be obtained in the brief window in which it is safe to maintain low/zero flow



Sunagawa, et al Ann Thorac Surg 2016

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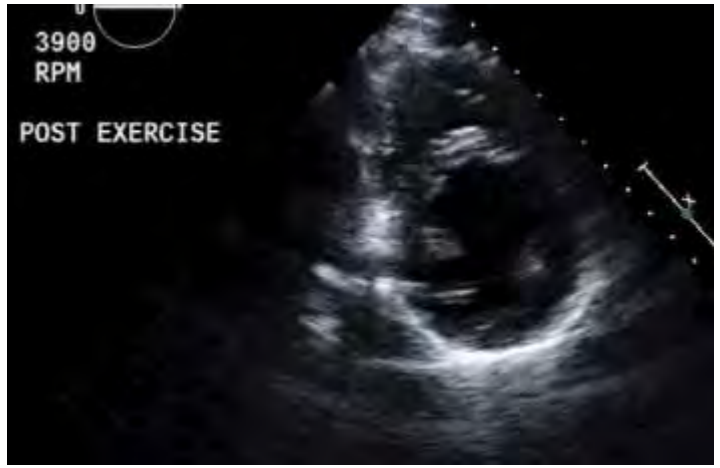
WEANING CONTINUOUS FLOW VADS – CHOP APPROACH

- Echo, cath, exercise with turndown to 3900 rpm
- Chest CTA
- Reverse anticoagulation preoperatively
- Anticipate vasoplegia



	7/31/20 – Baseline CPET	1/12/21 – Turndown CPET
Turndown RPM	5300	3900
Weight	67 kg	82 kg
BMI	21 kg/m2	25 kg/m2
Max VO2	1.456 L/min	2.337 L/min
Max VO2 (indexed)	22 mL/kg/min	29 mL/kg/min
Ectopy	No ectopy, frequent PVC at rest	No ectopy, occasional PVC at rest
Max Power	96 watt	124 watt
VAD PI	2.8	7.7

	5300 RPM	4000 RPM
Mixed venous saturation (RPA)	77%	76%
DAo saturation (pulse oximetry)	96%	96%
RA	2/3 m1	1/4 m2
RV	24/2	26/3
RPA	20/6 m14	22/8 m14
RPCW	m6	m6
CI (thermodilution)	2.9 L/min/m2	2.6 L/min/m2
CO (thermodilution)	5.7 L/min	5.1 L/min
PVRi	2.8 iWU	3.1 iWU
PVR	1.4 WU	1.6 WU

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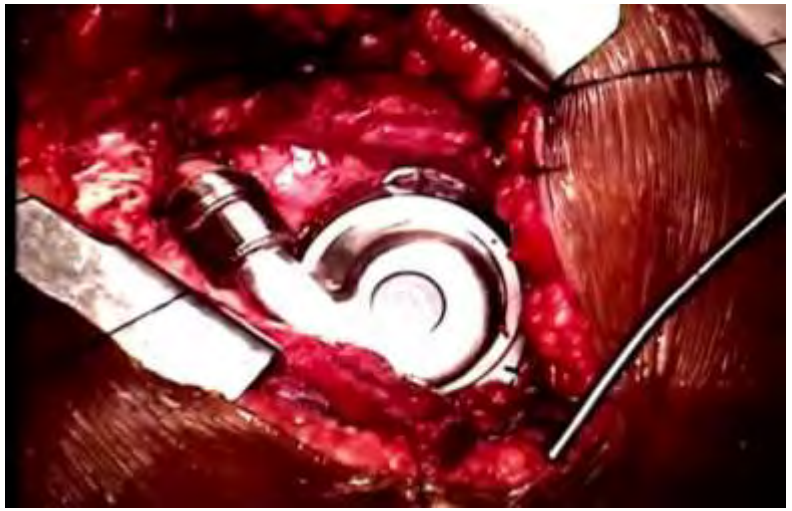
Off-Pump Explant of a Left Ventricular Assist Device Using a Recovery Plug in a Pediatric Patient

Tracy R. Geoffrion, MD, MPH,
Kendall M. Lawrence, MD, Matthew J. O'Connor, MD,
and Jonathan M. Chen, MD

