Pretransplantation and Post-Transplantation Liver Disease Assessment in Adolescents Undergoing Isolated Heart Transplantation for Fontan Failure

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Objective To describe the assessment of Fontan-associated liver disease and determine the clinical and imaging measures that may identify hepatic morbidity risk in isolated heart transplantation candidates and trend those measures post-isolated heart transplantation.

Study design Retrospective analysis of pre-isolated heart transplantation and post-isolated heart transplantation Fontan-associated liver disease (FALD) status using blood tests, magnetic resonance imaging (MRI), and liver biopsy analysis within 6 months before isolated heart transplantation and 12 months after isolated heart transplantation in 9 consecutive patients with Fontan. Pre- and post-isolated heart transplantation standard laboratory values; varices, ascites, splenomegaly, thrombocytopenia (VAST) score; Fontan liver MRI score; liver biopsy scores; Model for End-stage Liver Disease (MELD); MELD excluding the International Normalized Ratio (MELD-XI); AST to platelet ratio index, and cardiac catheterization data were compared.

Results Pretransplantation maximum MELD and MELD-XI was 15 and 16, respectively. Central venous pressures and VAST scores decreased significantly post-transplantation. In 5 paired studies, Fontan liver MRI score maximum was 10 pretransplantation and decreased significantly post-transplantation. Arterially enhancing nodules on MRI persisted in 2 patients post-transplantation. Pretransplantation and post-transplantation liver biopsy scores did not differ in 4 paired biopsy specimens.

Conclusions Patients with FALD and MELD <15, MELD-XI <16, Fontan liver MRI score <10, and VAST score ≤2 can have successful short-term isolated heart transplantation outcomes. Liver MRI and VAST scores improved post-transplantation. Post-transplantation liver biopsy scores did not change significantly. Pretransplantation liver biopsy demonstrating fibrosis alone should not exclude consideration of isolated heart transplantation. The persistence of hepatic vascular remodeling and fibrosis post-isolated heart transplantation suggests that continued surveillance for hepatic complications post-transplantation for patients with Fontan is reasonable. *(J Pediatr 2021;229:78-85)*.

The Fontan procedure was first described in 1971 to treat tricuspid atresia.[1] The indications for the surgery have subsequently broadened to include various forms of single-ventricle pathophysiology. It is now the most common congenital heart disease surgery performed after age 2 years.[2] Although overall patient survival with these lesions is increased by Fontan palliation, hemodynamic compromise typically progresses over time.[3-6] As a result of the complex physiological alterations subsequent to Fontan surgery, complications in other organ systems are also recognized.[3,4]

Owing to the development of extracardiac complications in this relatively large group of potential heart transplant recipients, the assessment of the impact of other organ system diseases on cardiac transplantation candidacy is important. The development and progression of Fontan-associated liver disease (FALD) is insidious and challenging to assess.[3-6] Hepatic function is jeopardized by clinical events during and after heart transplantation, and this impairment can affect the success of the surgery and the life of the patient.[7,8] The degree of pretransplantation hepatic dysfunction that precludes consideration of isolated heart transplantation in patients with Fontan is not well defined. Successful isolated heart transplantation has been reported in the presence of radiographically defined cirrhosis.[9] Other large transplantation centers have opted to perform combined heart/liver transplantation in nearly all candidates with Fontan, owing to the virtual universal presence of advanced hepatic fibrosis on analysis of pre-isolated heart transplantation liver biopsy specimens.[10] Rates of combined heart/liver transplantation in patients with congenital heart disease have increased in the US.[11]

AST	Aspartate aminotransferase
FALD	Fontan-associated liver disease
INR	International Normalized Ratio
MELD	Model for End-stage Liver Disease
MELD-XI	Model for End-stage Liver Disease excluding International Normalized Ratio
MRI	Magnetic resonance imaging
VAST	Varices, ascites, splenomegaly, thrombocytopenia

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Identifying which patients with Fontan can reasonably benefit from isolated heart transplantation as opposed to requiring combined heart/liver transplantation is important for appropriate utilization of scarce donor organs. Clinical decision making regarding optimal transplantation choice is further complicated by the fact that the pace at which FALD improves, if at all, and whether residual liver disease alters long-term post-transplantation patient outcomes has not been reported to any meaningful extent.

This retrospective study describes FALD assessment in pediatric heart transplantation candidates at our center, which follows more than 400 recipients of Fontan palliation. The study aimed to examine whether commonly available clinical measures prove useful in identifying candidates with Fontan who can successfully undergo isolated heart transplantation and whether short-term hepatic morbidity risk can be avoided post-transplantation. In addition, it attempted to evaluate whether the measured liver associated measures improved at 1 year after isolated heart transplantation.

