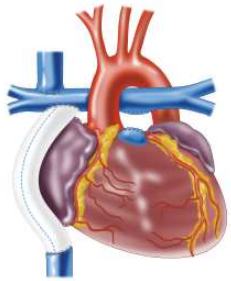


Transplant can work for some *but* is not for all and is not a cure

Cardiology
2018

21st Annual
Update on Pediatric
and Congenital
Cardiovascular Disease

Daphne T. Hsu, MD
Professor of Pediatrics, Albert Einstein College of Medicine
Division Chief and Co-Director, Pediatric Heart Center,
Children's Hospital at Montefiore



**Transplant can work for some
but
is not for all and is not a cure
*.....but neither is the Fontan***

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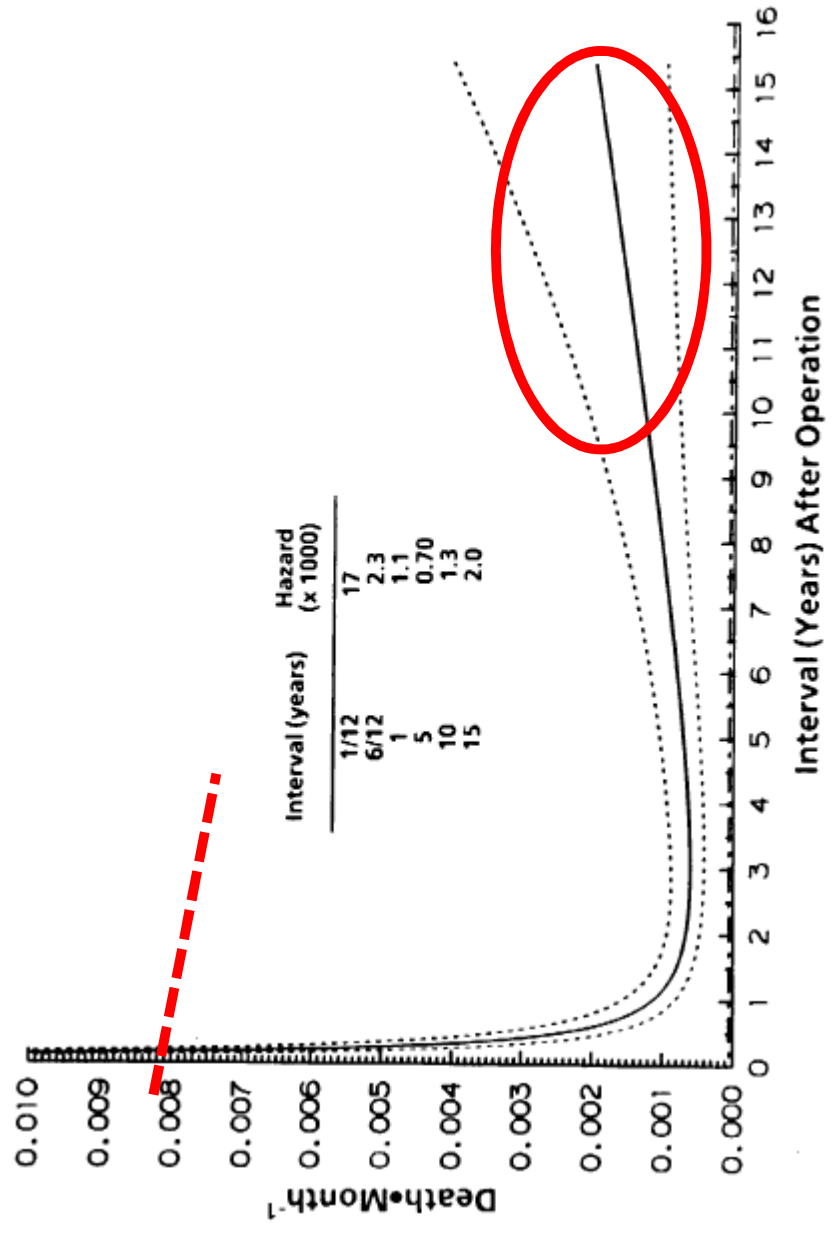
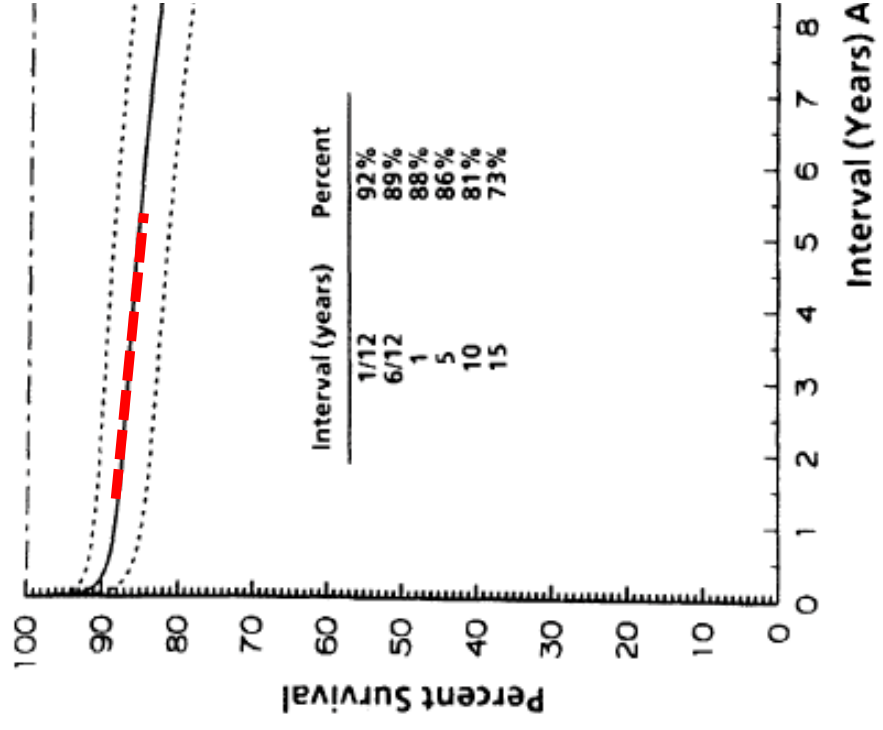
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Disclosures

