Pulmonary Perfusion: Out of Balance

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Disclosures

Proctor/Consultant:

- Abbott
- Edwards Lifesciences
- Medtronic, Inc.
- Cook Medical

Research Support:

- Edwards Lifesciences
- Siemens Medical Solutions USA, Inc.
- Renata Medical

Board Member:

- Intersocietal Accreditation Commission (IAC)

Will be discussing off-label use of devices

Goals

Aimee: "Gregor, what do you want me to discuss in this lecture?"

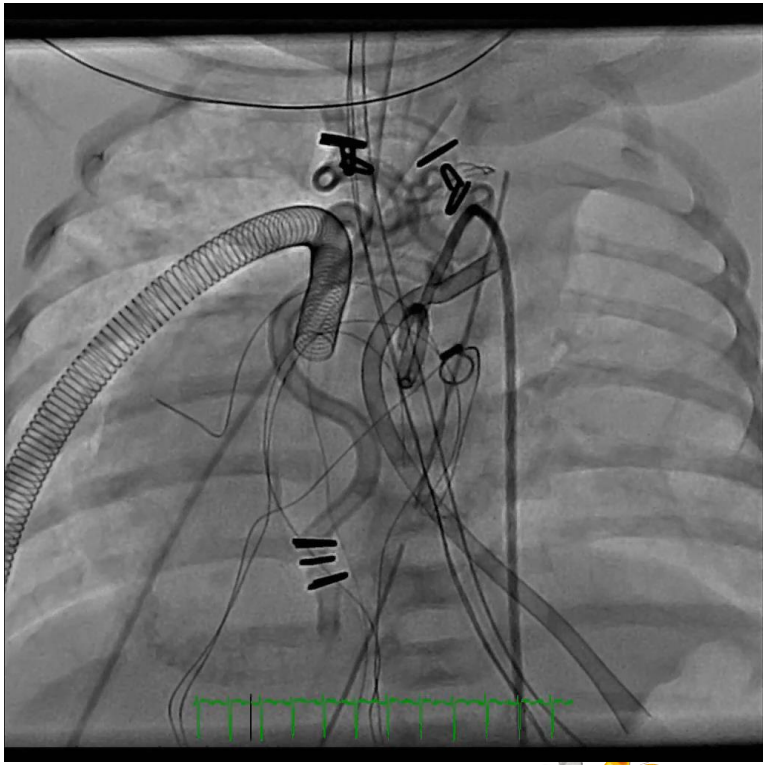
Gregor: "Since we cover the interval from postnatal through stage I, it would be good if you could talk on shunt and PA stenosis after Norwood and when and how to address them to generate even flow distribution to both branches."

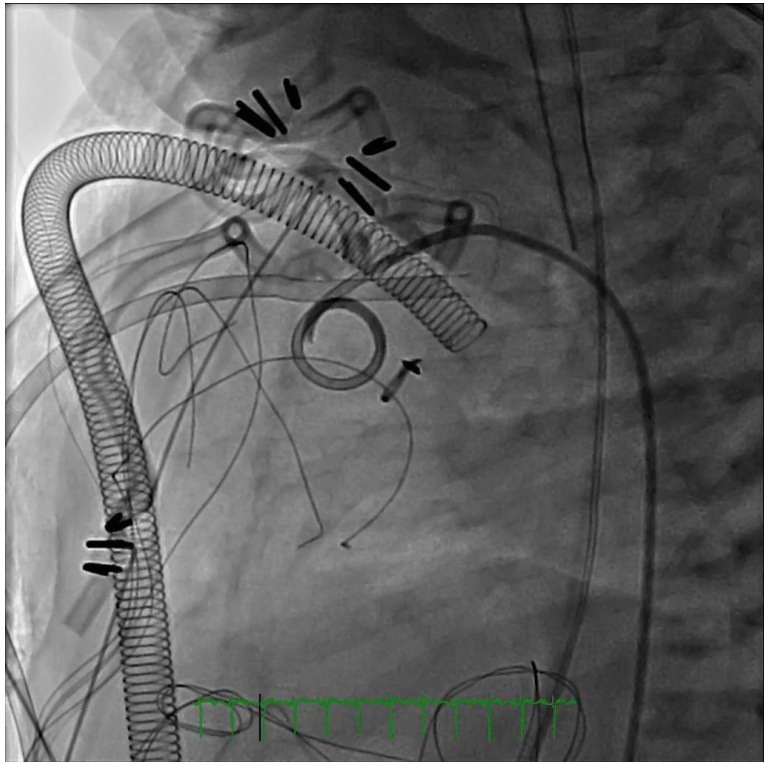
Well, great…
#1 I'm at an institution that does almost exclusively hybrid stage I
#2 There are probably no data on how to and why we should create even flow distribution after Norwood
#3 I know nothing about this topic

Out of Balance Case

- 25-day-old term female with HLHS (MA/AA), dextrocardia, aberrant right subclavian artery, stenosis of the retrograde arch at its junction with the ductus, and cor triatriatum sinister with moderate restriction
- At 6 days of age, underwent attempt at BAS, which was unsuccessful due to the complex anatomy
- Bilateral 3 mm branch PA bands placed to balance the circulation and delay Norwood, given complex anatomy
- At 3 weeks of age, Norwood procedure performed with resection of cor triatriatum, atrial septectomy, removal of PA bands, and placement of 3.0 mm Gore-Tex short central shunt posteriorly on the native MPA sinus
- Several hours after the operation, progressive hypoxemia led to a cardiac arrest requiring ECPR with central cannulation for V-A ECMO
- Shunt and PAs could not be seen on echo

Out of Balance Case





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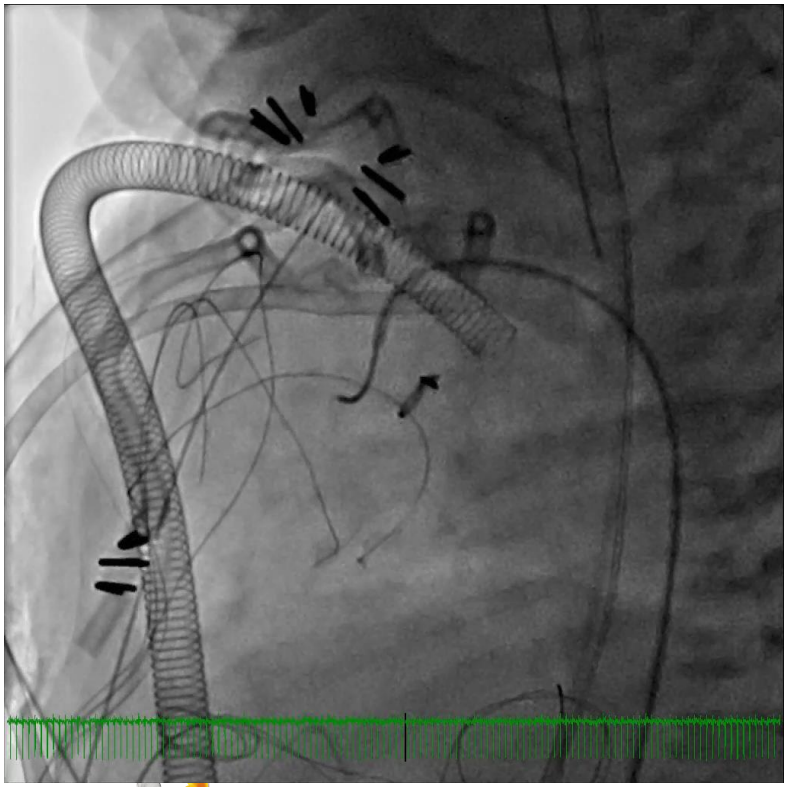

