Experimental Mechanical Assist for the Fontan Circulation

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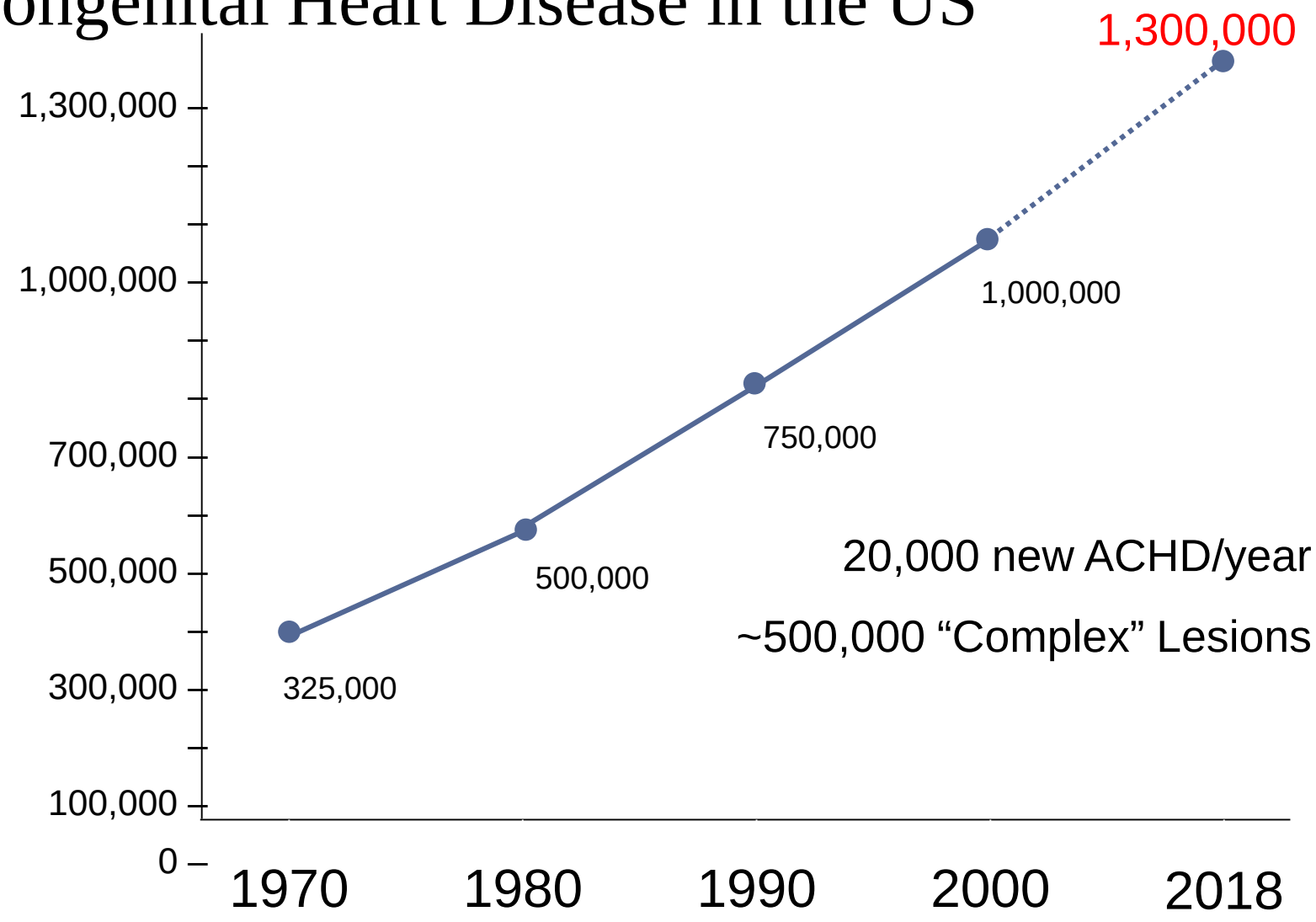
Adult Congenital Heart Disease in the US



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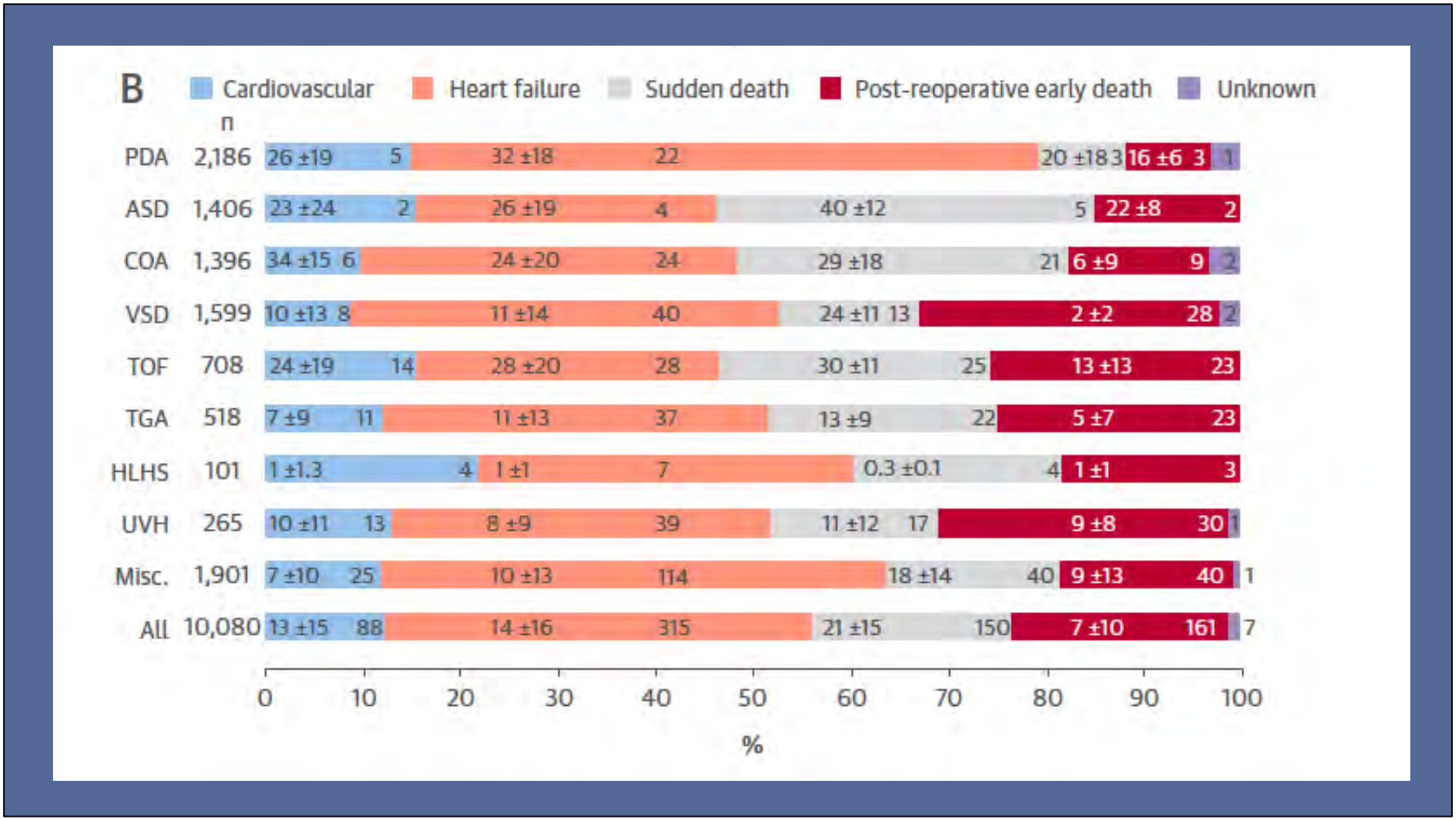
#1 Cause of Death in ACHD is Heart Failure



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Raissadati et. Al. JACC 2016. volume 68, no 5. Late Causes of Death After Pediatric Cardiac Surgery : A 60-Year Population-Based Study

Proportion of Patients Transplanted for CHD Has Increased Over Time

	1992-2000 (N = 37,146)	2001-2005 (N = 17,183)	2006-2012 (N = 22,318)	p-value
Cardiomyopathy	46.2%	48.2%	54.0%	<0.0001
Coronary artery disease	45.8%	42.7%	36.8%	
Valvular	3.9%	3.5%	2.8%	
Retransplant	1.9%	2.2%	2.5%	
Congenital	1.8%	2.7%	2.9%	
Other causes	0.4%	0.6%	0.9%	

Burchill et al: 85647 patients 2005-2010 3.2% of patients ACHD

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Burchill et. AlJ HeartLungTransplant 2014;33:1157–1163
Lund et al., J Heart Lung Transplant 2013;32:951

10% of Transplant Recipients Aged 18-39 Have Congenital Heart Disease

	N = 4,053
Recipient previous malignancy	4.3%
Creatinine at time of transplant	1.0 (0.6 - 2.1)
PVR (Wood units)	2.0 (0.2 - 5.6)
Diagnosis	
Cardiomyopathy	74.3%
Coronary artery disease	7.3%
Valvular	1.7%
Retransplant	5.3%
Congenital	9.9%
Other causes	1.4%

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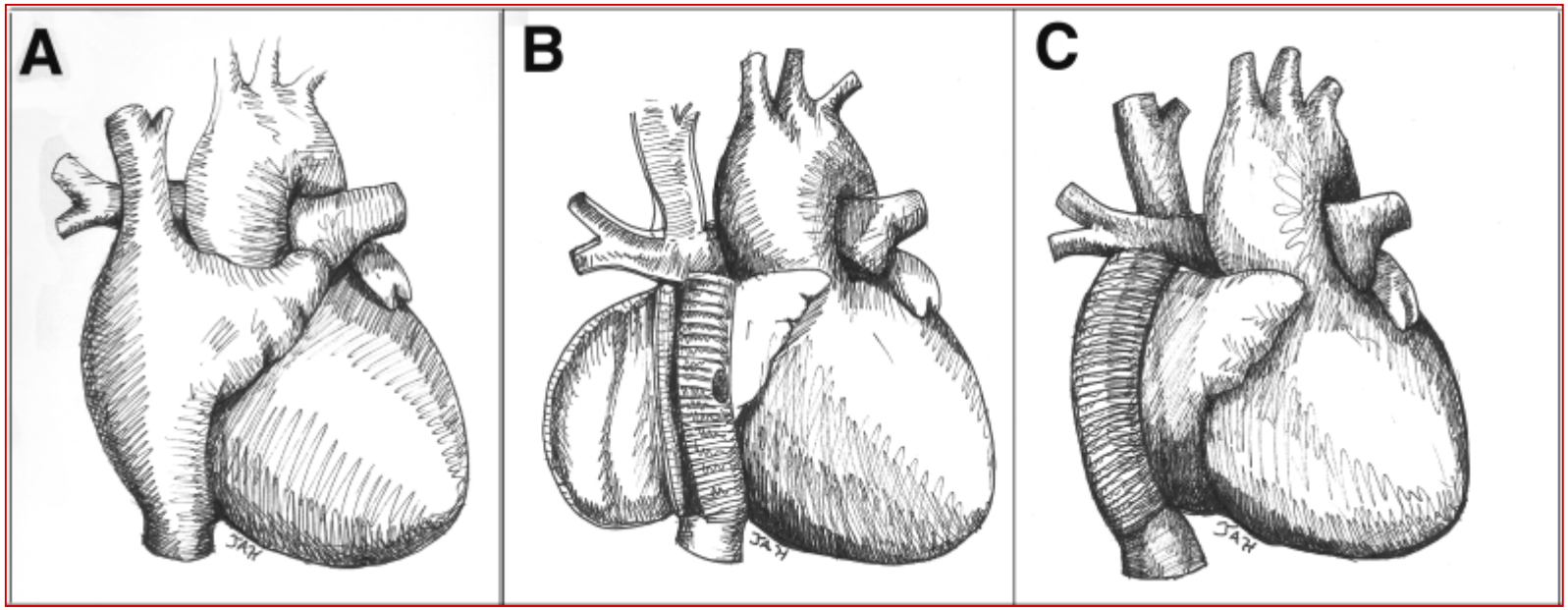
Lund et al., J Heart Lung Transplant 2013;32:951

The Fontan Procedure



A) RA-PA Fontan- 1971-1988

B) Lateral tunnel Fontan +/- fenestration- 1988- present

C) Extracardiac Fontan- 1990-present

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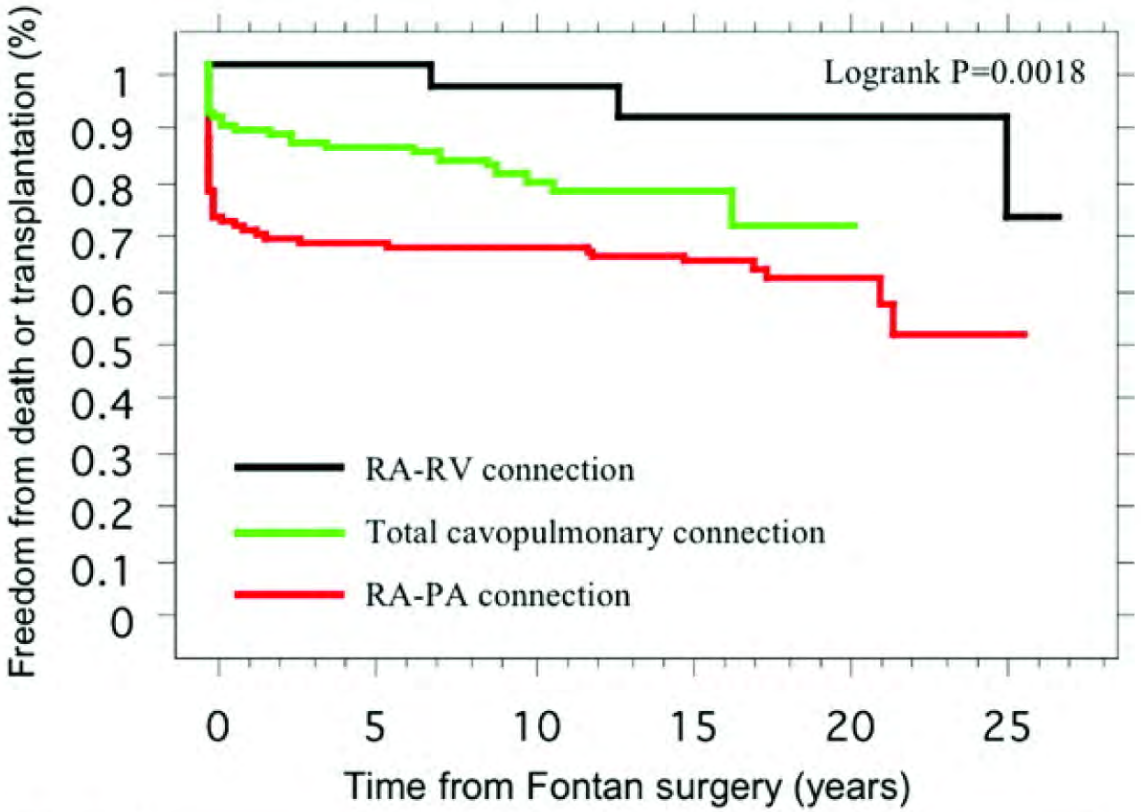
J. Aboulhosn, J.S. Child-CHD in Adults- Hurst's the Heart 12th edition-2008

Freedom from death or transplantation according to type of Fontan



Number at risk						
RA-RV	25	25	20	14	10	6
TCPC	122	77	57	27	1	0
RA-PA	135	85	77	61	23	3
TOTAL	**282**	**187**	**154**	**102**	**34**	**9**
Survival	80.1%	77.5%	74.8%	72.2%	68.3%	53.6%