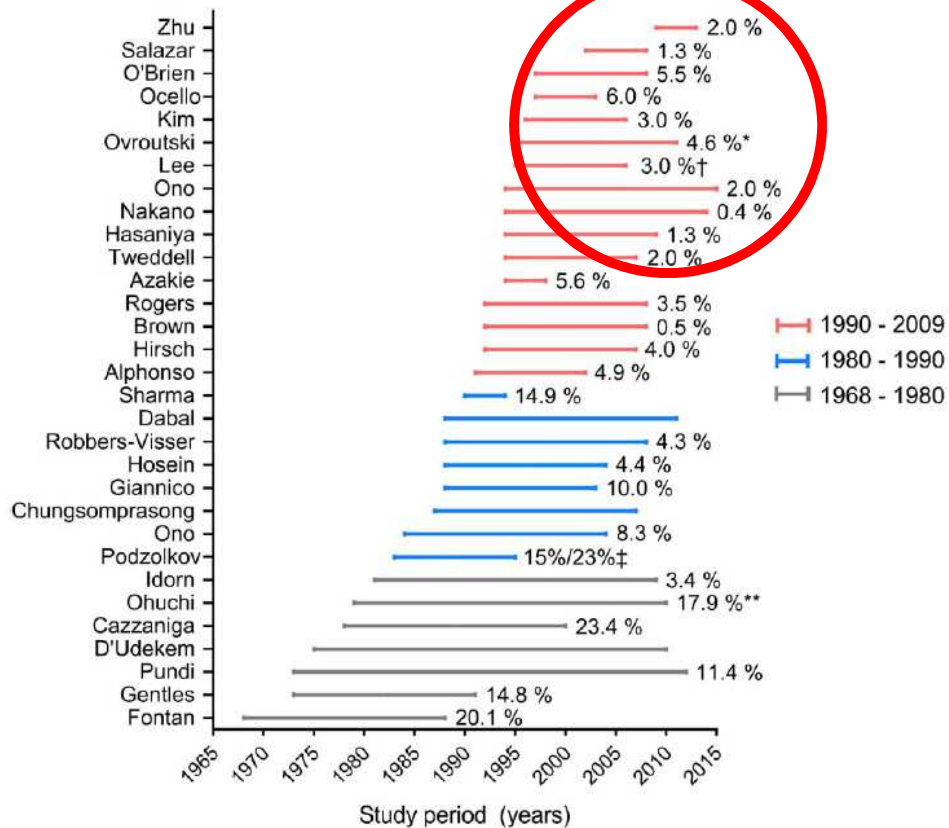
- None

Outcome After a “Perfect” Fontan Operation

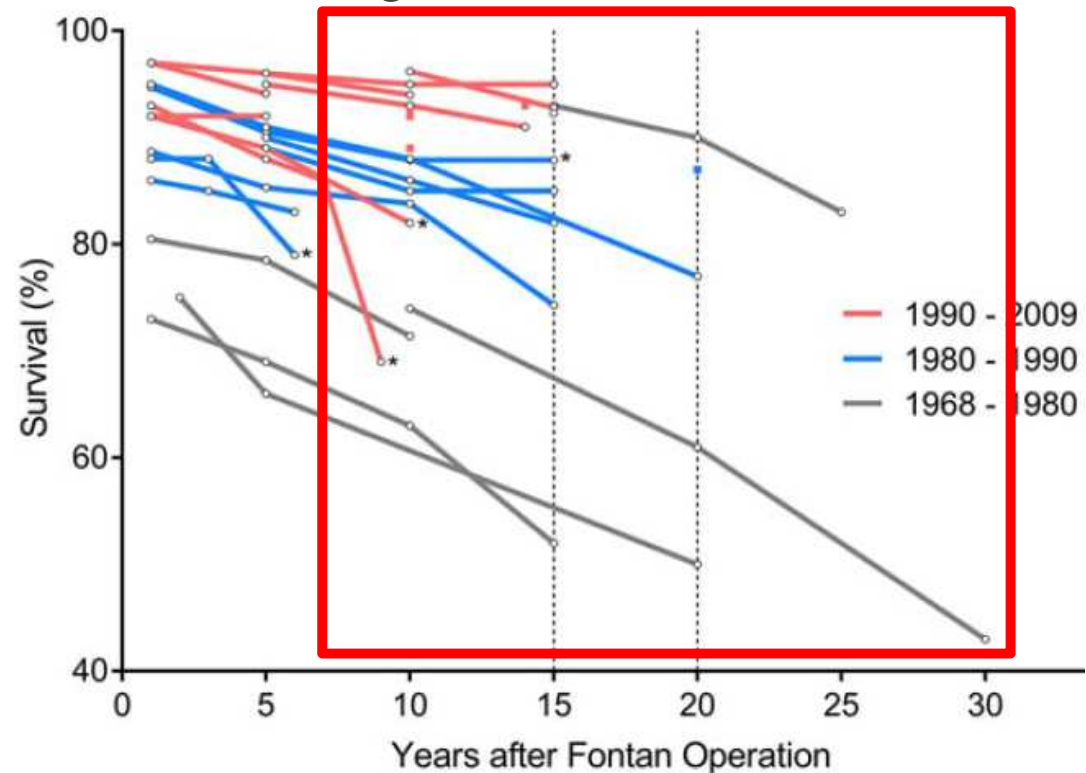


Five Decades of the Fontan Procedure

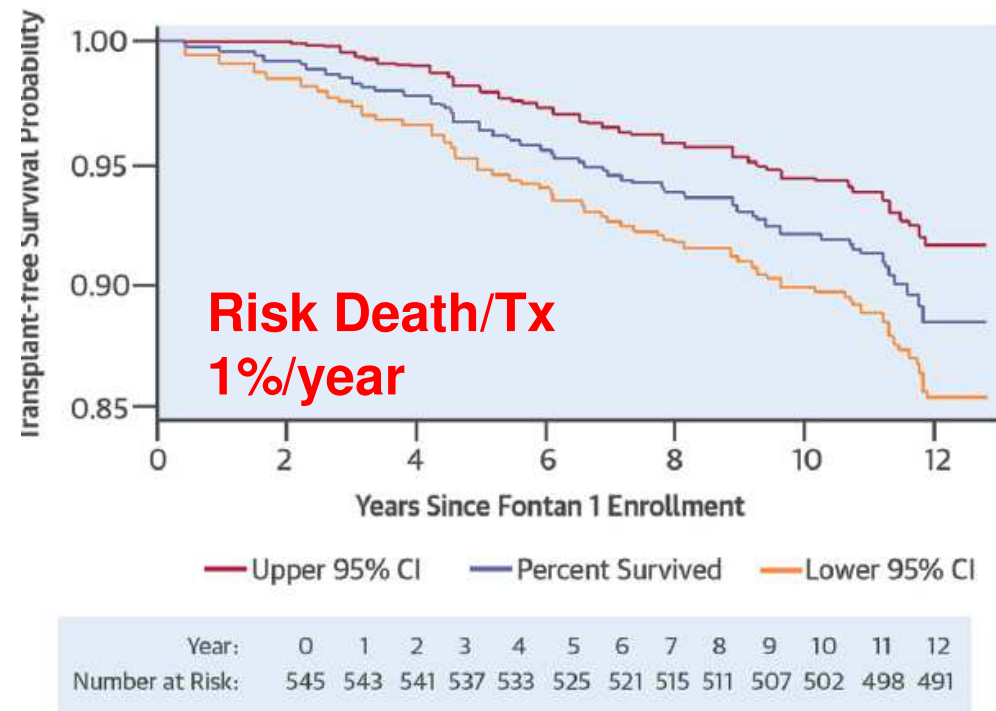
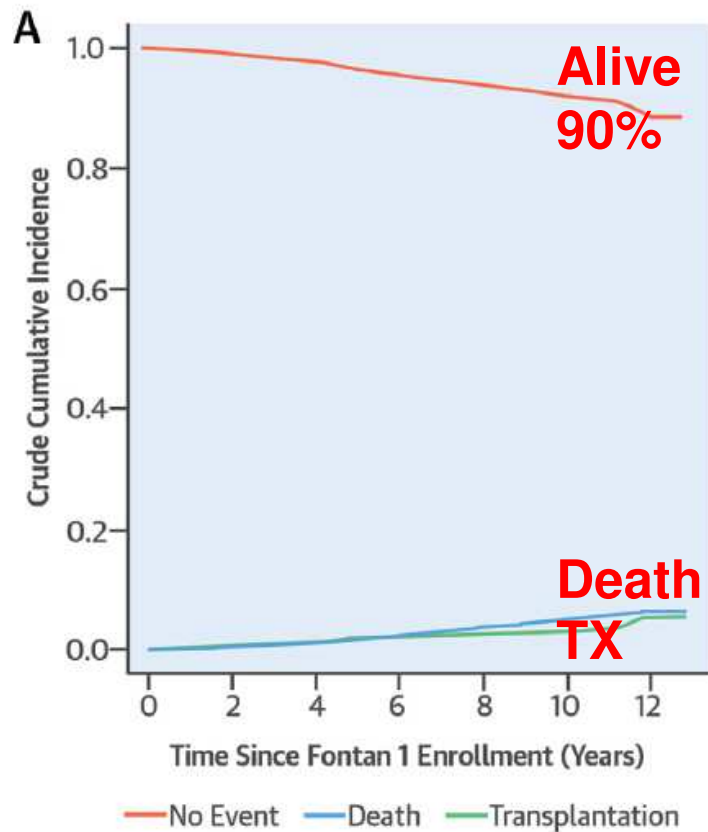
Early Mortality