Ann Thorac Surg 2021;111:e291-3



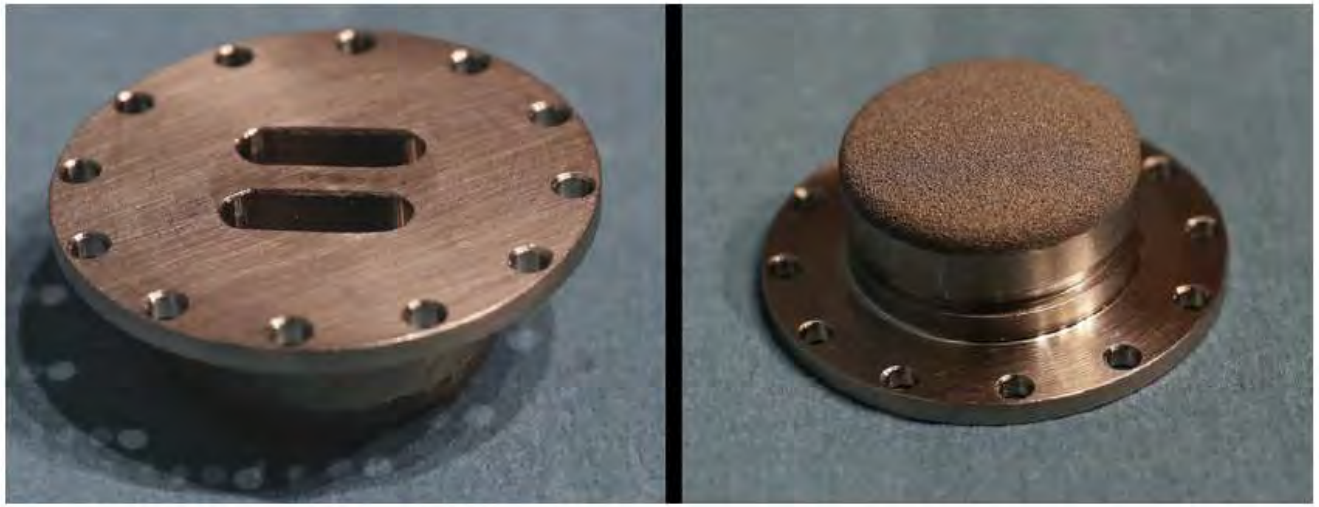


Figure 1. INNOVO Solutions custom PL-3 Recovery Plug for the HeartMate 3. Device specifications: 35-mm diameter, 13.5-mm height; medical grade titanium.

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BARRIERS TO VAD EXPLANT IN CHILDREN

- High proportion of diagnoses not suitable for recovery
  - DMD, failed Fontan, failed single ventricle palliation, etc
- Lack of familiarity/comfort with aggressive GDMT
  - GDMT is not well defined in children
- High transplant rate in children on VAD
  - ~50% of pediatric VAD implants have been transplanted by 6 months
- Weighing the long-term “unknowns” of explant against the “knowns” of transplant

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THANK YOU

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VAD EXPLANT: CHOP EXPERIENCE

- 110 VAD patients, 1998-2022
- 5 patients explanted

Year	Age	Diagnosis	Device	Support Duration	Outcome
2002	11 y	DCM	Thoratec	43 d	Alive
2016	13 m	Myocarditis	EXCOR	32 d	Alive
2017	16 m	Myocarditis	EXCOR	92 d	Alive
2018	12 y	DCM	HM3	310 d	Failed wean, transplanted 6 days post explant
2021	18 y	DCM (EAT)	HM3	301 d	Alive

