Congenital Heart Center Nevada

Fetus, Children & Adults

CHC Experience with Liver Biopsy Elastography & FALD

Western Society Of Pediatric Cardiology

2019

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Disclosures

- No conflicts of interest

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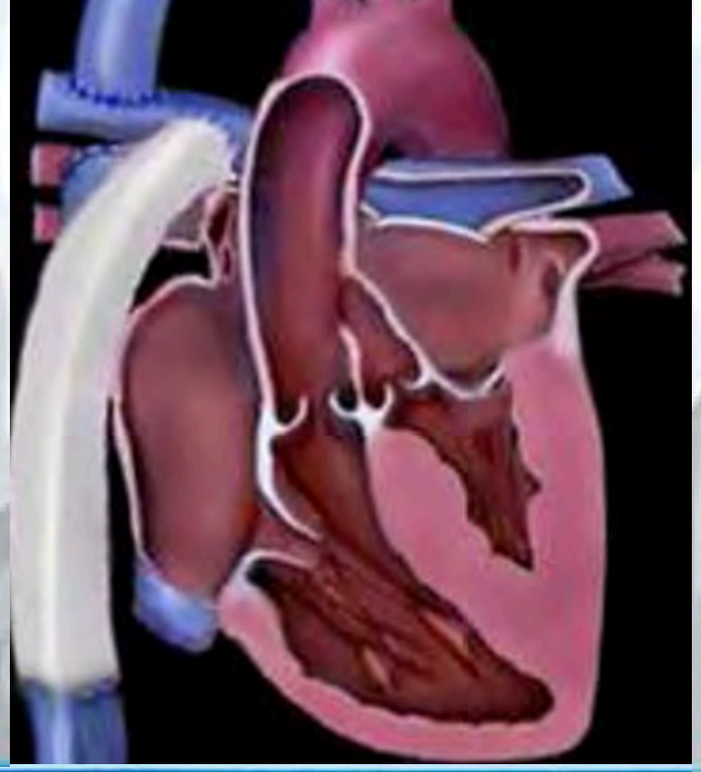
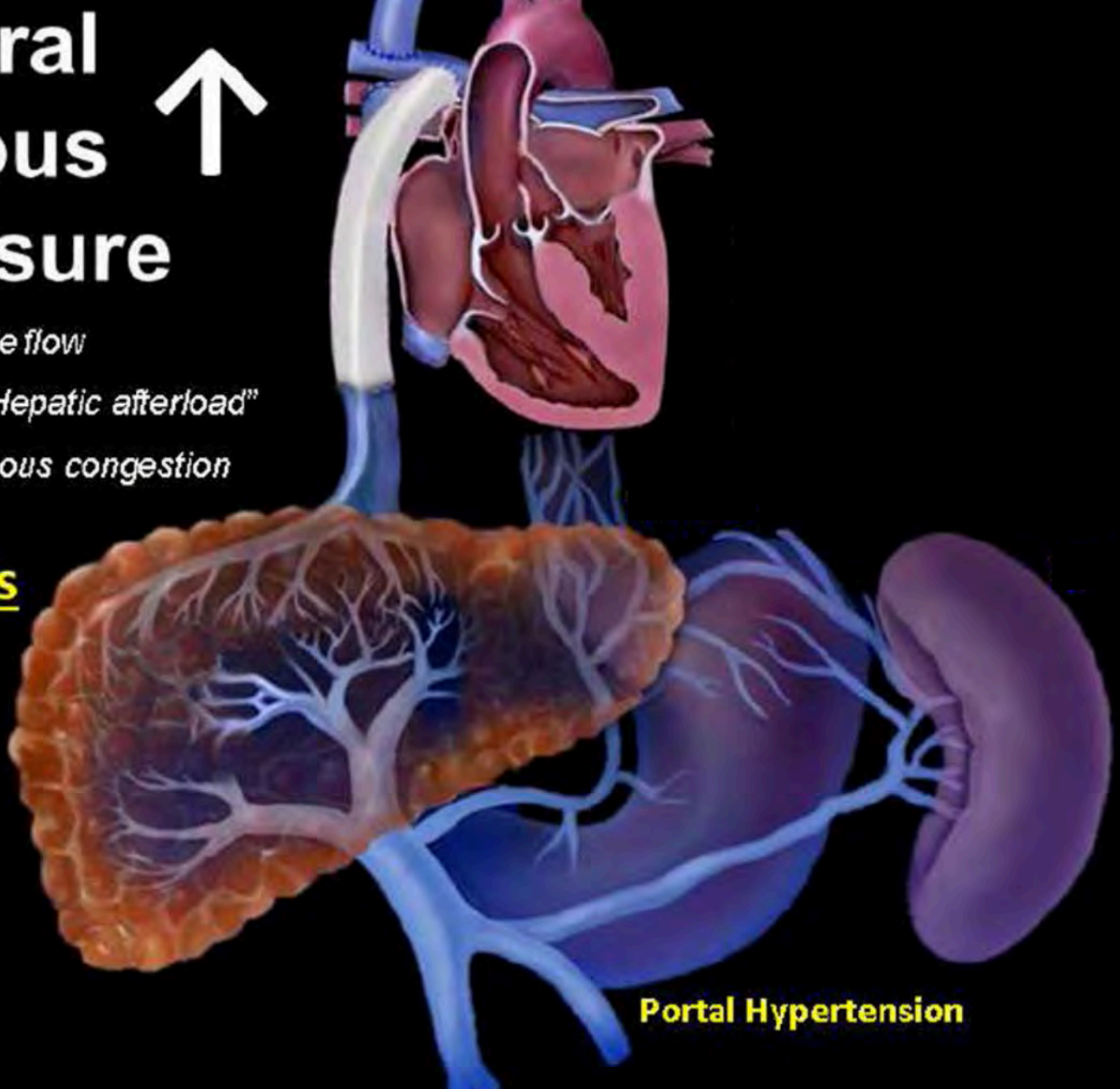


Central Venous Pressure ↑

- *Non-pulsatile flow*
- *Increased "Hepatic afterload"*
- *Passive venous congestion*

Cirrhosis



Fontan

- Increase in systemic oxygenation over Glenn

Fontan

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  - Additional source of pulmonary blood flow
  - Fenestration or not

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- Liver/gut systemic venous & portal venous congestion & HTN

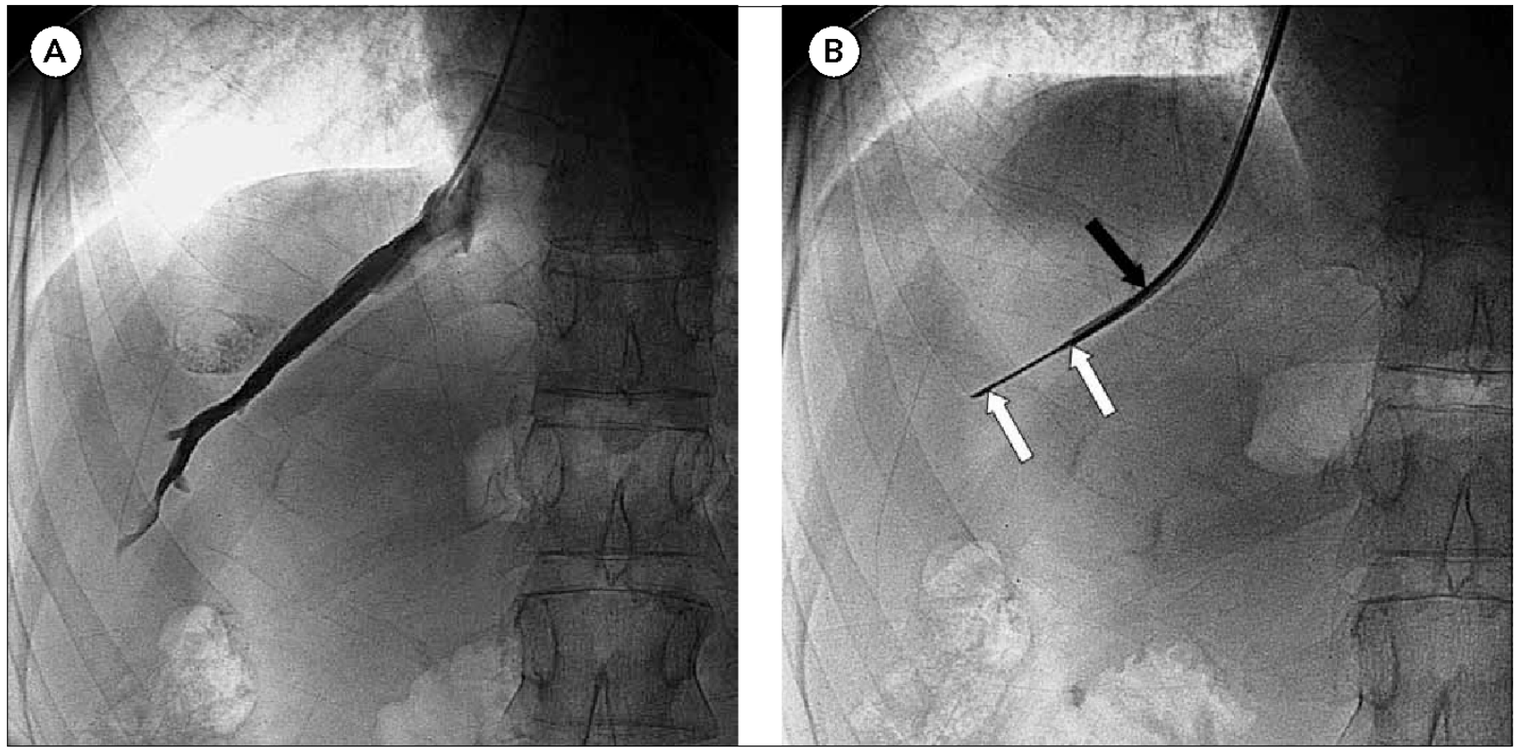
Fontan

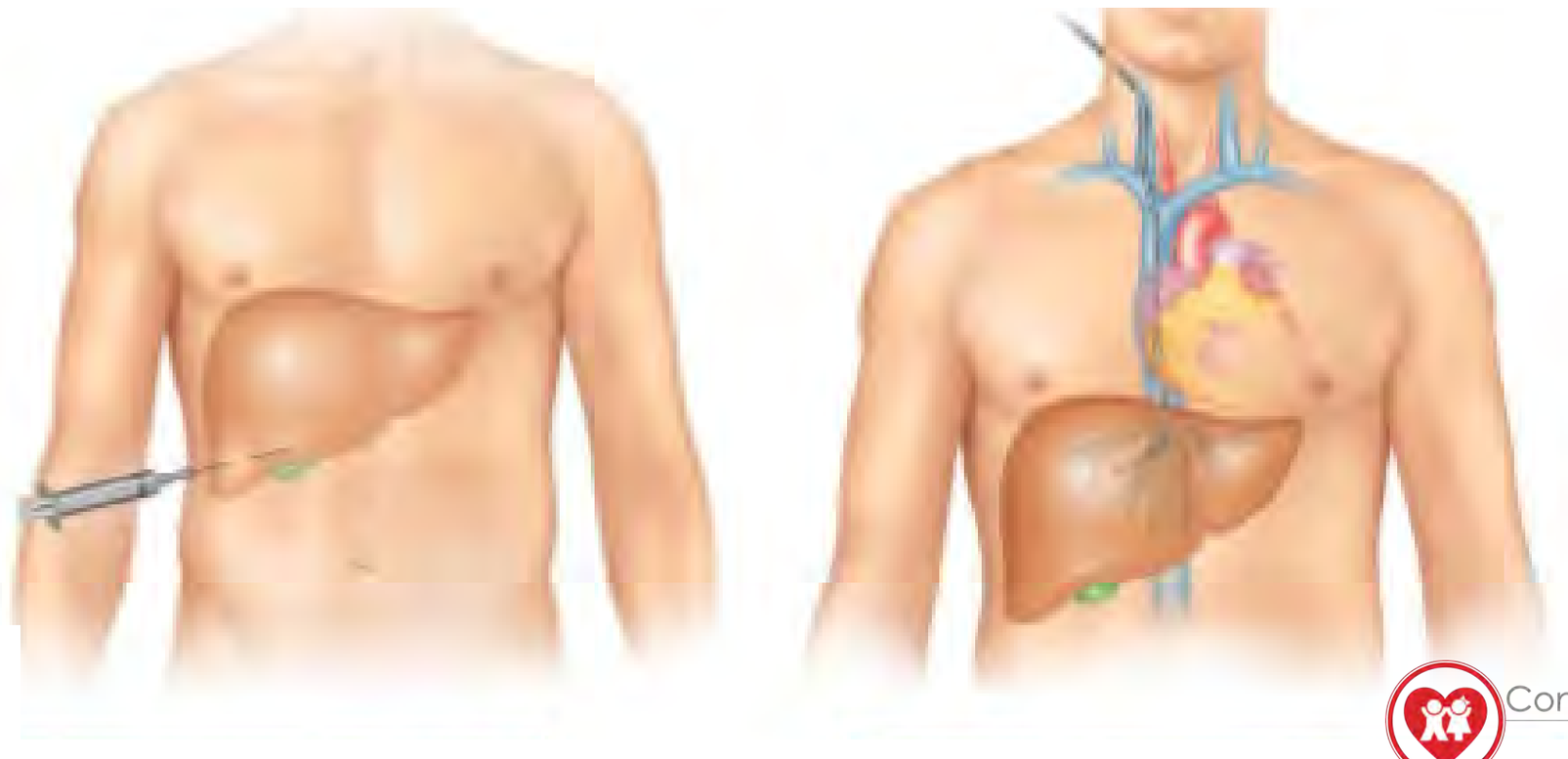
- Increase in systemic oxygenation over Glenn
  - Additional source of pulmonary blood flow
  - Fenestration or not
- Hepatic factor to the pulmonary circulation
- Liver/gut systemic venous & portal venous congestion & HTN
- FALD & PLE