Methods

This study was approved be the Children's Healthcare of Atlanta Institutional Review Board. The pediatric heart transplantation team has requested consultation with the pediatric liver transplantation team for FALD assessment in survivors of Fontan referred for heart transplantation evaluation as a routine practice since 2015. Between 2015 and 2018, 2 designated pediatric transplantation hepatologists and a single liver transplantation surgeon evaluated the liver status of all patients with Fontan in the evaluation phase. Pre-isolated heart transplantation hepatic testing included biochemical analyses, alpha 1 anti-trypsin level and phenotype, ceruloplasmin, anti-nuclear antibody, F-actin antibody, hepatitis B virus, hepatitis C virus, and HIV testing. Pretransplantation abdominal magnetic resonance imaging (MRI) or abdominal computed tomography angiography was performed. The decision regarding percutaneous liver biopsy as part of the transplantation evaluation was made by the hepatologists based on their interpretation of the clinical status of the patient after incorporation of history and physical examination, biochemical, and imaging findings and was not performed in all cases.

Follow up post-isolated heart transplantation was through the heart transplantation team. Cardiac catheterization and blood tests were performed at designated intervals according to routine clinical protocols. Reassessment by the same 2 pediatric hepatologists was performed at 12 months post-isolated heart transplantation in 5 patients. Repeat MRI and liver biopsy were obtained at 1 year after isolated heart transplantation in those 5 patients, concurrent with standard cardiac catheterizations for post-transplantation assessment at the discretion of the examining hepatologist.

All 9 patients who underwent Fontan surgical palliation and were referred for heart transplantation evaluation between October 2015 and October 2018 were included in these analyses. Data were abstracted from the electronic medical record at either heart transplantation evaluation or within 6 months before that date, and at 12 months (±6 months) post-transplantation during routine cardiac transplant follow up. Baseline demographic information included patient age at original Fontan surgery, type of Fontan surgery performed, race, sex, and date of heart transplantation. Pre-isolated heart transplantation heart catheterization data (Fontan pressure) at the time of evaluation or within 6 months before evaluation, and post-transplantation catheterization data (right atrial pressure) at annual visits were also obtained.

All laboratory data were abstracted from the same date in individual assessments and the same data elements used in clinical scoring calculations described below. The laboratory values included platelet count, creatinine, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase, gamma glutamyl transpeptidase, and International Normalized Ratio (INR). Using the laboratory data, Schwartz Pediatric Bedside estimated glomerular filtration rate; varices, ascites, splenomegaly, thrombocytopenia (VAST) score; Model for End-stage Liver Disease (MELD); MELD score excluding INR (MELD-XI); and AST to platelet ratio index score were calculated as previously described for the various time frames.[12-14]

Pre-isolated heart transplantation abdominal MRI and post-isolated heart transplantation abdominal MRI obtained at subsequent annual visits were reviewed. The radiology departmental imaging protocol includes axial T2-weighted images with and without fat suppression and T1-weighted gradient echo fat-suppressed 3D volumetric acquisition in precontrast, arterial, venous and delayed phases. Additional coronal thick slab magnetic resonance cholangiopancreatography, T1- and T2-weighted images, and axial diffusion-weighted images were acquired to complete the evaluation. The total scan time was approximately 30 minutes and was performed at either 1.5 T or 3.0 T (Aera, AvantoFit and TrioTim; Siemens Healthcare, Ehrlangen, Germany). A standard contrast dose of 0.1 ml/kg intravenous gadolinium was used.

A novel Fontan liver MRI score was determined after review of available pre-and post-isolated heart transplantation MRI by 2 blinded radiologists. Hepatic congestion, fibrosis, extent of varices, presence of splenomegaly, and the presence of arterially enhancing nodules and/or ascites were assigned numeric values and a total determined by individual reading and then finalized by consensus. MRI-based hepatic fibrosis scoring was based on the following scale: mild (1 point): fine reticular enhancement, most pronounced at the subcapsular margins; moderate (2 points): reticular enhancement throughout the liver parenchyma; severe (3 points): reticular enhancement and band-like enhancement suggestive of extensive fibrosis or areas of capsular retraction and/or nodular contour. Hepatic venous congestion was scored as follows: mild (1 point): periportal T2 prolongation (edema) and mild heterogeneous venous phase enhancement of the parenchyma; moderate (2