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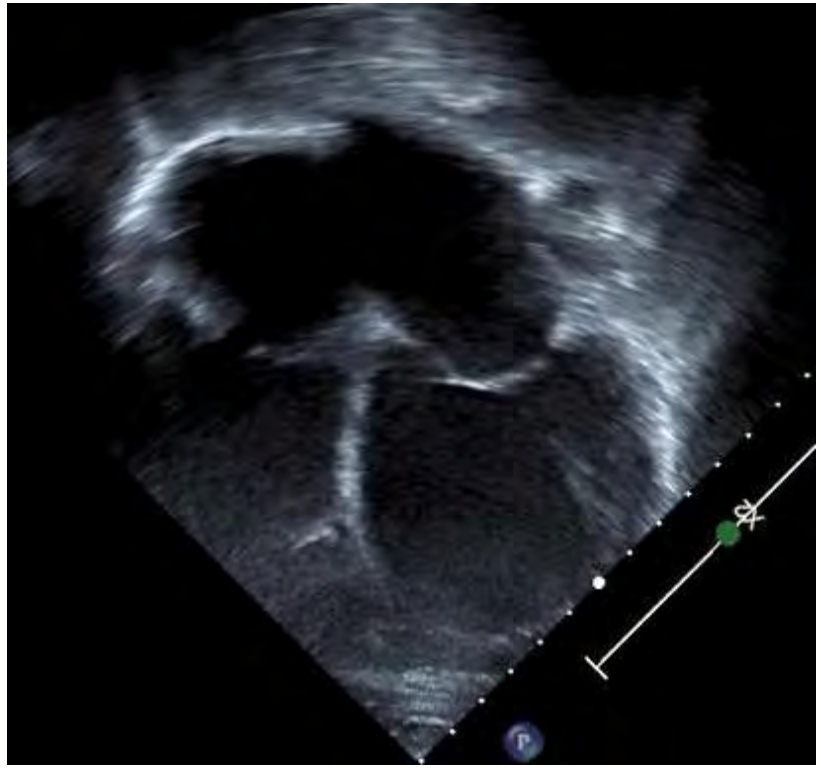
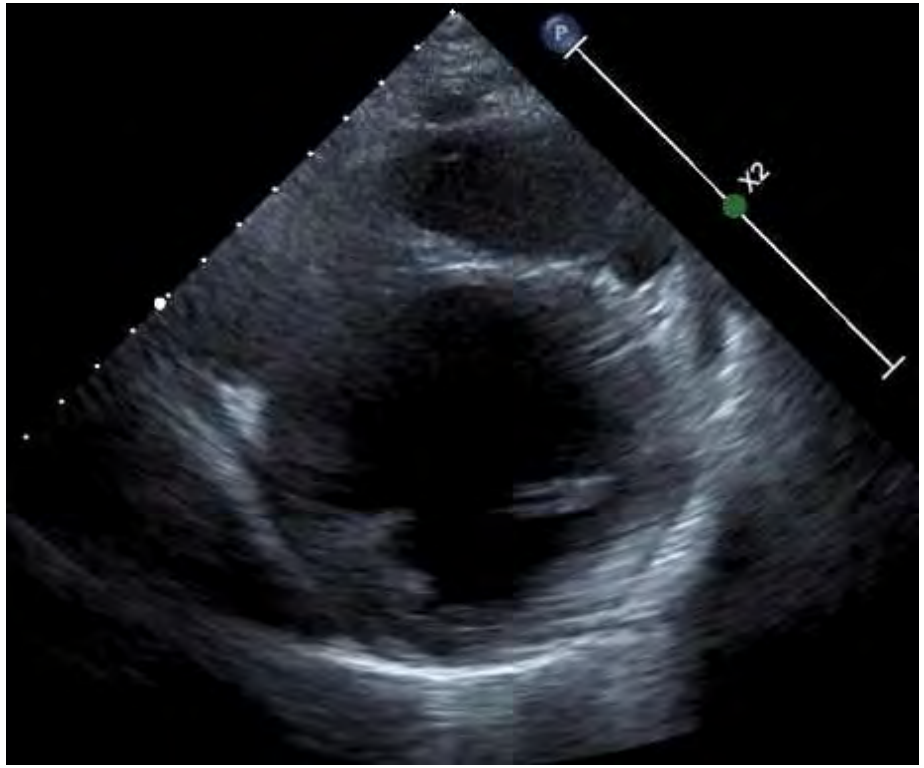
LESSONS LEARNED FROM A "FAILED" EXPLANT

- 13 y/o male with DCM likely related to myocarditis, *TTN* VUS
- Considered for HM3 explant; on device ~300 days
- Medications at time of explant
  - Carvedilol 25 mg BID
  - Digoxin 125 mcg daily
  - Eplerenone 25 mg daily
  - Losartan 50 mg BID
  - Sildenafil 20 mg TID
  - Warfarin
  - ASA
- Labs
  - Cr 0.4, total bilirubin 0.3, BNP 183