FALD – Liver BX Experience

- 280
- 233 (83%) extracardiac
- 47 (17%) either lateral tunnel or AP
- 126 underwent 139 caths & transvenous liver biopsies since 2012
- No complications & no overnight stays

Transvenous Hepatic BX @ Cath





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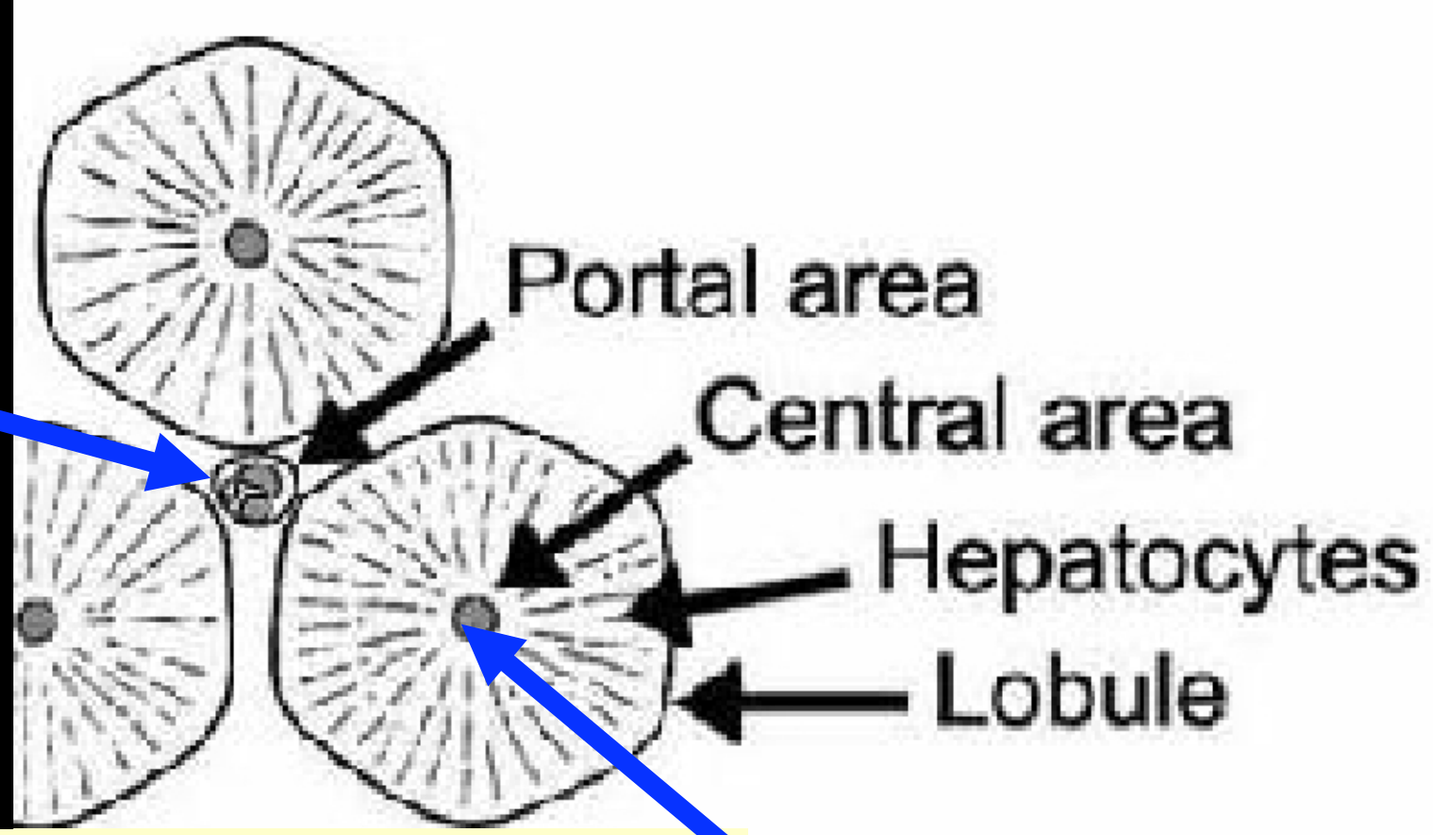


Portal triad

Central vein

bile duct

portal vein

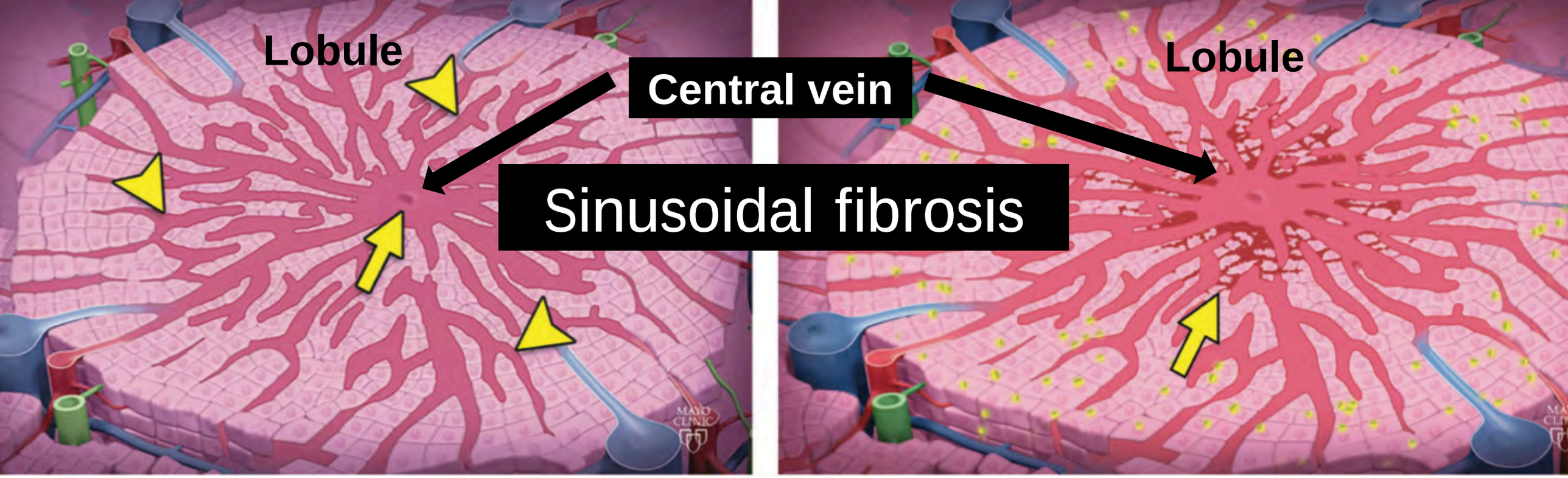
hepatic artery

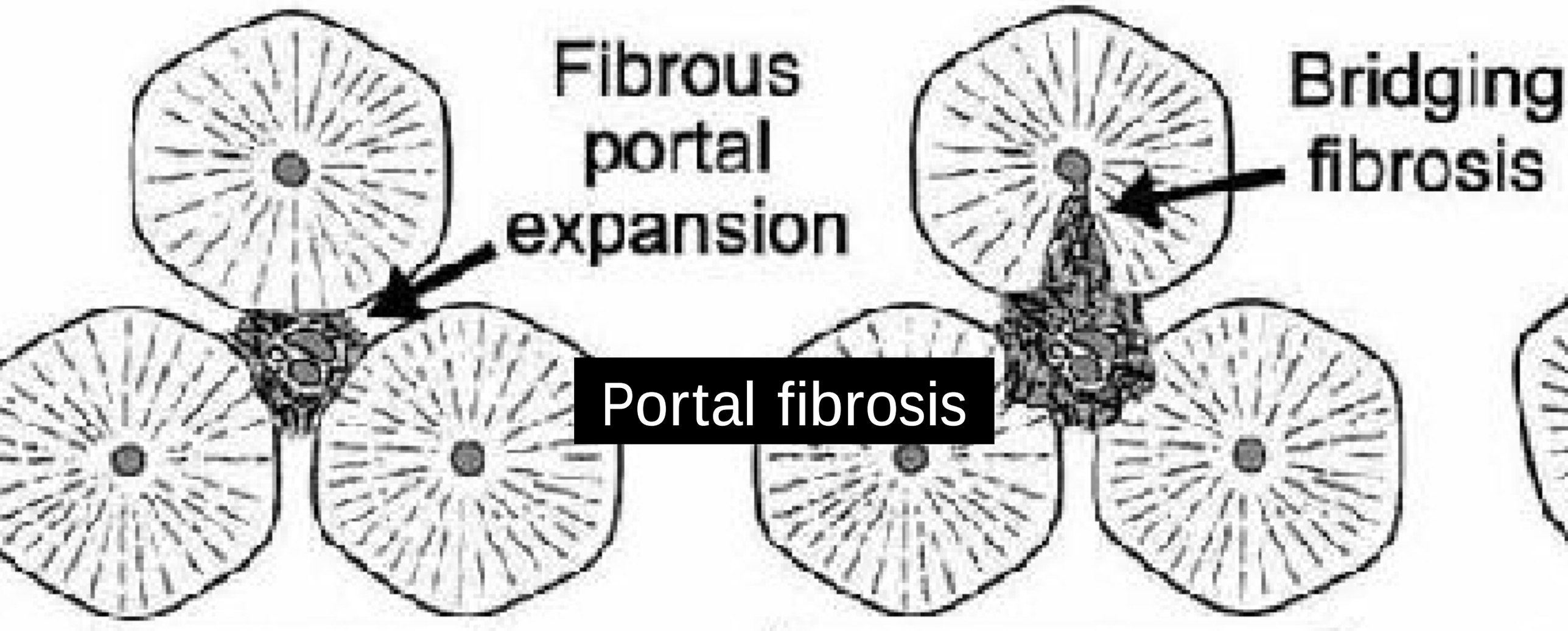
central vein

Lobule

blood flows thru sinusoids to central vein

Lobule


Lobule
Central vein
Sinusoidal fibrosis
Lobule


Fibrous portal expansion
Bridging fibrosis
Portal fibrosis

Hepatic Biopsy Fibrosis Scoring

- Sinusoidal 0-4
- Portal 0-4
- 0-none, 1-mild, 2-moderate, 3-bridging, 4-cirrhosis
- Total fibrosis score 0-8[1,2] (we use when correlating with other variables)

1. Evans WN et al (2014) Pediatr Cardiol 351273-1278
2. Poterucha JT et al (2015) Mayo Clin Proc 90:882-894

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Early Observation

- Compared 7 with neo HX obstructed Qp vs 7 with neo HX of unobstructed Qp
  - Similar age and Fontan duration
  - All NYHA 1
  - Situs solitus
  - Normal UV function and no significant AVVR
  - HX confluent PAs & Nakata > 200 mm^2/m^2
  - No Fontan connection or PA stenting
  - No pacemaker or amiodarone RX
  - No PLE
  - No differences in O2 sat, laboratory values, & hemodynamic values

Findings: statistically significantly higher TFS in those with HX of Ob Qp

Evans WN Pediatr Cardiol (2015) 36:657–661

Further Observation
n=56

- 4 Groups UV “type” and HX of neo Qp:
  - 1-LV no Qp obstruction n=10
  - 2-RV no Qp obstruction n=17
  - 3-LV yes Qp obstruction n=23
  - 4-RV yes Qp obstruction n= 6
- No differences: Fontan duration,O2 sat, pacing, UV dysFx, AVVR, IVCP, UVEDP, Qs, TPP, PVR
- Median TFS by groups:
  - 1-2*
  - 2-2
  - 3-3
  - 4-4*
  - *p = 0.031

Evans WN et al (2016) Pediatr Cardiol 37:30-36

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PLE Incidence Varies V-type & Qp HX

n=280 & 29 (10%) with PLE

UV Type & Qp obstruction n	LV No 41	RV No 99	LV Yes 96	RV Yes 44	p
PLE n (%)	2 (5%)*	6 (6%)	11 (11%)	10 (22%)*	0.04
Average Fontan Years	12	13	14	10	NS

No significant differences for: O2 sat, pacemaker, % with decreased UV fx, AVVR, IVCP, UVEDP, Qs, TPP, or PVR