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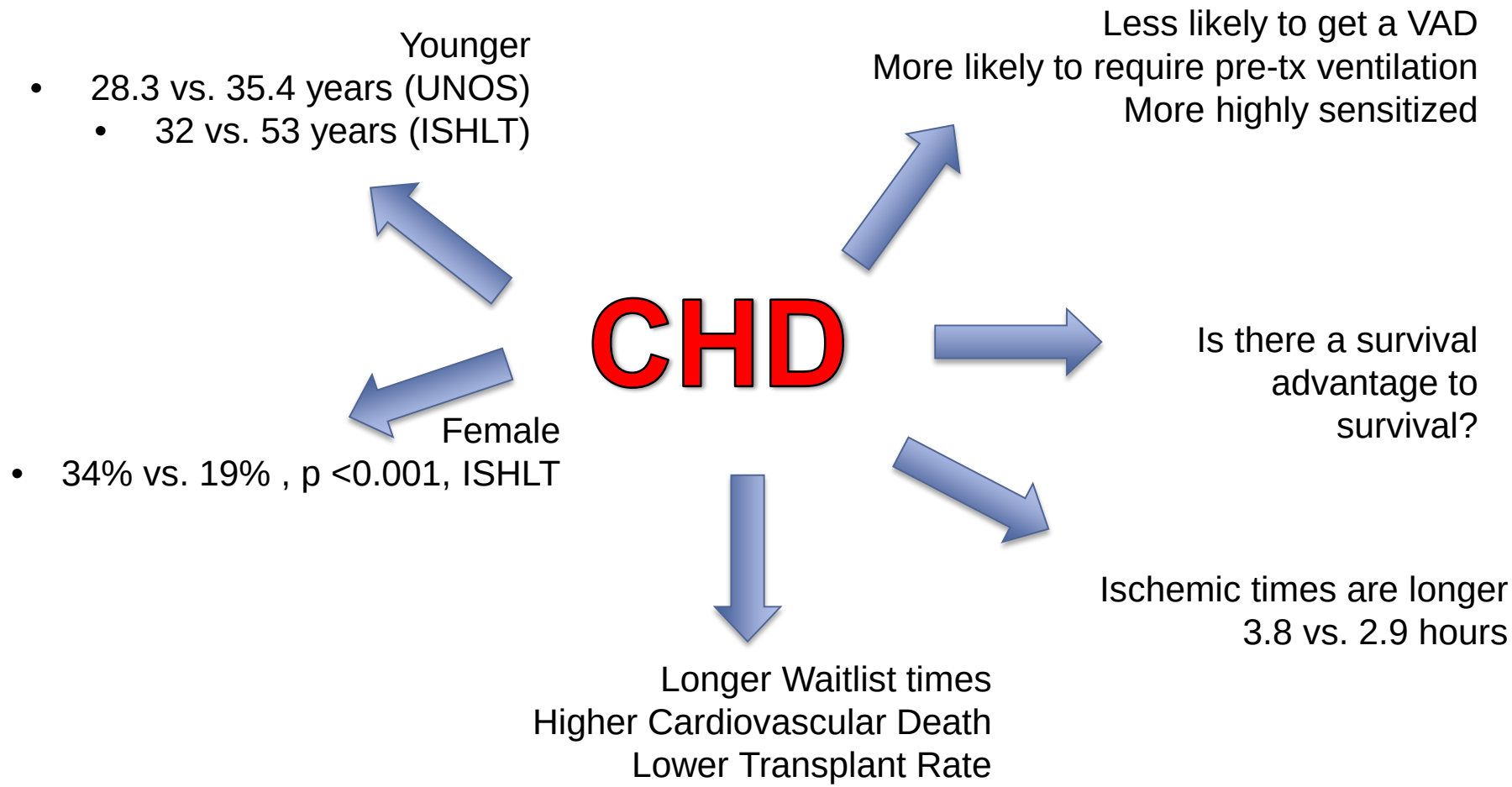
Khairy et al. *Circulation*. 2008;117:85-92

Congenital Heart Failure and Transplant Patients



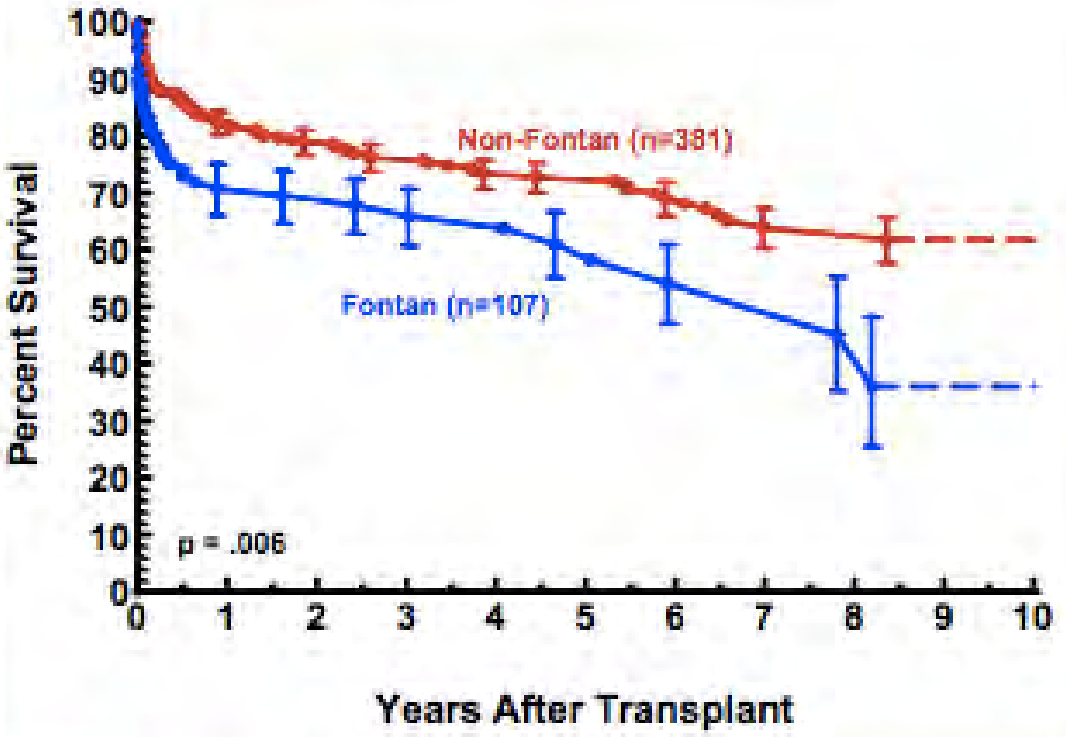


Figure 5 **Post-Transplant Survival: Fontan Versus Non-Fontan**

Kaplan-Meier survival comparing the survival post-transplant of Fontan patients with all other patients transplanted with congenital heart disease. The **vertical bars** surrounding the survival estimates represent 70% confidence limits.

UCLA Health

Lamour et al. J Am Coll Cardiol 2009;54:160–5

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DOI: 10.1111/ctr.13329

ORIGINAL ARTICLE

WILEY Clinical TRANSPLANTATION

Heart and heart–liver transplantation in adults with failing Fontan physiology

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Abstract

Background: As the population of patients with a Fontan palliation grows so does, the number of patients with cardiac failure necessitating orthotopic heart transplant (OHT) and combined heart–liver transplant (CHLT). There is recent evidence that current era cardiac transplant in Fontan patients has improved outcomes, but most studies have a preponderance of pediatrics patients in their cohorts. We examine our institutional experience with adult OHT and CHLT transplantation for failed Fontan physiology.

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DOI: 10.1111/ctr.13540

ORIGINAL ARTICLE

Clinical TRANSPLANTATION WILEY

Short-term outcomes of *en bloc* combined heart and liver transplantation in the failing Fontan

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Abstract

Patients with failing Fontan physiology and liver cirrhosis are being considered for combined heart and liver transplantation. We performed a retrospective review of our experience with *en bloc* combined heart and liver transplantation in Fontan patients > 10 years old from 2006 to 18 per Institutional Review Board approval. Six females and 3 males (median age 20.7, range 14.2-41.3 years) underwent *en bloc* combined heart and liver transplantation. Indications for heart transplant included ventricular dysfunction, atrioventricular valve regurgitation, arrhythmia, and/or lymphatic abnormalities. Indication for liver transplant included portal hypertension and cirrhosis. Median Fontan/single ventricular end-diastolic pressure was 18/12 mm Hg,

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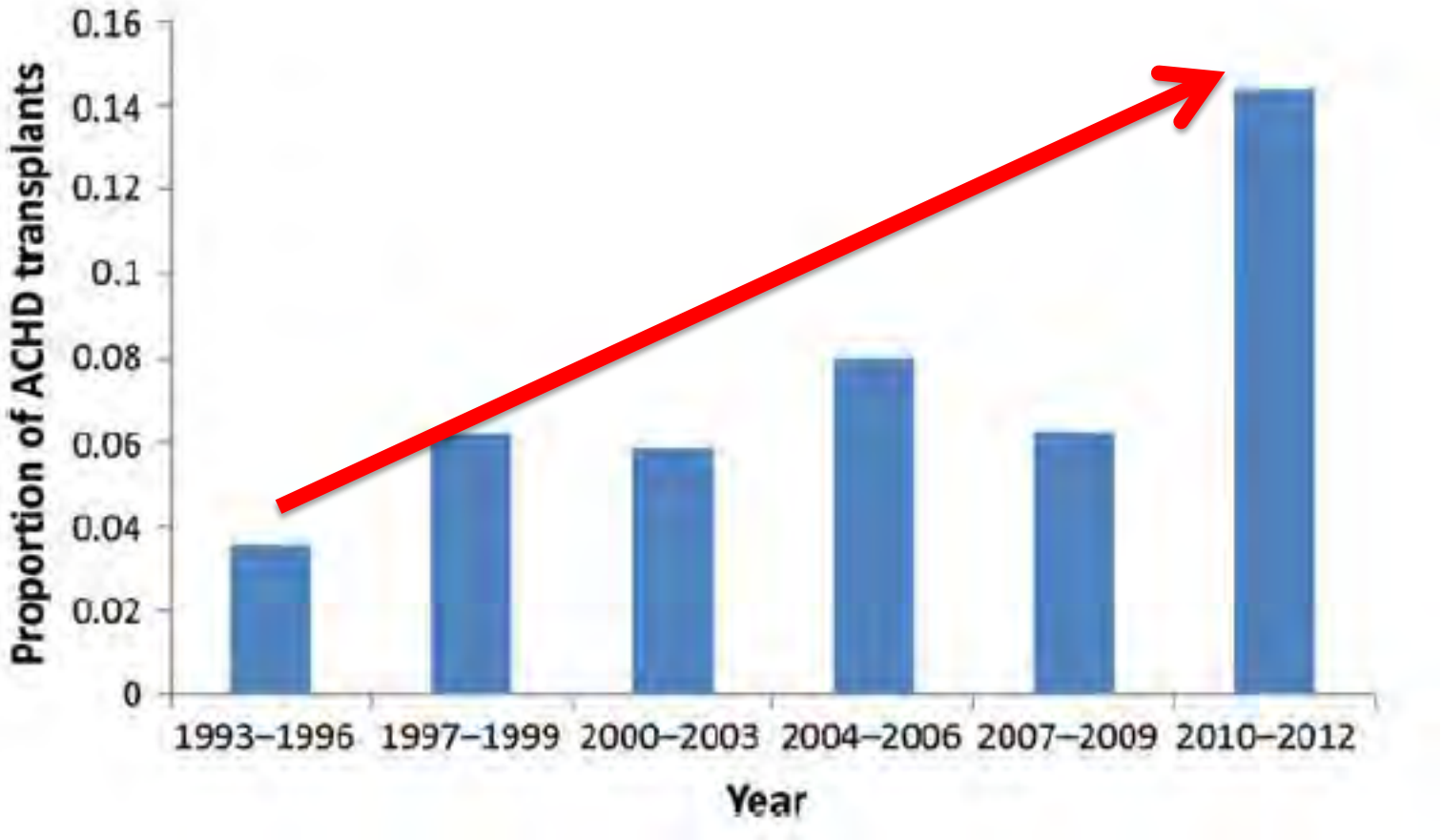
Proportion of ACHD Transplants Supported with MCS



LVAD 81%, RVAD 6%, BIVAD 7%, TAH 6%

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Maxwell et al., Eur J Cardiothorac Surg 2013 Oct 17

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

MCS REGISTRY IN CHILDREN – PEDIMACS

Second annual Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs) report: Pre-implant characteristics and outcomes

Elizabeth D. Blume, MD,[a] Christina VanderPluym, MD,[a] Angela Lorts, MD,[b] J. Timothy Baldwin, PhD,[c] Joseph W. Rossano, MD,[d] David L.S. Morales, MD,[b] Ryan S. Cantor, MSPH,[e] Marissa A. Miller, DVM, MPH,[c] James D. St. Louis, MD,[f] Devin Koehl, BS,[e] David L. Sutcliffe, MD,[g] Pirooz Eghtesady, MD, PhD,[h] James K. Kirklin, MD,[e] and David N. Rosenthal, MD[i] for the Pedimacs Investigators

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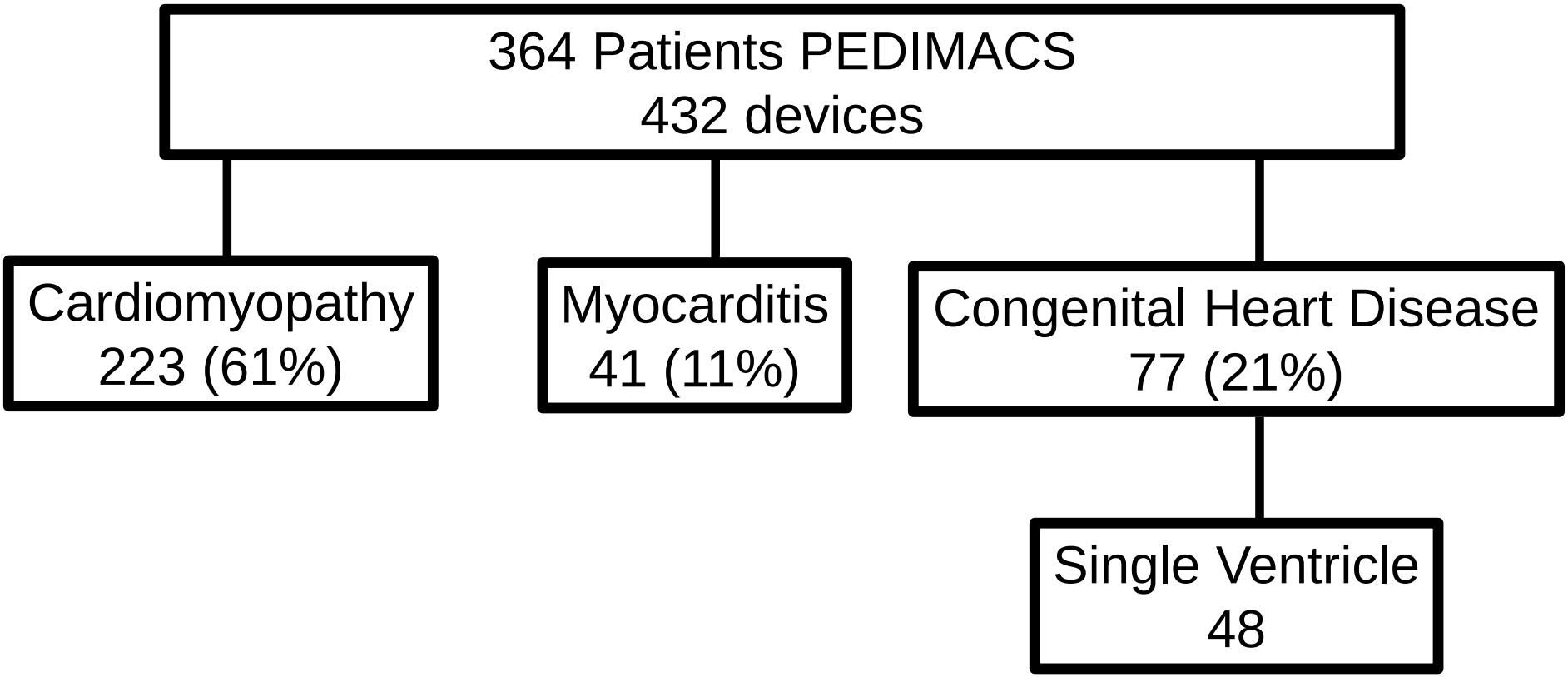
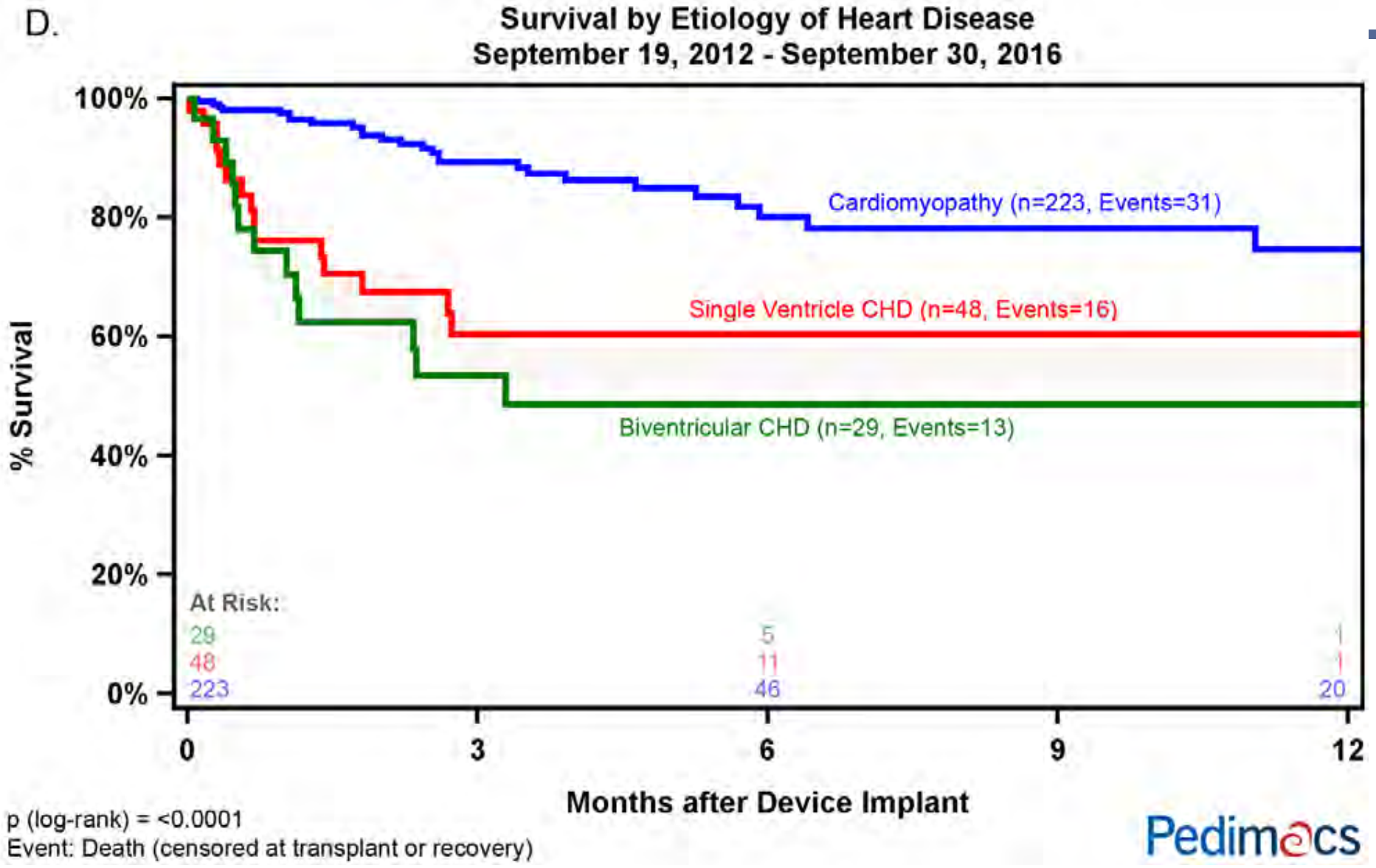

