

# Clinical and Laboratory Correlates of Impaired Cholate Clearance in the Adult Fontan

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*No disclosures*

*I will be discussing off-label use of dual cholate assay*

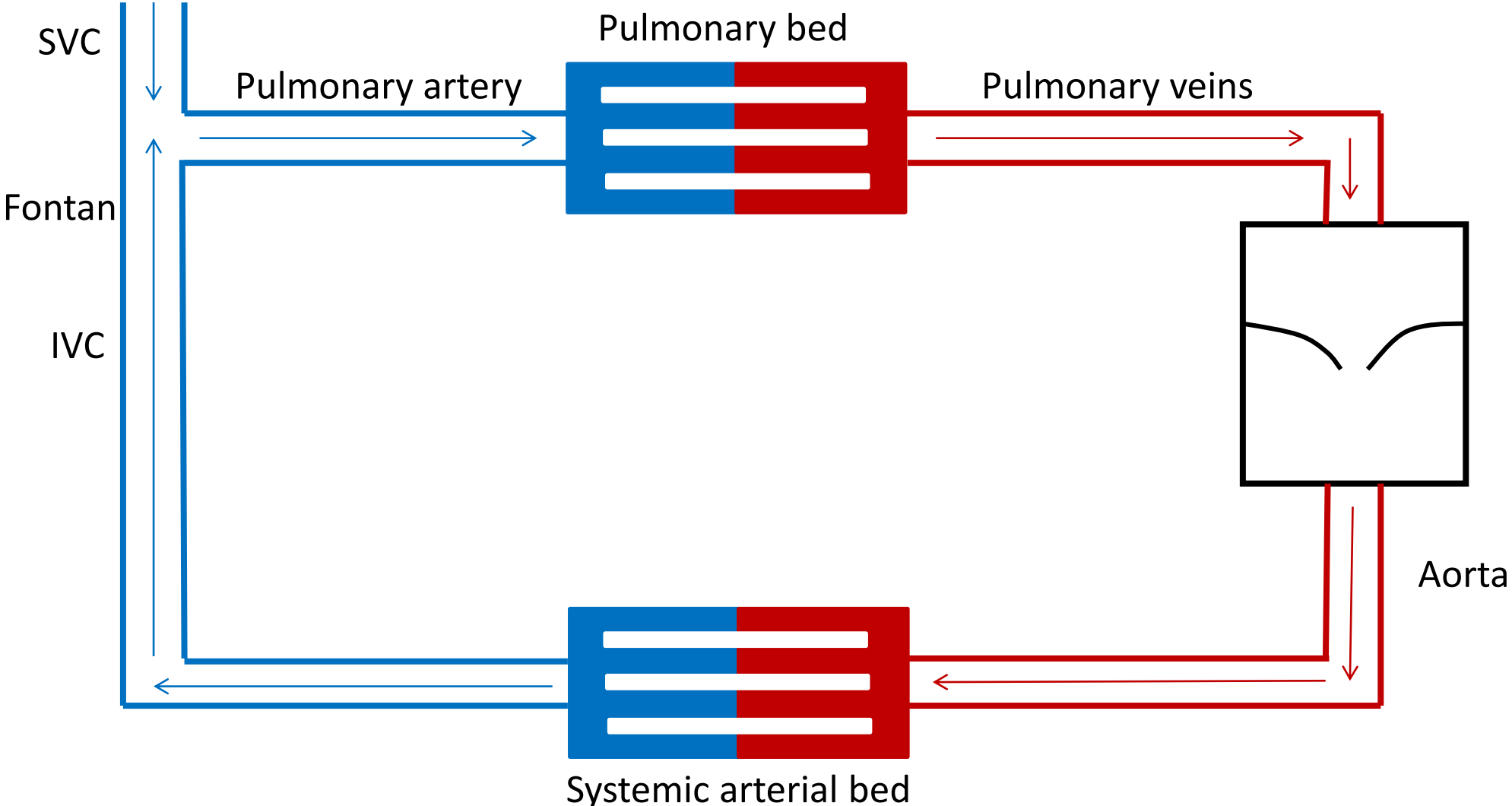
# Background

Fontan Associated Liver Disease (FALD) is universal.