points): hepatic parenchymal T2 prolongation (edema) throughout the liver, corresponding heterogeneous venous enhancement; severe (3 points): periportal and mild parenchymal edema, heterogeneous venous enhancement throughout the liver and/or subcapsular ascites or intra-abdominal ascites. The presence of varices and splenomegaly was assigned 1 point for the presence of splenomegaly with or without prominent gastrolienal veins, but with no gastroesophageal varices identified; 2 points for the presence of gastroesophageal varices and splenomegaly; and 3 points for the presence of splenomegaly, prominent gastrolienal veins, and gastroesophageal varices. A single point each was assigned for the presence of arterially enhancing nodules and/or the presence of ascites. The maximum possible Fontan liver MRI score was 11. Representative images for the hepatic congestion and fibrosis scoring system are shown in Figure 1.

Liver biopsies were performed during cardiac catheterizations by pediatric hepatologists using a standard percutaneous liver biopsy technique with ultrasound guidance. A 16-gauge spring-loaded biopsy needle was used to obtain a maximum of 2 core needle liver biopsy specimens with a maximum of 2 passes.[15] Liver biopsy specimens were formalin-fixed, paraffin-embedded, cut at 4 μm, and stained with hematoxylin & eosin and Masson's trichrome stains. Paired biopsy specimens from 4 of the 9 patients were available for retrospective evaluation. Two pediatric pathologists with hepatopathology expertise independently scored each biopsy specimen without knowledge of biopsy pairing or timing. Consensus determined final scores. Modified components of a previously described semiquantitative Fontan liver biopsy score were used to score the specimens.[16] Components included a traditional fibrosis score (METAVIR 0-4), presence or absence of central venous fibrosis, extent of sinusoidal fibrosis,[1-3] and extent of sinusoidal dilatation.[1-3] The maximum total liver biopsy score was 11.

Pre-isolated heart transplantation and post-isolated heart transplantation values at annual assessment were used for determination of group means and standard deviations. The pretransplantation and post-transplantation values were compared using the 2-tailed Mann–Whitney *U* test, with a *P* value <.05 considered to indicate statistical significance.

Results

During the study period, all patients with Fontan evaluated were referred for transplantation due to cardiac indications.