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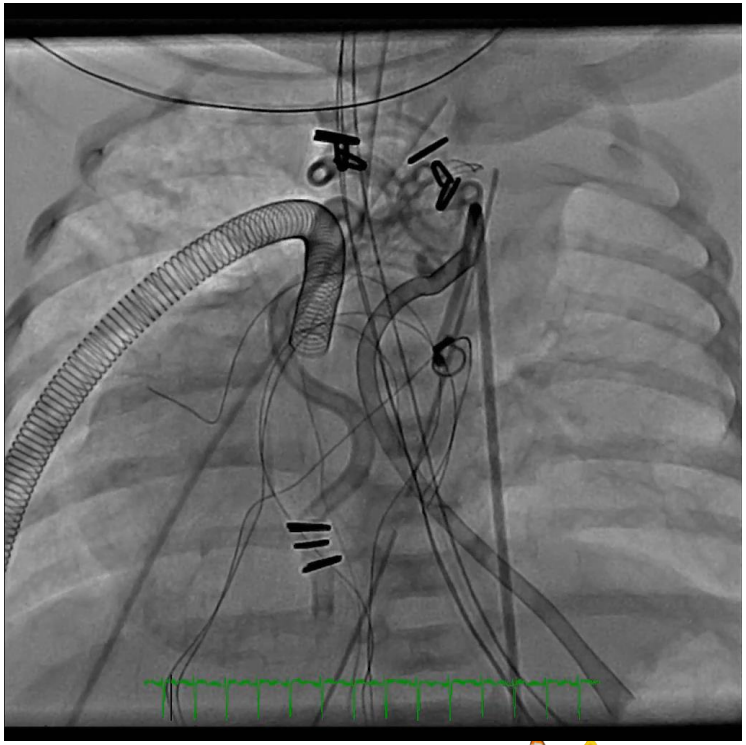

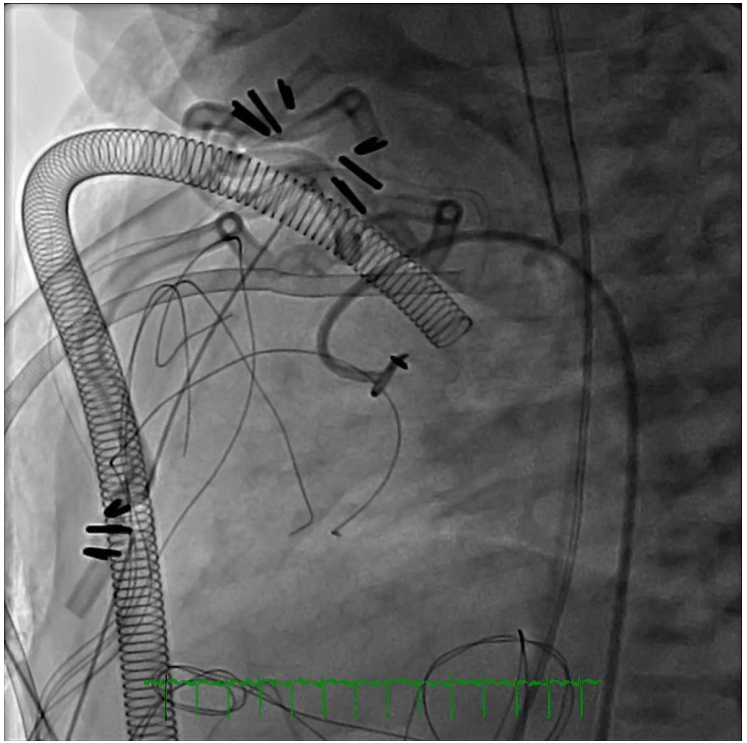

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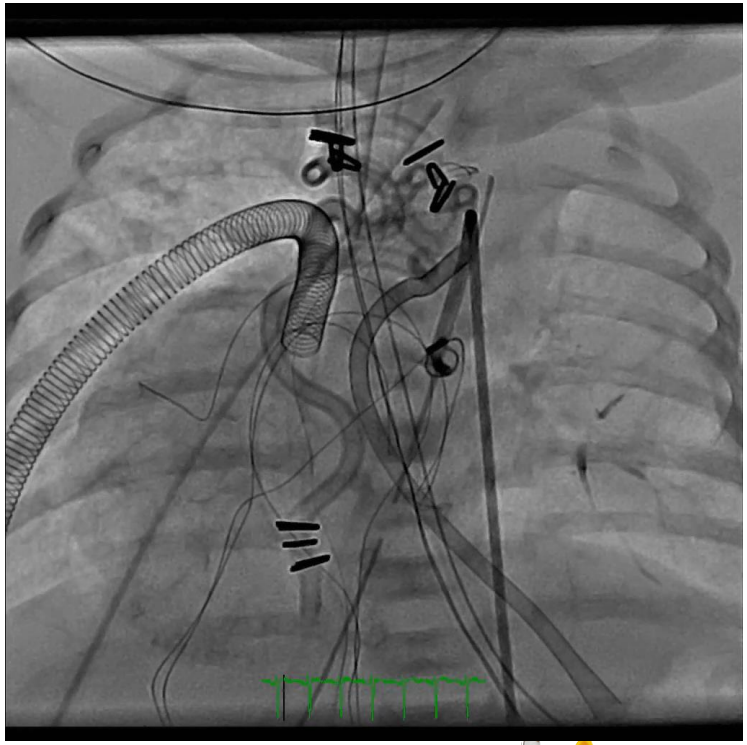