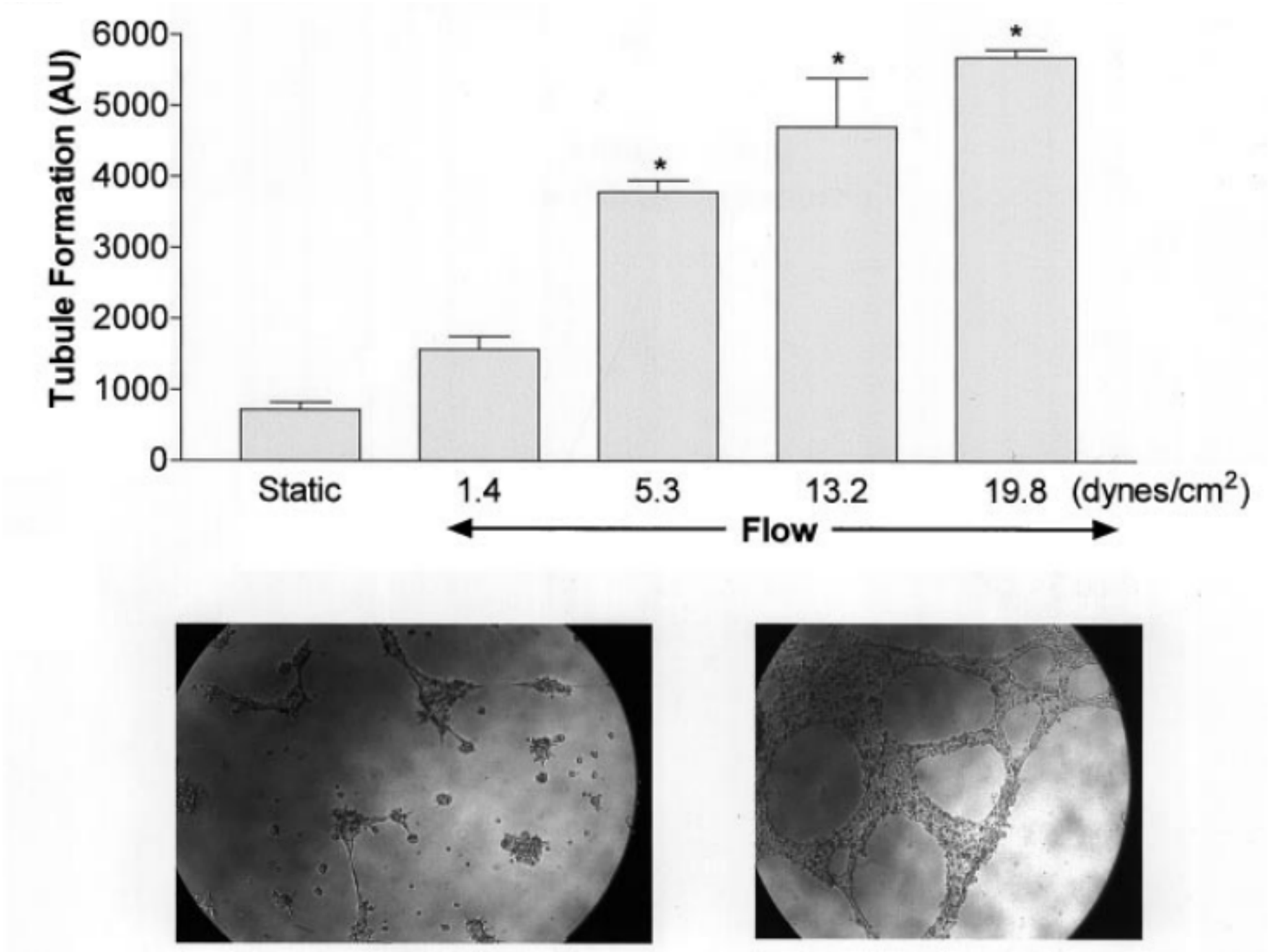
? Pulmonary Microvascular Development

- Haworth pulmonary atresia fewer intra-acinar arteries than normal
- Unobstructed pulmonary flow more intra-acinar arteries than normal
- Pulsatile pulmonary circulation - mechanotransduction - angiogenesis
- Pulmonary vascular development continues for several years
- Palliated UV no pulsatile Qp
- Fontan circuit “impedance” rather than “crude” Fick generated PVR
  - Direct IVC-Fontan recording of pressure and Doppler flow + offline Fourier transformation

Haworth SG, Reid L (1977) Quantitative structural study of pulmonary circulation in the newborn with aortic atresia. Thorax 32:121–128

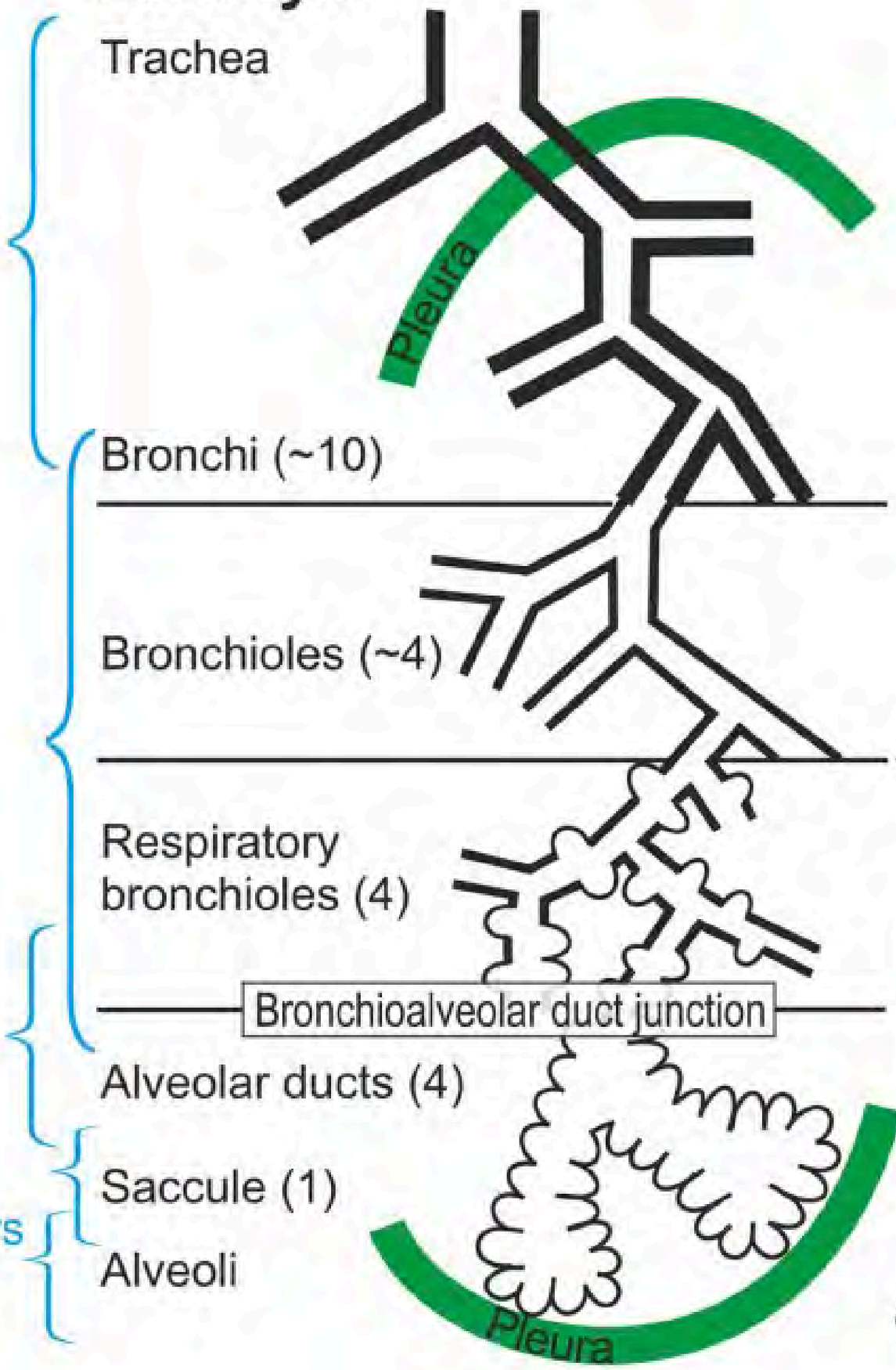
77) Quantitative structural study of pulmonary circulation in the newborn with pulmonary atresia. Thorax 32:129–133

Mechanotransduction-Angiogenesis



Cullen JP et al (2002) Arterioscler Thromb Vasc Biol 22:1610-1616

Airways



Arteries / Capillaries

Extrapulmonary artery
34 days

Lobular artery
44 days

Pre-acinar arteries
(conventional + supernummeraries)
5-17 weeks

Intra-acinar arteries
18-25 weeks

Alveolar duct arteries
25 weeks - 18 months postnatal

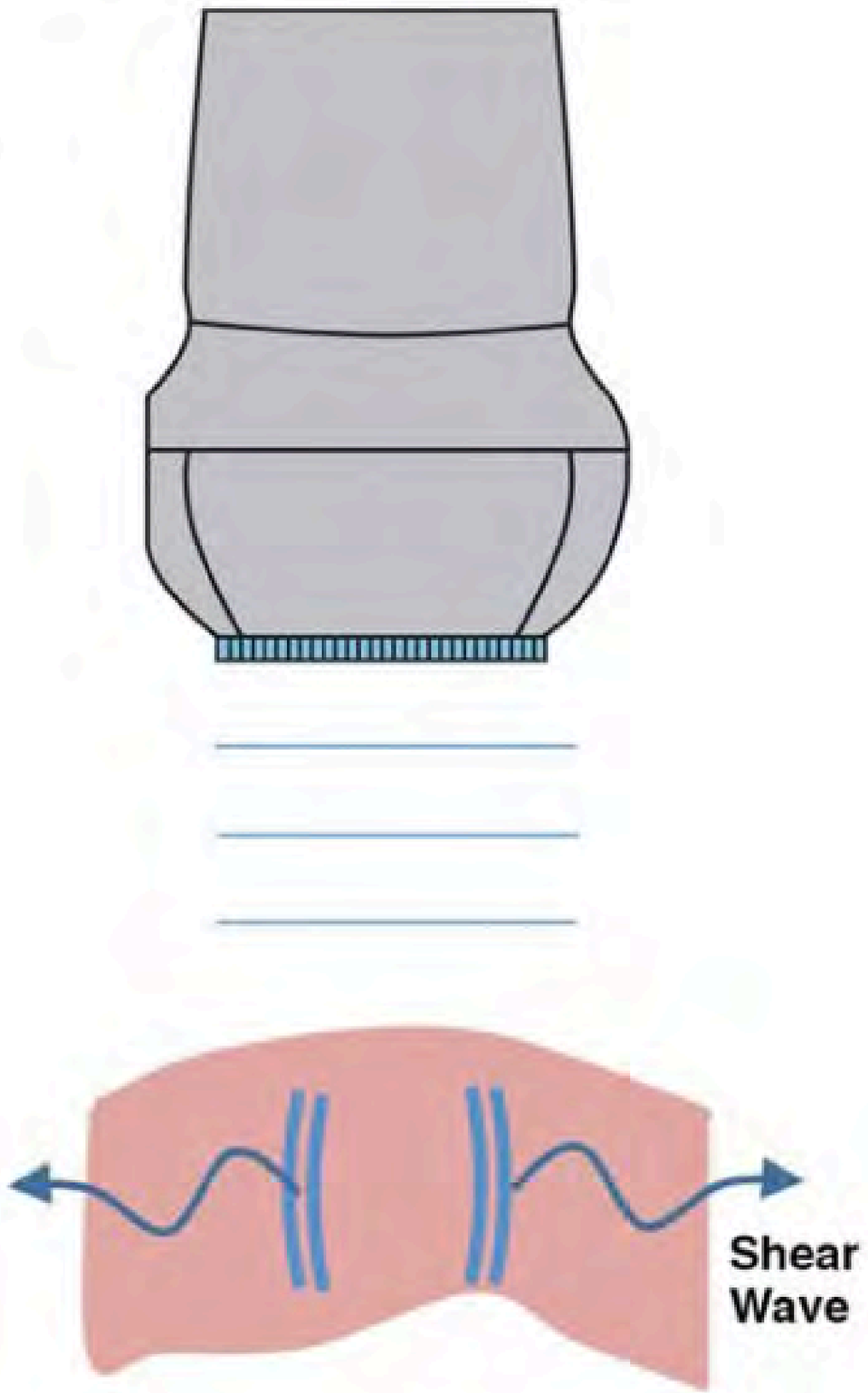
Microvascular maturation
36 weeks - ~21 years

Alveolar Capillaries
36 weeks - ~21 years

Following FALD

- Early and even advanced may have normal labs
- Invasive procedures infrequent
- Liver BX actually semiquantitative and subject to pathologist experience
- Non invasive methods
- MRI and ultrasound elastography