ECHO UPON PRESENTATION





LVEDd 7.1 cm
EF 26%

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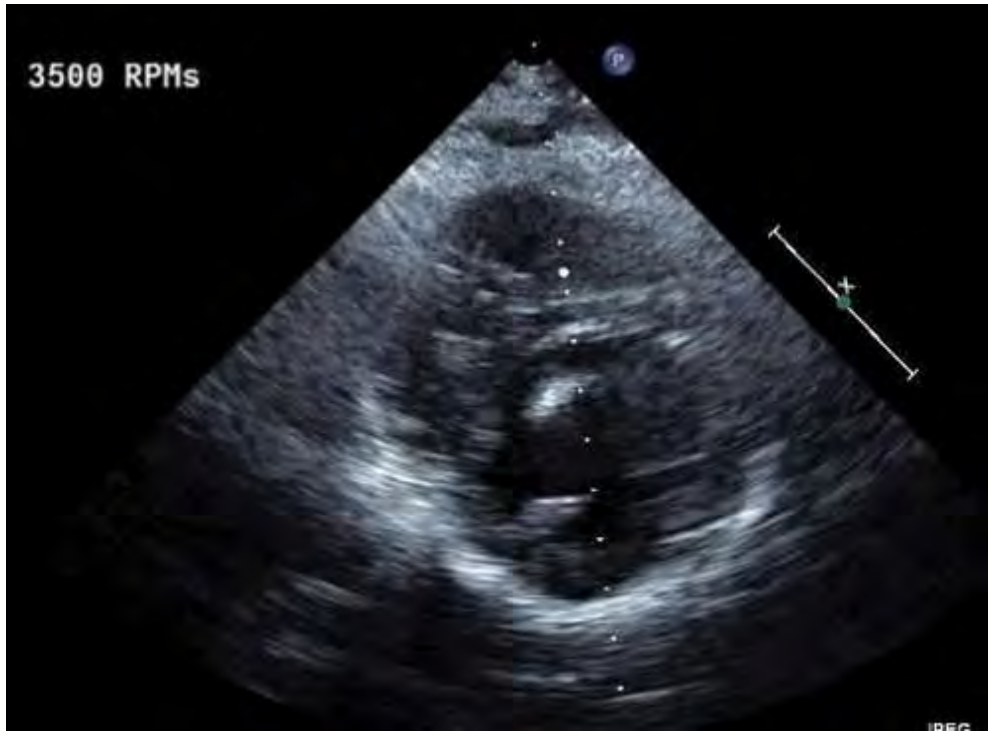
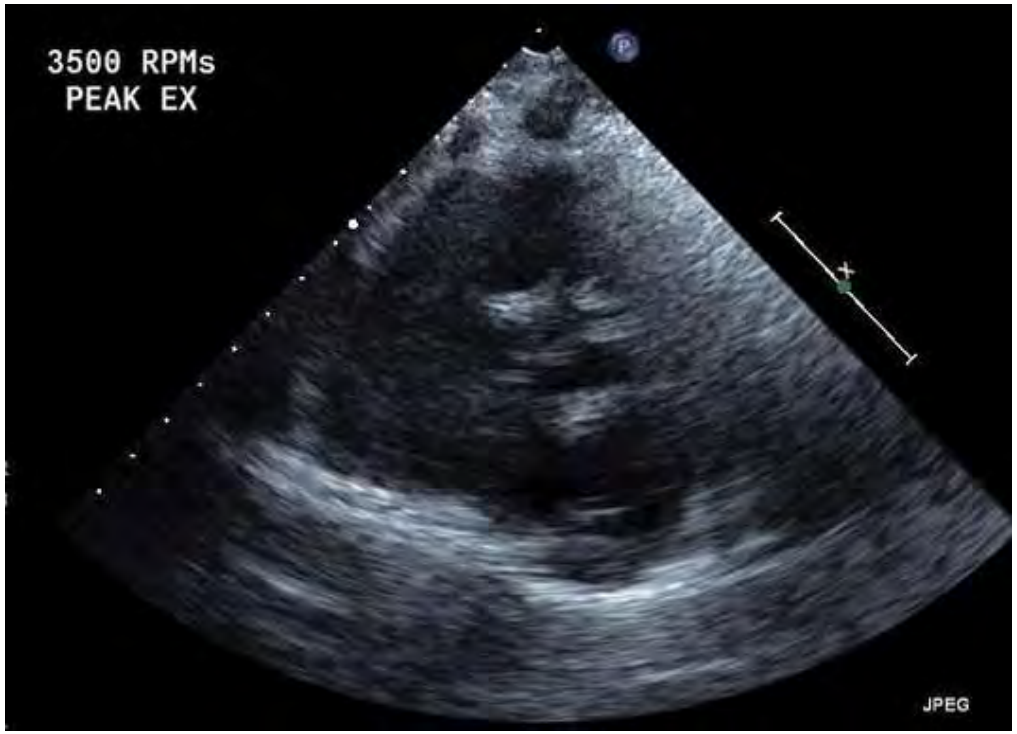
STRESS ECHO – 6 MONTHS LATER