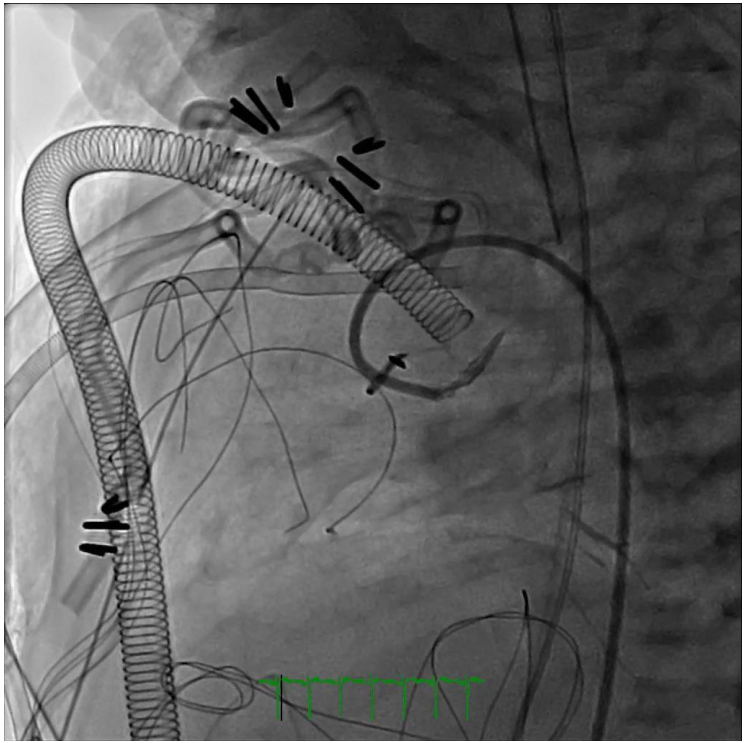

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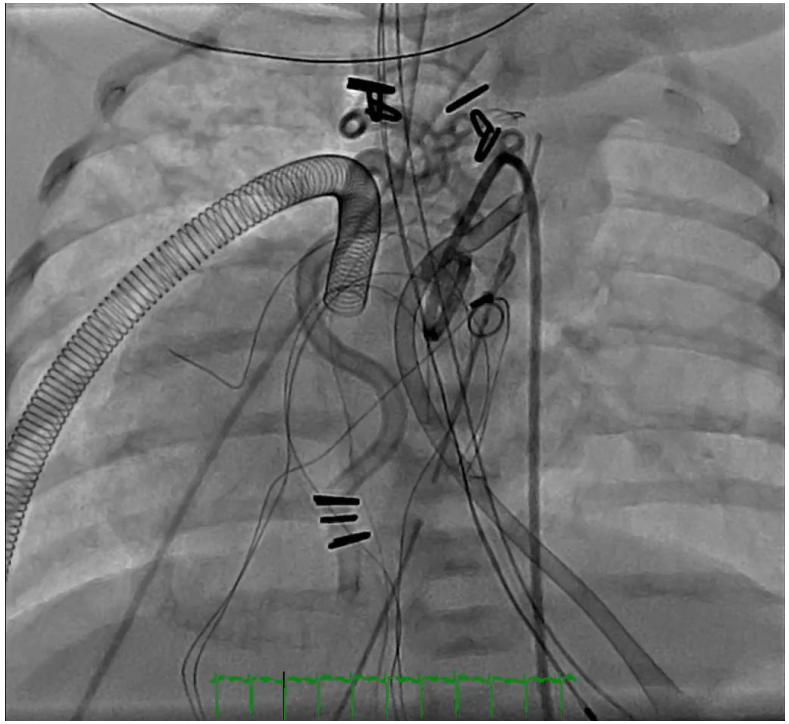
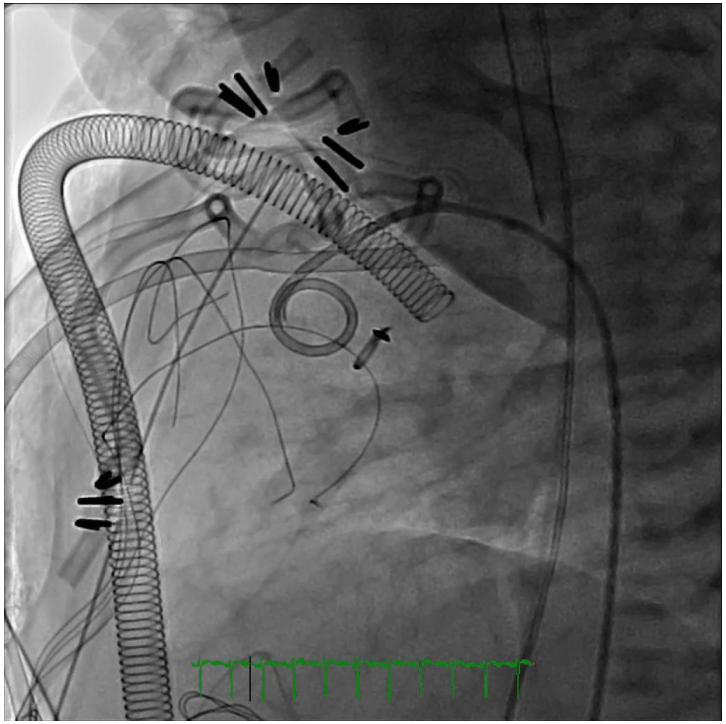
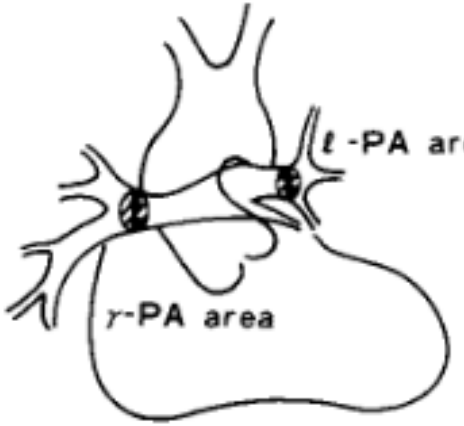




Nakata PA Index



$$\text{cross-sectional area} = \pi \left(\frac{\text{diameter}}{2 \cdot f} \right)^2$$

*f = magnification coefficient

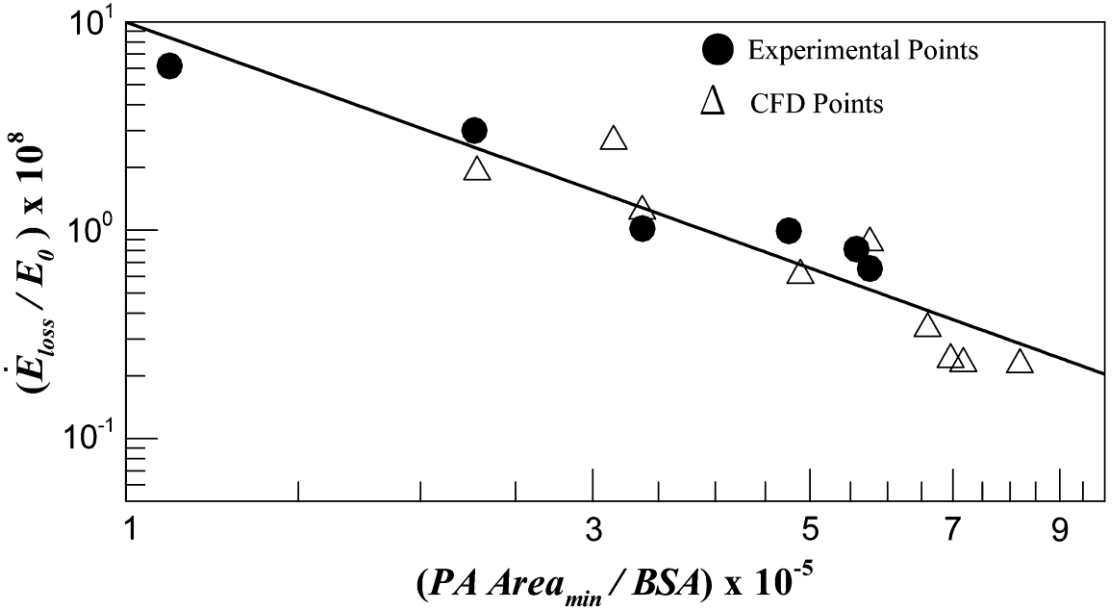
$$\text{PA index} = \frac{\text{r-PA area}(mm^2) + \text{l-PA area}(mm^2)}{\text{B.S.A.}(m^2)}$$