Long Term Survival



Contemporary Outcomes in Fontan Survivors: Pediatric Heart Network Fontan Longitudinal Study 2003-2014



Atz, A.M. et al. J Am Coll Cardiol. 2017;69(22):2735-44.

Predictors of Death/Transplant: PHN Longitudinal Study

TABLE 5 Cox Model for Predictors of Death or Cardiac Transplantation
(Total N = 545; 54 Events)

	Events/Total	Hazard Ratio (95% CI)	p Value*		Events/Total	Hazard Ratio (95% CI)	p Value*
Age at Fontan 1 enrollment	54/545	1.01 (0.94–1.09)	0.79	Fontan 1 exercise test completed	54/545	0.51 (0.29–0.88)	0.015
Ventricular type	54/545		0.11	Resting oxygen saturation, %	33/404	0.86 (0.81–0.91)	<0.001
Left		0.63 (0.30–1.32)	0.22	Percent predicted V _O ₂ at anaerobic threshold, %	22/316	0.98 (0.96–1)	0.038
Right		1.19 (0.59–2.44)	0.63	With maximum effort	32/400	0.82 (0.4–1.68)	0.59
Mixed		Reference		Percent predicted maximum V _O ₂ , %	12/165	0.99 (0.95–1.02)	0.46
Fontan type	54/545		0.60	Percent predicted maximum work rate, %	12/165	0.98 (0.94–1.01)	0.22
Atriopulmonary connection		Reference		Chronotropic index, 0.1-U increase	9/140	1.85 (1.01–3.38)	0.045
Intracardiac lateral tunnel		1.29 (0.50–3.32)	0.60	BNP >21 and CHQ-PF50 physical summary score <44	48/482	3.65 (2.00–6.65)	<0.001
Extracardiac conduit		1.75 (0.65–4.75)	0.27				
Other		2.00 (0.39–10.31)	0.41				
Fontan 1 CHQ-PF50 physical summary score	49/510	0.97 (0.95–0.98)	<0.001				
Fontan 1 CHQ-PF50 physical summary score	49/510		0.001				
<44		4.78 (1.98–11.59)	<0.001				
44–52		2.59 (1.01–6.63)	0.047				
>52		Reference					
Fontan 1 CHQ-PF50 psychosocial summary score	49/510	1.00 (0.98–1.03)	0.91				

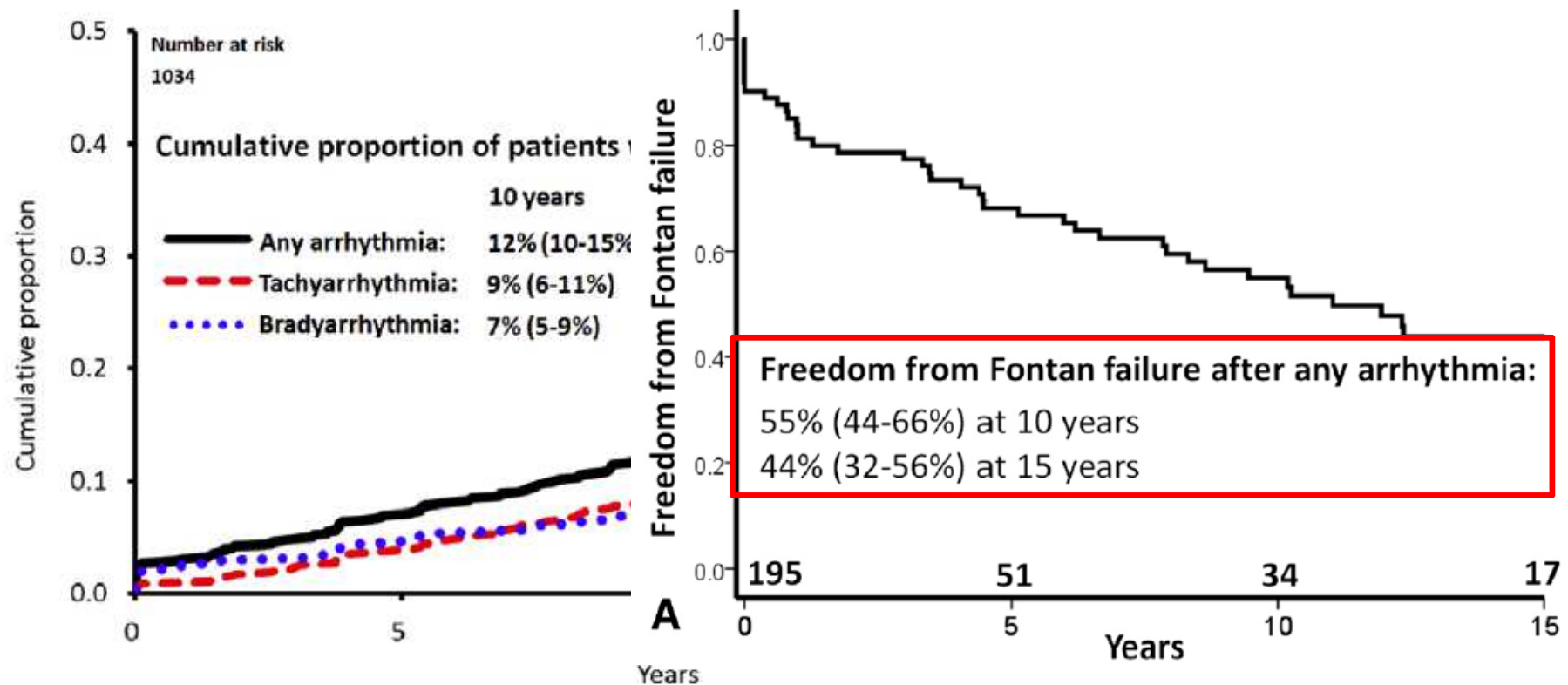
Late Morbidities In Patients Following the Fontan

- Arrhythmias/Sudden Death
- Decreased ejection fraction
 - Exercise intolerance and fatigue
 - Venous congestion
 - Poor growth
- Preserved ejection fraction
 - Venous congestion
 - PLE/Plastic Bronchitis
 - Ascites
- Thromboembolic Disease
- Extracardiac organ dysfunction
 - Kidney
 - Neurologic
 - Liver