LVEDd 4.8 cm
Resting EF 58%, exercise EF 76%

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CATH DATA – 6 MONTHS LATER

	VAD Flow	
	5400 RPM	3500 RPM
RPA saturation	80%	74%
Pulse oximeter	98%	98%
RA	4/5 (m 4)	5/8 (m 7)
RPA	28/12 (m 20)	34/18 (m 25)
RPCW	12/9 (m 10)	14/14 (m 12)
CI (Thermo)	3.5 L/min/m2	2.8 L/min/m2
	6.5 L/min	5.2 L/min
PVRi	2.9 iWU	4.6 iWU
	1.5 WU	2.5 WU

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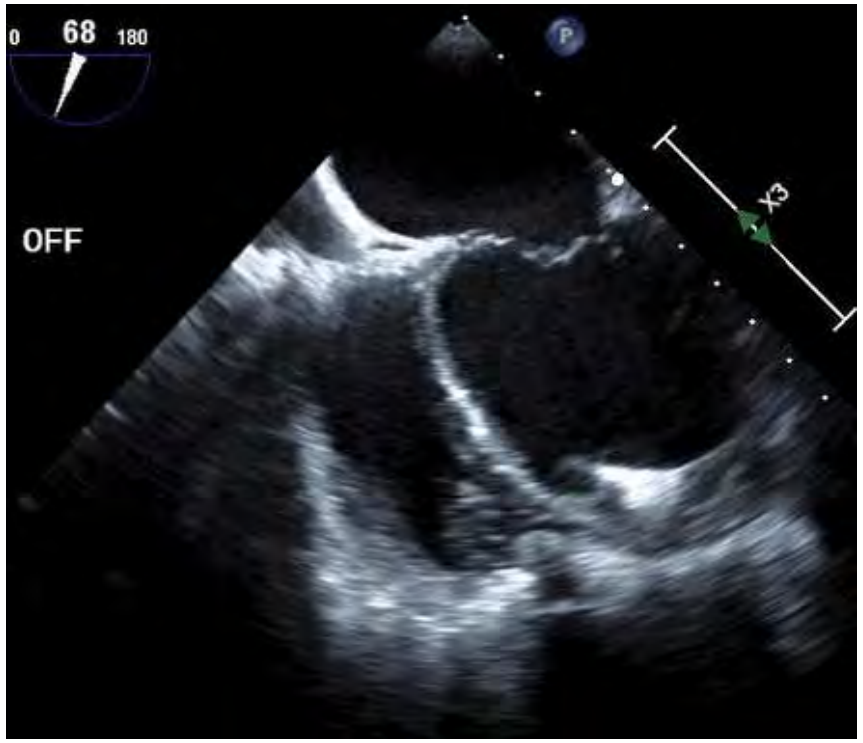
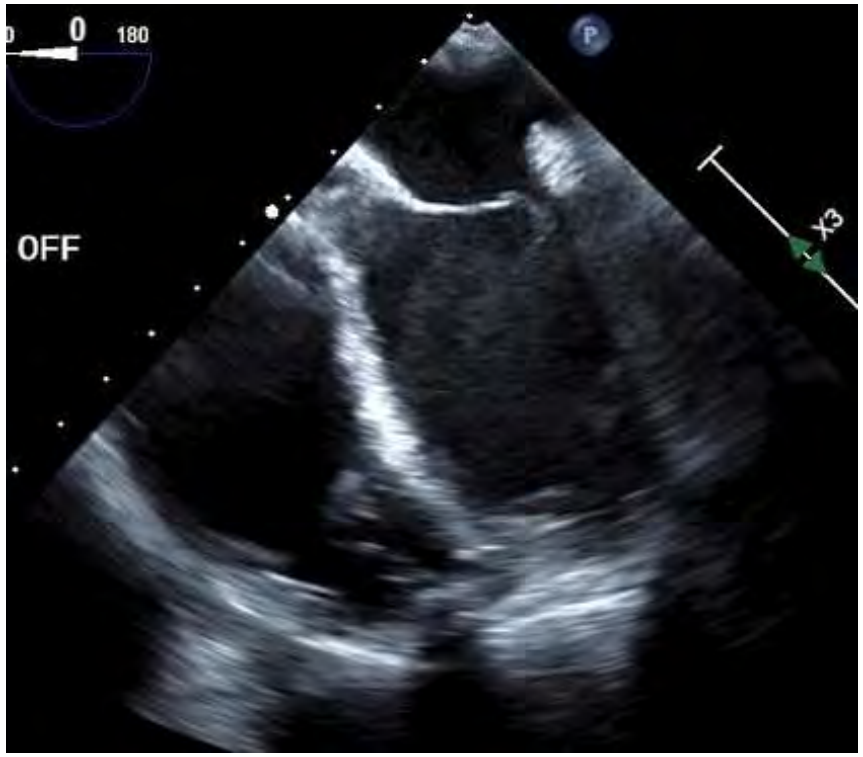
INTRAOPERATIVE COURSE



