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TRANSPLANTATION IN SINGLE VENTRICLE: TIMING AND STRATEGIES FOR SUCCESS

Battling Against Nature: Sustaining a Single Ventricle Circulation Throughout the Lifespan

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Kimberly Y. Lin, MD
Medical Director, Pediatric Cardiomyopathy Program
Children's Hospital of Philadelphia

Children's Hospital of Philadelphia Cardiac Center

Perelman School of Medicine University of Pennsylvania

22CME0420/PPT/01-23

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DISCLOSURES?

No financial disclosures

Irony: This talk is an impossible set up!

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OBJECTIVES

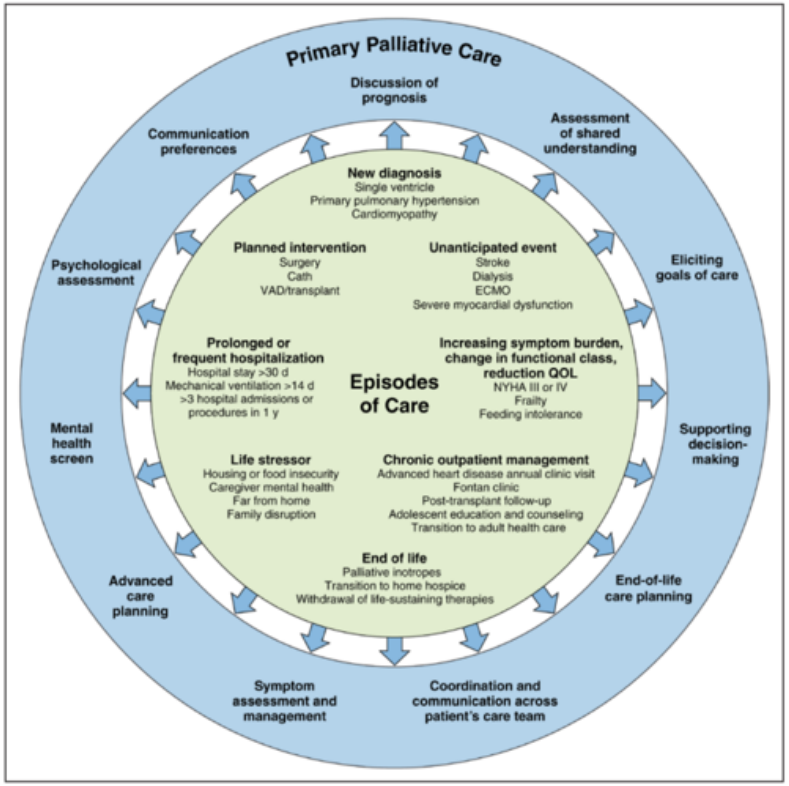
- Identify the perfect timing for referral for transplant evaluation
- Encourage you to stick your head in the sand, avoid talking to your single ventricle patients about long term prognosis
- Reassure you that your single ventricle patient will always be a great candidate for transplant
- Close out the conference on a high note, and on time

WE ALL EVENTUALLY DIE

MUCH OF WHAT WE DO IS PALLIATIVE CARE

THE SINGLE VENTRICLE CIRCULATION OFTEN FAILS

Palliative Care Across the Life Span for Children With Heart Disease: A Scientific Statement From the American Heart Association



Blume et al, Circ CV Qual Outcomes 2023

JUST CALL TRANSPLANT OUR “STAGE 5”?

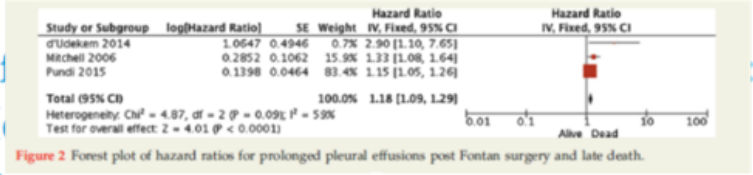


Figure 2 Forest plot of hazard ratios for prolonged pleural effusions post Fontan surgery and late death.