- Normal value: 330 ±30 mm^2/m^2
- Recommended for Fontan: >250 mm^2/m^2

Nakata S, et al. JTCVS 1984;88:610-619

Impact of PA Size on Fontan Outcomes

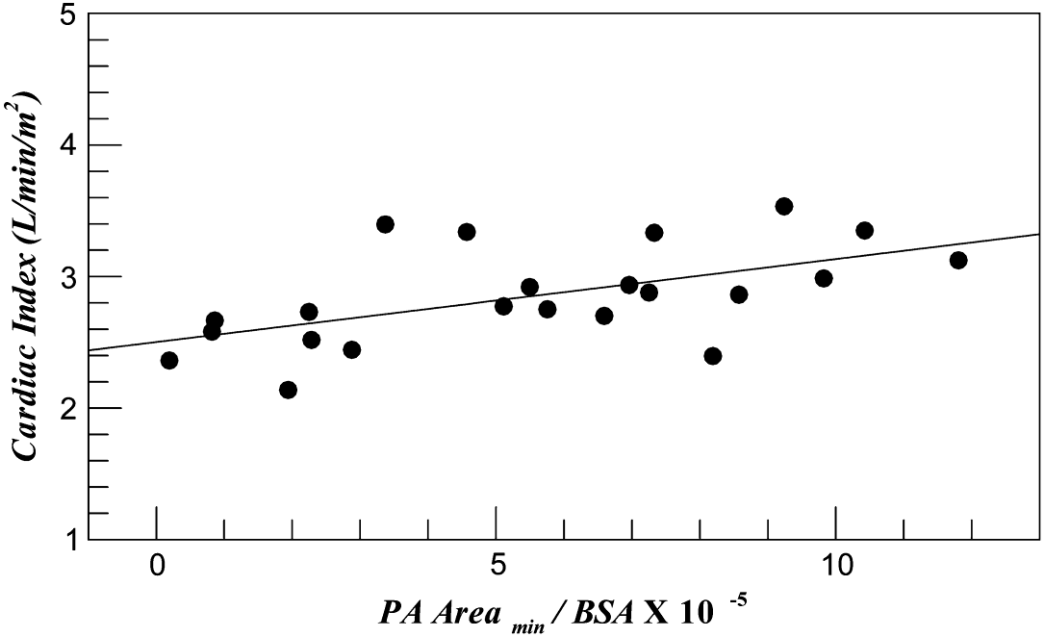
- Using CFD by MRI, minimum cross-sectional area of PAs governs the energy loss characteristics of the Fontan more strongly than variations in the shapes of EC and LT Fontan



Dasi LP, et al. JTCVS 2009;137(3):500-564

Impact of PA Size on Fontan Outcomes

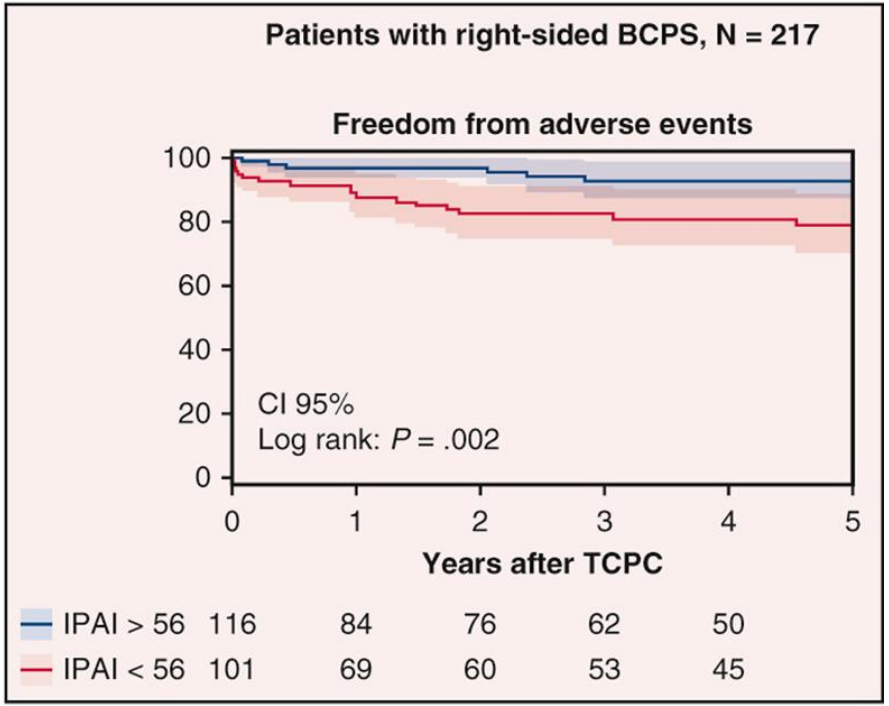
- Cardiac index significantly correlated with the minimum PA area (p=0.006), suggesting Fontan energy losses affect the resting CO



Dasi LP, et al. JTCVS 2009;137(3):500-564

Impact of PA Size on Fontan Outcomes

- 247 non-fenestrated Fontans between 2009-2021 in Munich
- Lower Nakata index:
  - Risk factor for chylothorax
  - Cutoff value of 170 mm^2/m^2
- In a right-sided Glenn subgroup, lower LPA index:
  - Risk factor for longer ICU stay
  - Risk factor for AEs (death, PLE, PB, thrombosis, NYHA Class 3-4)
  - Cutoff value of 56 mm^2/m^2



Kido T, et al. JTCVS 2023 (in press)

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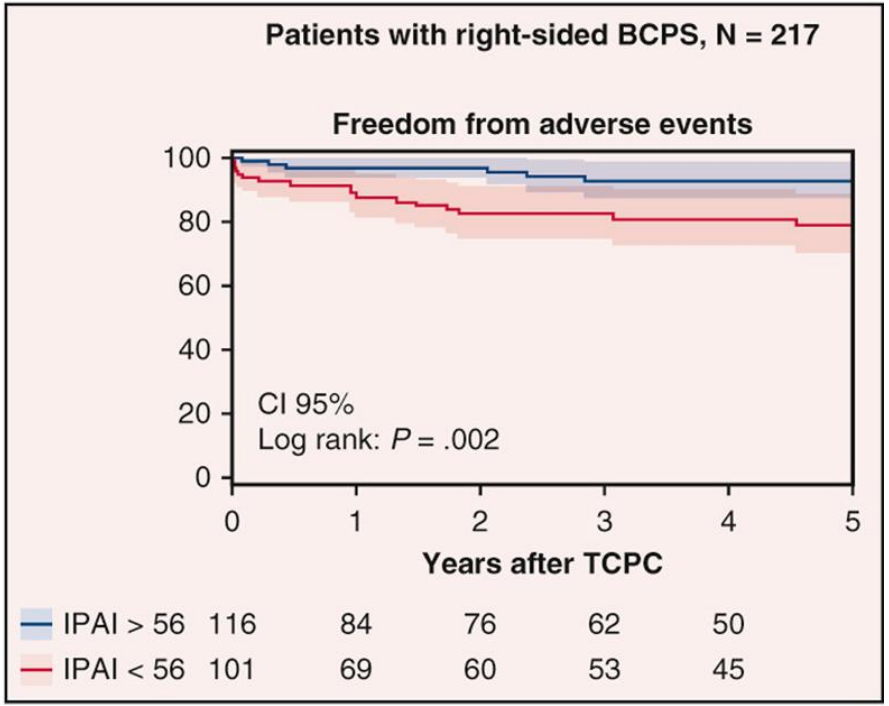
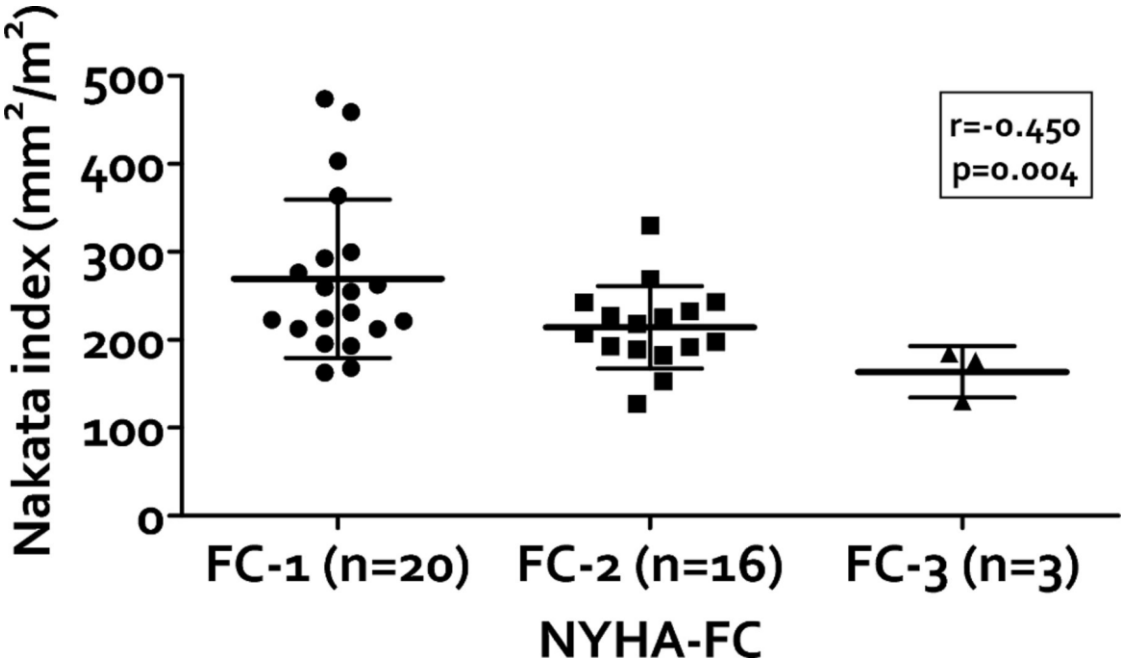


Kido T, et al. JTCVS 2023 (in press)

"Our findings further support the importance of [aortic arch] modifications in preventing LPA stenosis after stage 1 palliation."