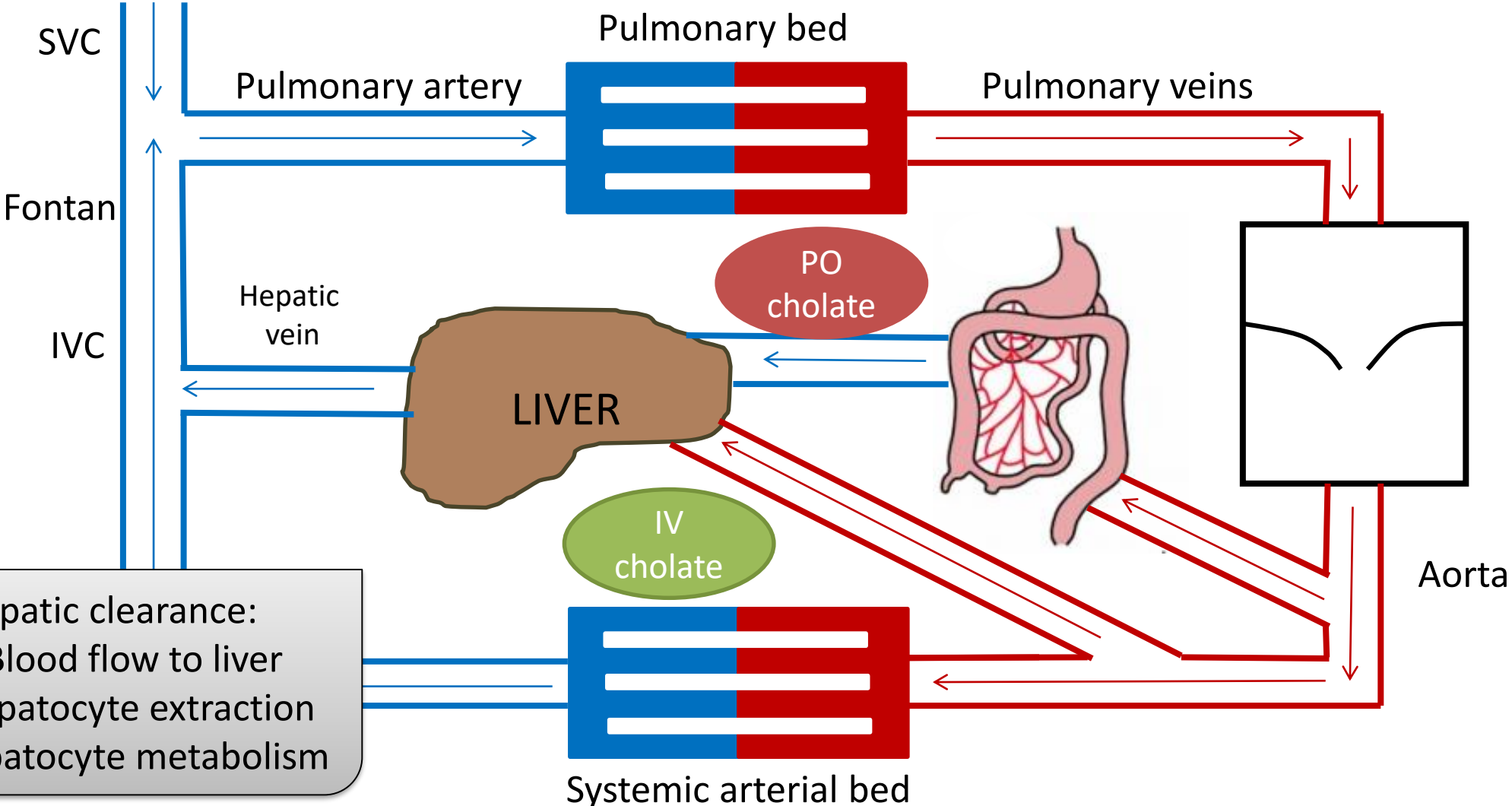
Dual cholate clearance has been shown to be impaired in adult Fontan.

We aim to explore associations between cholate clearance and clinical or laboratory parameters.