Inotropes added



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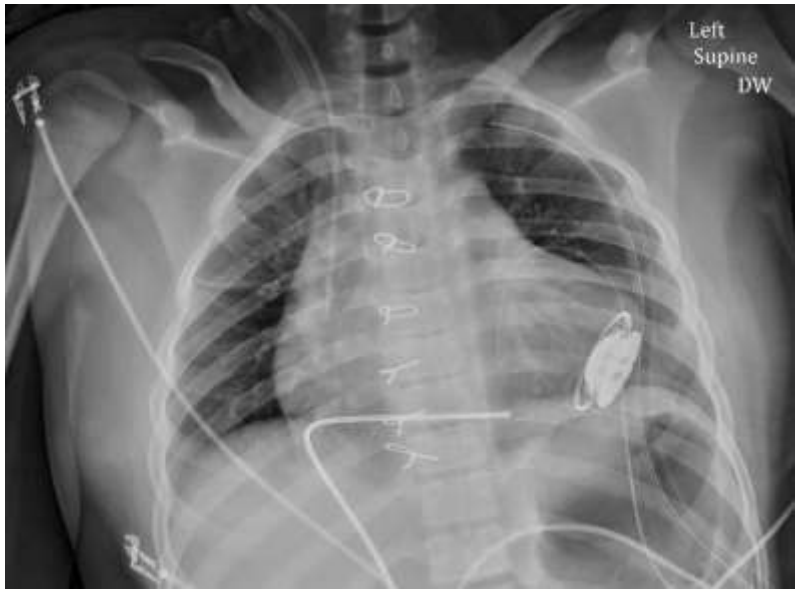
INTRAOPERATIVE COURSE

- Returned to ICU on milrinone, epinephrine infusions
- Extubated in operating room
- Worsening respiratory acidosis, pulmonary edema, desaturation
- Emergent re-intubation followed by cardiac arrest, ECMO cannulation



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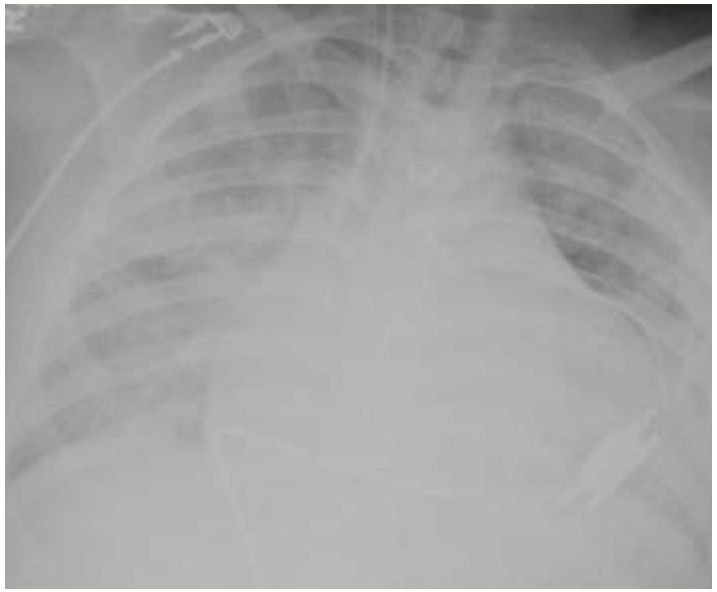

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POTENTIAL CONTRIBUTORS TO FAILURE

- Wrong substrate
- Inadequate GDMT
- Imperfect pre-explant hemodynamics
- Early extubation
- Insufficient monitoring (ie, no PA catheter)