Shear Wave Elastography-Stiffness



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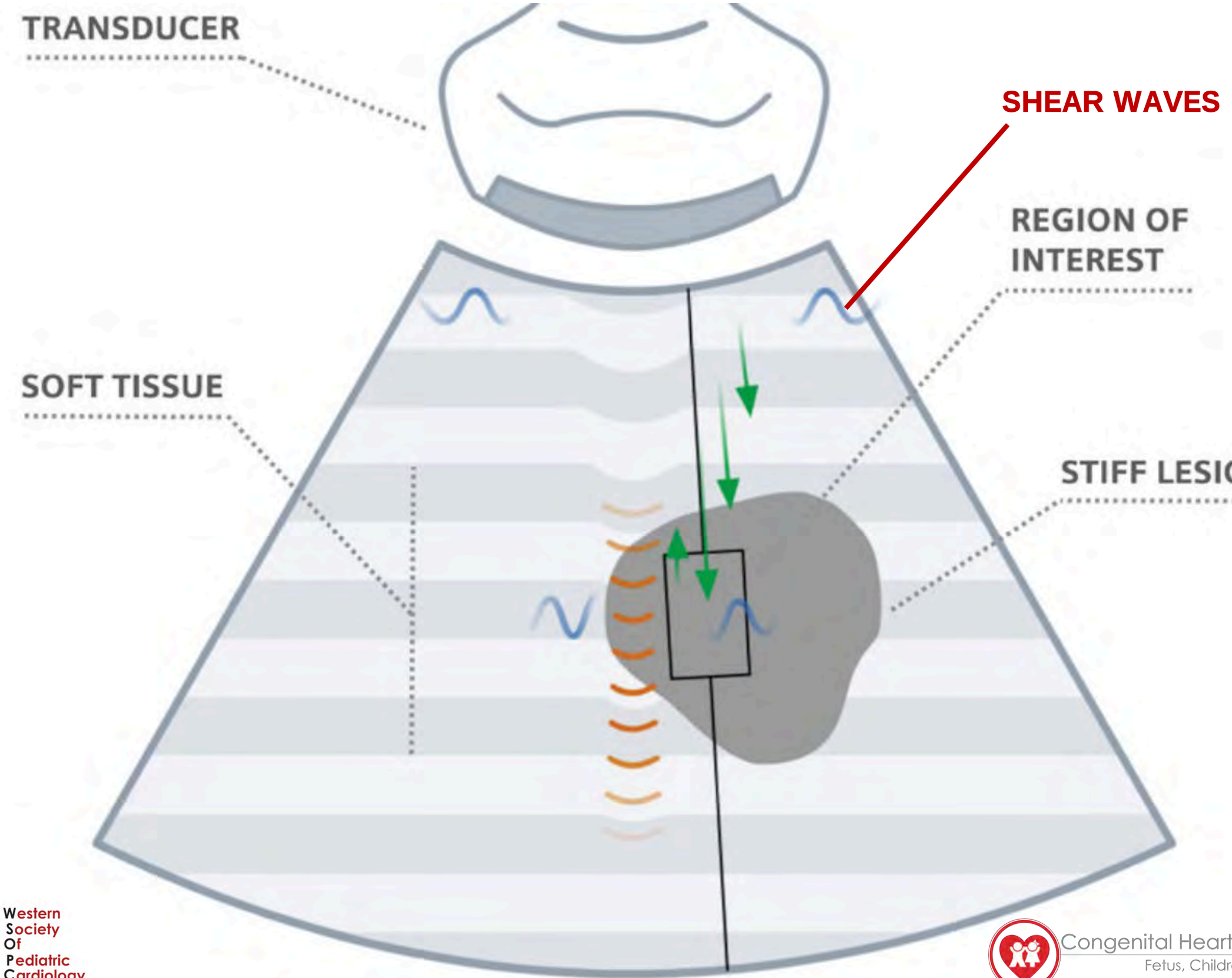
Shear Wave Elastography-Stiffness

- Stiffness in m/sec
  - Normal shear wave velocity ~1 m/sec
  - Cirrhosis shear wave velocity > 2 m/sec
- Stiffness in kPa
  - Normal ~ 3-5 kPa
  - Cirrhosis > 12 kPa
  - kPa ≈ 3 x SWV^2
- Baseline Fontan with congestion & no fibrosis may be higher than 5 kPa

US Shear Wave Elastography



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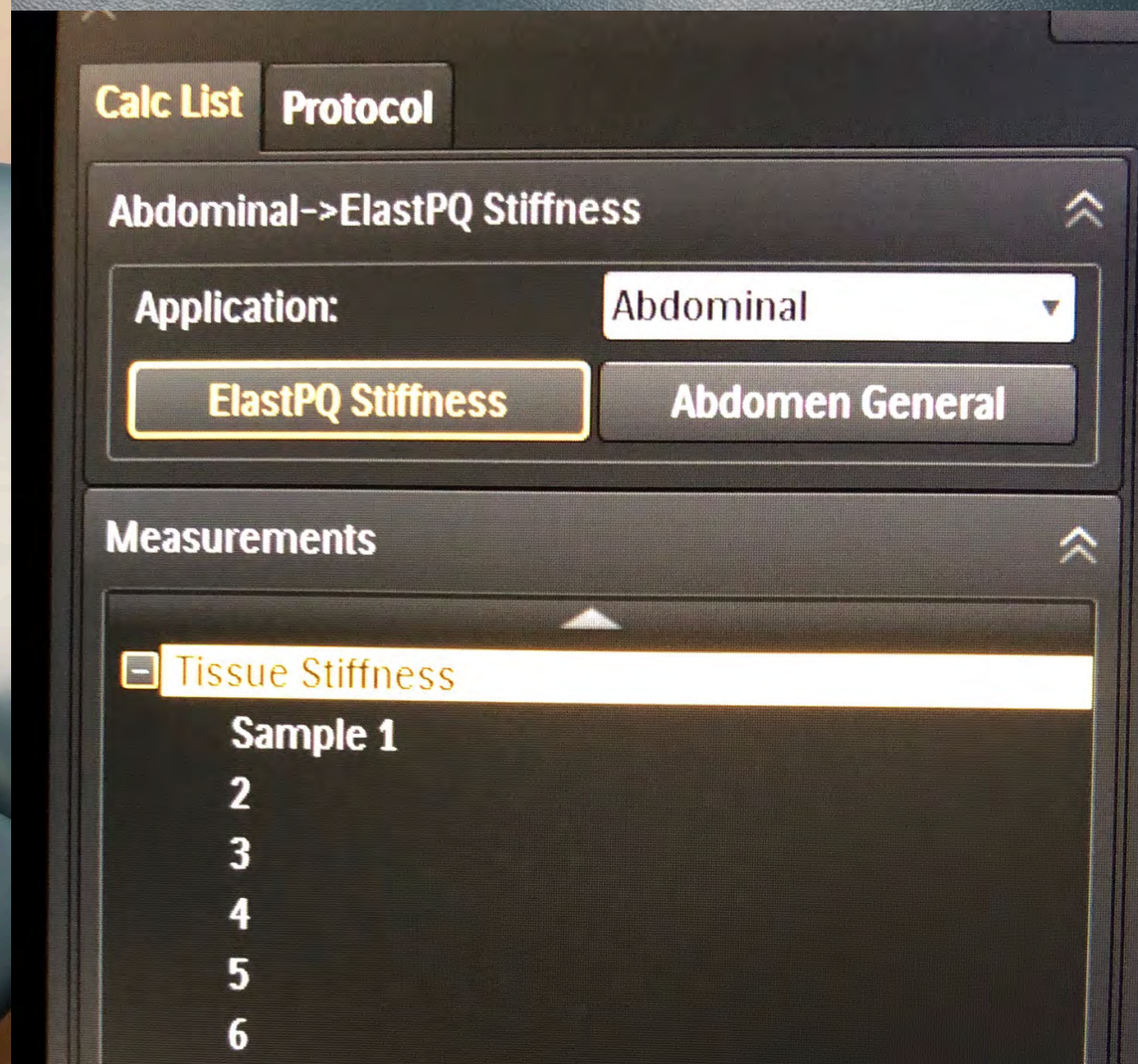
PHILIPS


C5-1
PHILIPS
PureWave


Calc List
Protocol
Abdominal->ElastPQ Stiffness
Application:
Abdominal
ElastPQ Stiffness
Abdomen General
Measurements
Tissue Stiffness
Sample 1
2
3
4
5
6

B
C5-1
16Hz
RP

2D
74%
Dyn R 55
P Med
Gen

ELASTPQ:
RP
68.3Hz

TIS0.2 MI 1.3

M3 M2

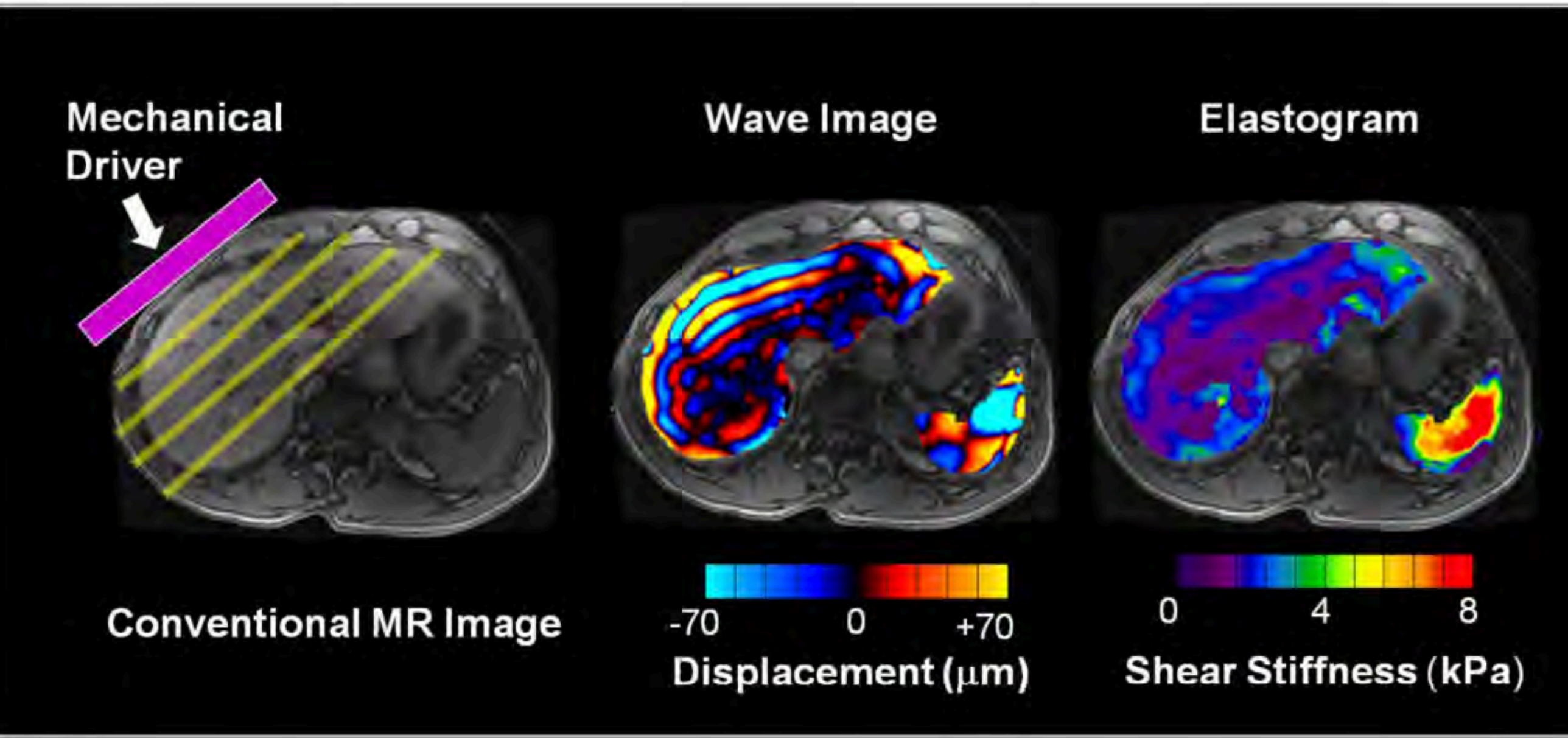
X3

G
P
R

6.99 ± 0.67 kPa

16cm

MRI Elastography



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MRI VS Ultrasound Elastography

- MRI maps large regions of the liver
- MRI less operator dependent than ultrasound
- Can include in abdominal MRI protocols for fat, focal disease, and varices
- MRI Can stage liver fibrosis or diagnose mild fibrosis with more accuracy
- **BUT** MRI facility based & ultrasound clinic based
- NV Medicaid - ultrasound elas: $32 vs MRI abd+elas: $175

Noninvasive Composite Indexes for Non-FALD fibrosis (many others)

- Fibro-Stiffness index = 5.7710 - 0.2662 [LS (kPa)] + 0.0749 [platelet count (× 10^4 /mL)] + 0.0560 [prothrombin time (%)]

- Forns index = (7.811 - 3.131 x ln(PLT count) + 0.781 x ln(gamma glutamyl-transferase (GGT)) + 3.467 x ln(age) - 0.014 x (cholesterol))