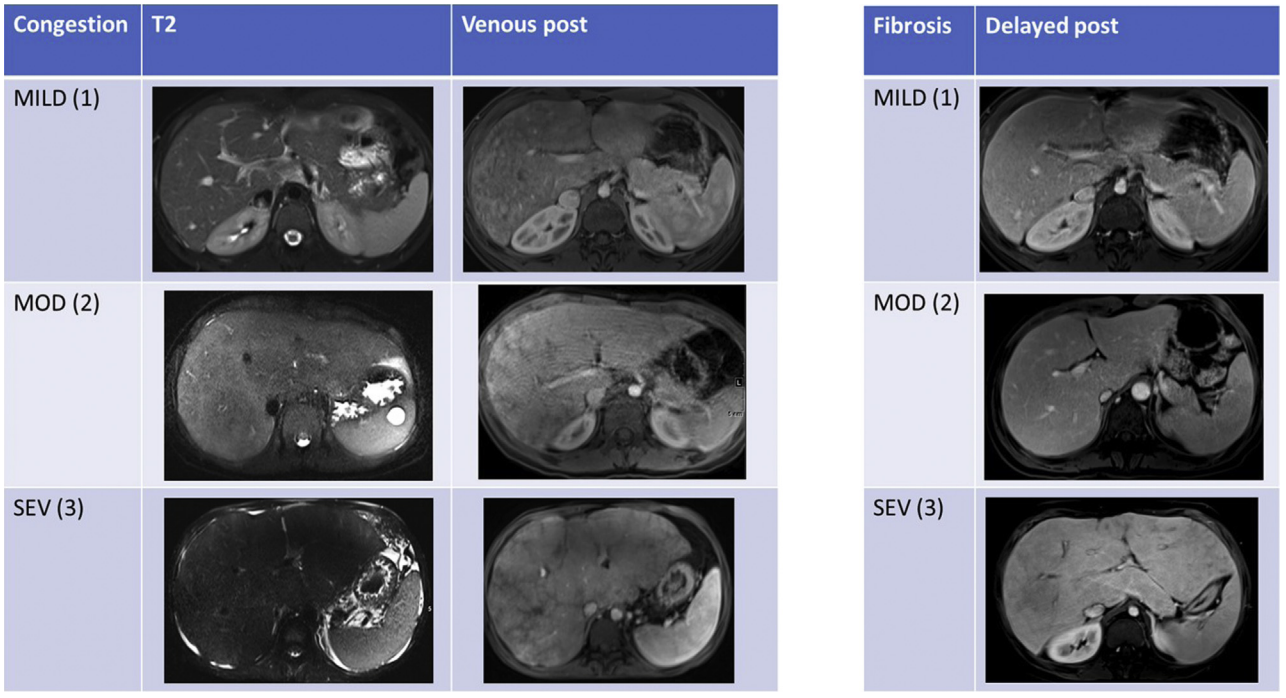

Figure 1. Representative images of liver MRI scoring system for congestion and fibrosis. The Methods section describes scores related to portal hypertensive related findings. (*Left* and *middle*) Hepatic venous congestion evaluated on fluid-sensitive and venous postcontrast phase sequences. Mild: periportal T2 prolongation (edema) and mild heterogeneous venous phase enhancement of the parenchyma. In this case, isolated to the right lobe. Moderate: hepatic parenchymal T2 prolongation (edema) throughout the liver, corresponding heterogeneous venous enhancement again more pronounced on the right. Severe: Periportal and mild parenchymal edema with subcapsular ascites and intra-abdominal ascites; heterogeneous venous enhancement is throughout the liver. (*Right*) Hepatic fibrosis evaluated on delayed postcontrast sequence. Mild: fine reticular enhancement, most pronounced at the subcapsular margins. Moderate: reticular enhancement throughout the liver parenchyma. Severe: reticular enhancement and band-like enhancement corresponding to bridging fibrosis; areas of capsular retraction and nodular contour.

No patient with Fontan was excluded from isolated heart transplantation because of concerns regarding pretransplantation FALD severity. All 9 evaluated patients underwent isolated heart transplantation and were alive with their original graft at the time of last follow-up (range, 21-42 months). Patients ranged in age from 10 to 19 years at the time of isolated heart transplantation. Eight of 9 patients had hypoplastic left heart syndrome as the underlying reason for their palliation. A single patient had an unbalanced atrioventricular canal defect. All patients had previous lateral tunnel Fontan surgeries with fenestrations. Pre–isolated heart transplantation MELD scores ranged from 6 to 15, and the maximum MELD-XI score was 16. Maximum INR and total bilirubin among all isolated heart transplantation recipients within 48 hours post-transplantation was 2.3 and 3.5 mg/mL, respectively, indicating no significant immediate postoperative hepatic decompensation. The initial post–isolated heart transplantation intensive care unit length of stay, used as a potential indirect indicator of morbidity or immediate postoperative hepatic dysfunction, ranged from 4 to 17 days, with the total initial isolated heart transplantation hospitalization ranging from 7 to 48 days. No significant differences in patients' pretransplantation and 1-year post-transplantation average laboratory values were identified (**Table I**; available at www.jpeds.com).

As expected, central venous pressures decreased significantly individually and collectively when comparing pretransplantation and post-transplantation measurements ($P < .0004$; **Figure 2**, A). Paired comparisons of MELD-XI scores reached significance on single-tailed analysis ($P = .05$), but were not significantly different on 2-tailed testing (**Figure 2**, B). Mean VAST scores and individual VAST scores decreased significantly at 1 year after isolated heart transplantation ($P = .006$; **Figure 2**, C).

Seven of 9 patients underwent pretransplantation MRI. The other 2 underwent computed tomography scan, 1 due to the presence of a pacemaker and the other because their clinical status did not permit sedation for the MRI. In the 5 patients with paired pretransplantation and post-transplantation MRI scores, mean and individual scores were significantly decreased post-transplantation ($P < .02$; **Figure 2**, D and **Figure 3**). Two patients had at least 1 arterially enhancing nodule on pretransplantation MRI. Both cases persisted at 1 year post-transplantation (**Figure 4**; available at www.jpeds.com). A single patient had identification of an arterially enhancing nodule