364 Patients PEDIMACS
432 devices
Cardiomyopathy
223 (61%)
Myocarditis
41 (11%)
Congenital Heart Disease
77 (21%)
Single Ventricle
48

D.



p (log-rank) = <0.0001
Event: Death (censored at transplant or recovery)

Pedimacs

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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Outcomes following implantation of mechanical circulatory support in adults with congenital heart disease: An analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)

Christina J. VanderPluym, MD,[a,1] Ari Cedars, MD,[b,1] Pirooz Eghtesady, MD, PhD,[c] Bryan G. Maxwell, MD, MPH,[d] Jill M. Gelow, MD, MPH,[e] Luke J. Burchill, MMBS, PhD,[e] Simon Maltais, MD, PhD,[f] Devin A. Koehl, BS,[g] Ryan S. Cantor, MSPH,[g,h] and Elizabeth D. Blume, MD[a]

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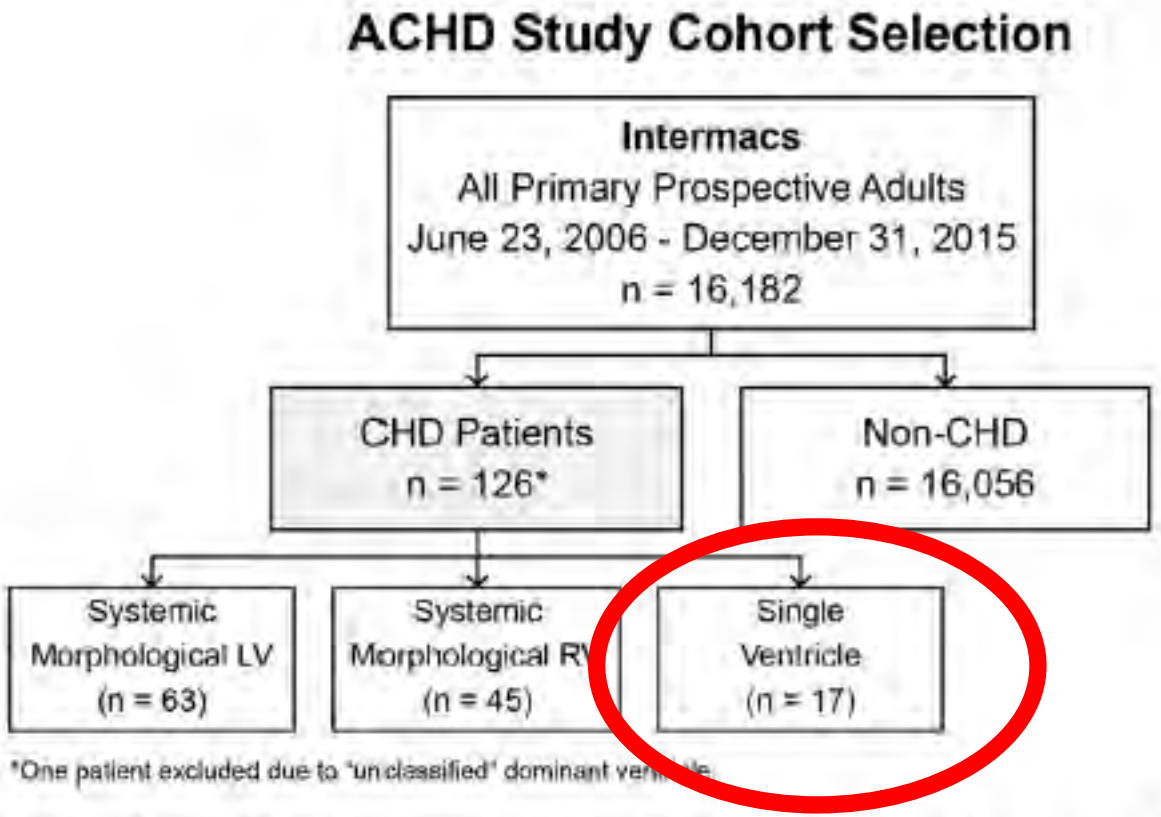
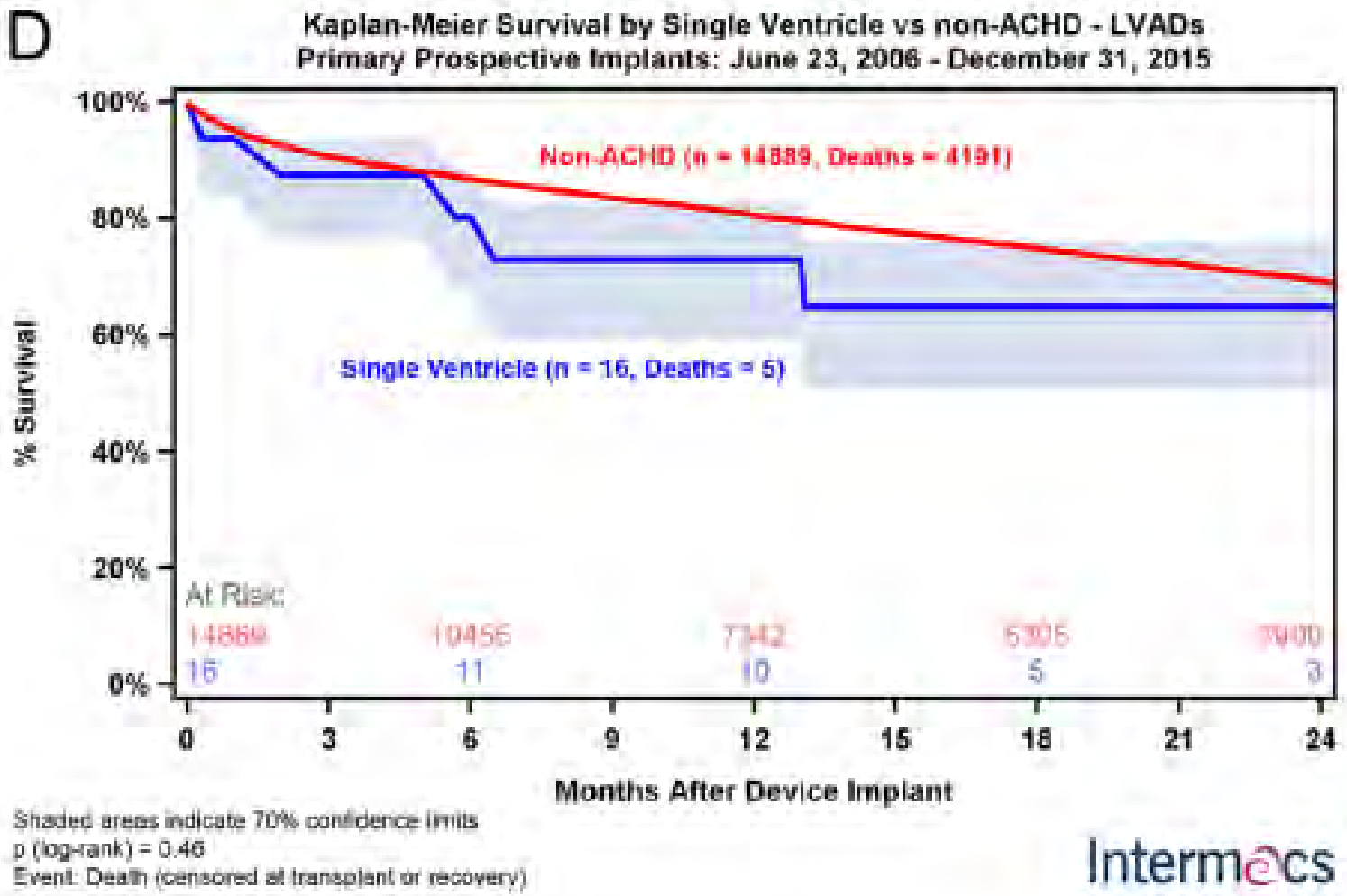


Figure 1 Graphic representation of patient selection and categorization into groups.


D
Kaplan-Meier Survival by Single Ventricle vs non-ACHD - LVADs
Primary Prospective Implants: June 23, 2006 - December 31, 2015
100%
80%
60%
40%
20%
0%
% Survival
Non-ACHD (n = 14889, Deaths = 4191)
Single Ventricle (n = 16, Deaths = 5)
At Risk:
14889 10456 7342 5305 3900
16 11 10 5 3
0 3 6 9 12 15 18 21 24
Months After Device Implant
Shaded areas indicate 70% confidence limits
p (log-rank) = 0.46
Event: Death (censored at transplant or recovery)
Intermacs

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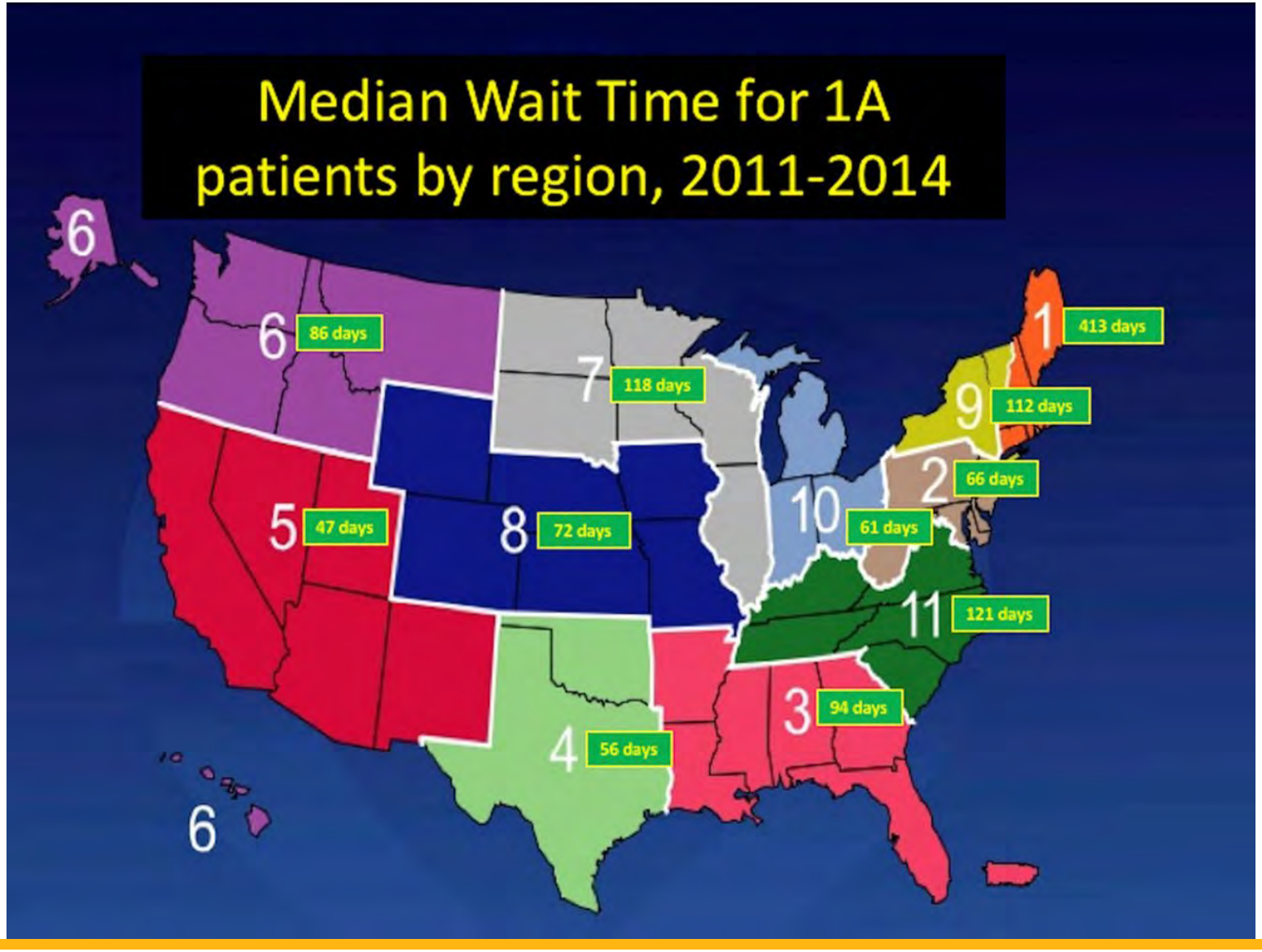

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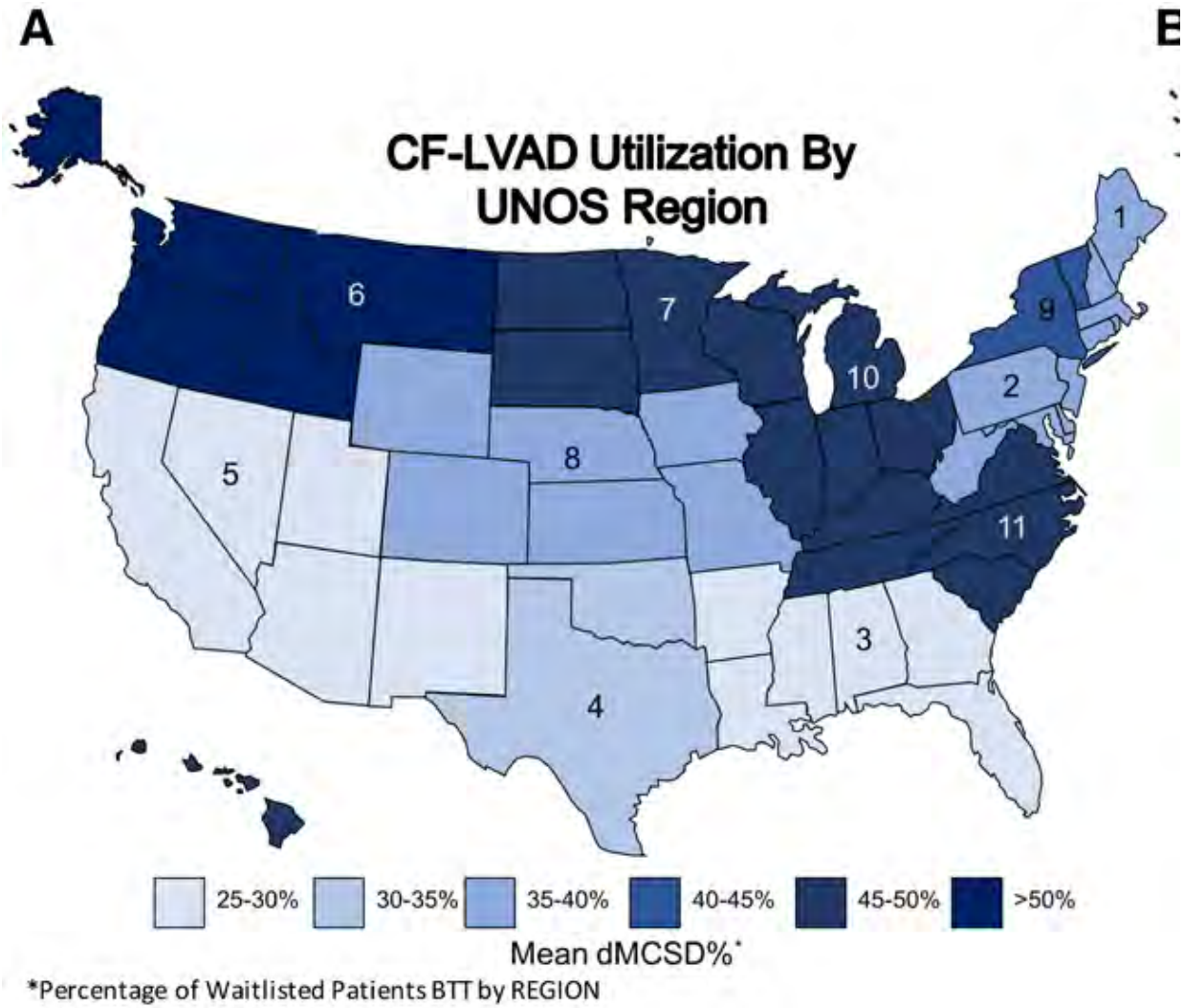
Schulze et. al. JACC: Heart Failure Vol. 2, No. 2, 2014



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Truby, et al. Circ Heart Fail. 2018;11:e004586.