- FIB-4 index = age ([yr] x AST [U/L]) / ((PLT [10^9/L]) x (ALT [U/L])(1/2))

Attempt at a FALD Composite Index

Received: 24 July 2017 | Revised: 3 October 2017 | Accepted: 15 October 2017

DOI: 10.1111/chd.12558

ORIGINAL ARTICLE

WILEY Congenital Heart Disease

A composite noninvasive index correlates with liver fibrosis scores in post-Fontan patients: Preliminary findings

William N. Evans MD[1,2] | Ruben J. Acherman MD[1,2] | Michael L. Ciccolo MD[1,3] |
Sergio A. Carrillo MD[1,3] | Alvaro Galindo MD[1,2] | Abraham Rothman MD[1,2] |
Gary A. Mayman MD[1,2] | Elizabeth A. Adams MD[1,2] | Leigh C. Reardon MD[1,4] |

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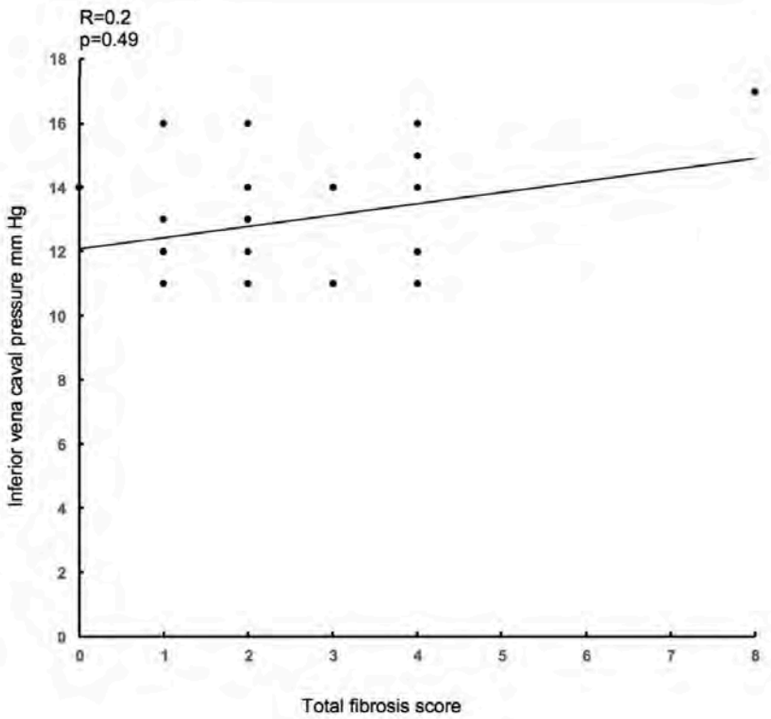
Attempt at a FALD Composite Index

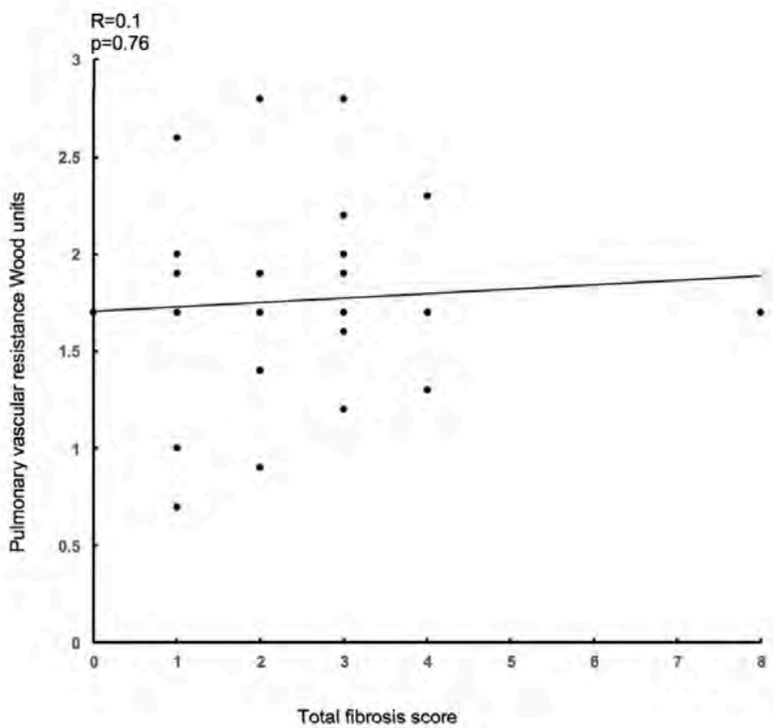
- 79 patients 86 caths & transvenous liver biopsies since 2012
- 30 with elastography

TFS vs Hemodynamic Values

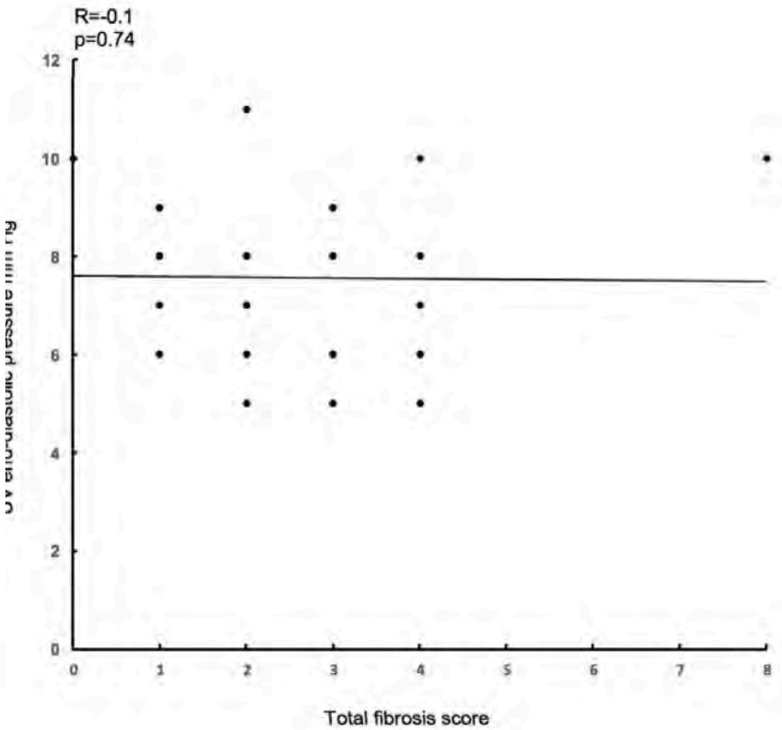
TFS vs IVCP
p=0.49



TFS vs PVR
p=0.76



TFS vs UVEDP
P=0.74



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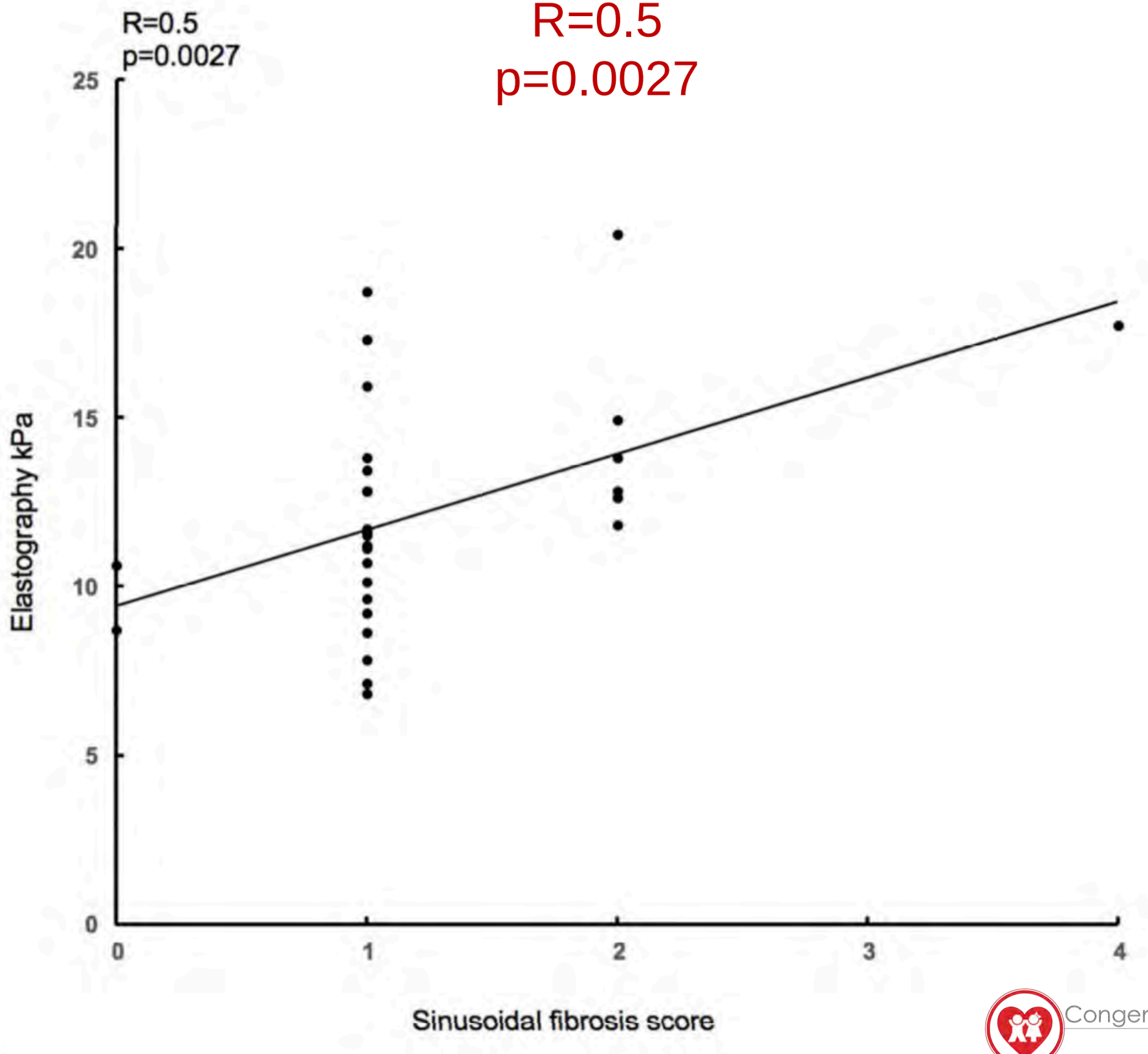
Sinusoidal Fibrosis vs Elastography



R=0.5
p=0.0027

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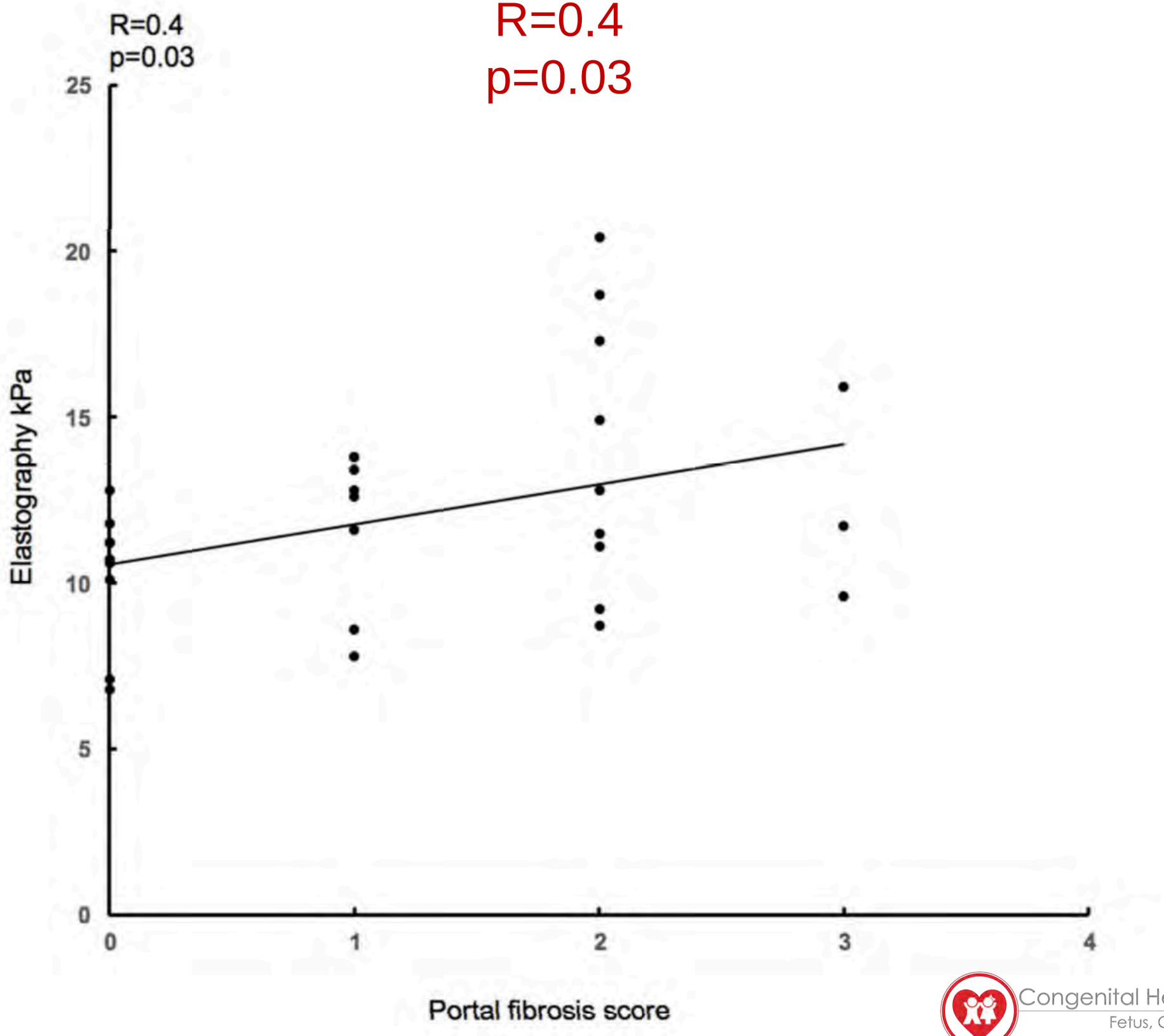
Portal Fibrosis vs Elastography