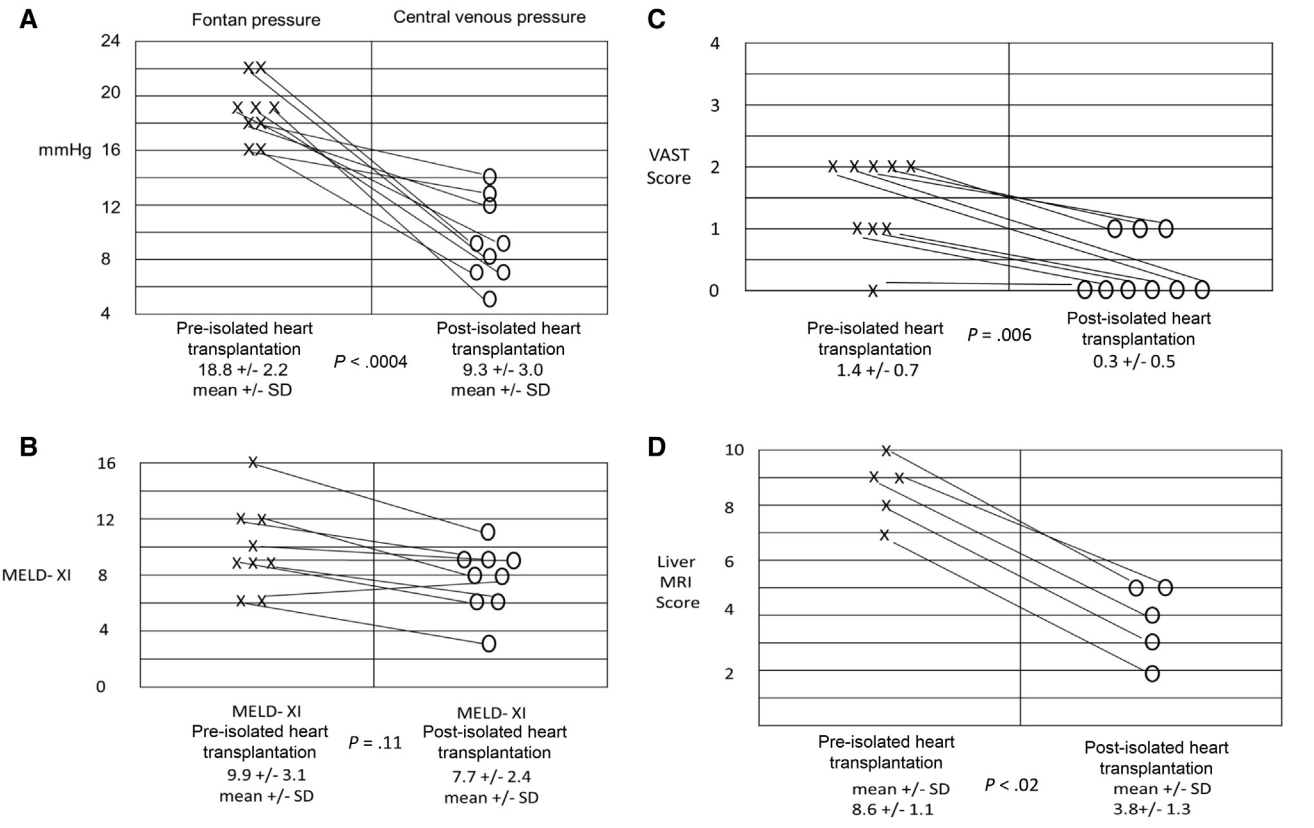

Figure 2. Spaghetti plots comparing individual and mean pre-isolated heart transplantation and post-isolated heart transplantation values. **A,** Fontan pressures and central venous pressure. **B,** MELD-XI values. **C,** VAST scores. **D,** Liver MRI scores. X indicates individual patient pre-isolated heart transplantation values; open circles, individual patient post-isolated heart transplantation values. Means and SDs calculated for pre-isolated heart transplantation and post-isolated heart transplantation values were compared using the paired Mann–Whitney *U* test, with a *P* value <.05 considered to indicate statistical significance.