Impact of PA Size on Fontan Functional Status

- 39 Fontan patients with concomitant CMR and CPET from 2012-2013
- Nakata index 238.6±78.5 mm2/m2



Ridderbos F-J S, et al. Heart 2020;106:233-239

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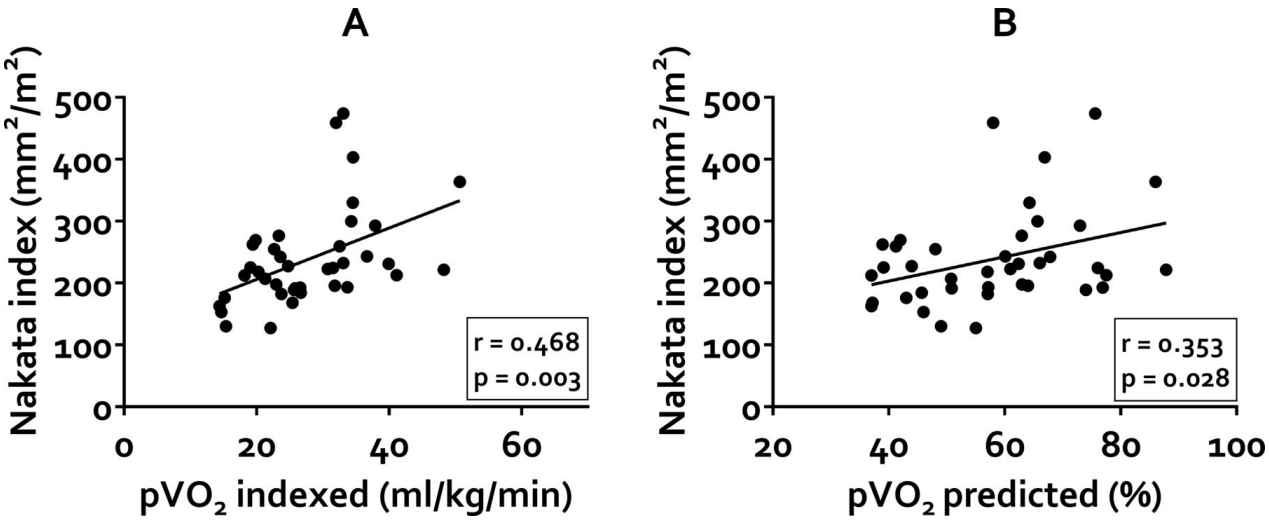
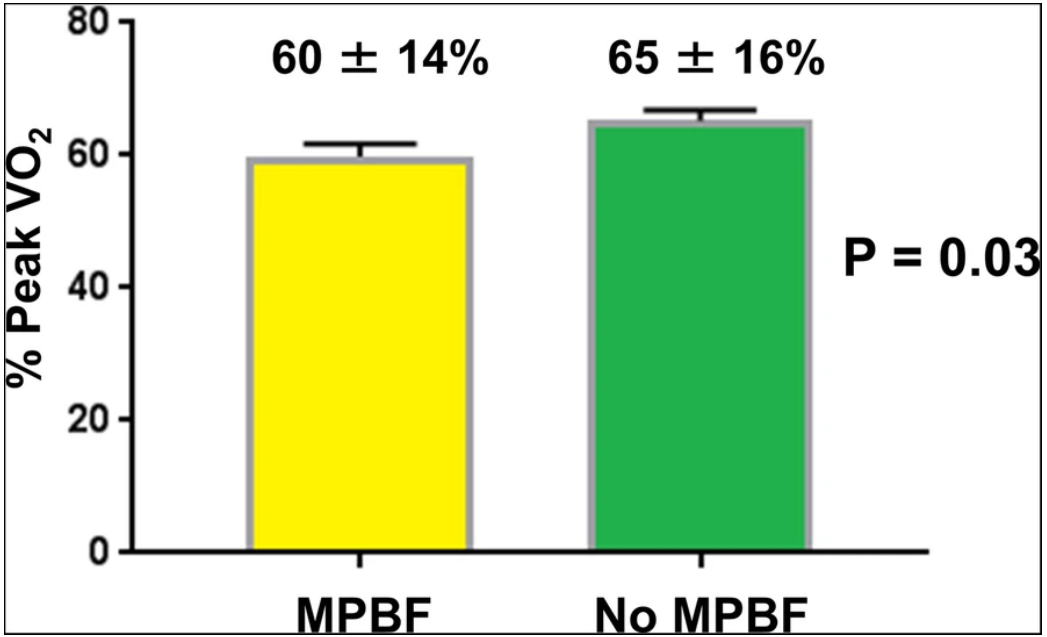


Ridderbos F-J S, et al. Heart 2020;106:233-239

Impact of PA Size on Fontan Functional Status

- 147 patients in Boston with CMR and CPET from 1999-2017 (median age 21.8 years)
- Median of 2.8 months from CMR to CPET
- Maldistribution of PA blood flow (MPBF) = >20% difference in branch PA flow
- 36% had MPBF
- Only compression by the AAO or aortic root was associated with MPBF