R=0.4
p=0.03



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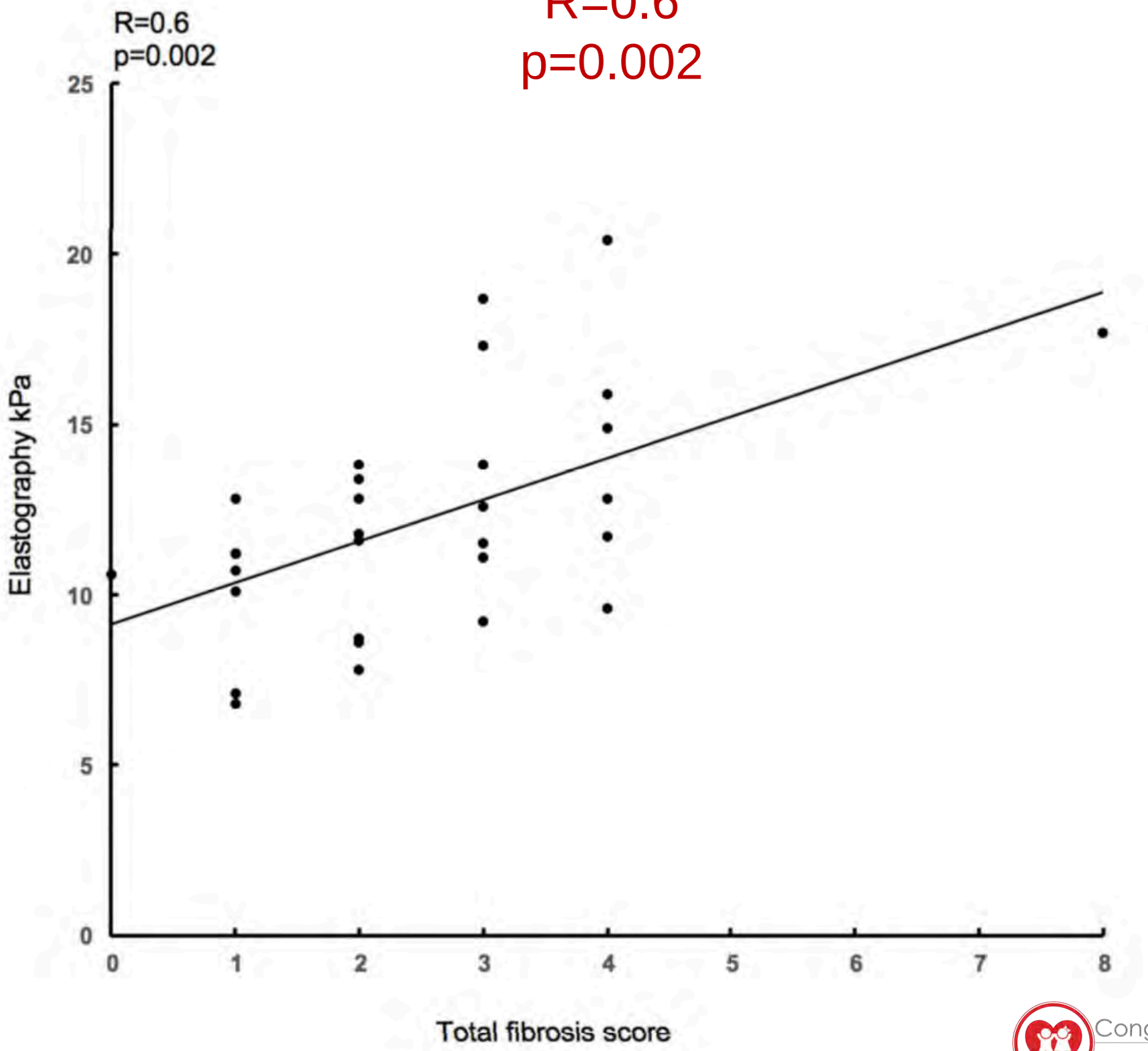
TFS vs Elastography

R=0.6
p=0.002



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MELD Scores

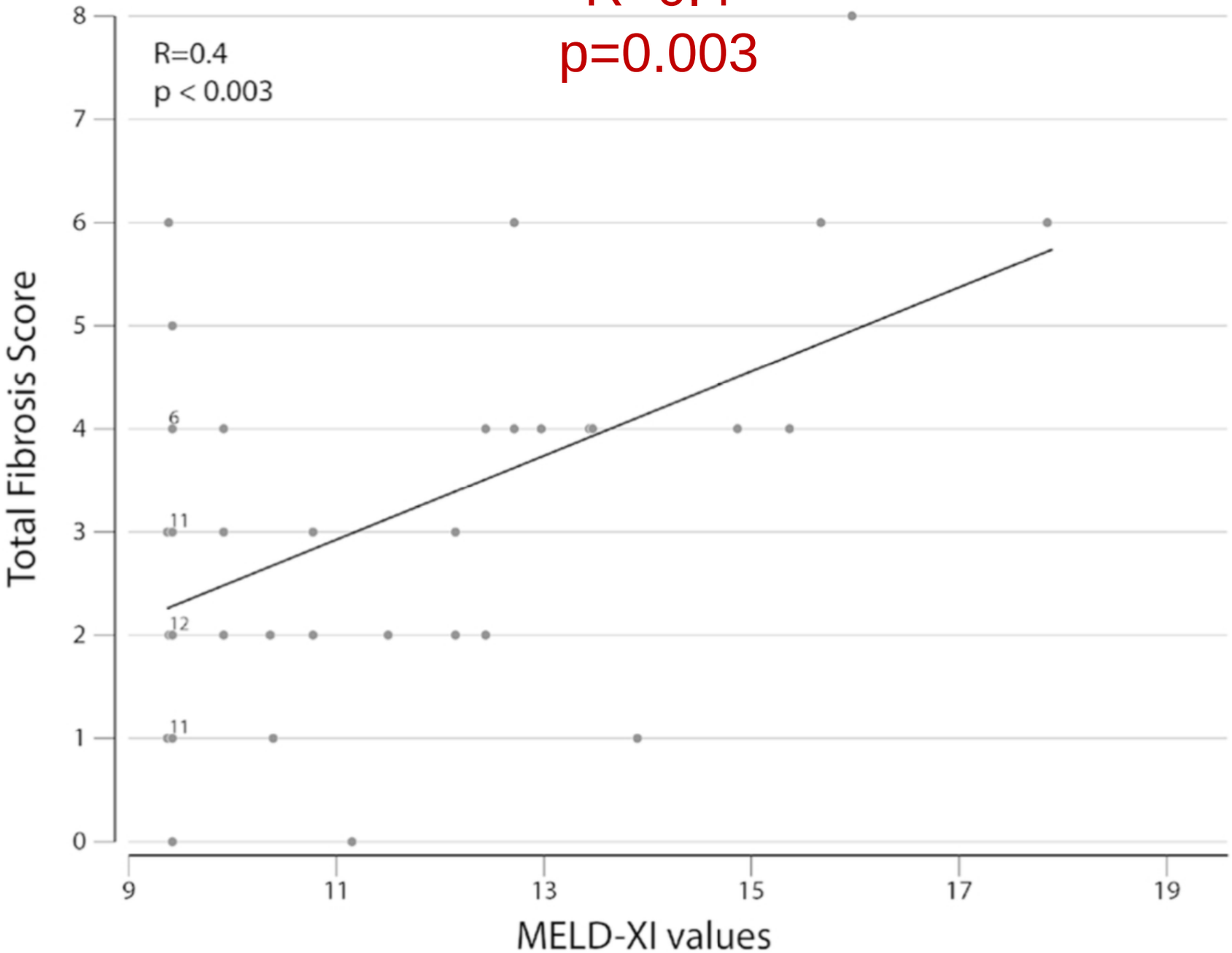
- The model for end-stage liver disease (MELD) & MELD-XI
- Formula: creatine, bilirubin, INR[1]
- XI excluding INR[2]
- MEDL-XI (5.11 x ln(total bili mg/dL) + 11.76 x ln(creatinine mg/dL) + 9.44)
- We compared TFS versus MELD-XI

1. Kamath PS et al (2001) Hepatology 33:464–470

2. Heuman DM et al (2007) Liver Transpl 13:30–37

TFS vs MELD-XI values

R=0.4
p=0.003



Evans WN (2016) Pediatr Cardiol 37:1274-1277

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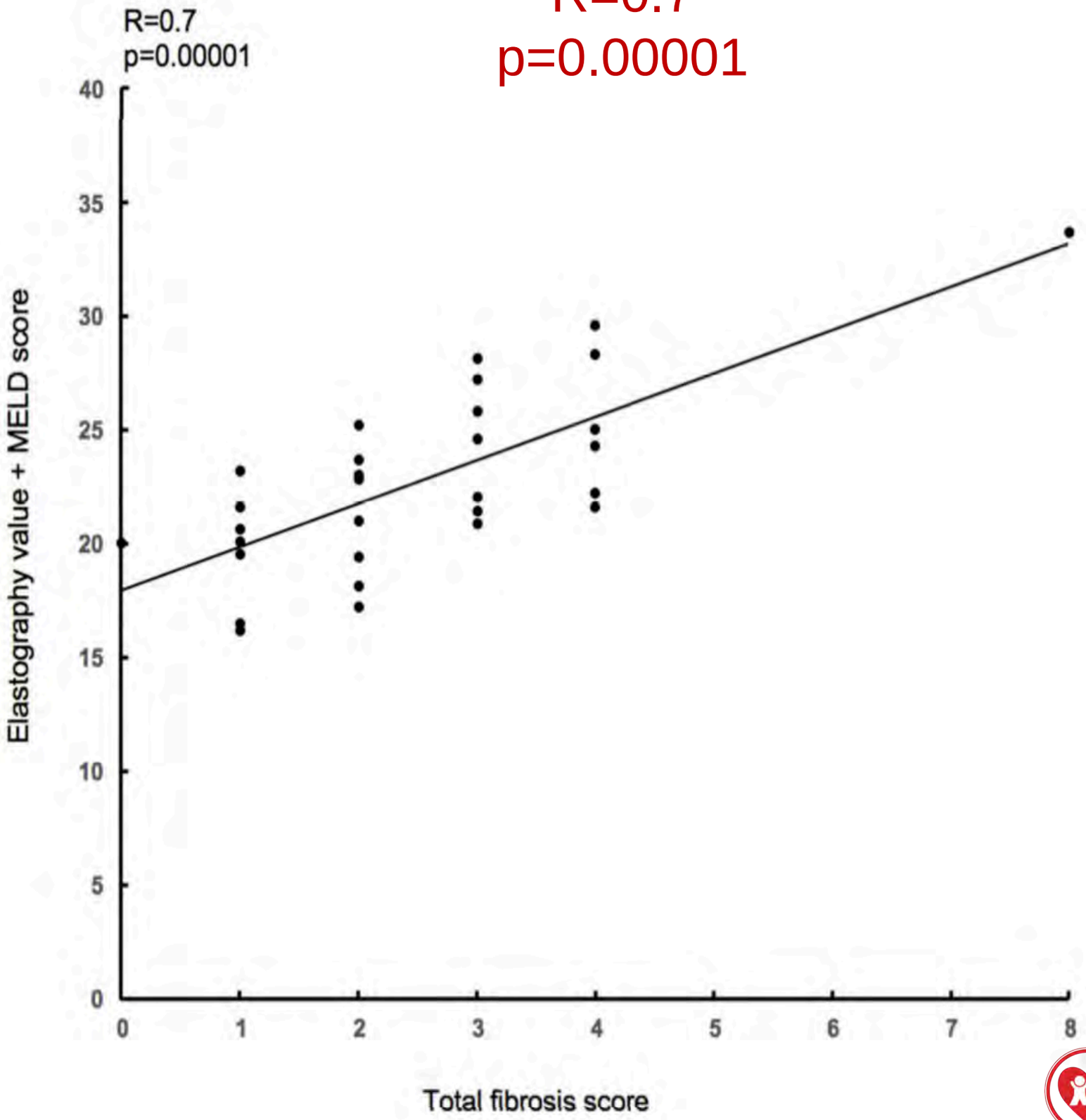
TFS vs Elastography (kPa) + MELD-XI