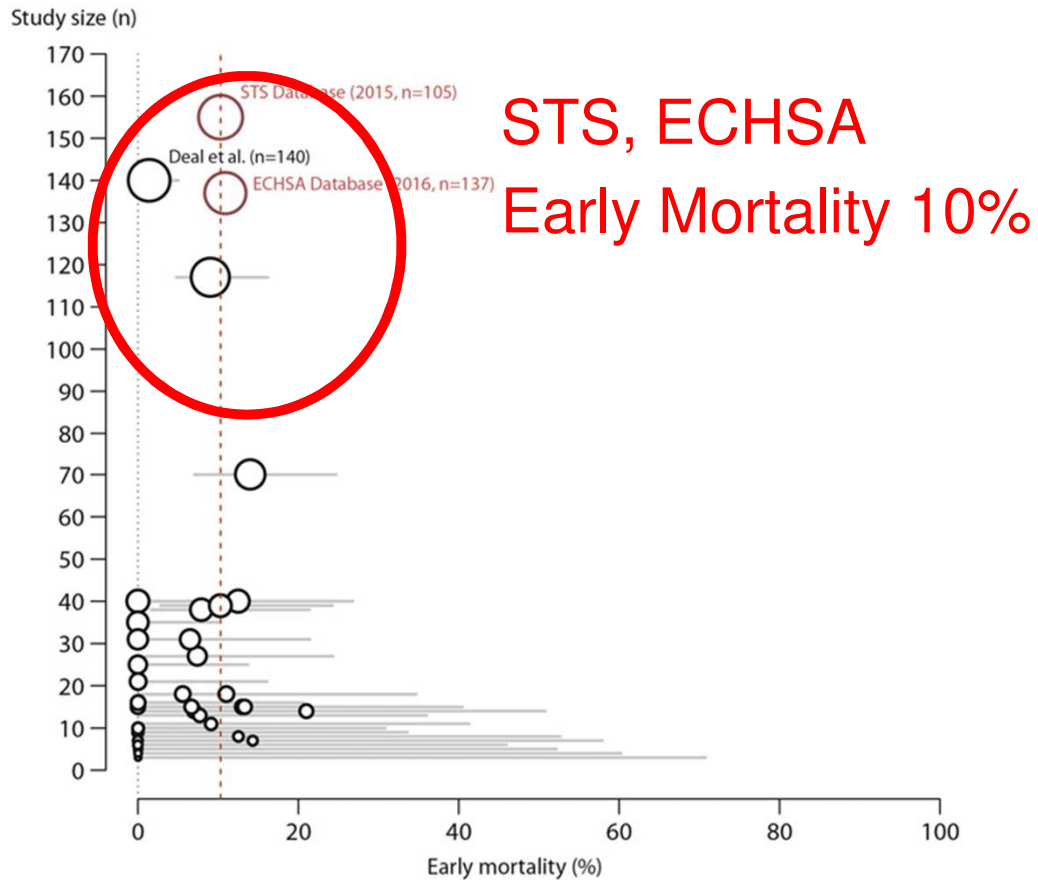
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Long-term outcomes after first-onset arrhythmia in Fontan physiology