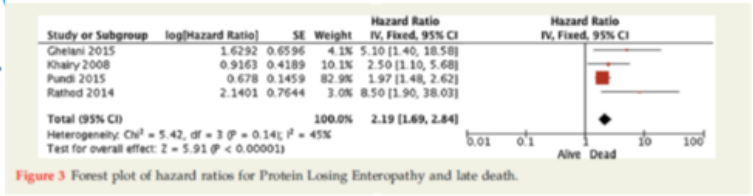


Figure 3 Forest plot of hazard ratios for Protein Losing Enteropathy and late death.

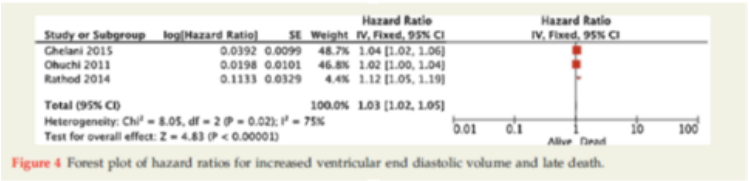


Figure 4 Forest plot of hazard ratios for increased ventricular end diastolic volume and late death.

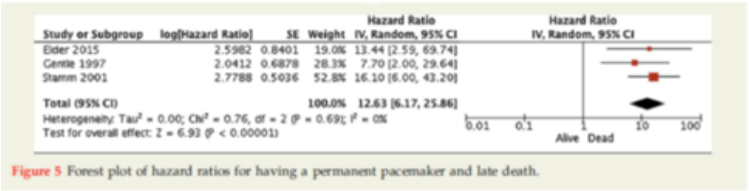
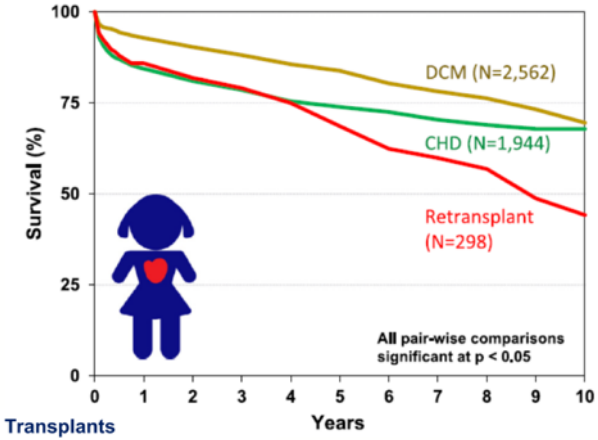
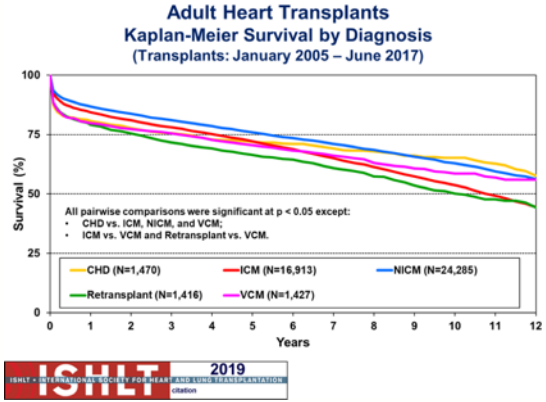


Figure 5 Forest plot of hazard ratios for having a permanent pacemaker and late death.





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Poh et al, Heart Lung & Circ 2018

www.ishlt.org 2016 & 2019 reports

ISHLT 2019

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WHEN IS THE *RIGHT TIME* TO REFER YOUR SV PATIENT FOR TRANSPLANT?