Pediatric Heart Transplant Criteria July 2016

1A	• Continuous mechanical ventilation • Intraortic balloon pump • Ductal dependent pulmonary or systemic circulation • Congenital heart disease with multiple low dose inotropes or 1 high dose • Mechanical circulatory support (does not require hospitalization)
1B	• Continuous infusion of 1 or more inotropes and does not qualify for 1A
2	• All Others

Adult Heart Allocation Criteria for Medical Urgency Status

The Organ Procurement and Transplantation Network announced that a new, six-tier adult heart allocation system will be implemented this year.

Status 1
- VA ECMO
- Non-dischargeable, surgically implanted, non-endovascular biventricular support device
- MCSD with life-threatening ventricular arrhythmia

Status 2
- Non-dischargeable, surgically implanted, non-endovascular LVAD
- IABP
- V-tach / V-fib, mechanical support not required
- MCSD with device malfunction/mechanical failure
- TAH, BiVAD, RVAD, or VAD for single ventricle patients
- Percutaneous endovascular MCSD

Status 3
- Dischargeable LVAD for discretionary 30 days
- Multiple inotropes or single high-dose inotrope with continuous hemodynamic monitoring
- VA ECMO after 7 days; percutaneous endovascular circulatory support device or IABP after 14 days
- Non-dischargeable, surgically implanted, non-endovascular LVAD after 14 days
- MCSD with one of the following: device infection, hemolysis, pump thrombosis, right heart failure, mucosal bleeding, aortic insufficiency

Status 4
- Dischargeable LVAD without discretionary 30 days
- Inotropes without hemodynamic monitoring
- Retransplant
- Diagnosis of one of the following: congenital heart disease (CHD), ischemic heart disease with intractable angina, hypertrophic cardiomyopathy, restrictive cardiomyopathy, amyloidosis

Status 5
- On the waitlist for at least one other organ at the same hospital

Status 6
- All remaining active candidates

OPTN | UNOS

Review Board (RB) Guidance for Adult Congenital Heart Disease (CHD) Exception Requests

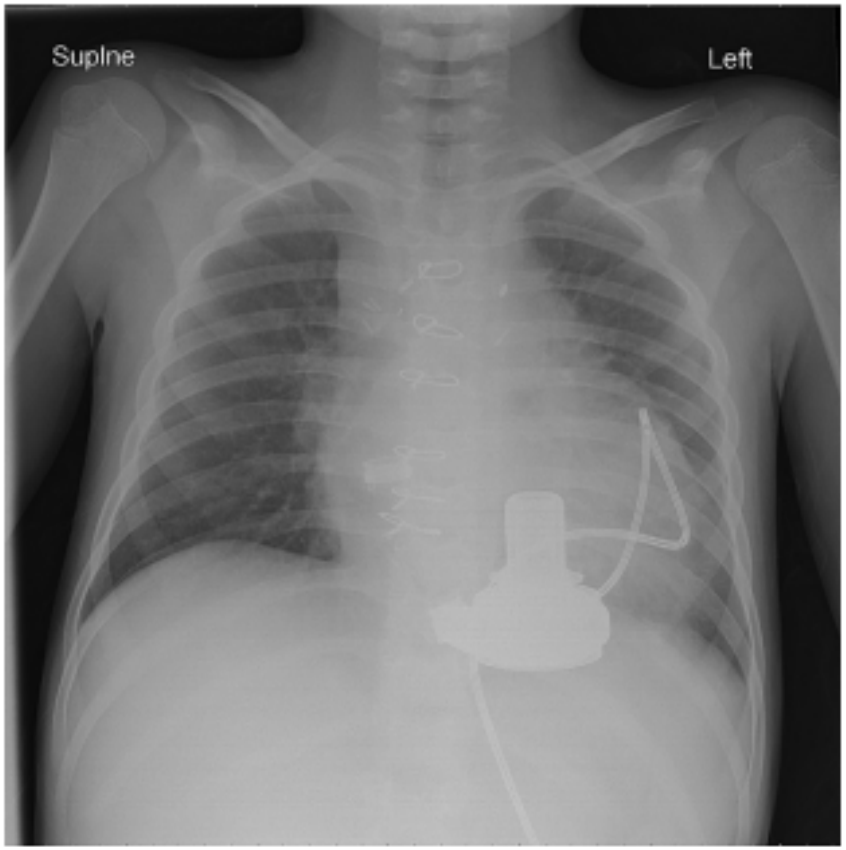
The OPTN/UNOS Board of Directors recently approved the Thoracic Organ Transplantation Committee's Modification *to the Adult Heart Allocation* proposal during their December 2016 meeting in St. Louis, MO. One of the major components of the new allocation system was the creation of three additional medical urgency statuses, for a new total of six. This new six-status system stratifies heart transplant candidates according to waiting list mortality.

During the development of the adult heart allocation policy, the Committee received feedback from the heart transplant community that adult congenital heart disease (ACHD) candidates may be disadvantaged by the new system, as they are a very heterogeneous candidate group and they may not always be optimal candidates for devices or inotropes.

The Committee acknowledged that some ACHD candidates may have higher waiting list mortality. The new allocation policy includes hemodynamic criteria in addition to criteria based on levels of support. Measurement of hemodynamics among patients with CHD can be complicated by altered anatomy and rendered meaningless. In addition, ACHD patients may not be candidates for the inotropic or mechanical support options. Thus CHD candidates may have difficulty meeting criteria for higher status according to policy, despite waitlist mortality equivalent to other candidates at higher status. Instead, the exception and review process will continue to accommodate these candidates, who can still apply for an exception at any status as their medical urgency and potential for benefit would warrant, including status 1, short-term. The Committee drafted this guidance with the goal of helping review board (RBs) standardize decision-making for ACHD exception requests.

Fontan VAD Support

- Single ventricular “systolic” failure.
- 11 year old patient supported with an HVAD for 148 days until he underwent OHT.



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Niebler et al. Ann Thorac Surg 2014;97:e115–6

HeartWare Ventricular Assist Device Implantation in Patients With Fontan Physiology

*Bartlomiej R. Imielski, †Robert A. Niebler, ‡Steven J. Kindel, and §Ronald K. Woods

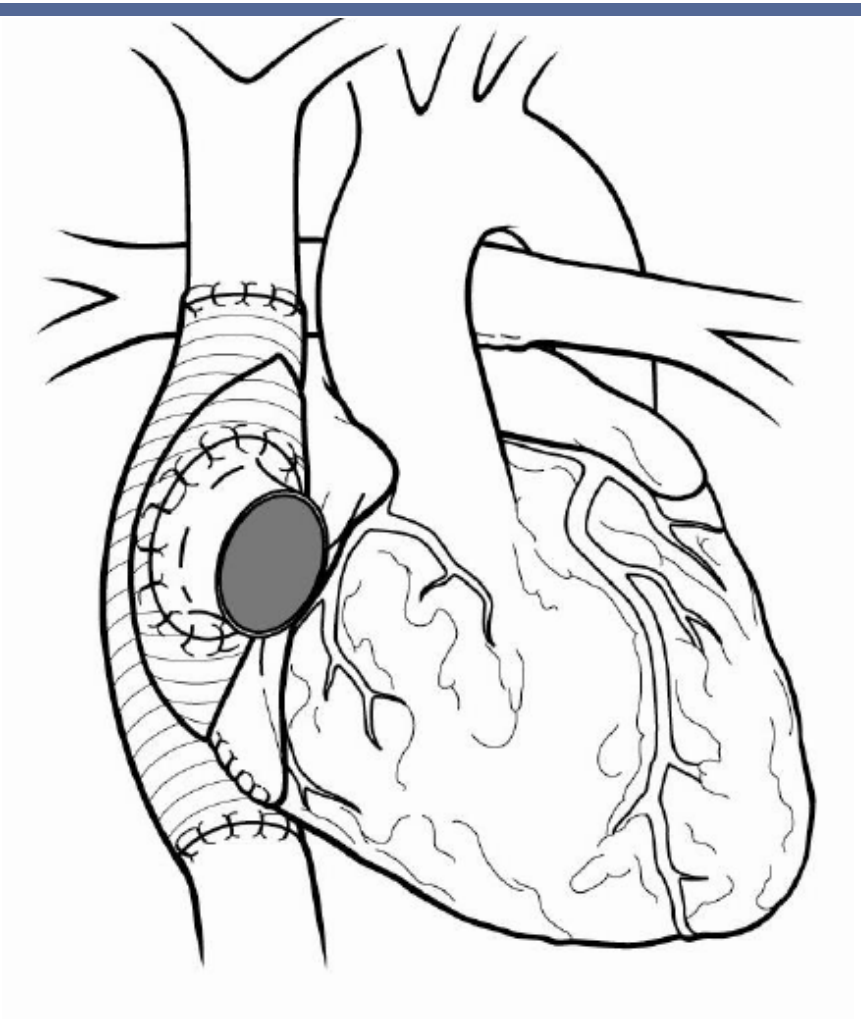
*Department of Cardiothoracic Surgery; †Department of Pediatrics, Section of Critical Care; ‡Department of Pediatrics, Section of Cardiology 3; and §Department of Cardiothoracic Surgery, Medical College of Wisconsin, Milwaukee, WI, USA

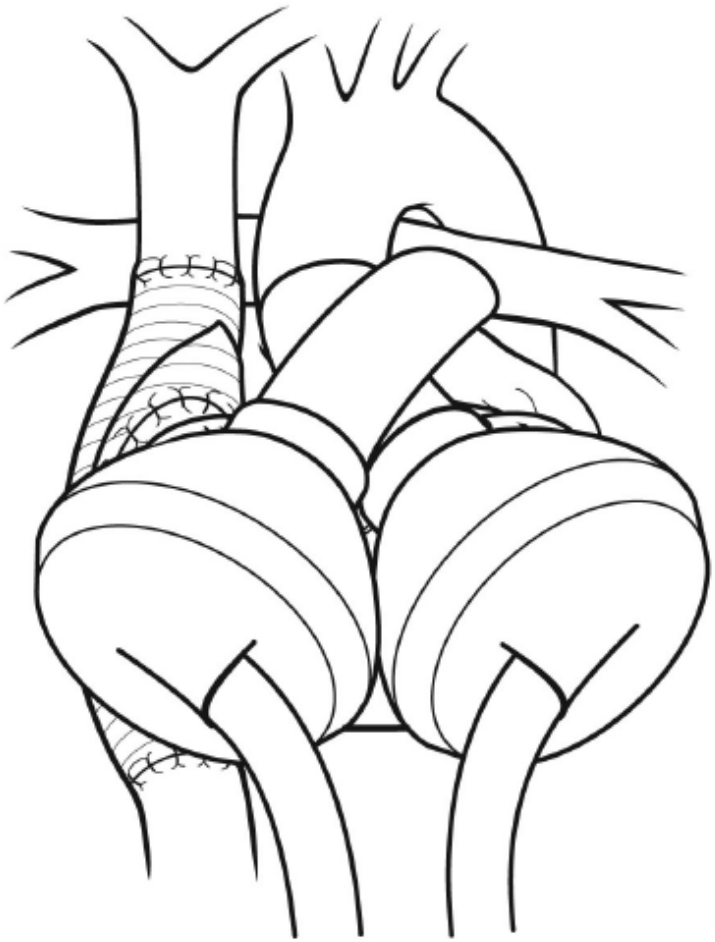
Artif Organs, Vol. 41, No. 1, 2017

TABLE 1. *Patient characteristics at implant*

	Patient 1	Patient 2	Patient 3
Age (years)	11.7	13.5	17.5
Weight (kg)	33.1	35.6	68.3
BSA (m^2)	1.13	1.22	1.92
Gender	Male	Male	Male
Primary anatomic diagnosis	HLHS	HLHS	HLHS
Fontan Type	Fenestrated Extracardiac Fontan	Fenestrated Extracardiac Fontan	Lateral Tunnel (device fenestration closure at 5 yrs, lateral tunnel stent placement in 12/2014 for narrowing)
Duration Fontan stage prior to HVAD implant (years)	9	11	16

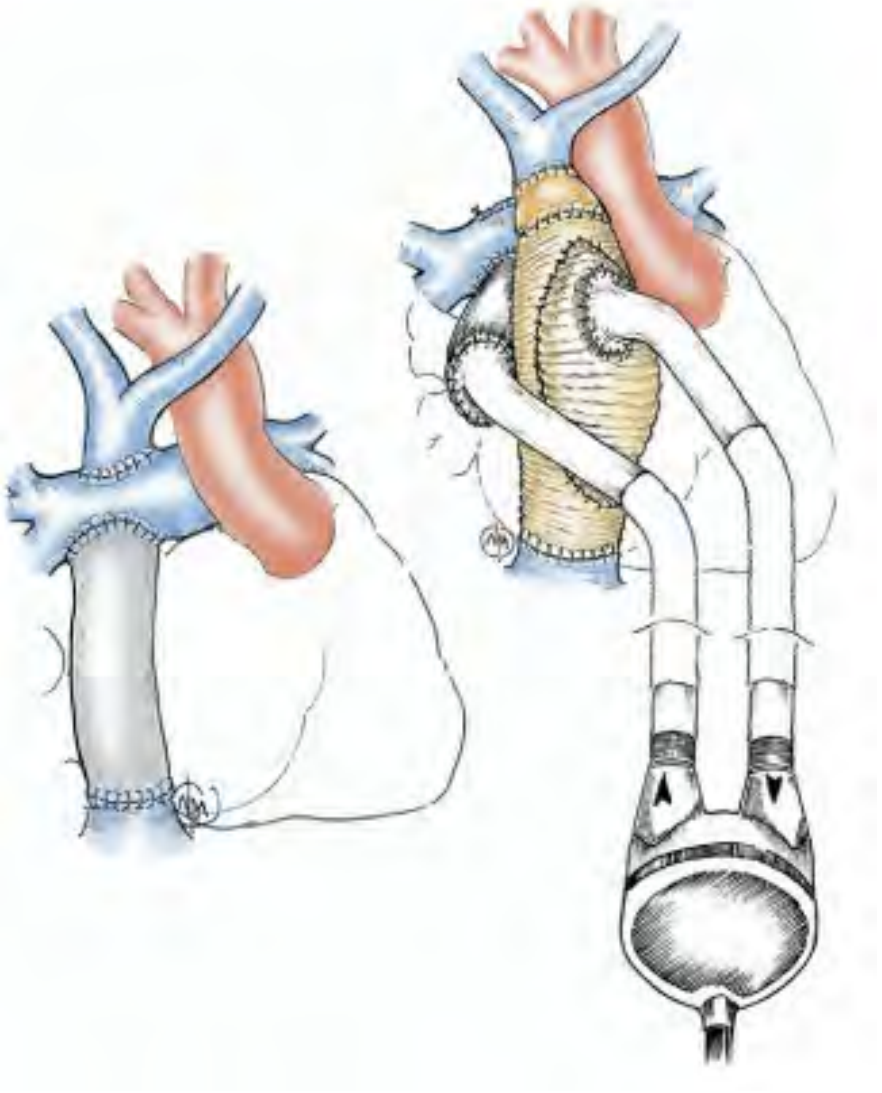
BSA, body surface area; HVAD, HeartWare ventricular assist device.





Fontan VAD Support

- 27-year-old male with Tricuspid atresia and a Björk Fontan underwent placement of a Berlin right sided device.
- Patient was transplanted after 13 months of support.



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Prêtre et al. Ann Thorac Surg 2008;86:1018–20

International Journal of Cardiology 176 (2014) 828–832

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Novel techniques of mechanical circulatory support for the right heart and Fontan circulation ☆

Gwendolyn Derk [a,b,*], Hillel Laks [b], Reshma Biniwale [b], Sanjeet Patel [b], Kim De LaCruz [e], Einat Mazor [d], Ryan Williams [a], John Valdovinos [c], Daniel S. Levi [f], Leigh Reardon [a,f], Jamil Aboulhosn [a,f]

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ABSTRACT

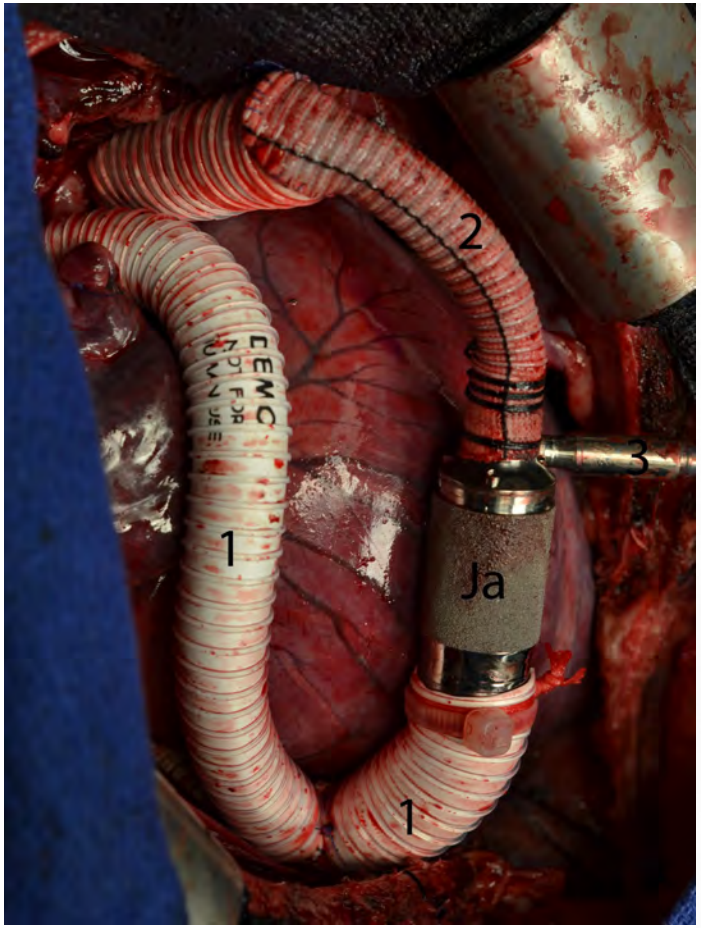
Background: Currently available ventricular assist devices are designed primarily for use in patients with left sided heart failure. This study evaluated the efficacy of the Jarvik 2000 ventricular assist device (VAD) as a pulmonary pump to power a Fontan circuit in a large animal model.