Alsaied T, et al. JCMR 2018;106:233-239

PA Growth After Fontan

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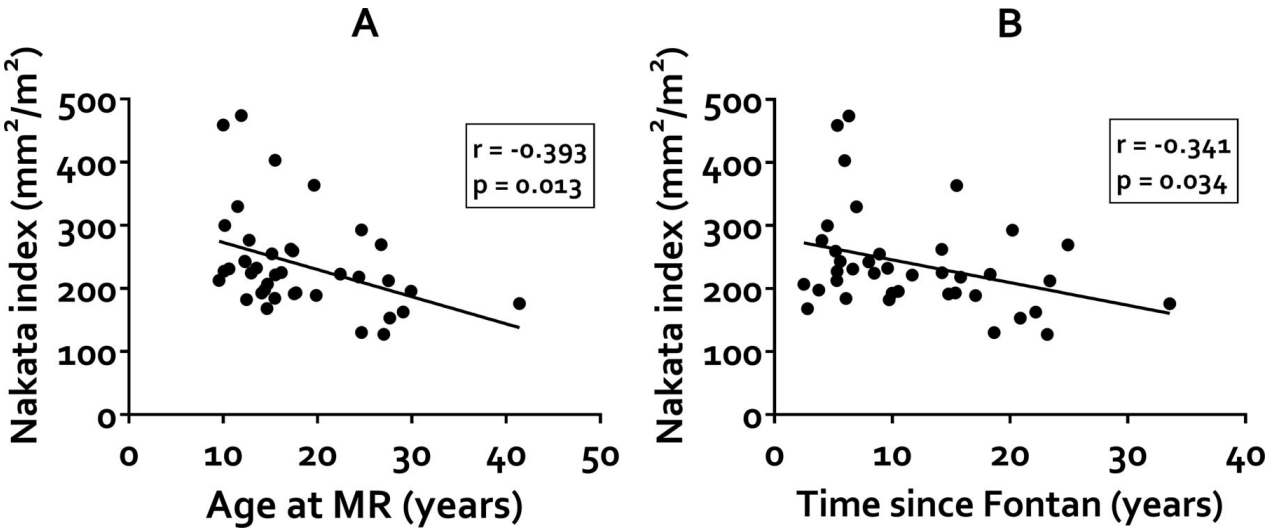
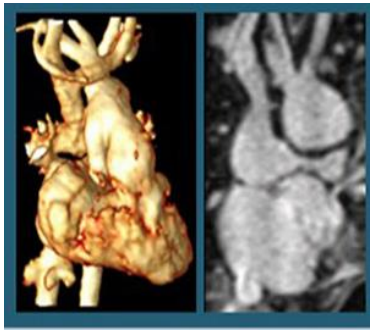
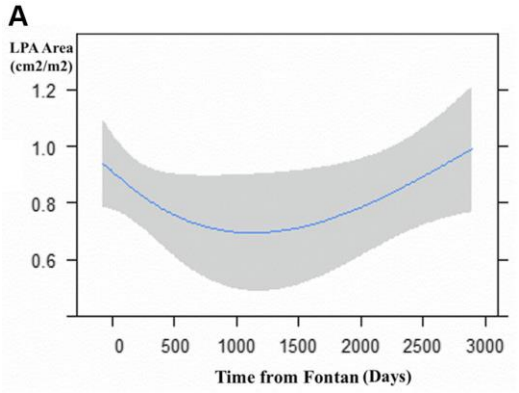


Ridderbos F-J S, et al. Heart 2020;106:233-239

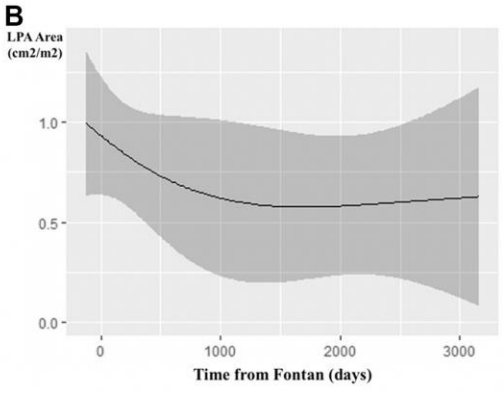
PA Growth After Fontan

- 119 single V patients with serial CMRs between 2008-2019 at CHOP
- Decrease in indexed LPA area with time from Fontan, whereas indexed RPA area remained the same





No DKS



DKS

Ghosh, et al. Ann Thorac Surg 2022 (online 8/18/22)

PA Growth After Glenn

- 247 patients between 2009-2021 in Munich
- Nakata index
  - 173 (127-242) mm^2/m^2 before Glenn
  - 162 (133-207) mm^2/m^2 before Fontan (p=0.002)
- In a right-sided Glenn subgroup, LPA index:
  - 74 (54-110) mm^2/m^2 before Glenn
  - 59 (44-79) mm^2/m^2 before Fontan (p<0.001)

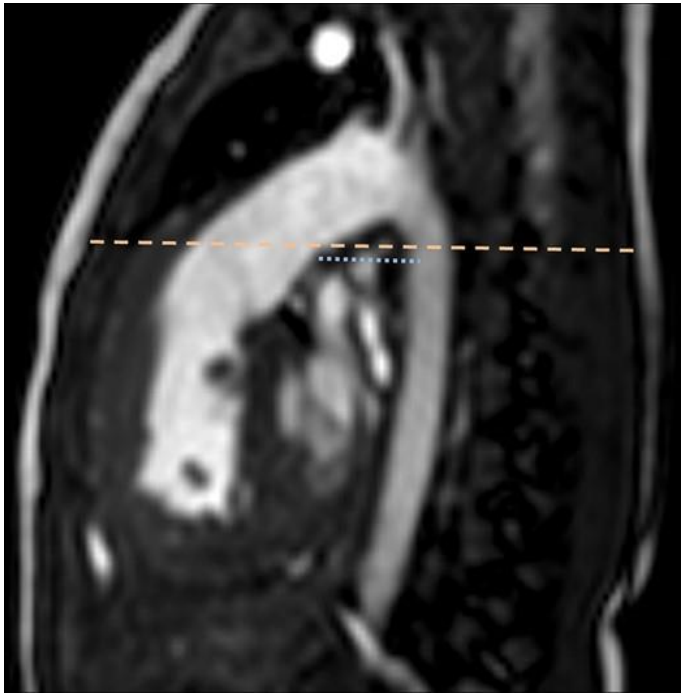
Kido T, et al. JTCVS 2023 (in press)

What Do We Know So Far?

- Larger PA size is important for:
  - Improving Fontan mechanics, cardiac output, and functional status
  - Decreasing AEs after Fontan
  - Decreasing ICU stay after Fontan
- Maldistribution of flow leads to:
  - Decreased peak VO2
- Nakata index decreases over time after Glenn and after Fontan, primarily due to the LPA and neoaortic interaction

Cause of LPA Stenosis After Norwood

- 47 HLHS patients at Evelina s/p Norwood with mBTS with MRI pre-stage II
- In multivariable analysis, only predictor of indexed mid-LPA area was the interaortic ratio (interaortic distance/chest AP distance)



Nassar MS, et al. Interactive CV and Thorac Surg 2015;20:631-635

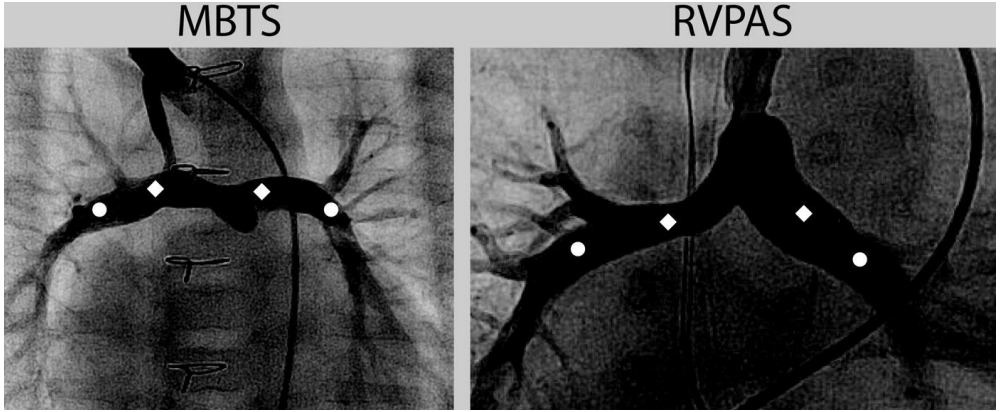
Single Ventricle Reconstruction Trial

- 555 HLHS patients undergoing Norwood enrolled
  - 279 assigned to MBTS
    - Distal RPA 6.1 mm by angio pre-stage II ($p<0.001$)
  - 276 assigned to RVPAS
    - Distal RPA 5.4 mm by angio pre-stage II ($p<0.001$)
  - Nakata index before the stage II was smaller in the RVPA shunt group than in the MBTS group ($p=0.009$)