2017: Metanalysis of Outcomes of Fontan Conversion



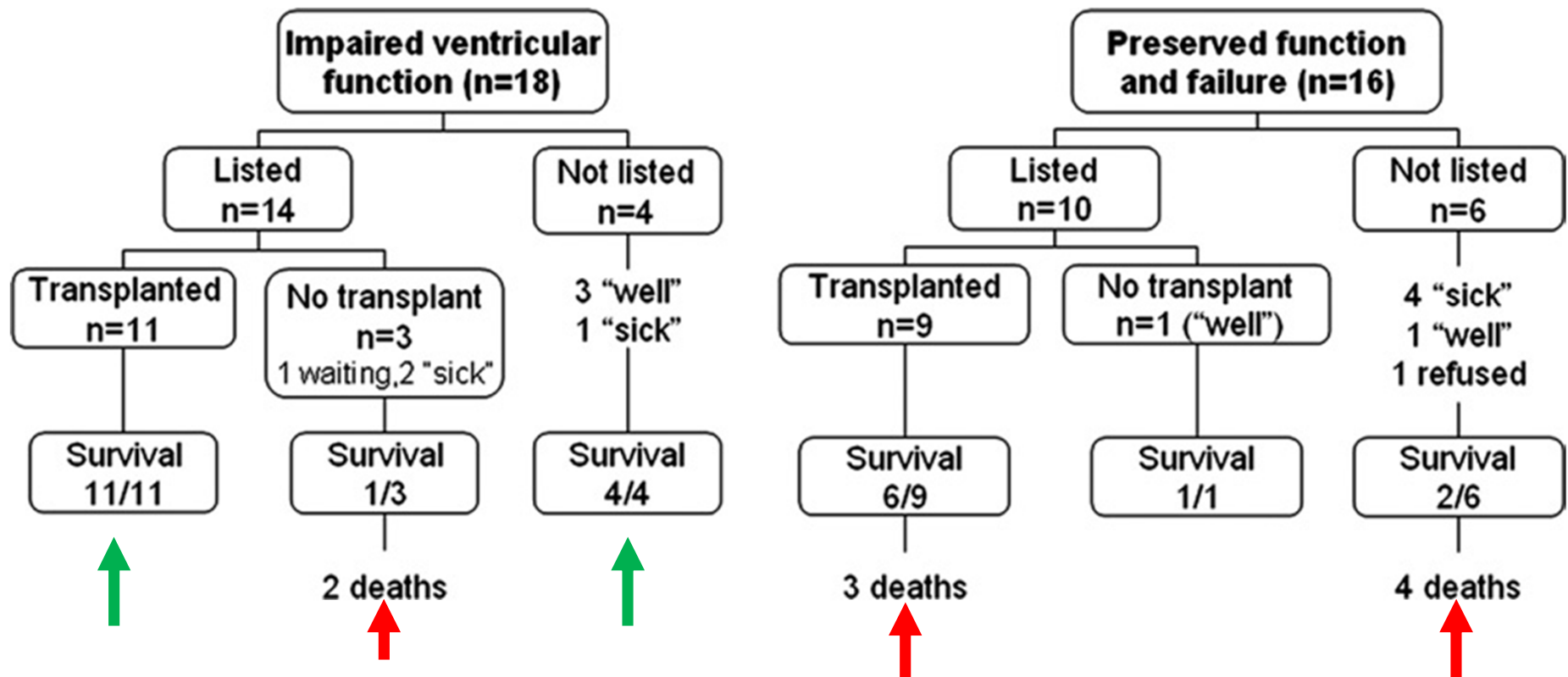
Indications

- Atrial tachyarrhythmia
- APC Fontan
- Younger age

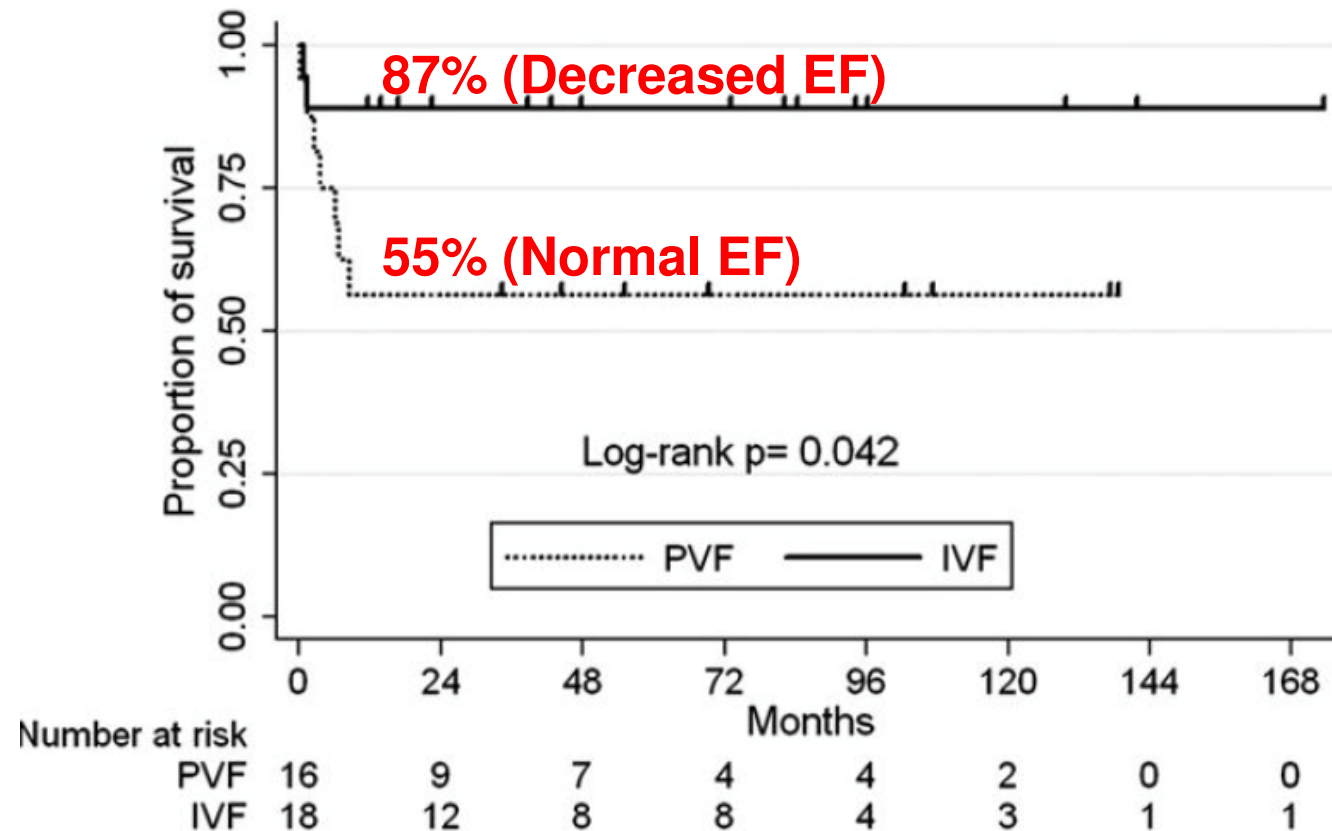
Contraindications

- Older age > 27 years
- Atrioventricular valve regurgitation
- Protein losing enteropathy
- Severe ventricular dysfunction
- Male gender
- Peak $VO_2 \leq 14$ ml/kg/m²

Outcomes of Fontan patients Referred for Transplant Decreased (n=18/34) vs. Normal (n=16/34) EF



Difference in One Year Survival After Transplant Evaluation by Ejection Fraction



Fontan Liver Disease: Japanese Survey

- Survey 2008-2009
- 75 centers, 2,700 patients
- 1.15% prevalence
 - Liver cirrhosis (LC) 12
 - Hepatocellular Carcinoma (HCC) 2
 - LC + HCC 3

Age at 1st diagnosis (years)	
LC	23 (13–34)
HCC	31 (22–44)
Age at 1st Fontan procedure* (years)	
8.2 (1–15)	
Time to diagnosis from the 1st Fontan procedure (years)	
LC	14.5 (5–24)
HCC	21.6 (7–31)
Mean NYHA heart failure classification (n=16)	
2.1	
NYHA heart failure classes (n)	
Class I	3
Class II	9
Class III	4
SpO₂ (%; n=16)	
88±6	

WHO SHOULD BE TRANSPLANTED AND WHEN?

Heart Transplant for Congenital Heart Disease

The New York Times

© 1967 The New York Times Company

NEW YORK, THURSDAY, DECEMBER 7, 1967

Heart Transplant Fails to Save 2-Week-Old Baby in Brooklyn

By RICHARD D. LYONS

A second attempt to transplant a human heart ended fatally at a Brooklyn hospital yesterday when an infant in whom surgeons had placed a heart from another baby boy died 6½ hours after the intricate operation.

Dr. Adrian Kantrowitz, the cardiac surgeon and researcher who performed yesterday's operation, said the transplanted heart had appeared to be working well until it "stopped suddenly" at 1 P.M.

The surgery, begun at 4:15 A.M., lasted 2 hours 15 minutes.

"We do not know at this time why this transplanted heart failed," Dr. Kantrowitz told a news conference at Maimonides Medical Center, where the surgery was performed.

Lines of tension and sleeplessness underscored the eyes of the surgeon as he told of the "heroic attempt" of his 22-member team of doctors, nurses and technicians to "salvage" the infant's life.

The team members were "disheartened and feel sad," he said.

"We were trying to make one whole individual out of two individuals who did not have a chance for survival when they were born," Dr. Kantrowitz said.

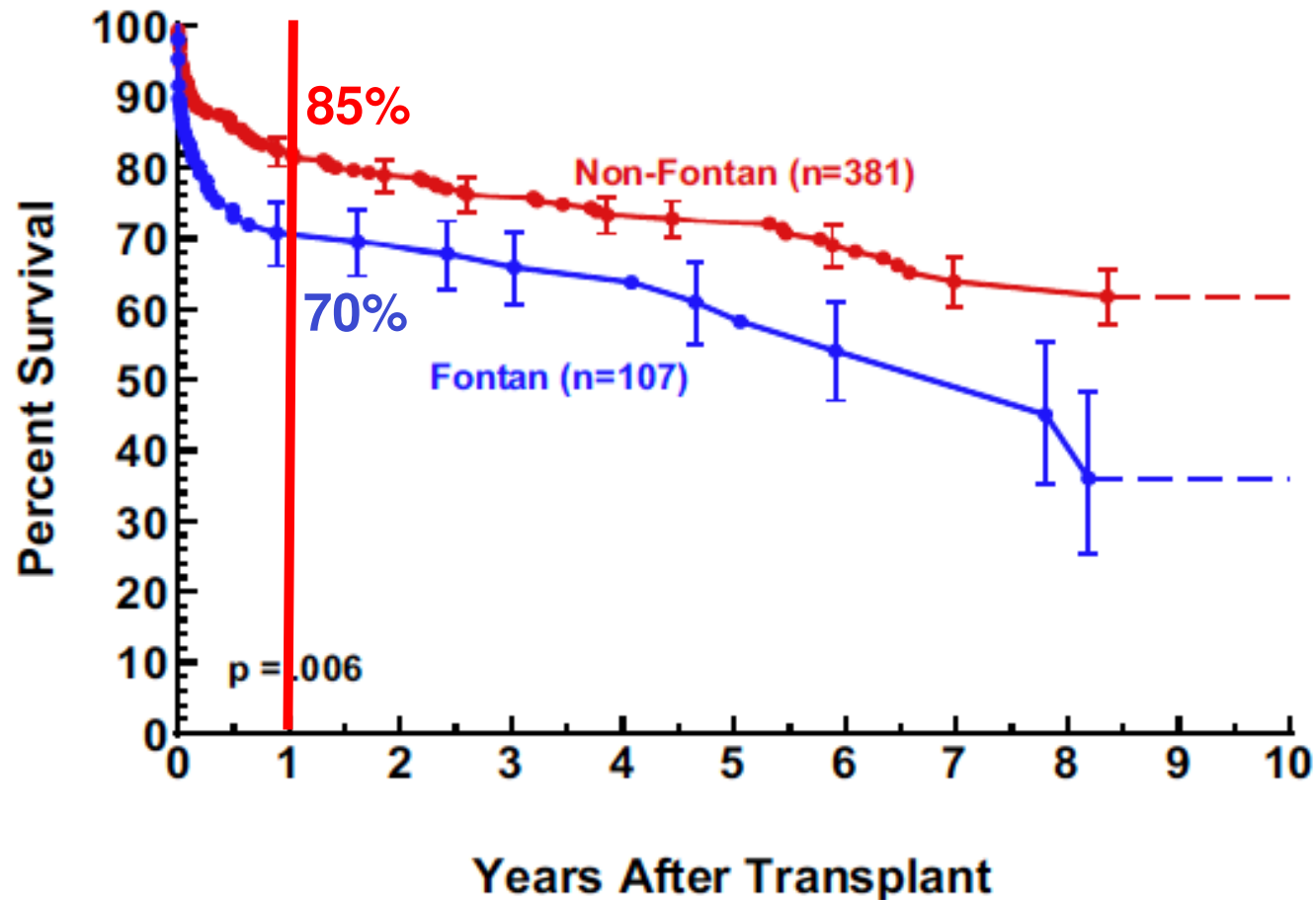
The baby in whom the heart was placed, the surgeon said, was born with a deformed heart valve that would have caused death "in days or a few weeks." This defect "precluded long-term survival," while the donor infant was born with a brain