R=0.7
p=0.00001



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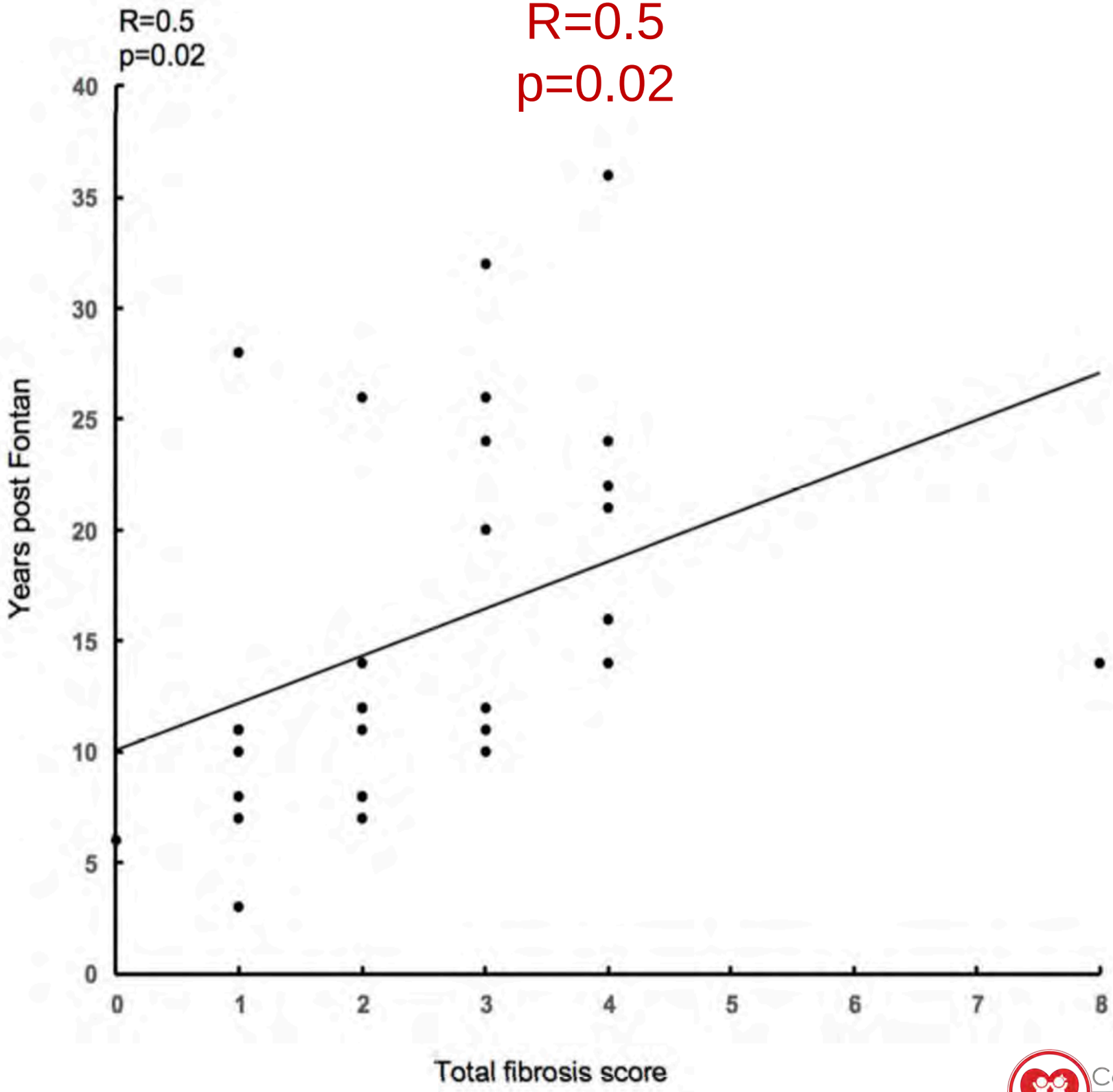
TFS vs Fontan Duration



R=0.5
p=0.02

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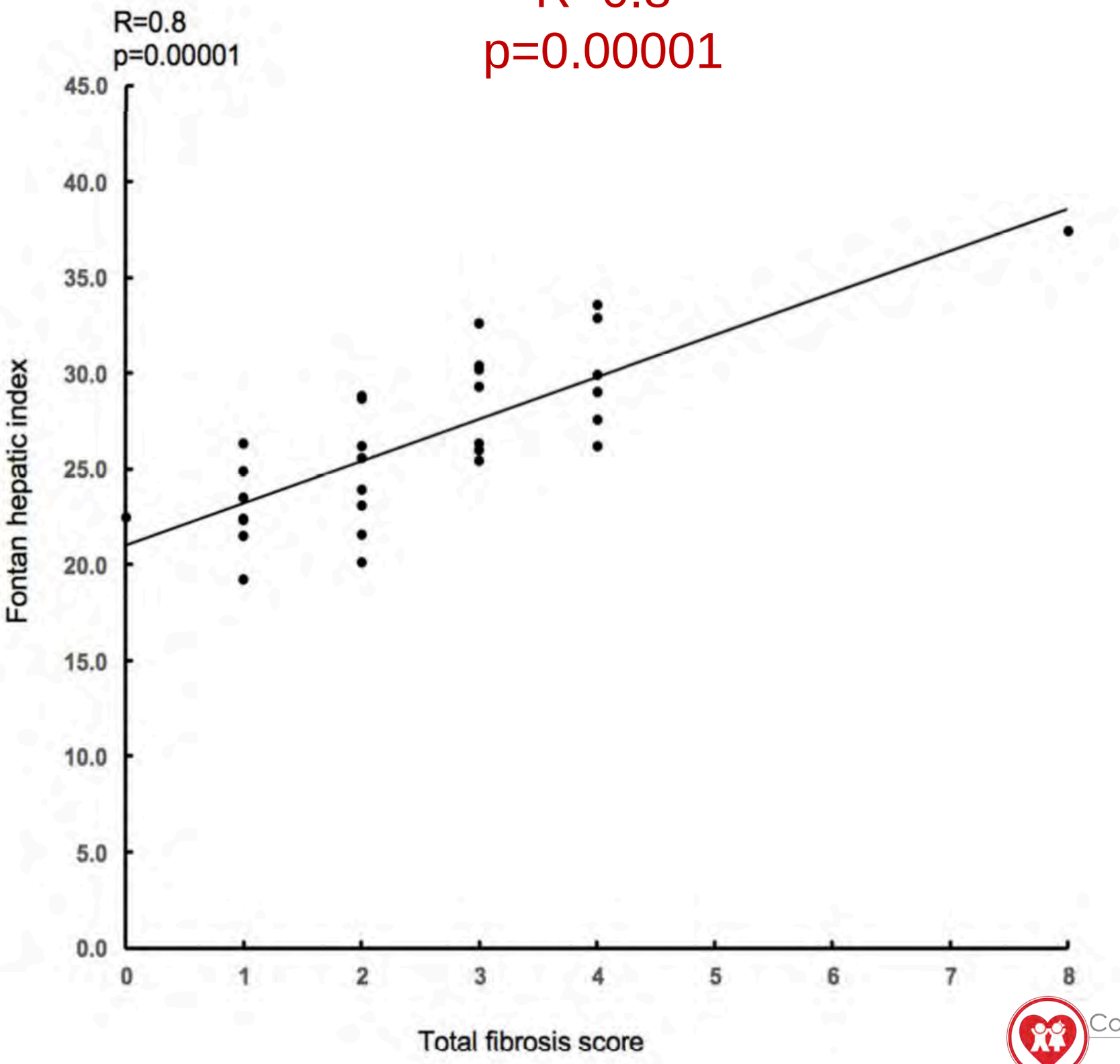
TFS vs Elas (kPa)+MELD-XI+√F Years

R=0.8
p=0.00001



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2019 paper

- 126 underwent 139 caths & transvenous liver biopsies
- 40 with elastography
- Attempt to refine FHI & validate cut off values for mild, mod, severe fibrosis

2019 paper

TABLE 1

Fontan type	N=40	Male n (%)	Arterial saturation	PLE n (%)	PM n (%)
EC ↑QP	10 (25%)	7 (70)	94	0	1 (10)
EC ↑QP/HLH	9 (23%)	6 (67)	91	1 (11)	1 (11)
EC ↓QP	7 (18%)	4 (57)	90	1 (14)	0
LT/AP ↑QP	9 (23%)	6 (67)	92	0	3 (33)
LT/AP ↓QP	5 (13%)	3 (60)	92	1 (20)	1 (20)

2019 paper

TABLE 1

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LT/AP ↑QP	9 (23%)	6 (67)	92	0	3 (33)
LT/AP ↓QP	5 (13%)	3 (60)	92	1 (20)	1 (20)

pacemakers: EC 2/26 (8%) vs LT/AP 4/15 (27%) p=0.33

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2019 paper

TABLE 2

Fontan type	n	Av TFS	Av kPa	Av Yrs F to E	Av TFS/Yrs F to E
EC ↑QP	10	1.7*	10.2*	11	0.15/y
EC ↑QP/HLH	9	2.2	11.1	11	0.20/y
EC ↓QP	7	3.1*	14.6*	12	0.26/y
LT/AP ↑QP	9	2.2	10.7	21	0.10/y
LT/AP ↓ QP	5	2.6	11.4	20	0.13/y
		*p=0.03	*p=0.009		

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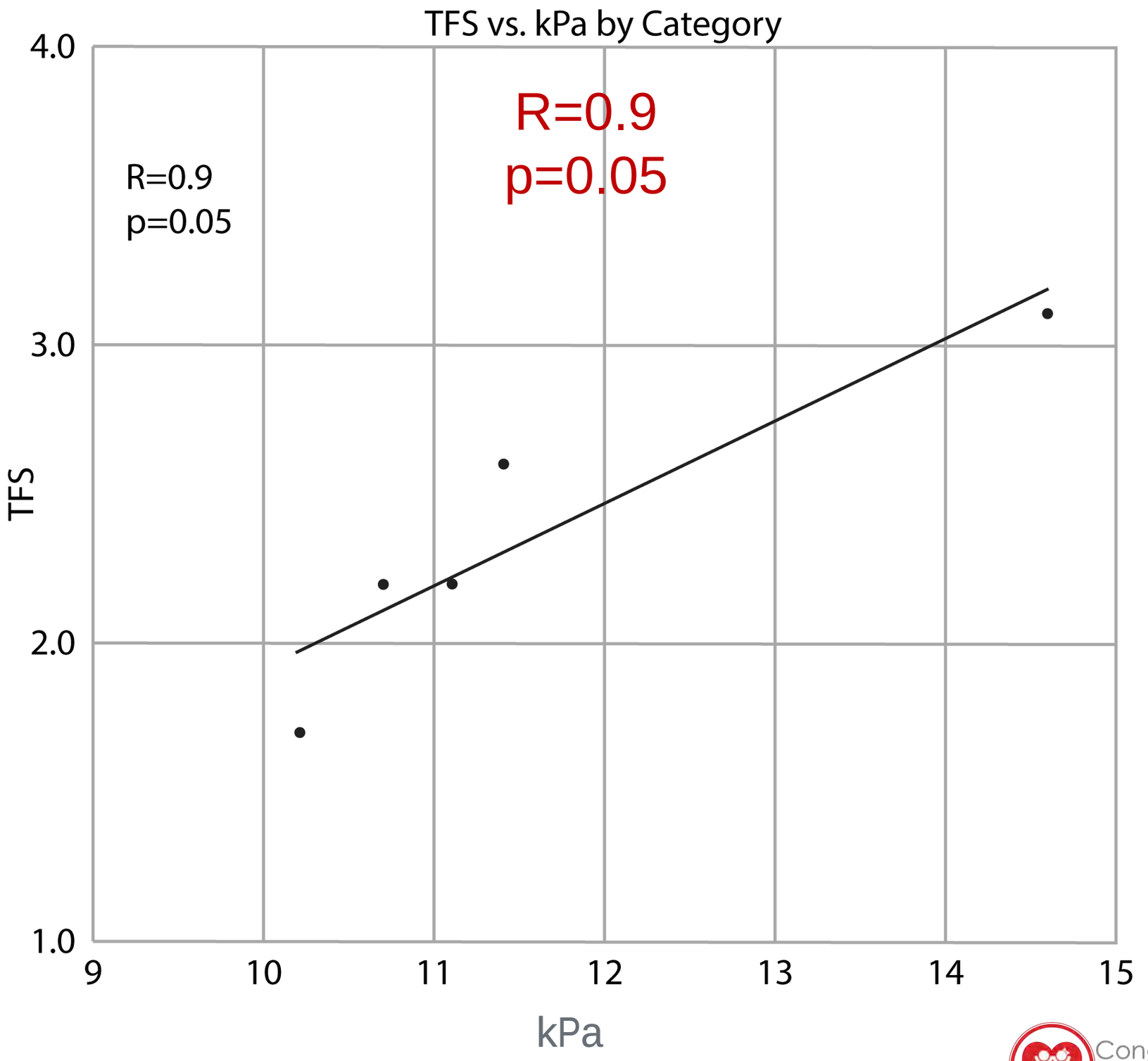