Ohye RG, et al. NEJM 2010;362:1980-1992

Single Ventricle Reconstruction Trial

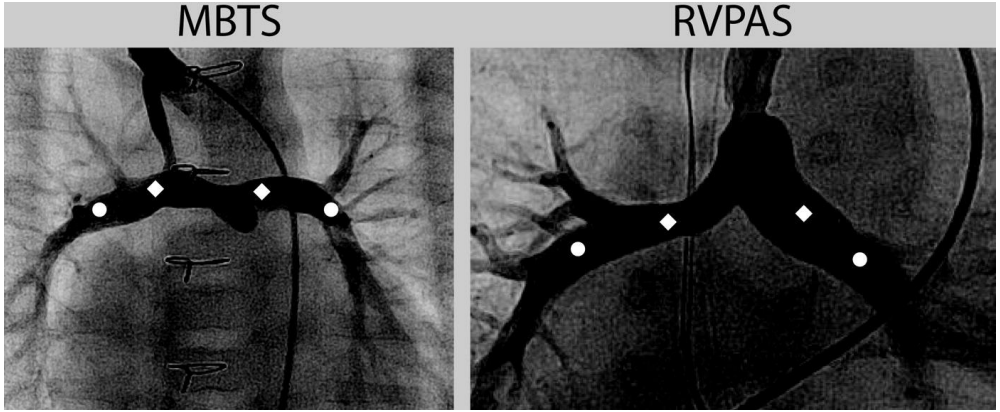
- 348 pre-stage II angios
  - 152 MBTS
  - 196 RVPAS
- 55% had shunt or PA stenosis
- 33% had moderate or severe branch PS (>35% stenosis)
- PA growth less in RVPAS ($p < 0.01$)
  - Nakata index 134 vs. 164
  - RLL PA 5.1 vs. 6.3 mm
  - Mid-main RPA 4.2 vs. 5.0 mm
  - Mid-main LPA 4.3 vs. 4.8 mm



Aiyagari R, et al. JTCVS 2014;148:1467-74

Single Ventricle Reconstruction Trial

- RVPAS
  - More mid-RPA stenosis (p=0.02)
    - 37% RVPAS
    - 25% MBTS
  - More severe LPA stenosis (p=0.003)
    - 9% RVPAS
    - 0.7% MBTS
  - More shunt stenosis (p=0.004)
    - 28% RVPAS
    - 14% MBTS



Aiyagari R, et al. JTCVS 2014;148:1467-74

Single Ventricle Reconstruction Trial

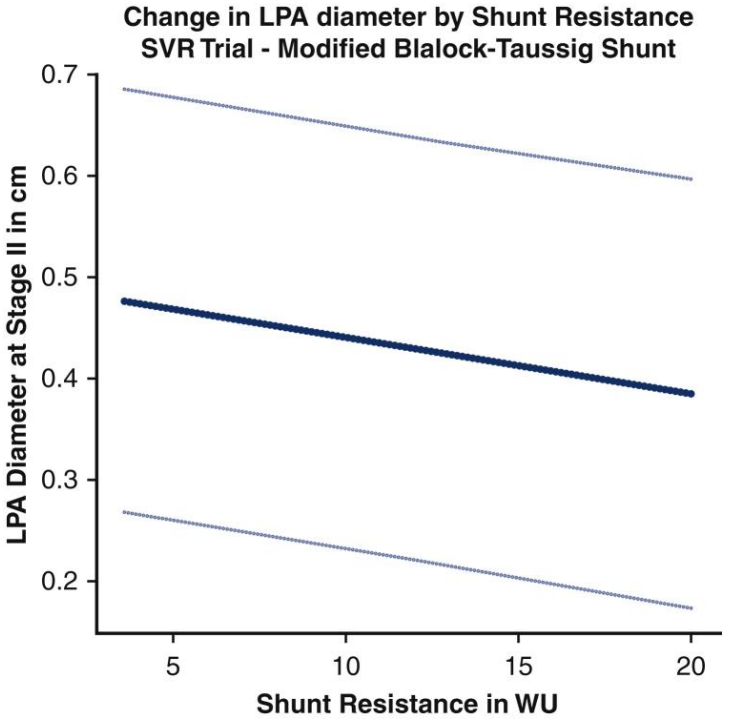
- 555 enrolled
  - 276 assigned to RVPAS
    - 41.2% had angioplasty of shunt or PA branch in the interstage* (p=0.01)
    - 7.3% had stent of shunt or PA branch in the interstage* (p=0.008)
  - 279 assigned to MBTS
    - 25.6% had angioplasty of shunt or PA branch in the interstage* (p=0.01)
    - 1.8% had stent of shunt or PA branch in the interstage* (p=0.008)

*Interstage includes stage II hospitalization

Ohye RG, et al. NEJM 2010;362:1980-1992

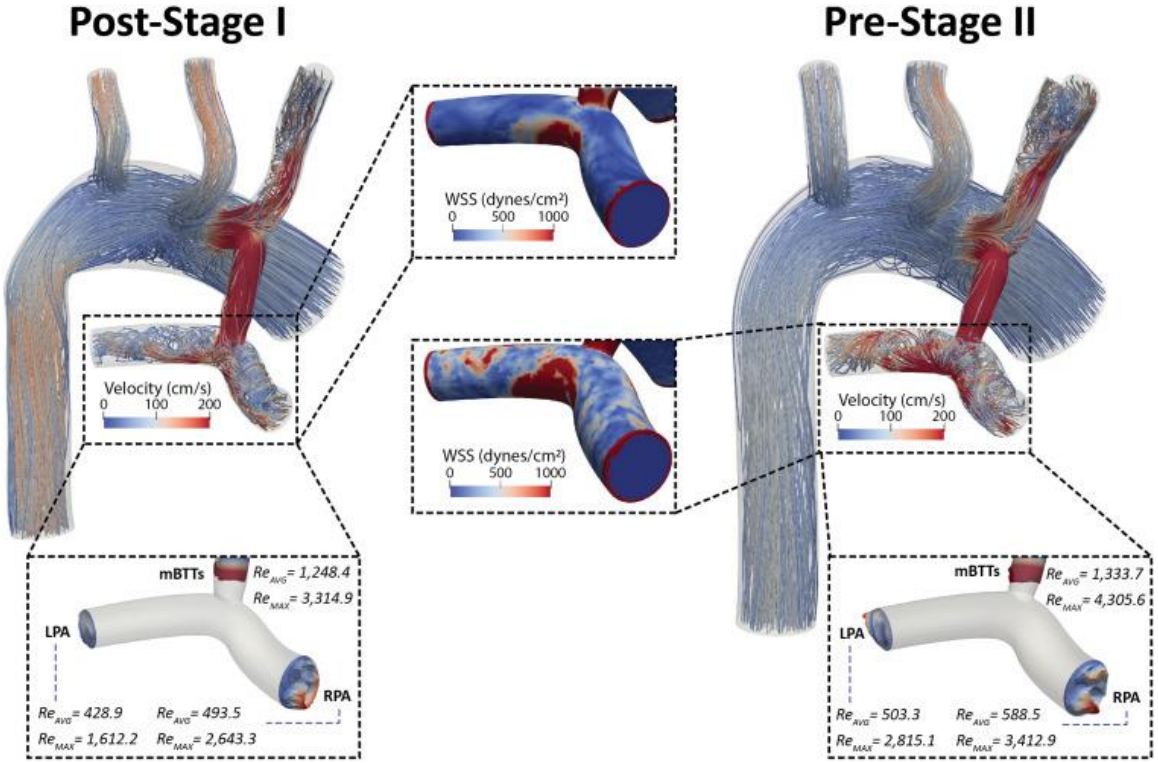
Single Ventricle Reconstruction Trial

- MBTS patients in the interstage (n=234)
- Shunt resistance = $\frac{8\mu L}{\pi r^4}$
- Lower shunt resistance associated with 1-year transplant free survival (p = .0001), even when controlling for initial shunt size
- Controlling for LPA diameter, for each WU increase in MBTS resistance, LPA diameter at stage II decreased by 0.6 mm
- Mean LPA diameter 0.39 ± 0.09 cm at Norwood and 0.44 ± 0.12 cm at stage II palliation