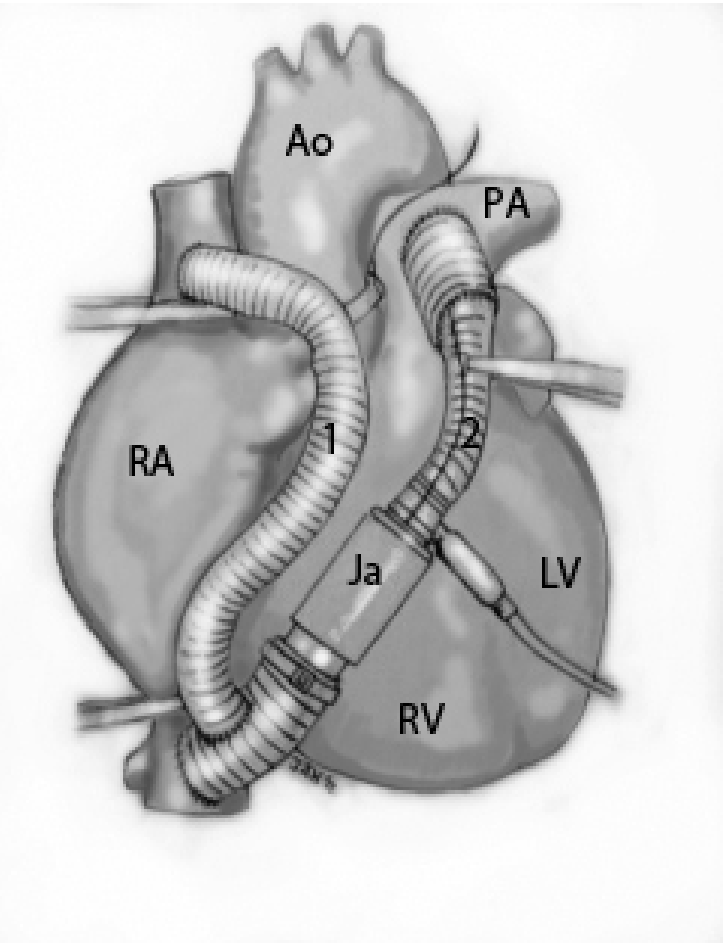
Methods: Without the use of cardiopulmonary bypass, Fontan circulations were surgically created in 4 pigs (50 kg) using synthetic grafts from the inferior and superior vena cavas to the main pulmonary artery. Subsequently, the VAD was implanted within the common Fontan graft to provide a pulmonary pump. Direct chamber pressures and epicardial Doppler images were taken during the various phases of the experiment. Heart rate, femoral artery blood pressure, oxygen saturation, and aortic flow rate were continuously recorded. The outflow cannula of the VAD was then partially banded by 50% and then 75% to mimic increased afterload.

Results: Fontan and VAD implantation was successfully performed in all 4 animals. Arterial pressure and aortic flow decreased dramatically with institution of the Fontan but were restored to baseline upon activation of the VAD. The pressure within the systemic venous circulation rose precipitously with institution of the Fontan circulation and improved appropriately with activation of the VAD. Adequate perfusion was maintained during increased afterload.

Conclusions: An axial flow VAD can restore normal hemodynamics and cardiac output when used as a pulmonary pump in a Fontan circulation. A VAD can rescue a failing Fontan as a bridge to transplant or recovery, even in the setting of high pulmonary resistance.

Creation of a Surgical Fontan Animal Model and the Use of a Ventricular Assist Device to Restore Cardiac Output





Extracardiac Fontan model with the Jarvik 2000 VAD

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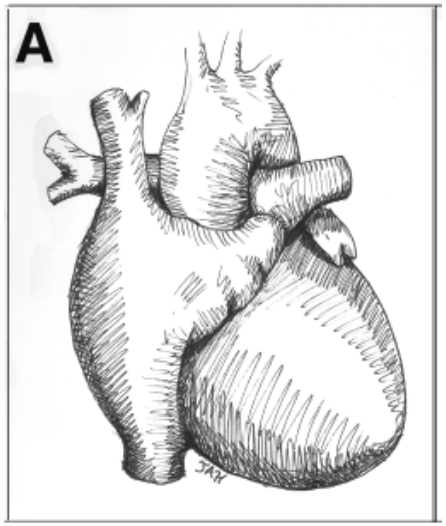
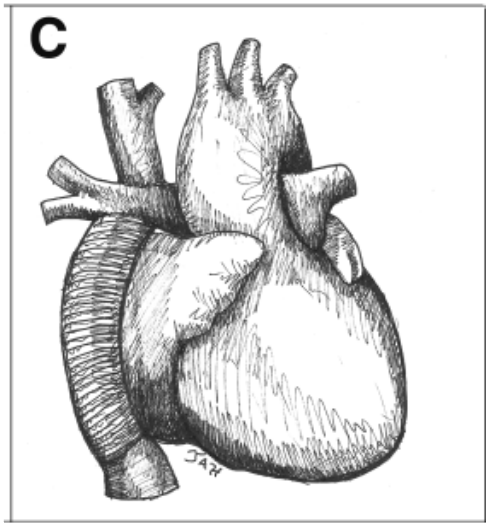
Derk et al. AJC August 2014.

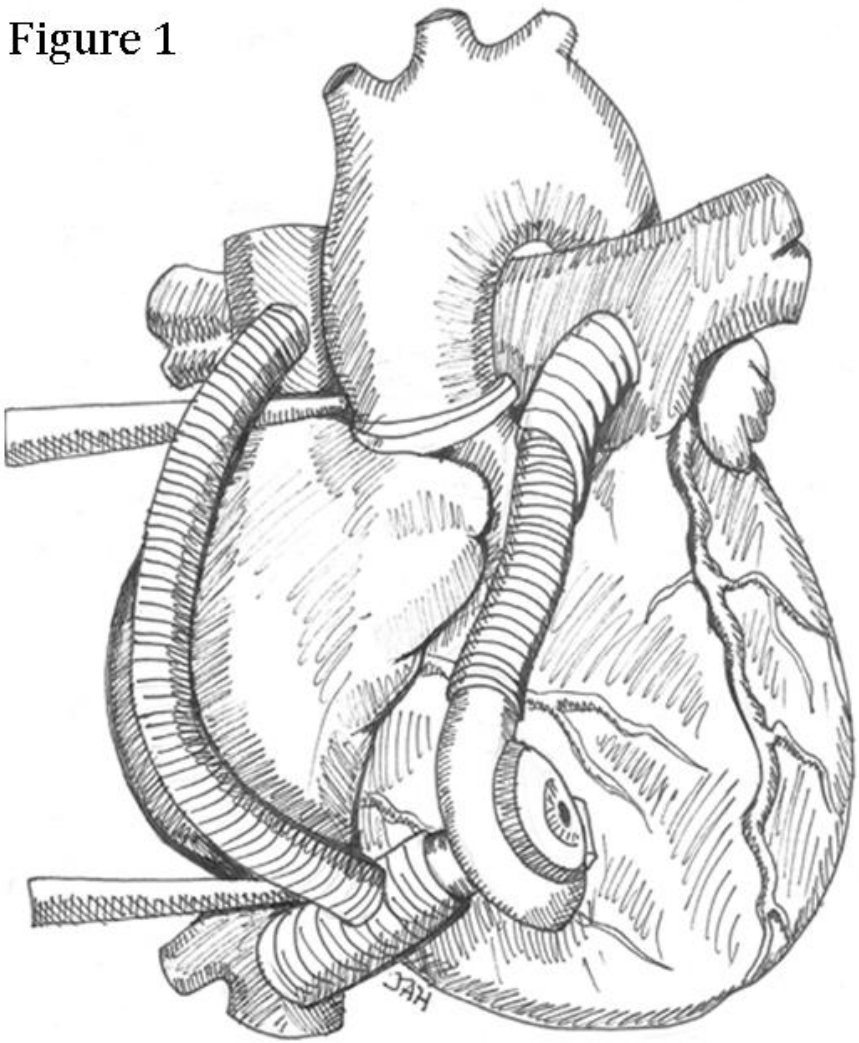
Heartware HVAD Model

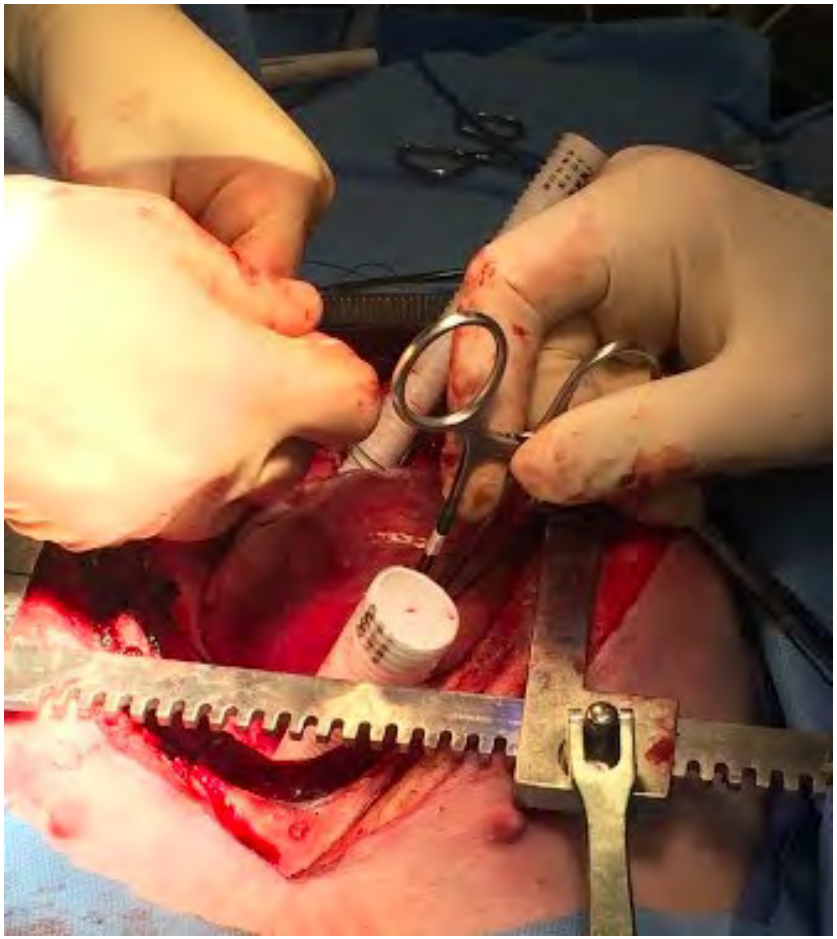
- Developed 2 models for right-sided Fontan support:
  - Extra-cardiac Fontan Model
  - RA-PA Fontan Model