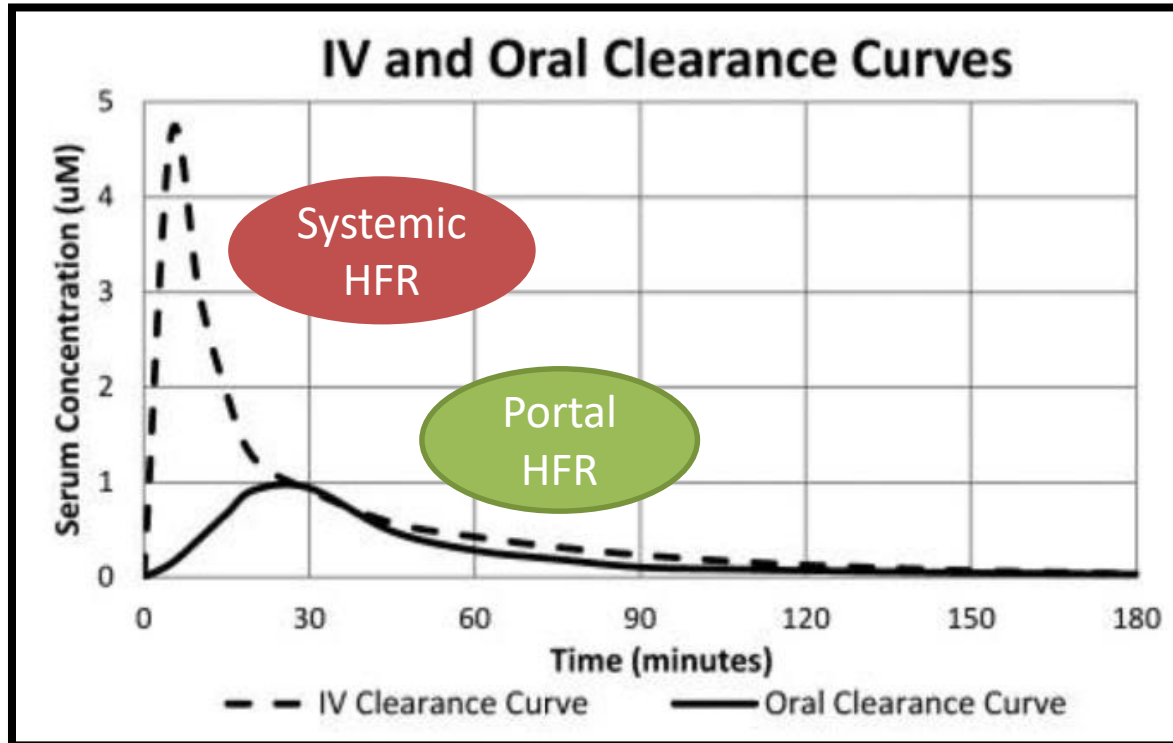
# Dual Cholate Assay



# Dual Cholate Assay



# Methods



## Systemic HFR

- IV cholate
- Systemic clearance

## Portal HFR

- Oral cholate
- Portal clearance

## SHUNT

- Systemic HFR/portal HFR
- Portal blood bypass liver
- 1st pass extraction

## DSI

- Composite score
- $DSI = A(\text{SHUNT}) - B(\text{Ln}(\text{Portal HFR})) - C(\text{Ln}(\text{Systemic HFR})) + D$

The coefficients A, B, and C and constant D were modeled from data patients with both early stage HCV and advanced fibrosis or compensated cirrhosis.