- 

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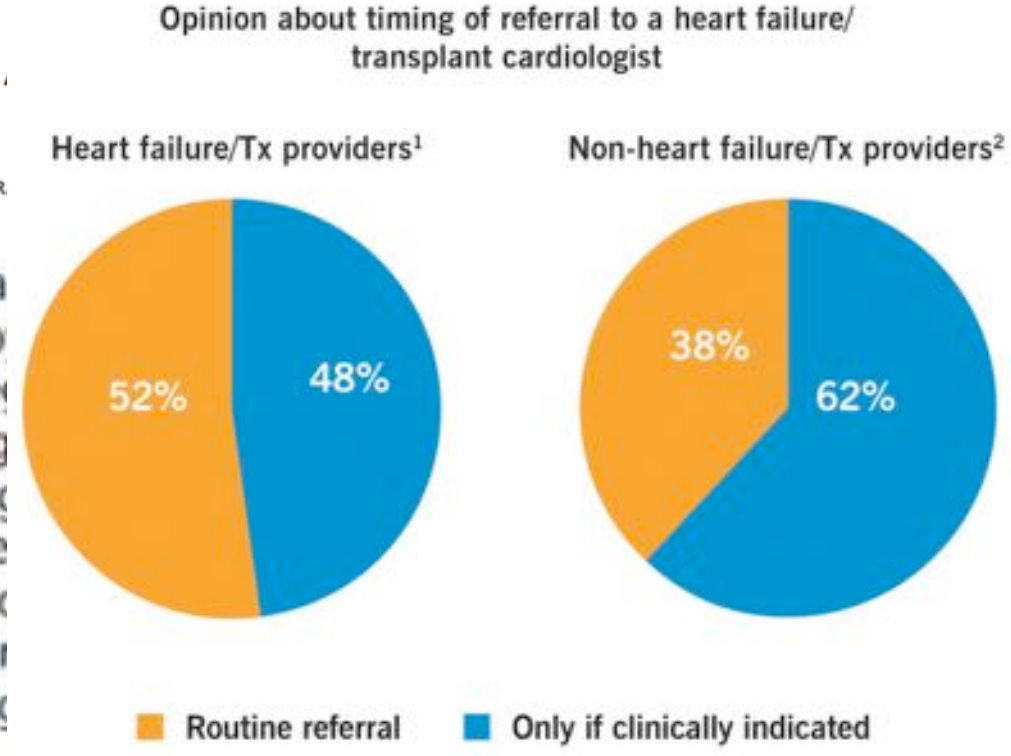
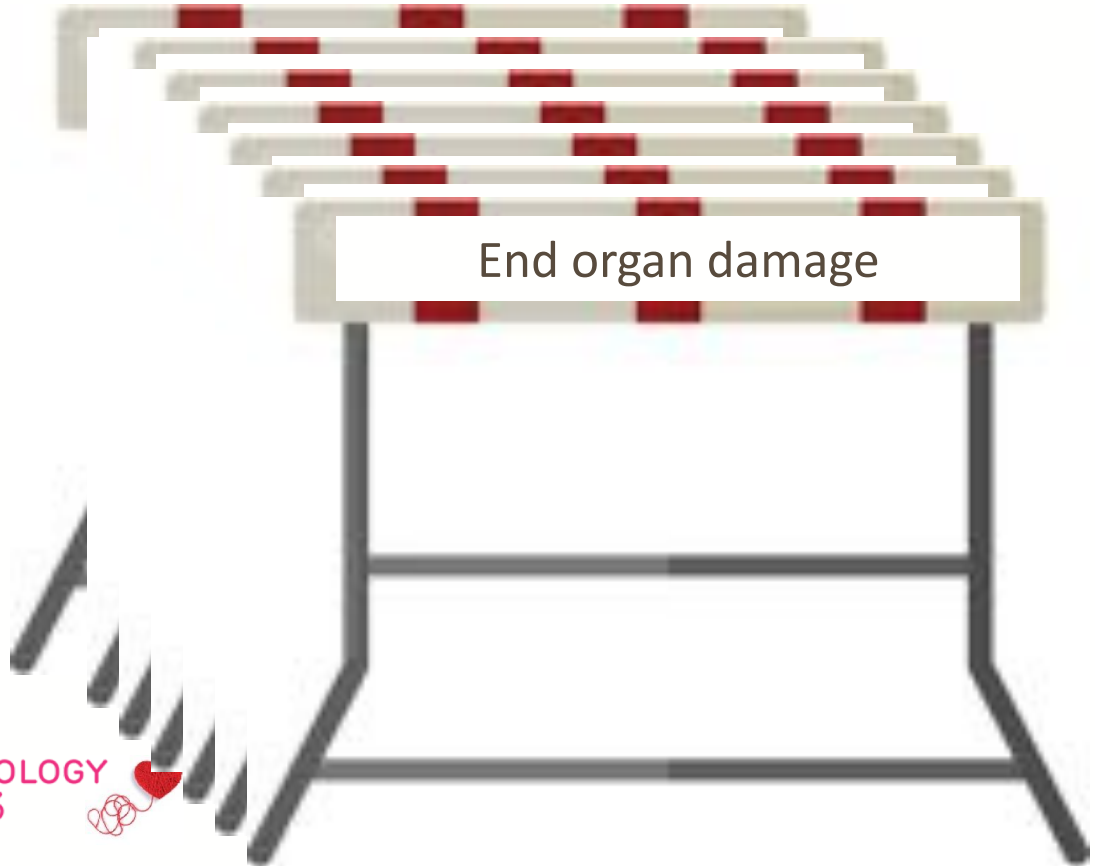
ROUTINE EVALUATION FOR EVERYONE?