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2019 paper

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EC ↑QP/HLH	9	2.2	11.1	11	0.20/y
EC ↓QP	7	3.1*	14.6*	12	0.26/y
LT/AP ↑QP	9	2.2	10.7	21	0.10/y
LT/AP ↓ QP	5	2.6	11.4	20	0.13/y
		*p=0.03	*p=0.009		

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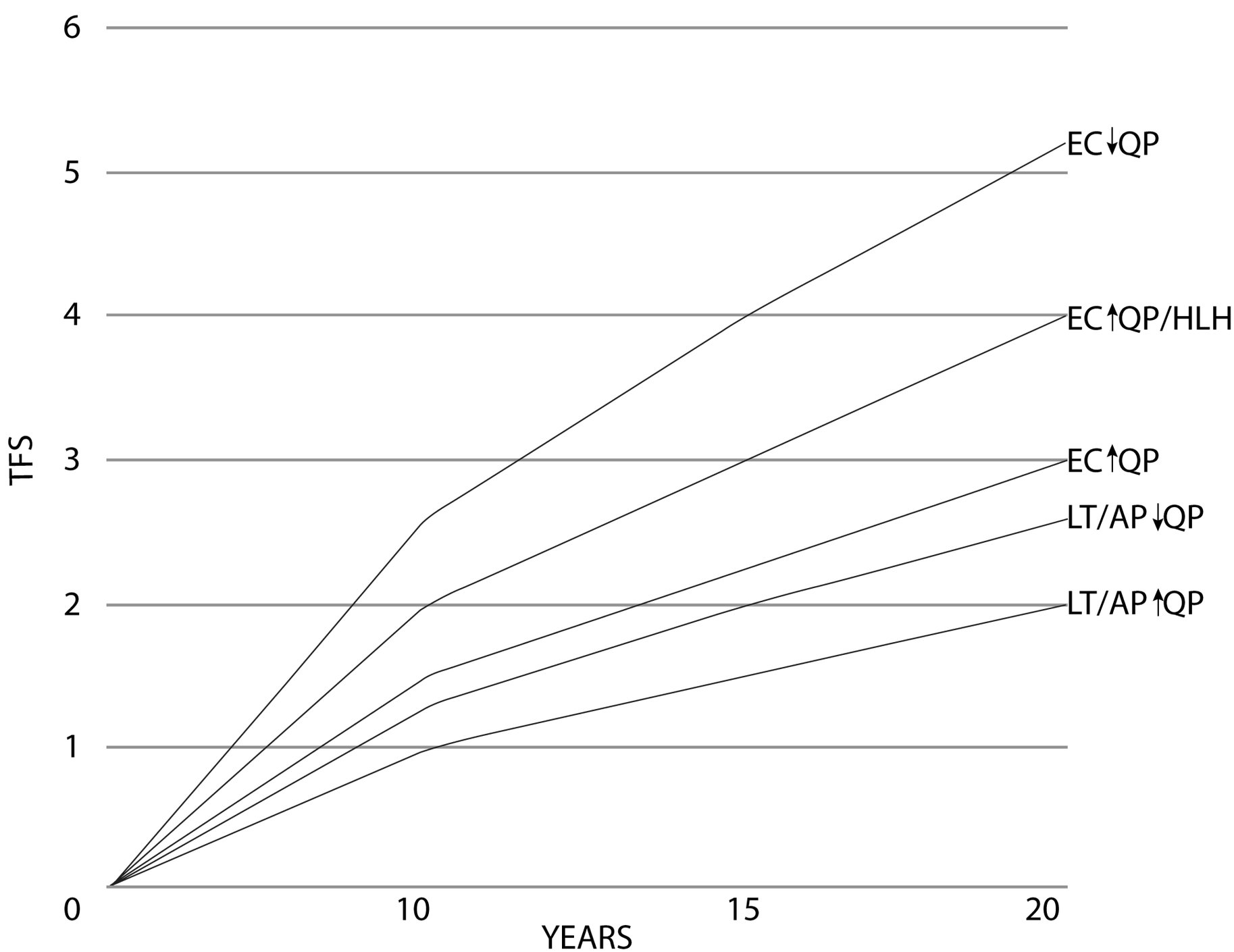

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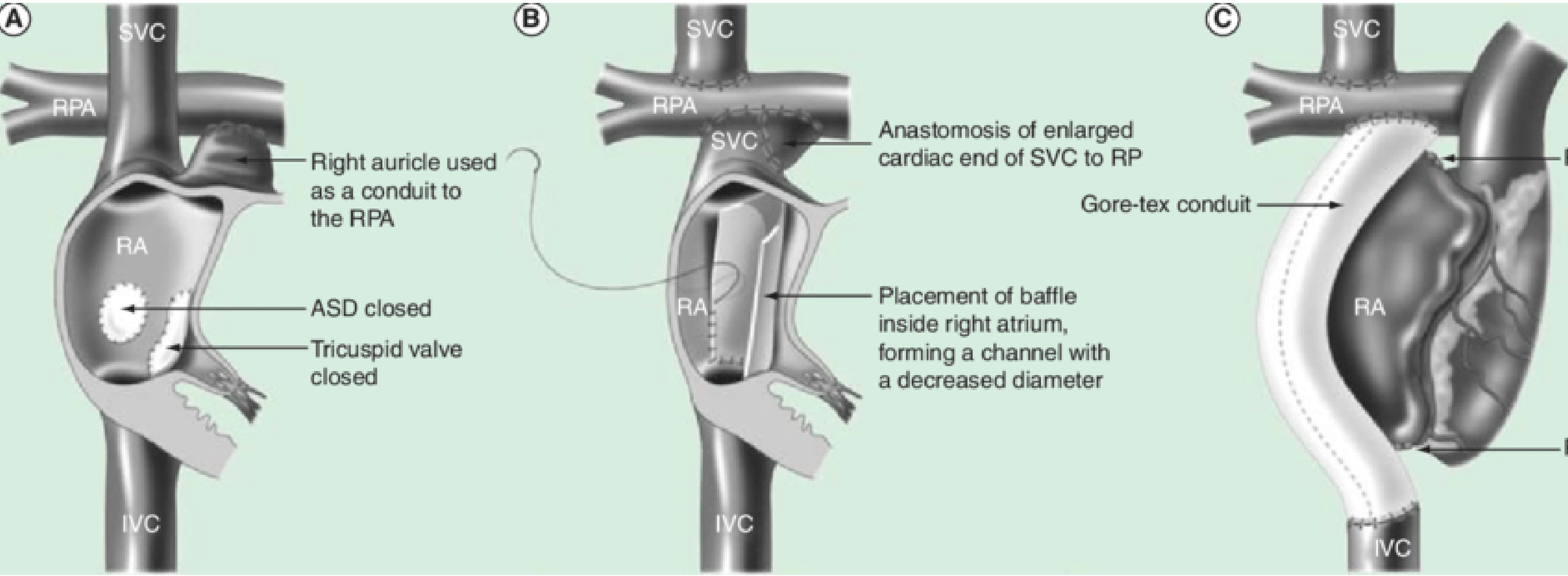
Hypothesis

- Pulmonary microvascular developmental abnormalities

- Fontan connection compliance

Fontan Connection Compliance



- AP Fontan significant energy loss*

de Leval MR et al (1988) J Thorac Cardiovasc Surg 96:682– 695

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Observation

- Noted low TFS in a small number of AP Fontans
- Compared two small groups: 3 LTF versus 3 AP Fontans
- Similar ages, Fontan duration, & IVCP, no PLE
- Atrial tachycardias 2/3 APF versus 1/3 in LTF
- TFS APF 0-1 versus LTF 3-5

Evans WN et al (2016) Pediatr Cardiol 37:1119-1122

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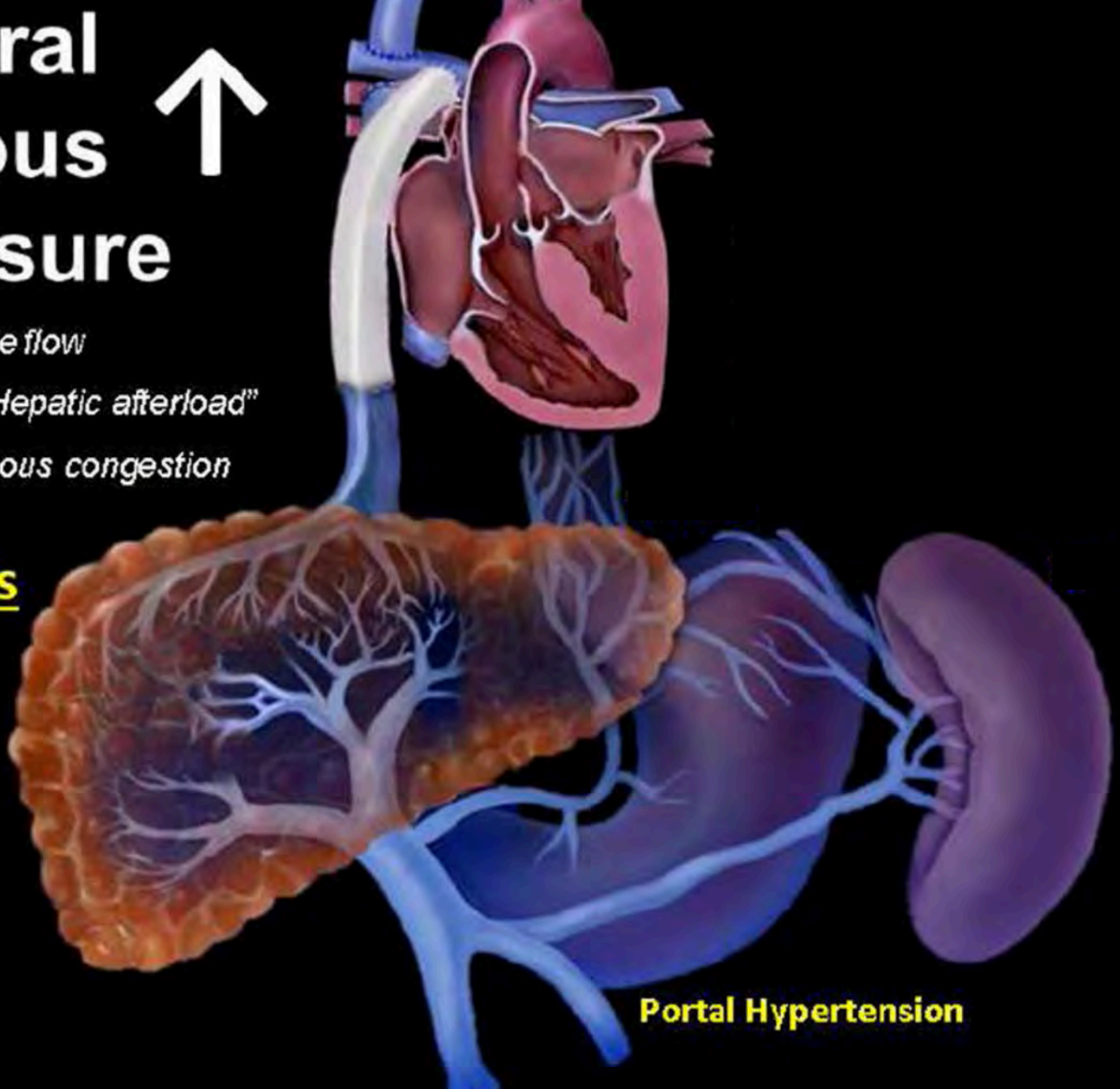
Hypothesis

- Pulmonary microvascular developmental abnormalities
- Fontan connection compliance
- Affect Fontan circuit “impedance” again not detectable by “crude” PVR
- In addition to gravity, breathing, and many other factors

Central Venous Pressure ↑

- *Non-pulsatile flow*
- *Increased "Hepatic afterload"*
- *Passive venous congestion*

Cirrhosis



Future

- ? Tailored approach for different anatomical types
- ? Leave fenestrations pop off systemic venous pressure
- ? Mild desaturation may be protective of oxidative stress
- ? “elastic” material for conduit
- ? Other – assist devices, other interventions
- ? Abandon - replace with Glenn + another source of Qp - heresy ???*

**Day RW et al (2006) Single ventricle palliation: greater risk of complications with the Fontan procedure than with the bidirectional Glenn procedure alone Int J Cardiol 106:201-210*


RENE-THÉOPHILE-HYACINTHE
LAËNNEC
(1781-1826)

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Thank you!

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William N. Evans, MD

Clinical Professor Pediatrics UNLV School of Medicine

Ball Squeezing Exercise
For Abdominal Compression