Continued on Page 34, Column 2

First human heart transplant in the USA

- Dec. 7, 1967
- 3 days after Dr. Christiaan Barnard transplanted adult patient in South Africa
- 19 day old with Tricuspid Atresia
- Baby died suddenly within 6 ½ hours

Post-Transplant Survival 1990-2002: Fontan vs. Other CHD



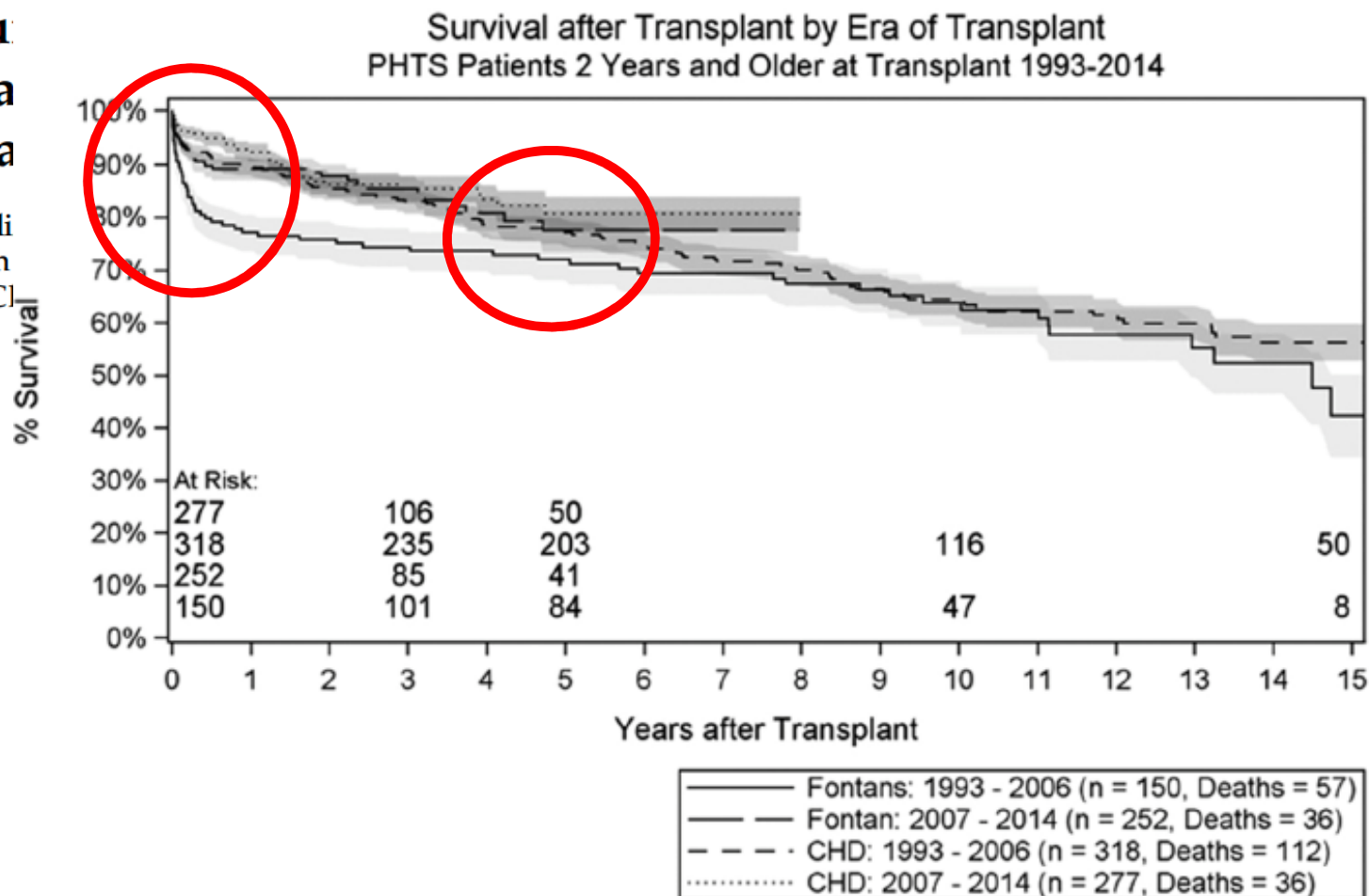
Lamour et al J Am Coll Cardiol 2009;54:160-5

Early and Late Risk Factors: Transplant for CHD 1990-2002

Variable	Relative Risk	p Value
Early phase		
Older recipient age	1.5	0.02
Previous Fontan operation		8.6
Longer ischemic time	2.5	0.002
Interaction of donor age and ischemic time	1.4	0.0007
Higher pre-Tx mean RAP (only in patients without previous Fontan)	2.4	<0.0001
Constant phase		
Younger recipient age	1.8	0.0001
Higher systolic transpulmonary gradient	2.0	0.01
CMV+ donor, CMV– recipient	2.8	0.001
Previous classical Glenn operation	3.1	0.01

Fontan Patient Survival after Heart Transplantation in the Current Era

Kathleen E. Simpson, MD, Eli David C. Naftel, PhD, Rakesh Aliessa P. Barnes, MD, and Cl