36 (9)
87 (22)
97 (24)
164 (41)
16 (4)

Sadat-Hossieny et al, JCF 2022

POTENTIAL HURDLES TO TRANSPLANT CANDIDACY IN SINGLE VENTRICLE PATIENTS



CAN WE REALLY GET THE TIMING JUST RIGHT?

RISK FACTOR, INDICATION, OR BOTH?

- Often the indications for transplant consideration overlap with the risk factors for a poor transplant outcome
- One risk factor may not preclude transplant, but cumulative risk may become prohibitive if transplant is considered too late

Table 4. Risk Factor Score

No. of Risk Factors[a] (Risk Score)	Patients No.	Mortality No. (%)
0	28	2 (7.1)
1	8	1 (12.5)
2	14	2 (14.3)
3	15	2 (13.3)
4	7	5 (71.4)
5	2	2 (100)

[a] Risk factors: single-ventricle congenital heart disease, biventricular assist device support, history of ≥4 sternotomies, preheart transplant panel reactive antibody >10%, prior operation at another institution, and pulmonary vein disease.

O'Connor et al, ATS 2018

GO EARLY: HYBRID VAD APPROACH

- Primary transplant without surgical intervention may not be feasible for many centers
- For some SV patients who are poor long-term single ventricle palliation candidates, VAD support at the time of hybrid procedure may be an option

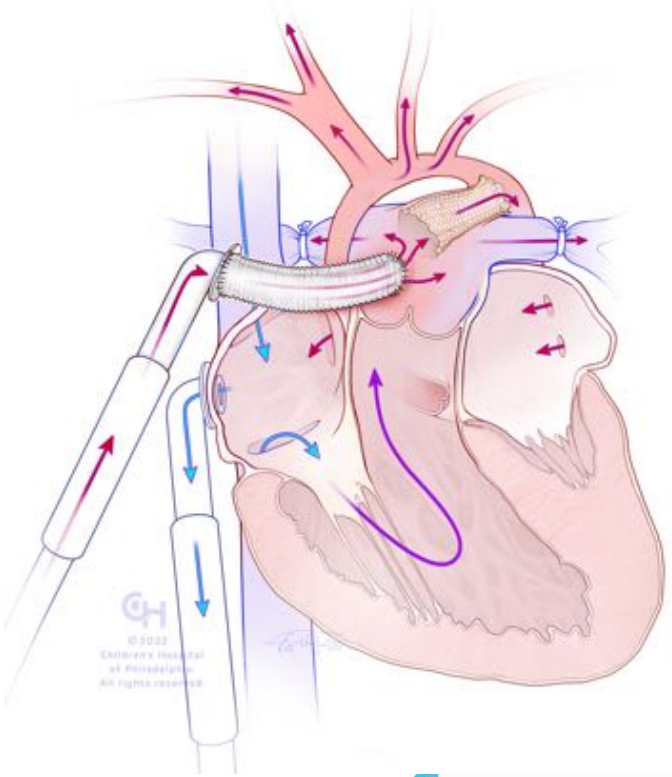


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Illustration: Eo Trueblood and Stream Studios