Spigel ZA, et al. JTCVS Open 2022;9:206-214

Disturbed Pulmonary Artery Hemodynamics



Primeaux J, et al. Frontiers in Physiology 2021;12:1-18

PA Interventions After Norwood

- 100 HLHS patients S/P Norwood from 2003-2011
  - RVPAS: 67
    - PA angioplasty in interstage: n=6, 14%
    - No PA stenting before Glenn
    - 22/44 (50%) had surgical PA patch plasty at Glenn
  - mBTS: 33
    - No catheter interventions done on PAs before or after the Glenn in 38 total procedures
    - 9/21 (43%) had surgical PA patch plasty at Glenn

Gist KM, et al. JTCVS 2013;145:1485-1492

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  - mBTS: 33
    - No catheter interventions done on PAs before or after the Glenn in 38 total procedures
    - 9/21 (43%) had surgical PA patch plasty at Glenn
  - Largest proportion of catheter-based PA interventions was performed between the BDG and Fontan procedures (32% in the RVPAS group and 0% in the mBTS group)

Gist KM, et al. JTCVS 2013;145:1485-1492

PA Interventions After Norwood

- 317 Norwood procedures between 1997 and 2014
  - 54 mBTTS
  - 82 left-sided RVPAS
  - 181 right-sided RVPAS
- 25 pts (7.9%) had catheter intervention

Table 2: Unplanned procedures in the interstage I

	No. of patients
Surgical procedure	
Sano conduit change	17
Sano conduit revision	3
mBTS instead of Sano conduit	2
mBTS change	6
Tricuspid valve repair	3
Aortic arch repair	2
Atrial thrombectomy	1
Pacemaker implantation	1
Total	35
Interventional procedure	
Aortic arch dilatation	11
RV-PAC stent (1 plus isthmus stent)	7
APCA coilings	5
LSVC coiling	1
LPA dilatation	1
Total	25

Sames-Dolzer E, et al. European J Cardio-Thorac Surg 2017;51:1044-1050

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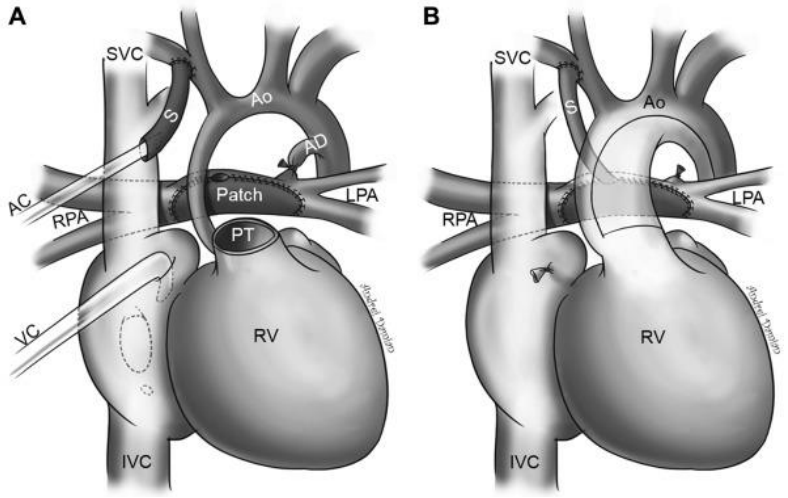
Why Isn't PA Intervention Undertaken in the Interstage?

- Need to cross shunt to intervene
- Long segment stenoses unlikely to respond to angioplasty
- Stenting is needed for most long-segment stenoses
  - Patients may not tolerate stenting through the shunt
  - Difficult to take siting angiograms through shunt
  - Only option is coronary stent that will need to be removed or fractured
  - Lack of bioresorbable stents and stents that can be dilated to adult size
- Lack of data supporting a need to intervene in the interstage and guidance as to when intervention should be undertaken for branch PS

LPA Patching During the Norwood

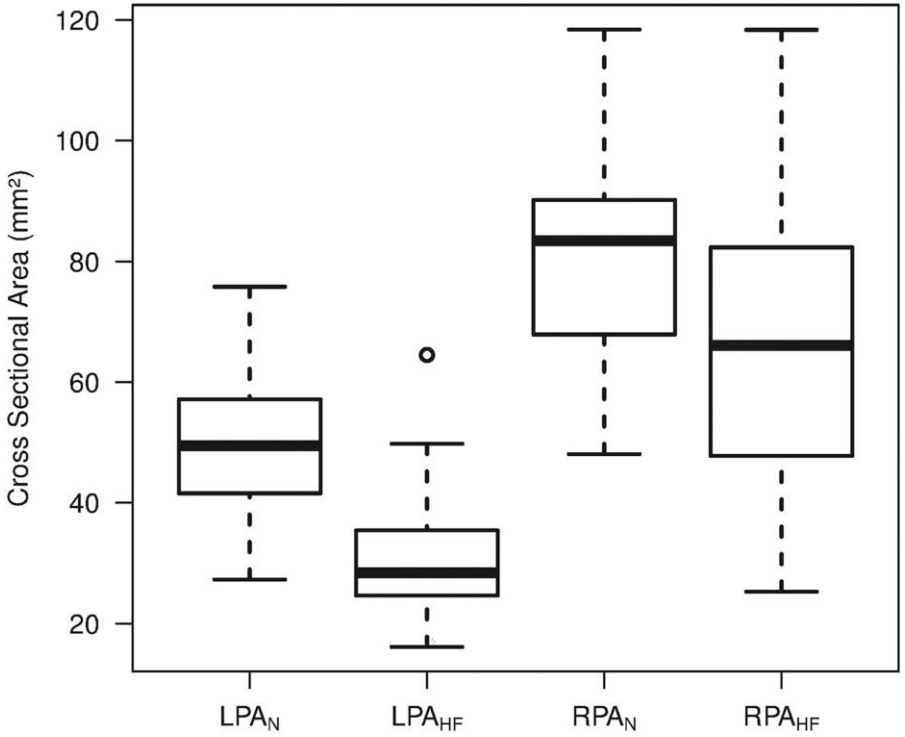
- 51 HLHS in Kiel, Germany:
  - Group N: 20 pts with LPA patch during Norwood
  - Group HF: 31 pts with LPA patch during HFP



Ravesh MS, et al. Ann Thorac Surg 2018;105:1447-54

LPA Patching During the Norwood

- 51 HLHS underwent MRI around 3 years of age:
  - Group N: 20 pts with LPA patch during Norwood
  - Group HF: 31 pts with LPA patch during HFP
  - No LPA reinterventions (surgical or cath)



Ravesh MS, et al. Ann Thorac Surg 2018;105:1447-54

Summary

- Larger PA size and even flow distribution are important for Fontan outcomes and functional status
- Nakata index, particularly of LPA, decreases over time after stage II and after Fontan, due to compression from the neo-aorta
- PA angioplasty and stenting are rarely done in the interstage, particularly after MBTS
- Larger PA size and/or decreased need for PA intervention associated with:
  - Large interaortic ratio
  - MBTS (vs. RVPAS)
  - Less shunt resistance
  - LPA patching at the Norwood stage (prior to HFP)

What Does the Future Hold?

- Bioresorbable stents
- Low profile stents that can be dilated to adult size
- Data supporting intervention on the PAs in the interstage
- The question of how transcatheter stage I with PA flow-restrictors will impact PA growth

Thank You!