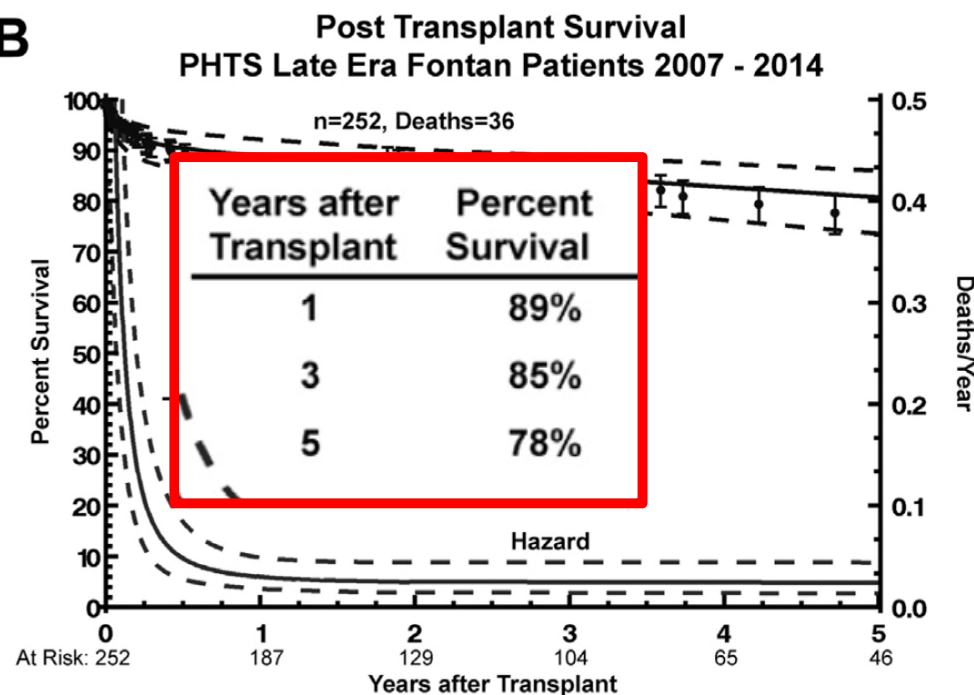


Shaded areas indicate 70% confidence limits
p (log-rank) = 0.0466
Event: Death after Transplant

Improved Post-Transplant Survival: 2007-2014

Variable ^a	Early Era (1993–2006) (n = 150)	Late Era (2007–2014) (n = 252)	p Value
Male	99 (66.00)	144 (57.14)	0.08
White race	119 (79.33)	193 (76.59)	0.52
eGFR, mL/min per 1.73m ²	86 ± 35.7	103.8 ± 94.4	0.0008 ^b
At listing for transplant			
Renal insufficiency	5 (3.33)	17 (6.75)	0.15
Protein-losing enteropathy	31 (20.67)	85 (33.73)	0.005 ^b
Failure to thrive	27 (18)	76 (30.16)	0.007 ^b
At transplant			
Inotropes	79 (52.67)	166 (65.87)	0.009 ^b
Ventilator	15 (10)	12 (4.76)	0.04
ECMO support	1 (0.68)	1 (0.4)	0.7
Age at Fontan, y	4.44 ± 3.12	3.31 ± 1.82	0.0008 ^b
Fontan to transplant, y	5.23 ± 4.29	6.71 ± 5.12	0.007 ^b
Transplant ≤6 months of Fontan	16 (15.09)	10 (4.72)	0.002 ^b

B

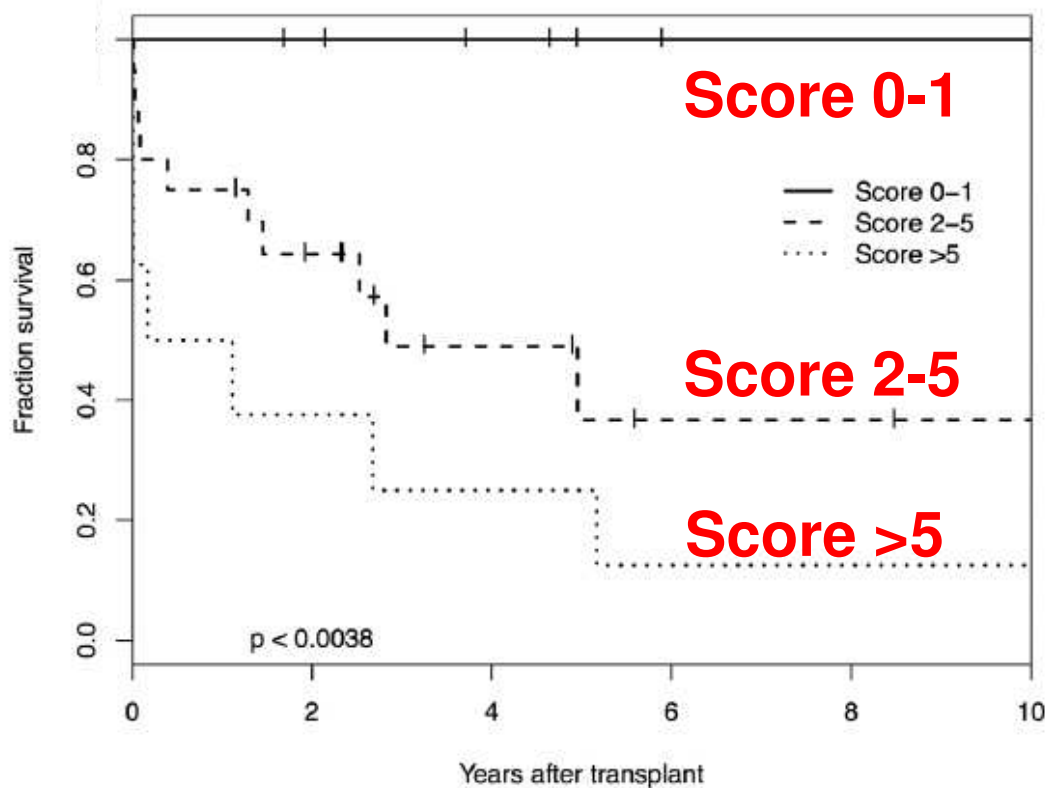


Mortality Risk Stratification in Fontan Patients Who Underwent Heart Transplantation

Christopher J. Berg, MS^a, Brenton S. Bauer, MD^{a,b,c}, Abbie Hageman, BS^{a,d},
Jamil A. Aboulhosn, MD^{a,c,d}, and Leigh C. Reardon, MD^{a,c,d,e,*}

Am J Cardiol 2017;119:1675e 1679

- Systemic EF < 20%
- AV valve regurg ≥ moderate
- Fontan pressure > 16 mmHg
- Renal replacement therapy
- ECMO
- MELD XI excluding INR