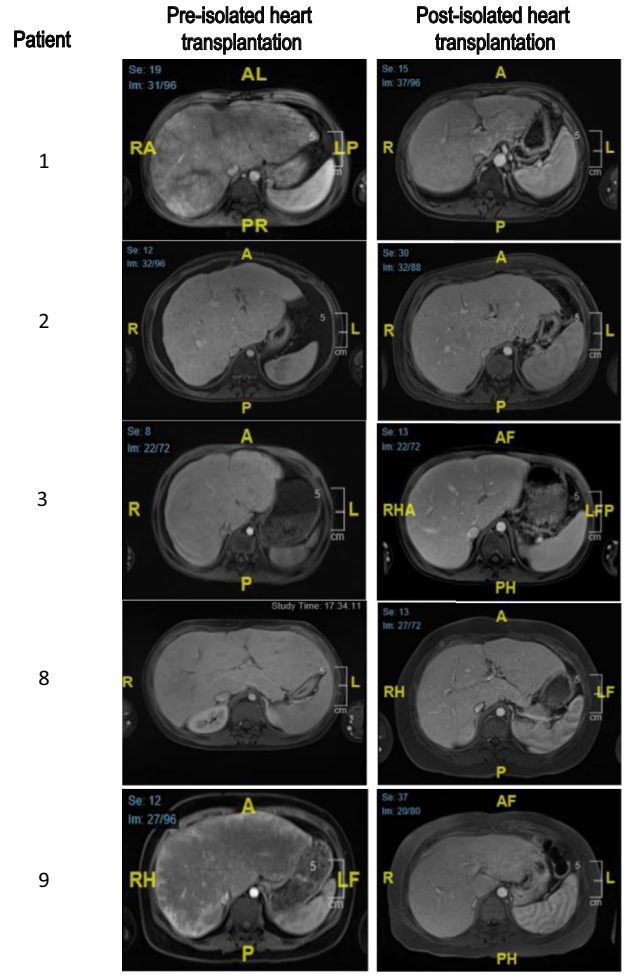

Figure 3. Paired pre- and post-isolated heart transplantation MRI comparisons in 5 patients. All images are axial volumetric T1 gradient echo fat-suppressed venous phase images.

post-transplantation not seen on pretransplantation imaging. In both pretransplantation and post-transplantation MRI of these cases, delayed venous phase images did not reveal characteristics suspicious for hepatocellular carcinoma.

Paired biopsy specimens from 4 of the 9 patients were available for retrospective evaluation. The liver biopsy total scores did not show improvement at 1 year post-transplantation with a single exception (**Table II**; available at www.jpeds.com).

Discussion

The measures and decision making process used to determine which patients with Fontan due to the presence of FALD require isolated heart transplantation vs combined heart/liver transplantation are not uniform and are still evolving.[9,10,17,18] Expert opinion articles emphasize the difficulties regarding FALD evaluation for isolated heart transplantation candidacy in patients with Fontan failure.[4,19,20] The impact of isolated heart transplantation on the subsequent evolution of liver disease or residual liver disease effects on post-transplantation outcome are not known. Although limited by the small sample size, incomplete collection of data, and retrospective approach, this is the first study focused on the pre–heart transplantation assessment of FALD in the pediatric and young adult population that measures and reports any comparison of pretransplantation and 1 year post-transplantation hepatic outcomes.

That various standard laboratory measurements are not significantly different after isolated heart transplantation is not surprising, given the lack of change in these values in most pretransplantation patients with Fontan.[21-23] Scoring systems have been developed for the assessment of portal hypertension, synthetic impairment, and risk of death from liver disease.[24] The AST to platelet ratio index score was used in this study because it could be readily calculated retrospectively from routinely available clinical data and was not significantly different post-transplantation.[25] The role of other calculations or commercially available laboratory-based assessments of hepatic fibrosis to predict pretransplantation hepatic morbidity risk is not addressable in this study.

MELD scores were calculated for our patients because they correlate well with death on the liver transplantation waitlist and with morbidity after cardiac surgery.[26] In our cohort, all patients had a calculated MELD scores pretransplantation <15, which is generally considered too low to favor proceeding with isolated liver transplantation in the vast majority patients with typical liver diseases.[27] Post-transplantation MELD scores were not available for comparison due to the lack of post-transplantation INR values. Our study suggests that patients with traditionally regarded low MELD scores on pretransplantation evaluation tolerate isolated heart transplantation and have acceptable short-term outcomes. The upper limit of MELD scores in patients with Fontan who are acceptable candidates for isolated heart transplantation was not identified in this study.

The MELD-XI score was developed to assess mortality risk in patients with liver disease on anticoagulation and thus has been applied to assess hepatic compromise in patients with cardiac disorders.[28,29] This calculation correlates with post–cardiac surgery liver disease morbidity.[30-34] MELD-XI scores tended to decrease at 1 year post–isolated heart transplantation in our study, but the difference was not statistically significant on 2-tailed analysis. A statistically significant decrease in MELD-XI score if verified in a larger sample size could be clinically important, suggesting a decreased post–isolated heart transplantation liver-associated mortality risk.[28,29] Our data suggest that patients with an MELD-XI score <16 can undergo isolated heart transplantation with acceptable survival. The upper limit of MELD-XI values for a successful isolated heart transplantation also remains unknown.

The VAST scoring system has been shown to highly correlate with liver disease–related morbidity and mortality in patients post-Fontan.[13] In our present cohort, none had a pretransplantation VAST score >2. Whether a VAST score

>2 alters post-transplantation outcome is not known, and this could be a focus of future multicenter studies.