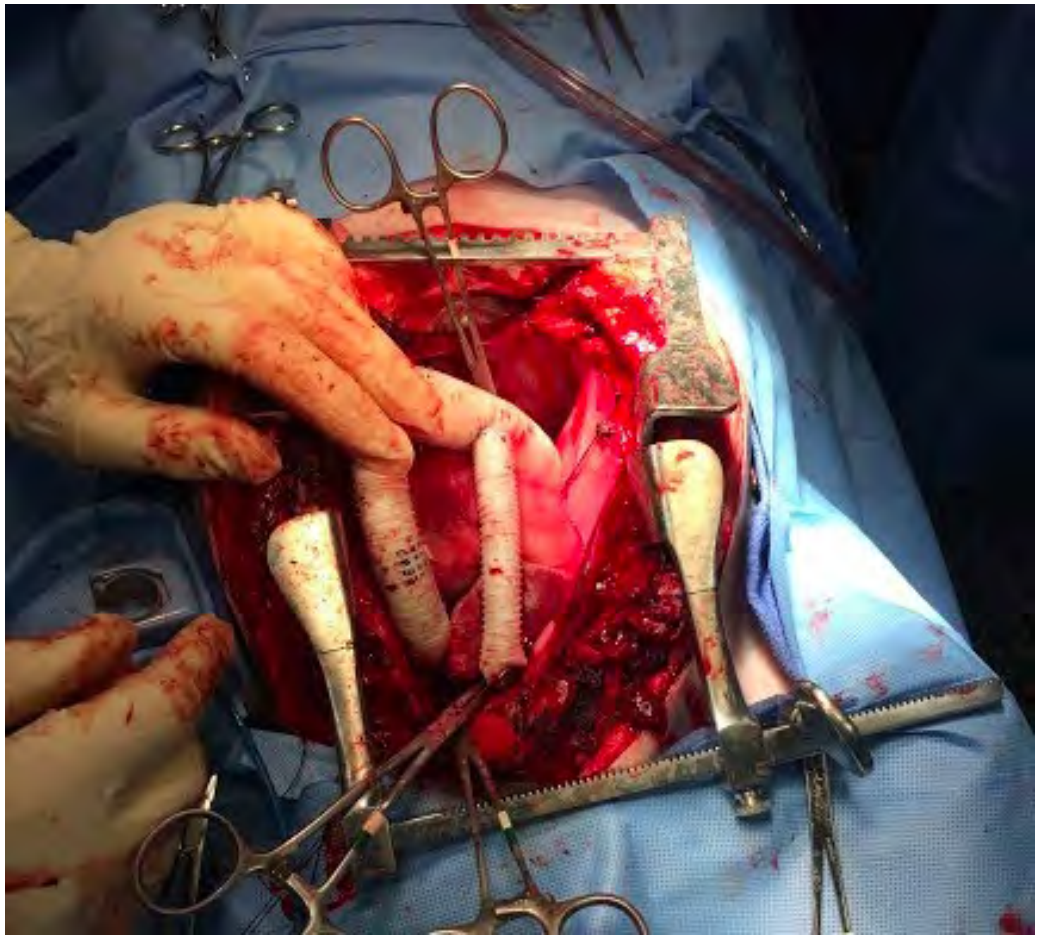


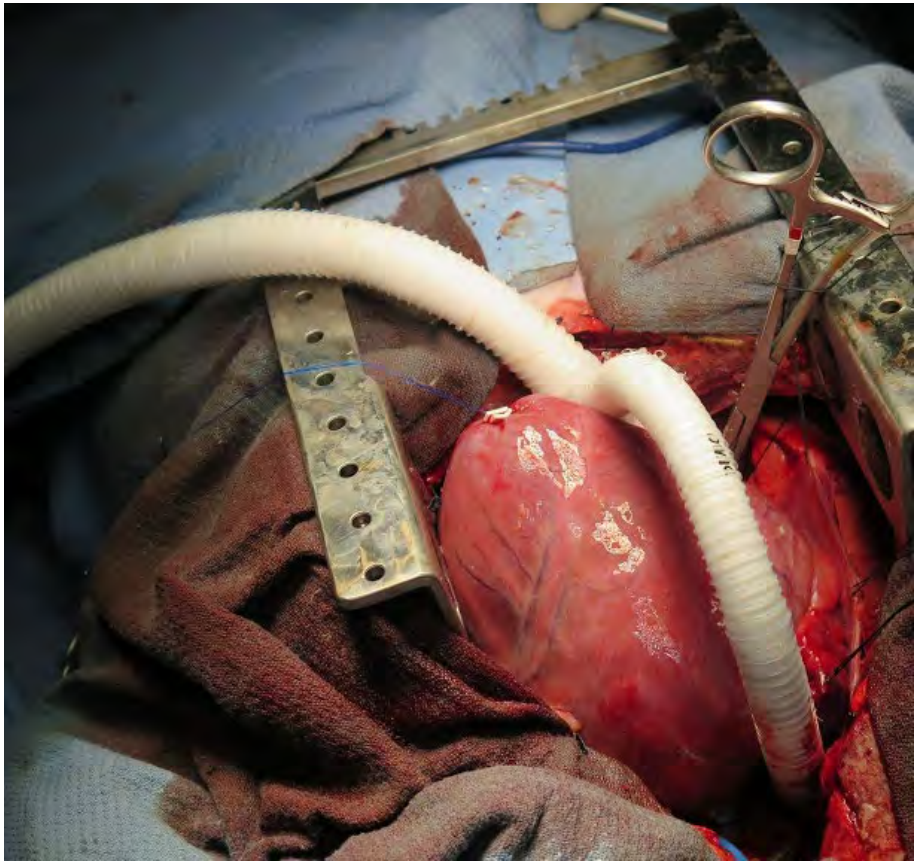


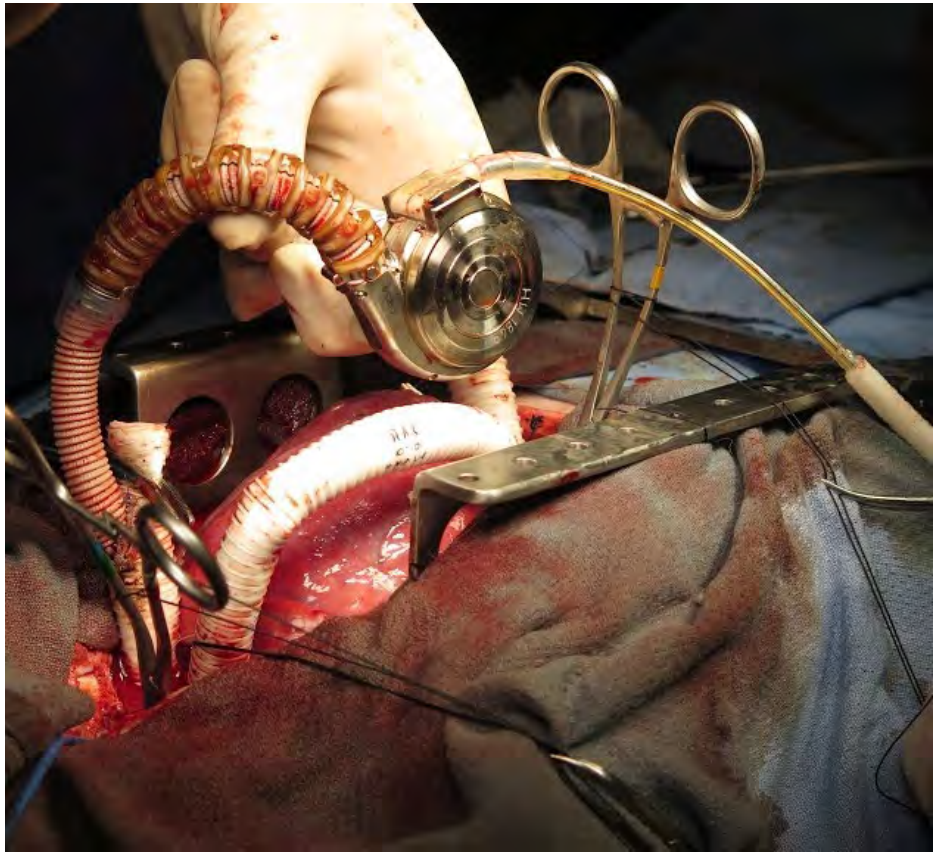
Extracardiac Fontan Model



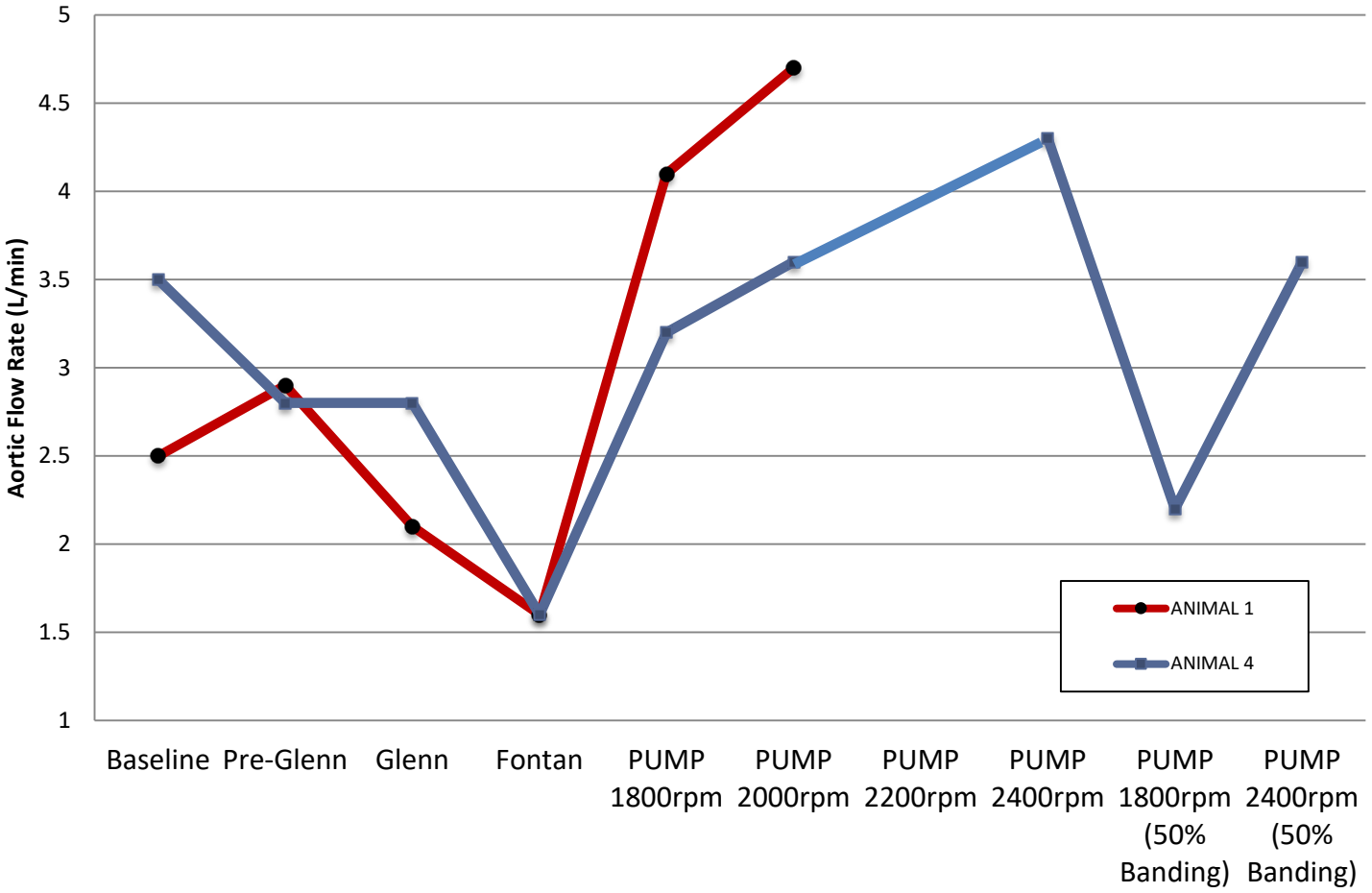








Extracardiac Fontan Model: Cardiac Output



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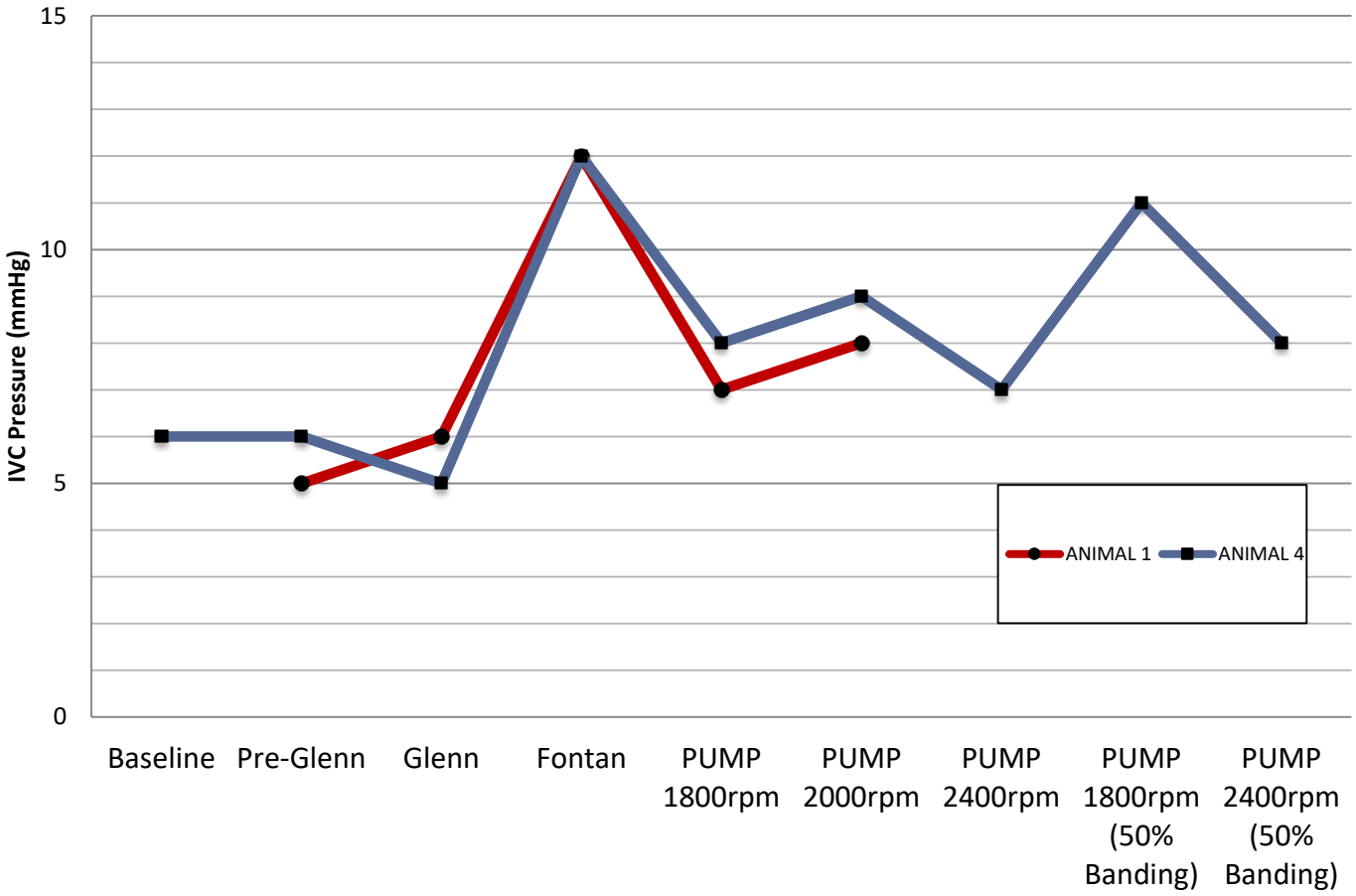
Extracardiac Fontan Model: IVC Pressures



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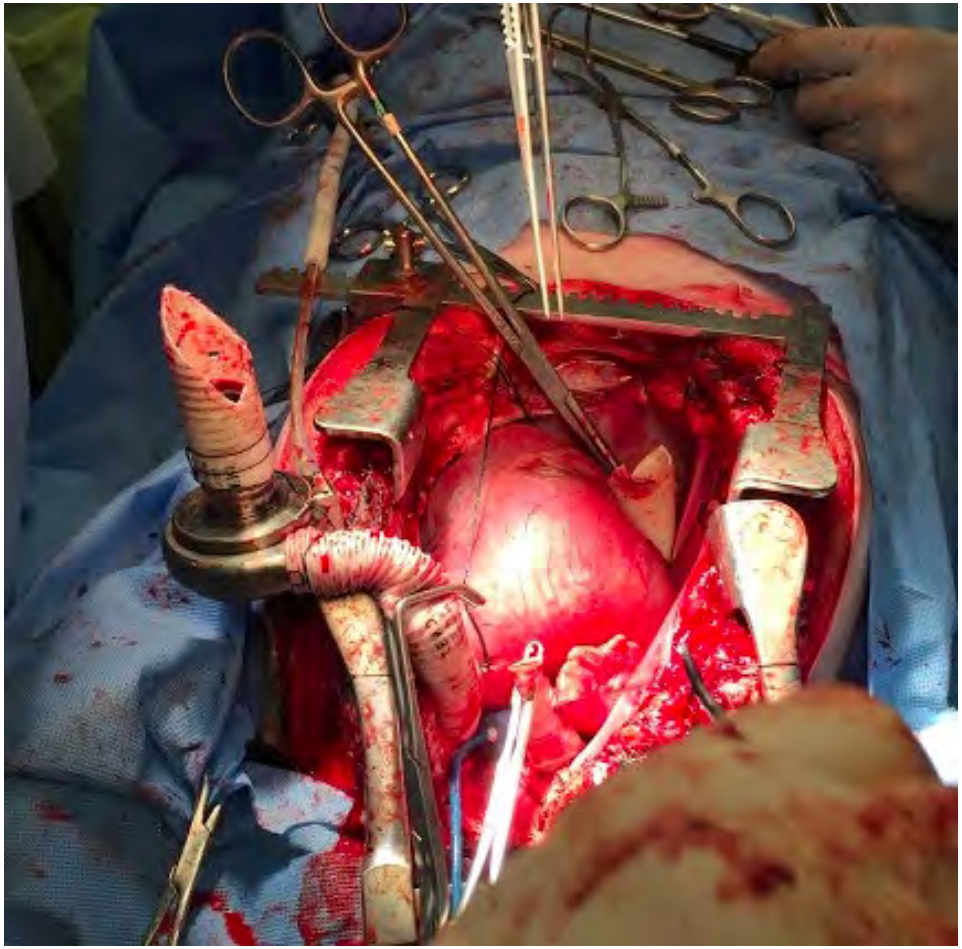