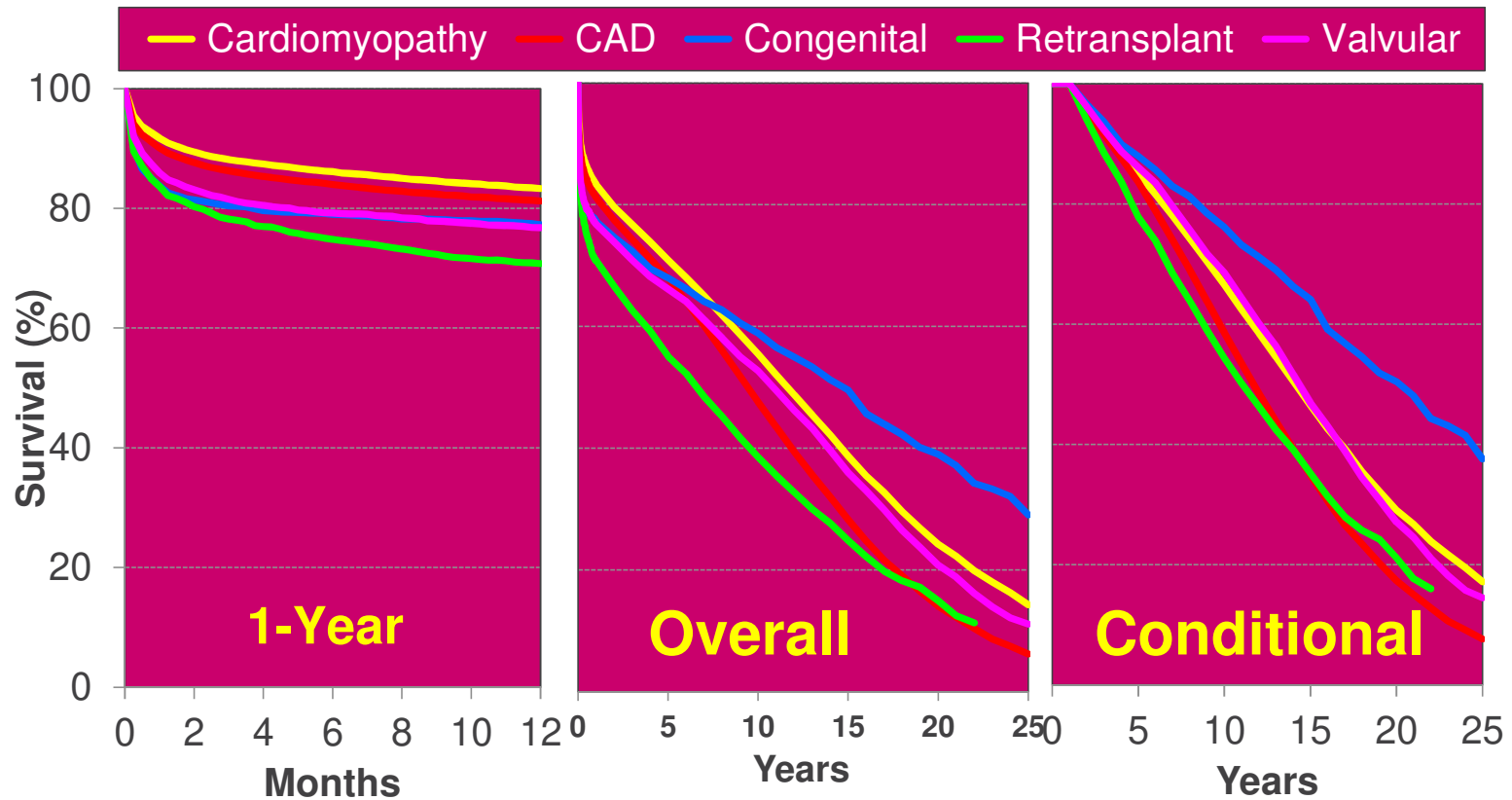
US Organ Allocation Changes: Patients ≥ 18 years

Status	Proposed Criteria
1	<ul style="list-style-type: none"> i. ECMO ii. Mechanical ventilation iii. Non-dischargeable BiVAD or RVAD iv. Mechanical circulatory support with life-threatening ventricular arrhythmia
2	<ul style="list-style-type: none"> i. Intra-aortic balloon pump ii. Acute circulatory support device iii. Ventricular tachycardia/ventricular fibrillation, mechanical support not required iv. Mechanical circulatory support with device malfunction/mechanical failure v. Total artificial heart vi. Dischargeable BiVAD or RVAD
3	<ul style="list-style-type: none"> i. LVAD for up to 30 days ii. Status 1A exception iii. Multiple inotropes or single high-dose inotropes with continuous hemodynamic monitoring iv. Mechanical circulatory support with device-related complications other than infection, thromboembolism, device malfunction/mechanical failure or life-threatening ventricular arrhythmia v. Mechanical circulatory support with device infection vi. Mechanical circulatory support with thromboembolism
4	<ul style="list-style-type: none"> i. Diagnosis of congenital heart disease (CHD) with: <ul style="list-style-type: none"> a. Unrepaired/incompletely repaired complex CHD, usually with cyanosis b. Repaired CHD with two ventricles (e.g., TOF, TOGV) c. Single ventricle repaired with Fontan or modifications ii. Diagnosis of ischemic heart disease with intractable angina iii. Diagnosis of hypertrophic cardiomyopathy
	<ul style="list-style-type: none"> v. Stable LVAD candidates after 30 days vi. Inotropes without hemodynamic monitoring vii. Diagnosis of amyloidosis viii. Retransplant ix. Status 1B exception
5	Combined organ transplants: heart-lung; heart-liver; heart-kidney
6	All remaining active candidates
7	Inactive/not transplantable

Qualification:

1. Candidate is admitted to the transplant hospital that registered the candidate on the waiting list
2. Transplant physician believes, using acceptable medical criteria, that a heart candidate has an urgency and potential for benefit comparable to that of other candidates at the requested status

Transplant Survival by Underlying Diagnosis One Year, Overall, Conditional



Who Should Be Transplanted?

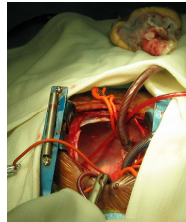
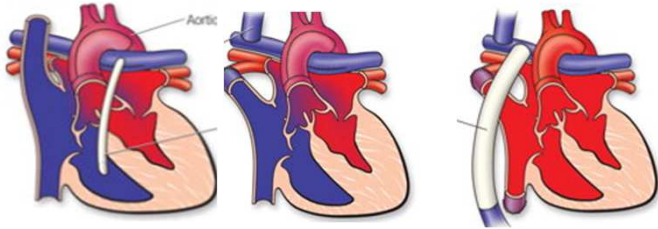
- Heterotaxy, unbalanced AV canal, pulmonary stenosis
- Bidirectional Glenn (4 years), EC Fontan completion (9 years)
- Ages 9-21 years: graduated high school, travelled the world, graduated college, worked as LPN
 - Ventricular function mildly depressed
 - Intermittent nonsustained atrial tachycardia @125-130, (5-10 min, 3/wk)
- Age 22 years: starting nursing school
 - IVC narrowed on echo, Stent IVC (IVC mean 12, PA mean 10 mmHg)
 - Liver fibroscan score 15, ultrasound normal
- 23 years: Graduating from nursing school this summer. Complaints of tachycardia, dizziness
 - IART and atrial tachycardia up to 180 bpm
 - Liver fibroscan score 25

Transplant vs Management of Fontan Morbidities?

- Pro-Transplant
 - Survival one year 90-95%, 10 year survival 70-80%
 - Ongoing risk progressive liver dysfunction would preclude transplant
 - Risk of recurrent arrhythmias, ventricular dysfunction, PLE
 - Timing: graduating school, parental insurance
- Pro- Continued management of Fontan
 - One year mortality 5-10%, Ten-year mortality 20-30%
 - Have not tried pulmonary vasodilators, stent redilation, arrhythmia management
 - Risk of post-transplant morbidities

TRANSPLANT: THE FOURTH STAGE

LIVING WITH A SINGLE VENTRICLE



**? Artificial Heart
Xenotransplant
Bioreplacement**

Stage 1: Balance pulmonary and systemic blood flow

Stage 2: Decrease volume load on heart

Stage 3: Improve oxygen delivery

Stage 4: Prevent morbidity from Fontan physiology

Stage 5: Prevent morbidity from transplant

**Transplant can work for some
but is not for all and is not a
cure...**

***and
has a greater chance of
success if offered earlier
before patients develop
significant morbidities from
the Fontan***