Hepatic fibrosis is a nearly universal finding in long-term survivors of Fontan.[3,35-38] Liver biopsy sampling error is a major limitation in the assessment of suitability for isolated heart transplantation post-Fontan.[3] The right hepatic lobe, the area typically biopsied, is disproportionately affected by fibrosis in patients with Fontan.[39] The role of liver biopsy in assessing the functional reserve of the liver in patients post-Fontan is uncertain.[16] No pretransplantation patient was identified as having cirrhosis in this cohort, but all had at least a stage 2 or 3 (out of 4) portal and/or sinusoidal fibrosis. Based on our data and given the universality of hepatic fibrosis, the presence of portal or sinusoidal fibrosis on histological assessment should not be the sole criterion used to exclude consideration of isolated heart transplantation for patients with Fontan.

Of the patients who underwent pre- and post-transplantation liver biopsy, multicomponent aggregate scoring of the liver biopsy did not change at 1 year. It may be that improvement in hepatic fibrosis may take longer than 1 year, may lag behind post-transplantation MRI changes, or may be subject to sampling error. A recent case report noted histological improvement of the liver at 18 months after isolated heart transplantation in a patient with Fontan.[40] Whether all hepatic histological abnormalities are ultimately reversible with heart transplantation, or whether lack of complete reversibility impacts the future health of post-transplantation recipients of Fontan is still unknown and requires longer-term follow-up. For these reasons, we conclude that post–isolated heart transplantation follow-up with a hepatologist to monitor for residual FALD-related complications is reasonable.

MRI of the liver in patients with Fontan can provide multiparameter assessment of hepatic status that includes qualitative and/or quantitative estimates of hepatic fibrosis, hepatic congestion, bowel edema, ascites, and vascular consequences of portal hypertension, such as the extent and location of varices and splenomegaly and abnormal perfusion patterns.[39,41-43] In this study, we used a novel scoring system that guided the blinded, qualitative assessment of the principal MRI features of FALD: congestion, fibrosis, arterially enhancing hepatic nodules, and radiologically evident portal hypertension. All patients had a Fontan liver MRI score of <10 at the time of isolated heart transplantation. Patients undergoing MRI at 1 year post-transplantation shower clear improvement in cumulative MRI scores, driven primarily by changes in congestion and qualitative fibrosis scores.

Given documented post–isolated heart transplantation decreases in central venous pressures and hepatic congestion in MRI, it could be hypothesized that liver stiffness measures, such as MRI elastography, would also show improvement. A recent cardiac catheterization and liver biopsy cohort reported that in their pre-transplant patients, central venous or "Fontan pressure" greater or equal to 14 mmHg and MRI elastography liver stiffness of >4 kiloPascals was associated with more advanced hepatic fibrosis.[44] In another study, pretransplantation MRI elastography value >4.5 kPa correlated with "Fontan failure."[45] If MRI elastography measurements show improvement in future post-isolated heart transplantation studies, it may not be appropriate to conclude that histological resolution of fibrosis had occurred without correlation with liver biopsies from at least 2 different sites. MRI elastography cutoff points predicting successful isolated heart transplantation vs need for combined heart/liver transplantation have not been reported to date.

Pre–isolated heart transplantation arterially enhancing nodule(s) on MRI persisted at 1 year after isolated heart transplantation in our patients. The vast majority of arterially enhancing lesions in patients with Fontan have radiologic characteristics compatible with focal nodular hyperplasia[46,47]; however, distinguishing these lesions from hepatocellular carcinoma can be challenging.[47-49] The persistence of these imaging abnormalities at 1 year after isolated heart transplantation suggests that pretransplantation screening to identify arterially enhancing nodules may be important. A single patient developed a lesion post-transplantation that had not been identified pretransplantation. Continued surveillance for arterially enhancing lesions and for the possible development of hepatocellular carcinoma, in a now immunosuppressed post-isolated heart transplantation population with potentially incompletely resolved liver injury is justifiable.