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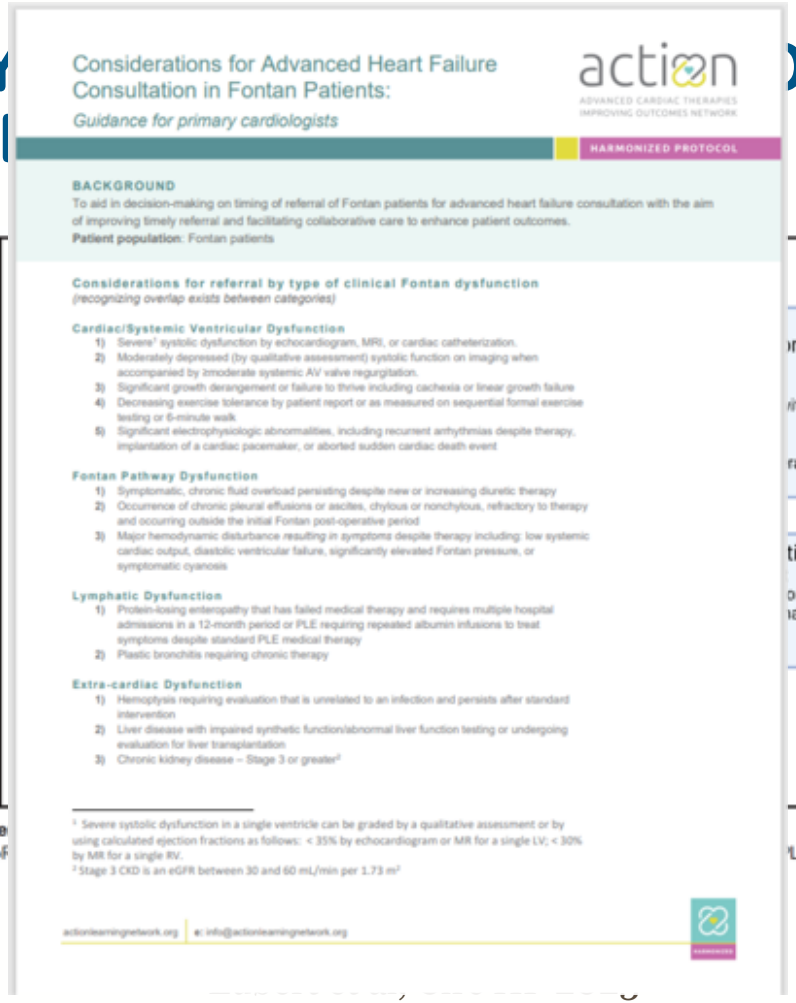
REFER EARLY … OM THE ACTION …



Considerations for Advanced Heart Failure Consultation in Fontan Patients:

Guidance for primary cardiologists

action
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]

[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 m²

actionlearningnetwork.org | e: info@actionlearningnetwork.org

Figure. Conside… Created with BioF… enteropathy.

…LE, protein-losing

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https://myactioneducation.org/wp-content/uploads/2021/12/Failing-Fontan-Referral-Document-10_21_19.pdf

EVIDENCE OF SUCCESS: PLE AND TRANSPLANT

- PLE resolved in 42 of 43 HTx survivors at a median of 1 month post-HTx
- Post-HTx survival in PLE patients was similar to what we see in non-PLE patients (92% at 1 month, 83% at 1 year, and 72% at 5 years)

Fontan-associated protein-losing enteropathy and post–heart transplant outcomes: A multicenter study

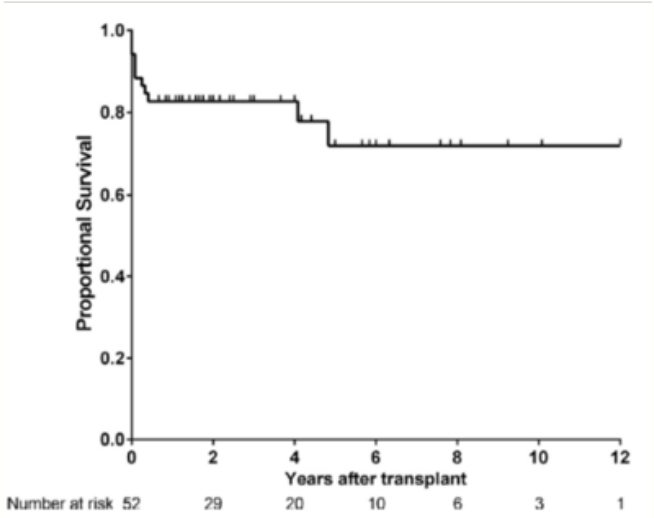


Figure 1 Post-HTx survival.