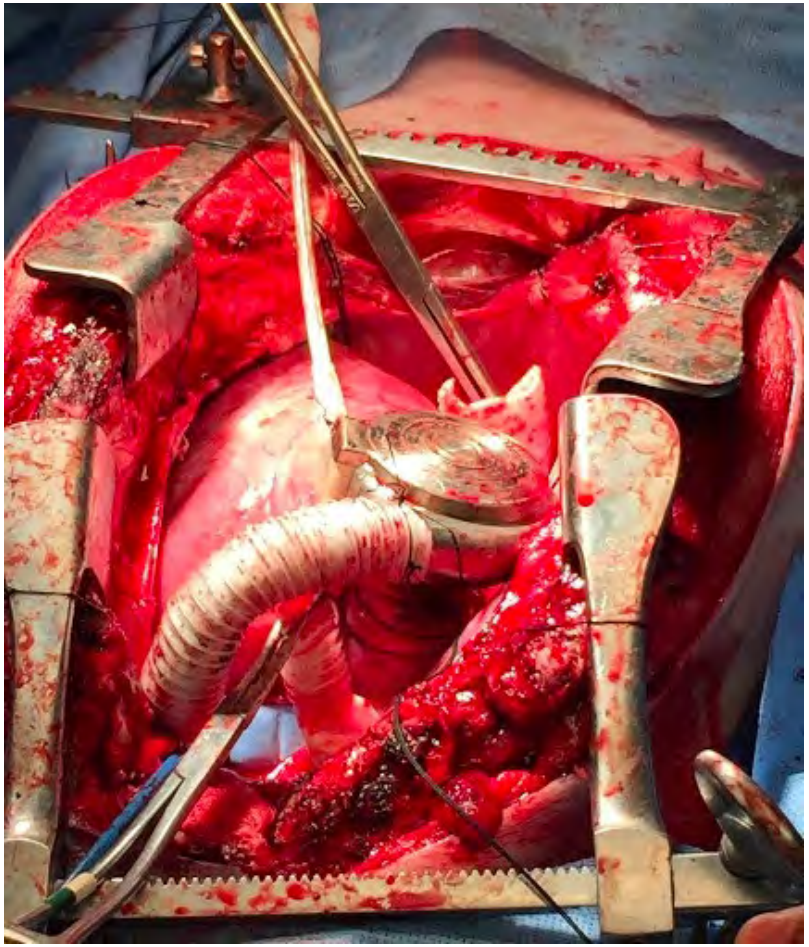

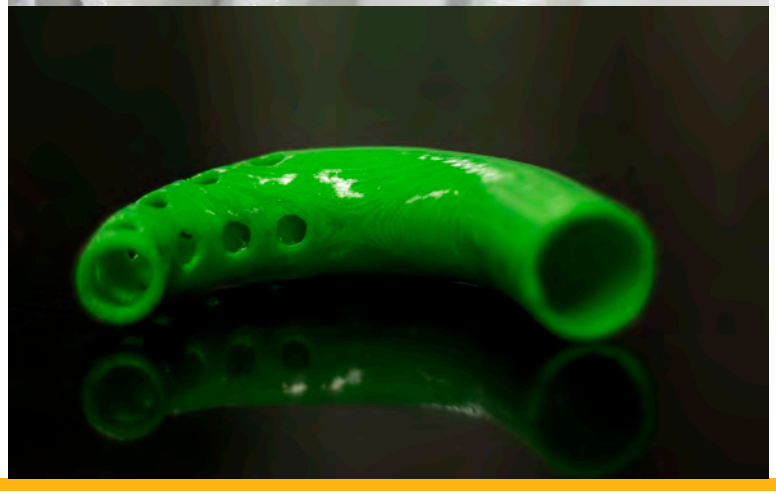

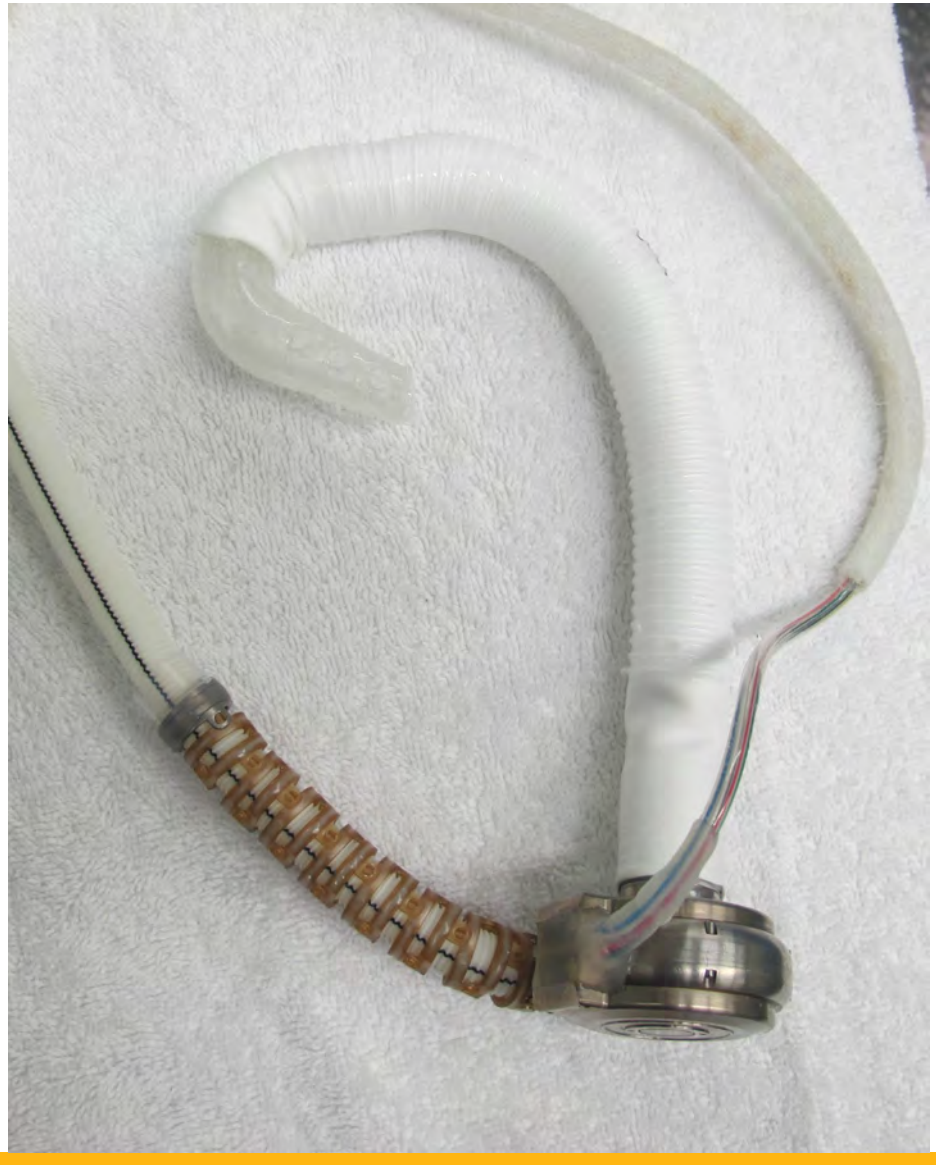

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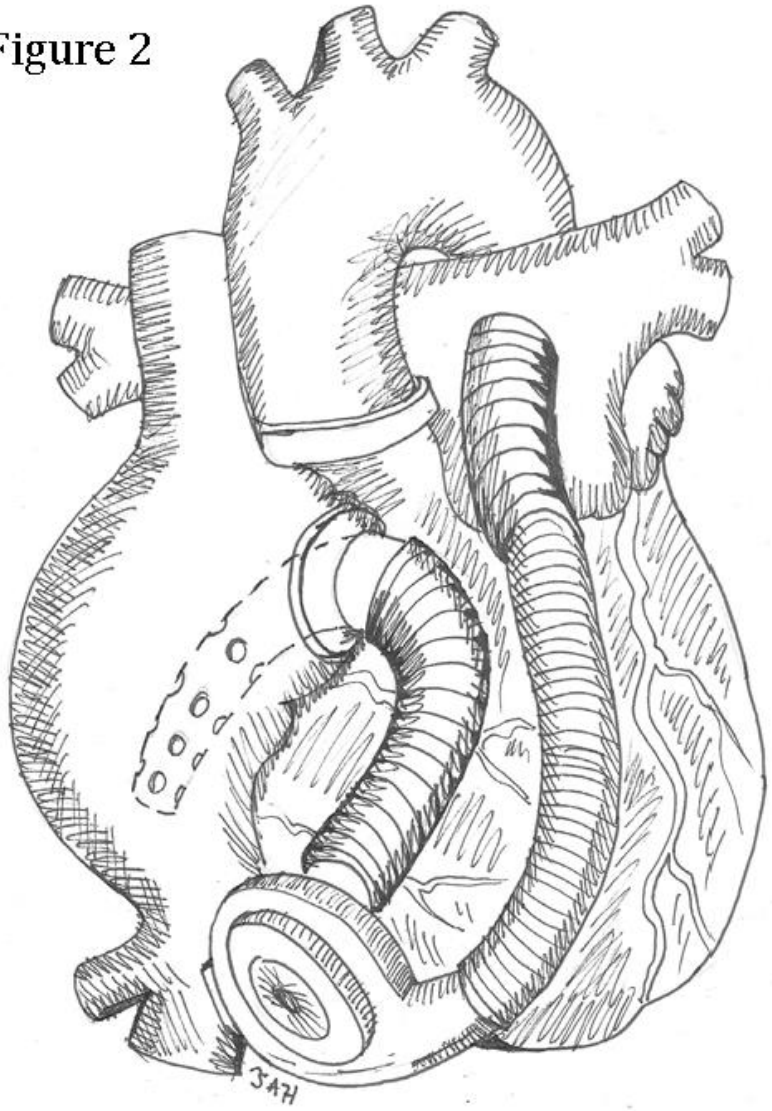
RA-PA Fontan Model



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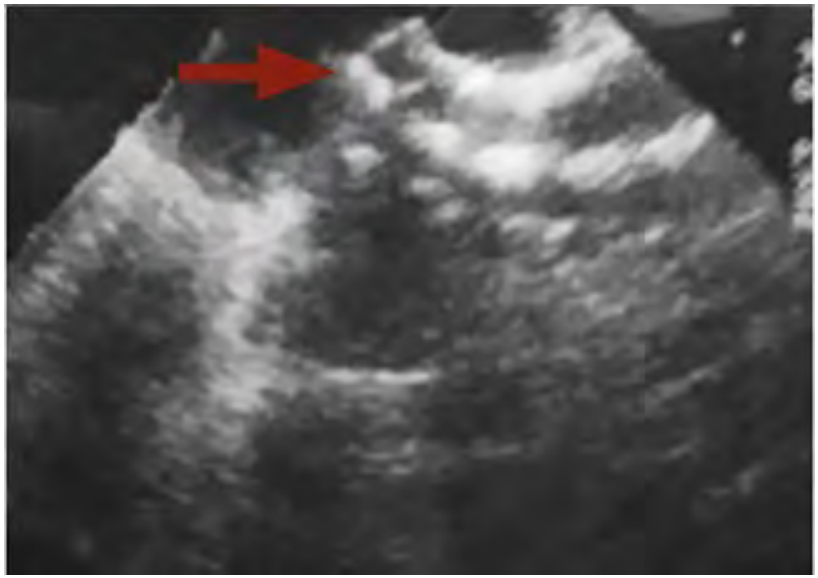
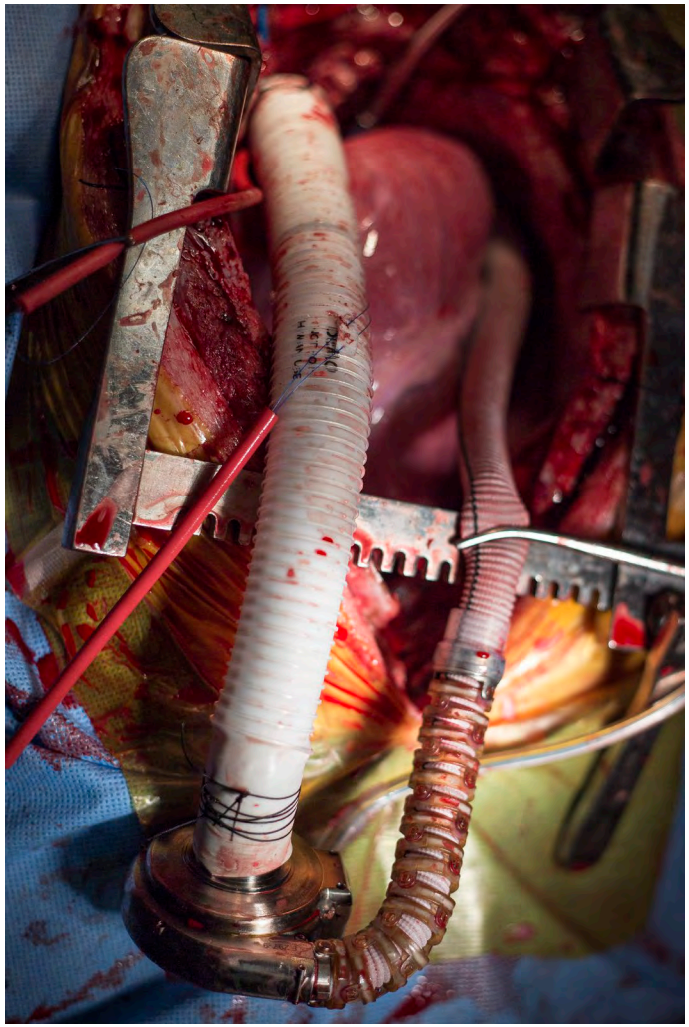
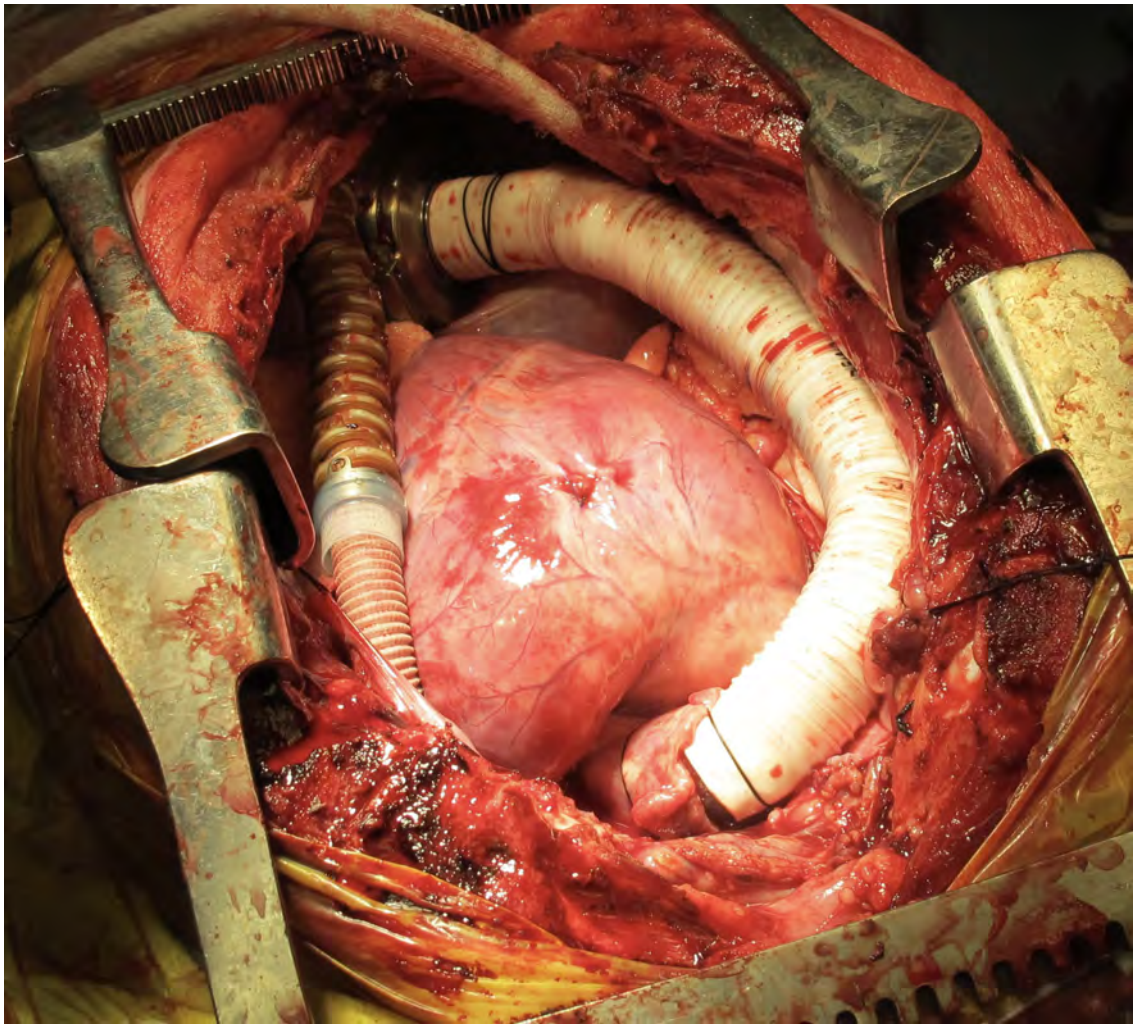
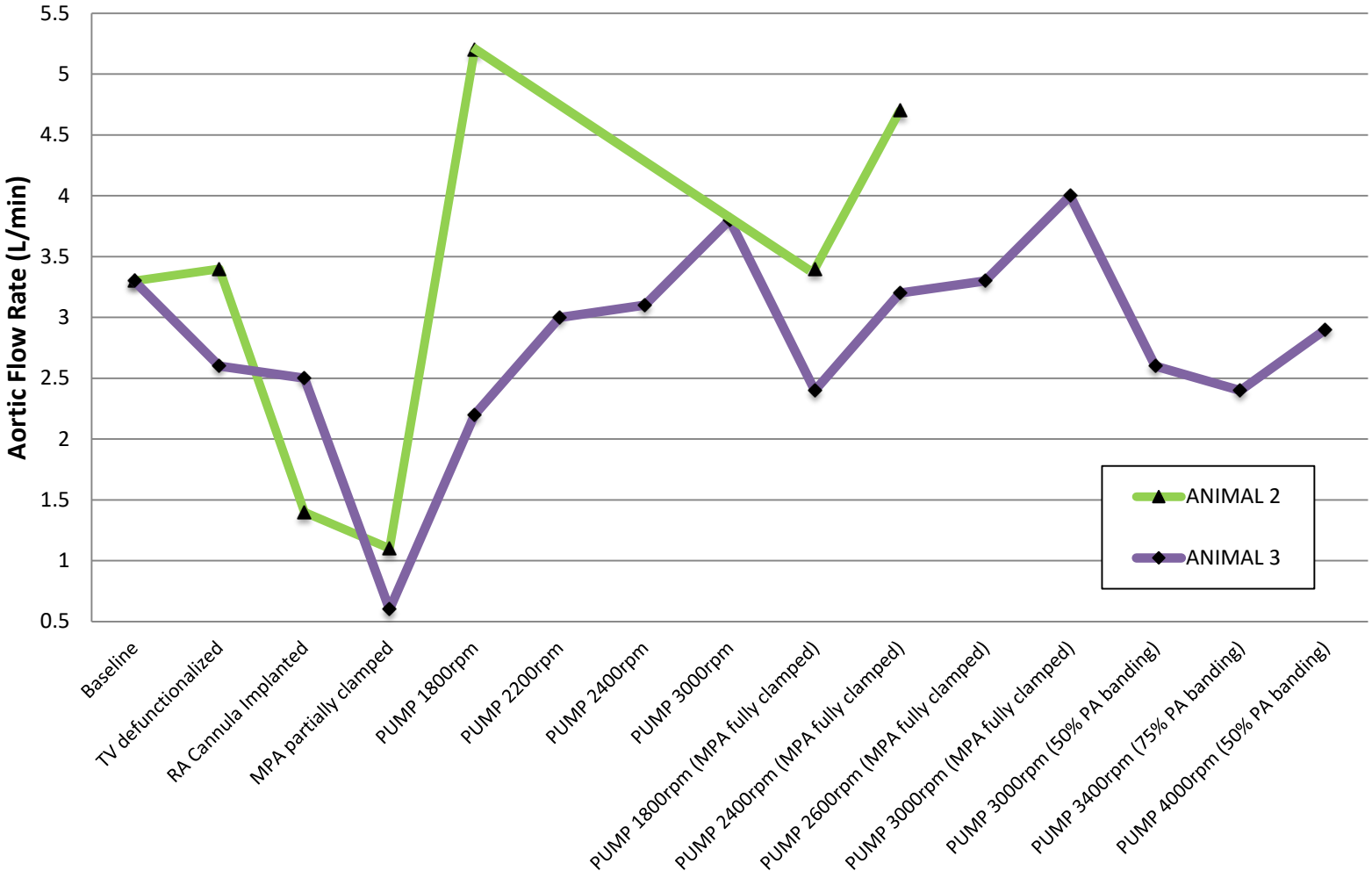