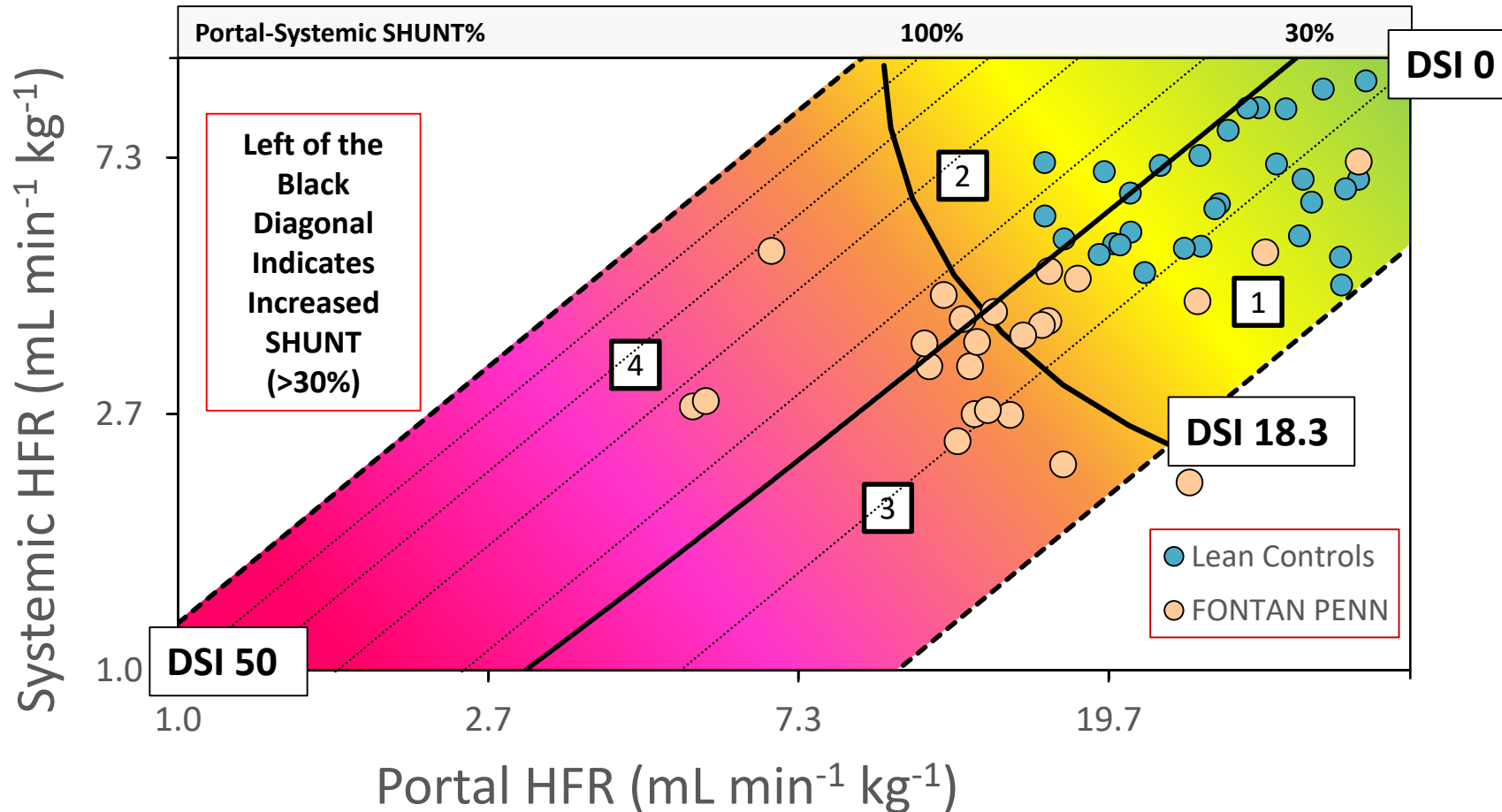
Table 1. Patient characteristics	n=24
Age (yr)*	30.3 (25.0 – 36.5)
Female	50%
White	92%
Age at Fontan (mos)*	32.6 (24.4 – 66.0)
Type of Fontan	
Lateral tunnel	13/24 (54.2%)
Extra-cardiac	5/24 (20.8%)
Right atrial to pulmonary artery	4/24 (16.7%)
Other	2/24 (8.3%)
Cardiac morbidities	
Atrial arrhythmias	11/24 (45.8%)
Heart failure	4/24 (16.7%)
Protein losing enteropathy	4/24 (16.7%)
Desaturation (<90%)	3/24 (12.5%)
History of thrombus	3/24 (12.5%)
Valve replacement	1/24 (4.2%)
Liver morbidities	
Cirrhosis (imaging or biopsy)	19/24 (79.2%)
Clinical ascites	3/24 (37.5%)
Hepatocellular carcinoma	2/24 (8.3%)

\*Median (interquartile range)

Table 2. Clinical variables*	
Cardiac index (L/min/m <sup>2</sup> )	2.9 (2.5 – 3.2)
Total bilirubin (mg/dL)	1.0 (0.6 – 1.2)
AST (U/L)	29.5 (21.0 – 38.3)
ALT (U/L)	26.5 (20.8 – 36.3)
Alkaline phosphatase (U/L)	75.5 (68.3 – 94.8)
Albumin (g/dL)	4.7 (4.3 – 4.7)
Platelets (10 <sup>3</sup> /μL)	177 (142.8 – 189.3)
Alpha fetoprotein	2.0 (1.9 – 3.0)

Table 3. Cholate clearance assay *	
Portal HFR (mL/min/kg)	13.5 (12.1 – 16.5)
Systemic HFR (mL/min/kg)	3.6 (2.8 – 4.2)
Shunt (%)	25 (19.7 – 30.0)
DSI	19.3 (17.0 – 21.0)

# Function Map of FONTAN Cases and Lean Controls



Quadrant 1: normal DSI and normal SHUNT (n=9)

Quadrant 2: normal DSI and increased SHUNT (n=0)

Quadrant 3: Increased DSI and normal SHUNT (n=9); consistent with decline in effective hepatic blood flow.