Schumacher et al, JHLT 2019

IS TRANSPLANT AN OPTION FOR SV PATIENTS WITH MULTI-ORGAN DYSFUNCTION?

- Successful heart-alone transplantation has been reported in CHD patients with single lung physiology
- Successful heart-alone transplantation can be performed in Fontan patients with evidence of liver cirrhosis
- ACHD patients undergoing multi-organ transplant have worse survival than heart-alone transplant (primarily driven by heart-lung outcomes)

Heart transplantation in the setting of complex congenital heart disease and physiologic single lung

Warren A. Zuckerman, MD,[a] Marc E. Richmond, MD, MS,[a] Teresa M. Lee, MD,[a] Emile A. Bacha, MD,[b] Paul J. Chai, MD,[b] Jonathan M. Chen, MD,[c] and Linda J. Addonizio, MD[a]

Liver cirrhosis in Fontan patients does not affect 1-year post-heart transplant mortality or markers of liver function

Kathleen E. Simpson, MD,[a] Amir Esmaeeli, BA,[b] Geetika Khanna, MD,[c] Francis White, MD,[d] Yumirle Turnmelle, MD,[a] Pirooz Eghtesady, MD,[e] Umar Boston, MD,[e] and Charles E. Canter, MD[a]

Outcomes of Multi-Organ Transplant in Adult Patients With Congenital Heart Disease

Kristen Wong, MD; Kristen Tecson, PhD; Ari Cedars, MD

Zuckermann et al, JTCVS 2015; Simpson et al, ATS 2017; Wong et al, JAHA 2019

WHEN WILL WE HAVE MORE TO OFFER?!

News | Heart Failure | March 05, 2020

Abbott's In-Development Fu
Earns FDA's Breakthrough D

World's Fi
Thymus Ir
Milestone Coul

By Morgan deBlecourt
March 09, 2022

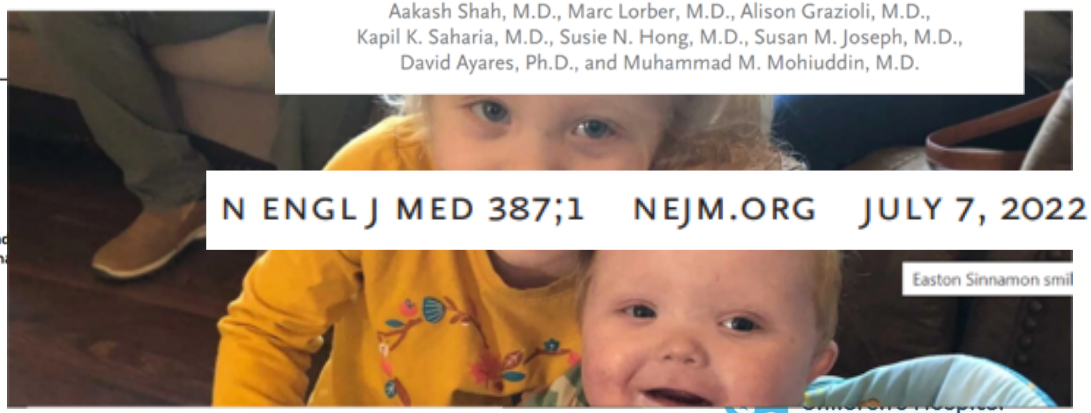
The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Genetically Modified Porcine-to-Human Cardiac Xenotransplantation

Bartley P. Griffith, M.D., Corbin E. Goerlich, M.D., Ph.D., Avneesh K. Singh, Ph.D., Martine Rothblatt, Ph.D., Christine L. Lau, M.D., Aakash Shah, M.D., Marc Lorber, M.D., Alison Grazioli, M.D., Kapil K. Saharia, M.D., Susie N. Hong, M.D., Susan M. Joseph, M.D., David Ayares, Ph.D., and Muhammad M. Mohiuddin, M.D.