RA-PA Fontan Model: Cardiac Output



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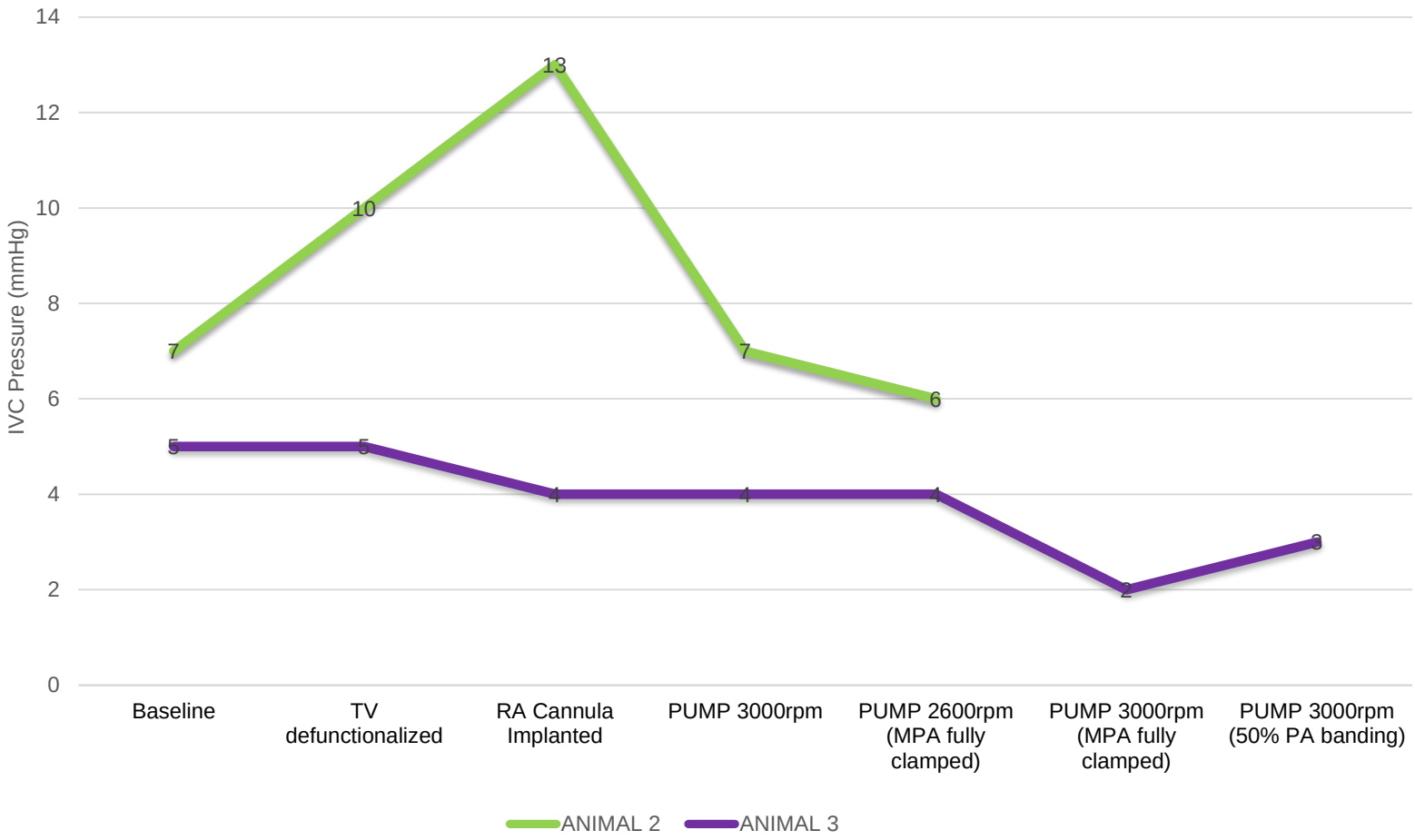
RA-PA Fontan Model: IVC Pressures



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Original Article

Mechanical Circulatory Support for the Failing Fontan: Conversion to Assisted Single Ventricle Circulation—Preliminary Observations

World Journal for Pediatric and Congenital Heart Surgery
2018, Vol. 9(1) 31-37

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Abstract

Background: Mechanical circulatory support (MCS) of a failing Fontan circulation remains challenging. We hypothesized that MCS can be provided by converting the Fontan circulation into a mechanically assisted single ventricle parallel circulation (MASVC). **Methods:** A porcine model of functionally univentricular circulation was created under cardiopulmonary bypass (CPB) by performing an atrial septectomy, tricuspid valvectomy, and interrupting antegrade pulmonary blood flow. A centrifugal flow pump was placed with inflow from the common atrium. Eight millimeter Dacron grafts anastomosed to the ascending aorta and main pulmonary artery supplied systemic (Qs) and pulmonary (Qp) blood flow. Ultrasonic flow probes were used to measure Qs and Qp after weaning from CPB. The Qp/Qs ratio was regulated using an adjustable clamp. Hemodynamic and laboratory data were recorded. **Results:** All four animals were successfully weaned from CPB onto the MASVC for a duration of two hours. Mechanically assisted single ventricle parallel circulation achieved satisfactory hemodynamics. As anticipated, the arterial oxygen saturation and partial pressure of oxygen in arterial blood were lower in the MASVC compared to baseline biventricular circulation. At the conclusion of the study, there was a trend towards a decrease in the mixed venous saturation with increasing oxygen extraction compared to the baseline. Serum lactate levels increased after weaning from CPB and did not return to baseline after two hours of support. **Conclusion:** Mechanically assisted single ventricle parallel circulation can be established in a single ventricle animal model. This strategy could potentially provide MCS of a single ventricle circulation. Studies with longer duration

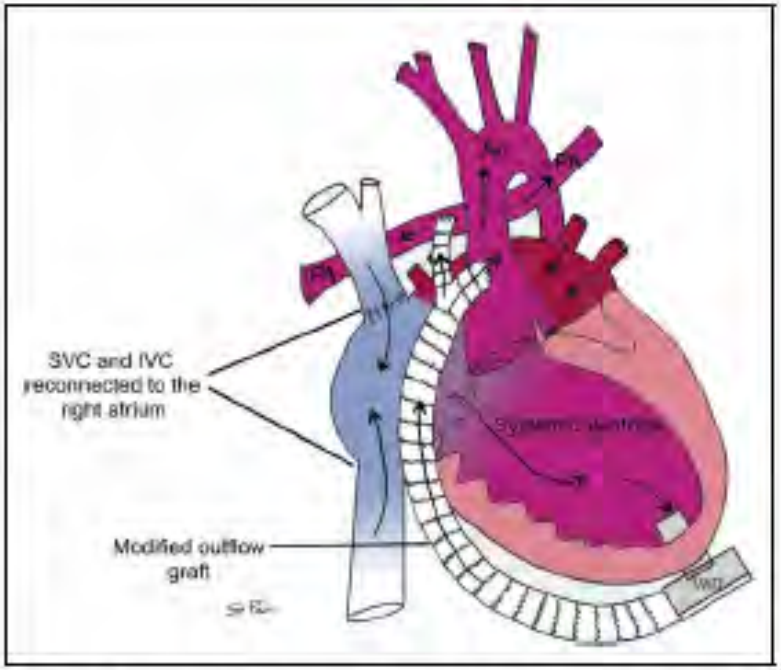

Figure 1. Proposed mechanically assisted single ventricle circulation. Ao indicates aorta; IVC, inferior vena cava; PA, pulmonary artery; SVC, superior vena cava; VAD, ventricular assist device.

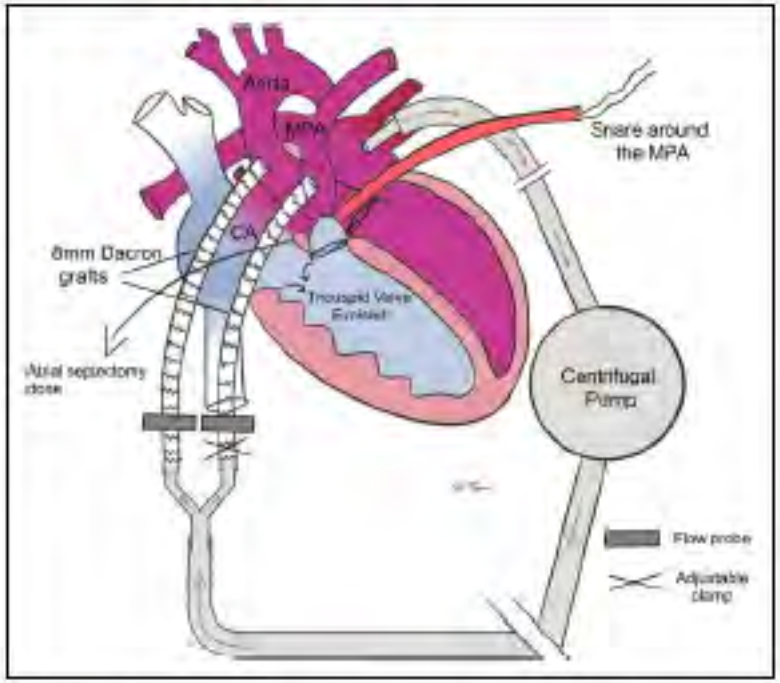

Figure 2. Porcine single ventricle model created by performing atrial septectomy, tricuspid valvectomy and interrupting antegrade pulmonary blood flow. CA indicates common atrium; MPA, main pulmonary artery.

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In Vitro Examination of the VentriFlo True Pulse Pump for Failing Fontan Support

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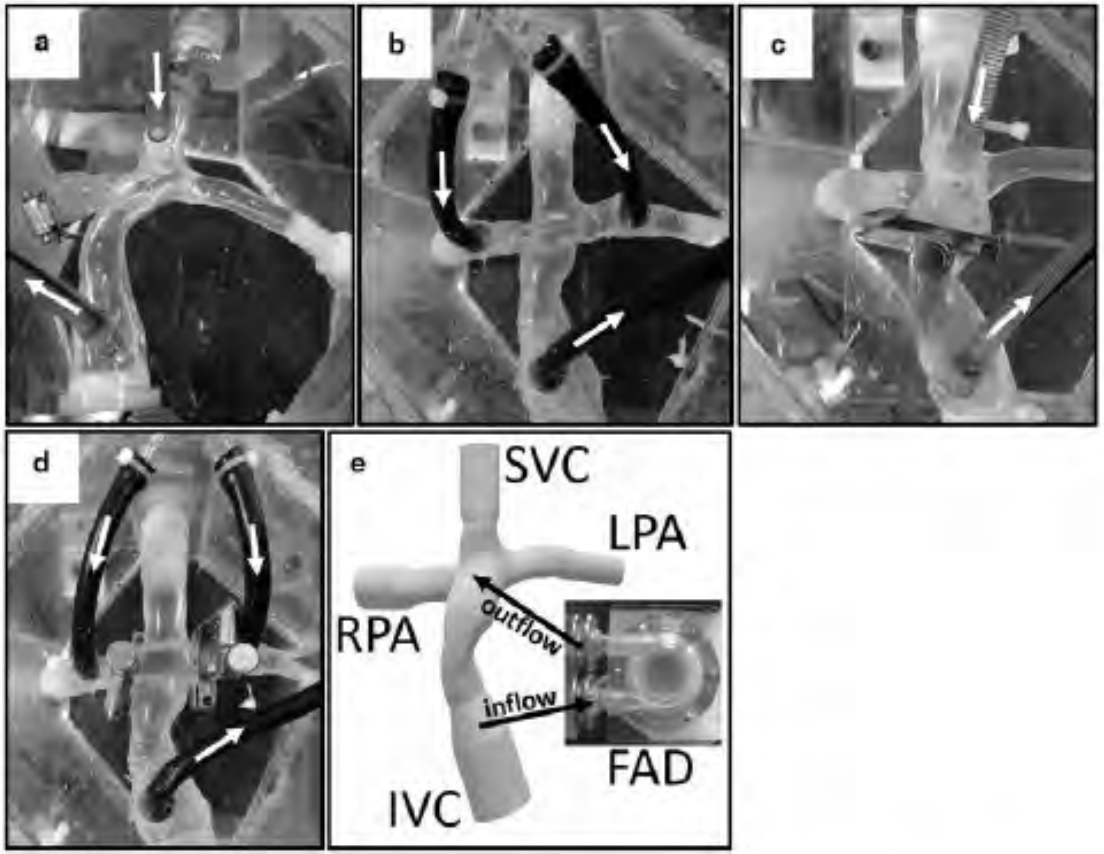


FIG. 2. Cannulation strategies. (a) FAD in parallel with single outflow cannula. (b) FAD in parallel with Y-graft outflow cannula. (c) FAD in series (complete Fontan baffle restriction). (d) Fontan takedown configuration (vena cava separated from pulmonary arteries). (e) Schematic of TCPC and FAD with vessels and cannula labeled. Outflow cannula will vary based on cannulation strategy.

Artificial Organs, Vol. 43, No. 2, 2019

What next?

- Initial proof of concept for right sided support
- Innovative approach to future development
- Use of 3D modeling and VR to determine fit

Figure 7. Transapical MVAD.
Reprinted with permission from HeartWare Inc. Intraventricular MVAD across aortic valve configuration.

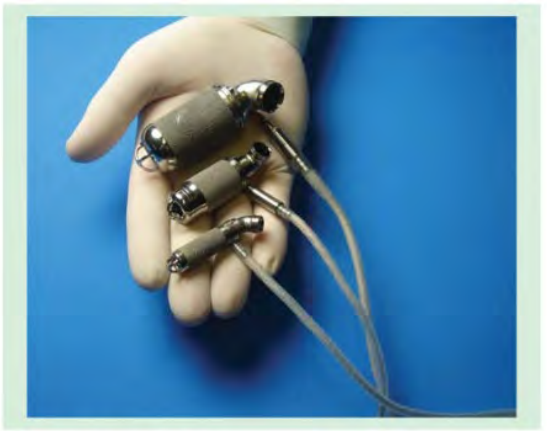
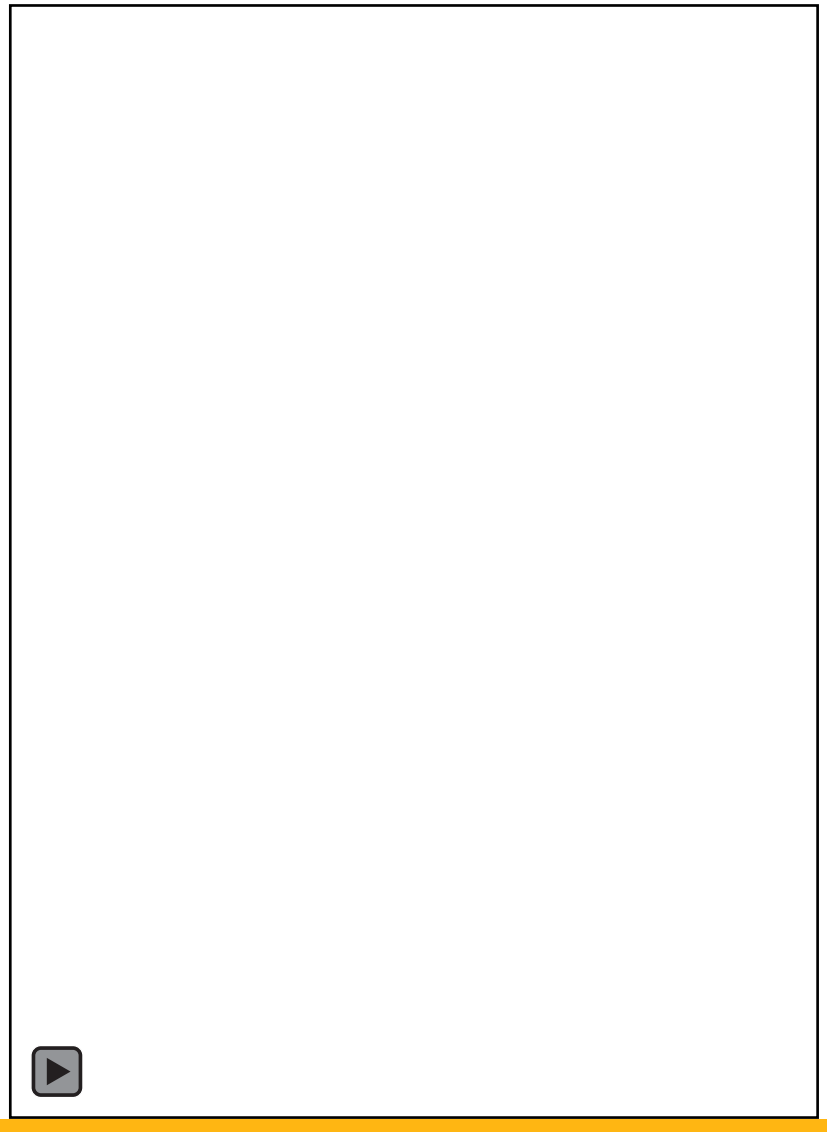


Figure 4. Jarvik 2000.
Reprinted with permission. Adult, child and infant Jarvik 2000.

Expert Rev. Cardiovasc. Ther. 13(4), 417–427 (2015)



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