Quadrant 4: Increased DSI and increased SHUNT Fraction (n=6); consistent with development of intrinsic liver disease.

	Abnormal DSI Abnormal shunt N = 6	Abnormal DSI Normal shunt N = 9	Normal DSI Normal shunt N = 9	p-value
Shunt fraction (%)†	44.65 [33.60, 53.23]	20.50 [18.70, 25.70]	24.00 [16.40, 25.60]	<b>&lt;0.01</b>
DSI†	22.18 [19.46, 27.23]	20.86 [20.06, 21.15]	15.42 [12.62, 17.03]	<b>&lt;0.01</b>
Time since Fontan (year)†	26.71 [25.80, 30.21]	24.33 [22.48, 28.90]	27.13 [21.70, 32.90]	0.69
Oxygen saturation (%)†	90.50 [90.00, 91.00]	92.00 [92.00, 94.00]	93.00 [92.00, 96.00]	<b>0.04</b>
Cardiac testing				
At least mild ventricular dysfunction*	4 (66.7)	2 (22.2)	4 (45.4)	0.26
Cardiac index (L/min/m <sup>2</sup> )†	2.62 [2.42, 3.24]	3.03 [2.70, 3.18]	2.90 [2.50, 2.94]	0.63
Peak VO <sub>2</sub> (ml/kg/min)†	25.50 [13.60, 26.40]	21.60 [20.50, 26.43]	23.55 [19.25, 33.10]	0.87
Fontan pressure (mmHg)† n=19	16.00 [16.00, 17.00]	13.00 [12.00, 14.75]	12.00 [9.75, 14.25]	<b>0.06</b>
Liver imaging*				
Cirrhosis	5 (83.3)	9 (100.0)	5 (55.6)	<b>0.08</b>
Focal liver lesion	4 (66.7)	1 (11.1)	3 (33.3)	0.10
Splenomegaly	3 (50.0)	3 (33.3)	5 (55.6)	0.68
Laboratory†				
Total bilirubin	1.25 [1.10, 1.48]	0.90 [0.70, 1.10]	0.80 [0.60, 1.00]	0.19
Albumin	4.70 [4.32, 4.70]	4.60 [4.50, 4.80]	4.40 [4.10, 4.70]	0.55
Platelet count	177.50 [141.00, 182.50]	159.00 [147.00, 184.00]	178.00 [144.00, 205.00]	0.81
AST	31.50 [22.25, 37.00]	25.00 [21.00, 38.00]	30.00 [21.00, 39.00]	0.98
ALT	28.50 [20.00, 35.50]	27.00 [22.00, 37.00]	22.00 [21.00, 34.00]	0.84
Alkaline phosphatase	95.50 [91.75, 159.25]	76.00 [69.00, 87.00]	74.00 [56.00, 75.00]	<b>0.03</b>
Creatinine	0.89 [0.70, 1.02]	0.77 [0.70, 1.00]	0.92 [0.70, 1.00]	0.92
Alpha fetoprotein	5.00 [3.25, 6.15]	2.00 [1.70, 2.80]	2.00 [1.30, 2.00]	<b>&lt;0.01</b>
NTproBNP	407.00 [97.00, 416.00]	157.50 [62.75, 237.00]	338.50 [84.25, 512.00]	0.35

†Expressed as median [interquartile range]

\*Expressed as counts (%) as assessed by abdominal ultrasound, magnetic resonance imaging, or computed tomography

AOR, Adjusted Odds Ratio; CI, Confidence Interval; DSI, Disease Severity Index; VO<sub>2</sub>, NTproBNP, N-terminal pro brain natriuretic peptide; Peak Oxygen Consumption



# Limitations

## Assay characteristics

- Results may be related to flow or decreased cardiac output.

## Selection bias

- Only patients undergoing cardiac cath or CMR are recruited.

## Underpowered

- Challenging to detect trends with small numbers.

# Conclusions

Cholate clearance correlates with markers of liver disease in the Fontan:  
AFP, alkaline phosphatase, cirrhotic imaging.

↑ Fontan pressure and desaturation  
are also associated with decreased cholate clearance.

Cholate clearance assay may provide a framework for  
Understanding the pathophysiology of FALD.