N ENGL J MED 387;1 NEJM.ORG JULY 7, 2022



Pediatric Cardiology (2022) 43:1481–1493
https://doi.org/10.1007/s00246-022-02872-6

ORIGINAL ARTICLE

Autologous Cardiac Stem Cell Injection in Patients with Hypoplastic Left Heart Syndrome (CHILD Study)

Sunjay Kaushal[1] · Joshua M. Hare[2] · Aakash M. Shah[3] · Nicholas P. Pietris[4] · Judith L. Bettencourt[5] · Linc
Aisha Khan[2] · Abigail Snyder[3] · Riley M. Boyd[1] · Mohamed Abdullah[1] · Rachana Mishra[1] · Sudhish Sharma
Timothy C. Slesnick[6] · Ming-Sing Si[7] · Paul J. Chai[8] · Barry R. Davis[5] · Dejian Lai[5] · Michael E. Davis[6,9] ·
William T. Mahle[9]

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SUMMARY

- Advances in our field with respect to the care of single ventricle patients have improved survival
- Those survivors, however, may accrue morbidity that endangers their eventual transplant candidacy
- An early referral for failing single ventricle physiology may help keep the option for transplant open
- Early discussions about long term prognosis and goals of care may also be helpful for framing future decisions
- Better options for recognizing, supporting, and prioritizing single ventricle circulation are on the horizon


GRACIAS

CHILDREN DON'T OFTEN GET TRANSPLANTED WITHOUT ADVANCED HF THERAPY

Status	Criteria	% of transplants
1A	VAD Inpatient and on ventilator, IABP, ductal dependent, CHD on inotropes	79.3%
1B	Inotropes but doesn't qualify for 1A HCM or RCM and <1yo	16.9%
2	Others	3.8%

https://srtr.transplant.hrsa.gov/annual_reports/2020/Heart.aspx#HR_dist_ped_waiting_urg_b64

ADULT HEART TRANSPLANT CRITERIA: DISADVANTAGE FOR SV PATIENTS?

Status	Criteria	Average waitlist time
1	ECMO, surgical/non-dischargeable BiVAD, MCSD with life-threatening arrhythmia	<1 month
2	Surgical/non-dischargeable LVAD, MSCD with malfunction, temporary VAD/IABP, VT/VF, MCSD with malfunction, SV VAD	< 1 month
3	30 days on LVAD, inotropes with Swan, MCSD with complication, ECMO > 7 days, temporary VAD > 7 days, IABP or surgical, non-dischargable LVAD > 14 days	< 1 month
4	LVAD > 30 days, inotropes without Swan, CHD, ischemic heart disease with intractable angina, re-transplant, amyloidosis, HCM, RCM	5-9 months
5	Multi-organ listing at same institution	Not calculable
6	Others	9-11 months

https://srtr.transplant.hrsa.gov/annual_reports/2020/Heart.aspx#HR_dist_ped_waiting_urg_b64

ETHICAL DILEMMAS

- Multi-organ transplant
- Pediatric vs adult listing criteria
- What if we transplant too early?
- Should lack of Fontan candidacy be reason for transplant candidacy?

INDICATIONS FOR HEART TRANSPLANT CONSIDERATION IN SV AND OTHER CHD PATIENTS

- Stage D heart failure, refractory to other interventions
- Life-threatening arrhythmias refractory to alternative interventions
- Stage C heart failure associated with reactive PHTN
- Stage C HF associated with systemic ventricular dysfunction; often the main symptom is growth failure in children
- CHD with normal ventricular function but no good surgical intervention to offer for:
  - Moderate-to-severe valvar stenosis or regurgitation
  - Symptomatic cyanosis
  - Persistent protein-losing enteropathy
  - Plastic bronchitis not amenable to catheter-based intervention
- Primary transplantation is not indicated for most complex CHD
  - Exceptions may include PA/IVS and single ventricle heterotaxy
- Acute Fontan failure is often best treated by Fontan takedown rather than urgent transplant listing

Ross et al, AHA Scientific Statement on Tx and MCS in CHD, Circulation 2016