Although this report is limited by its single-center retrospective design, and also by the fact that not all patients underwent paired imaging and liver biopsies, it nonetheless reinforces that fact that isolated heart transplantation is possible and associated with good short-term outcomes and little immediate hepatic disease associated morbidity in well-selected candidates post-Fontan. Adolescent and young adult patients with MELD <15, MELD-XI <16, VAST score <2, and Fontan liver MRI score <10 can undergo successful isolated heart transplantation. Such patients can demonstrate improvement in Fontan liver MRI score and VAST score at 1 year after isolated heart transplantation. This FALD-related data in adolescents and young adults add additional insights to reports from our center indicating favorable post-transplantation outcomes in young patients with Fontan undergoing transplantation for cardiac indications.[50] Given the near universality of hepatic fibrosis in these patients, the presence of hepatic fibrosis alone on pretransplantation liver biopsy should not be the exclusive criterion to decline heart transplantation candidacy. Because the histological alterations of fibrosis and arterialized FNH-like lesions of the liver may persist post-transplantation, continued surveillance for hepatic complications in post-transplantation patients with Fontan is reasonable. The development of hepatocellular carcinoma, given the use of immunosuppression in the presence of previous hepatic injury, remains at least a theoretical possibility.[20] With a growing number of survivors post-Fontan, the difficulties in managing transplantation decision making will not ease in the future and will require continued multidisciplinary collaboration and investigation. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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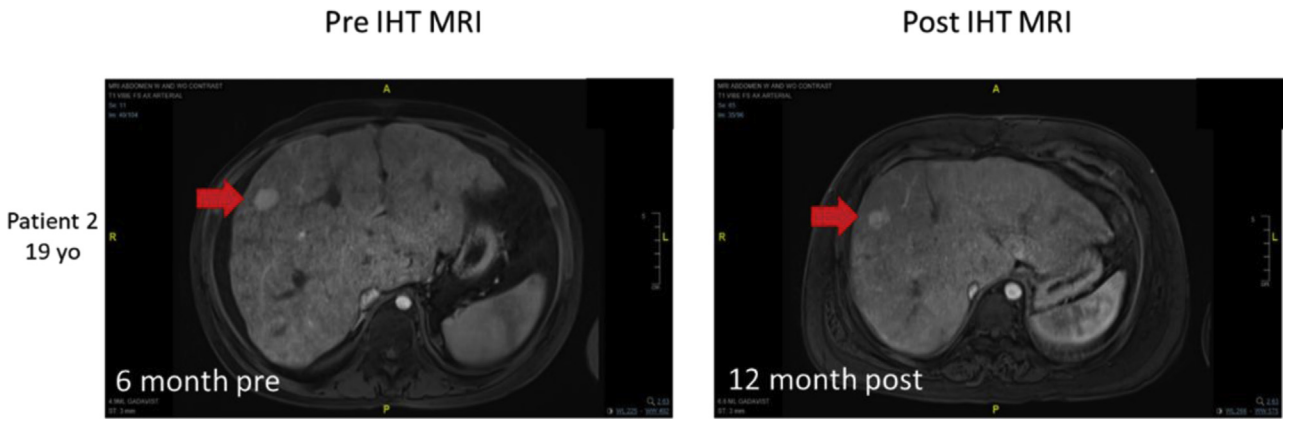

Figure 4. Arterially enhancing liver nodule (*red arrow*) persisting one year Post-isolated heart transplantation. All images are axial volumetric T1 gradient echo fat suppressed late arterial phase images.

Table I. Clinical parameters, pairwise comparisons pre-isolated heart transplantation and post-isolated heart transplantation

Patient	Platelets pre-IHT, $\times 10^3/\mu L$	Platelets post-IHT, $\times 10^3/\mu L$	TB pre-IHT, mg/dL	TB post- IHT, mg/dL	INR pre-IHT	INR post-IHT	eGFR pre-IHT, mL/min/1.73 m^2	eGFR post-IHT, mL/min/1.73 m^2	APRI Pre-IHT	APRI post-IHT
1	267	170	0.2	0.3	1.3	1.0	126	107	0.272	0.195
2	396	349	0.3	0.1	1.0	1.1	102	126	0.199	0.339
3	373	192	0.3	0.3	1.1	1.2	79	82	0.227	0.426
4	366	175	0.3	0.2	0.9	ND	120	168	0.224	0.329
5	191	281	0.8	0.2	2.0	ND	72	102	0.238	0.237
6	183	213	0.6	0.5	1.5	ND	63	91	0.232	0.171
7	162	143	0.6	0.5	1.7	ND	89	112	0673	0.509
8	78	162	0.6	0.3	1.2	1.2	100	125	1.166	0.486
9	95	126	1.3	0.5	1.2	1.1	82	111	1.053	0.986
Mean ± SD	234 ± 121	201 ± 71	0.6 ± 0.3	0.3 ± 0.1	1.3 ± 0.4	1.1 ± 0.08	92 ± 21	114 ± 25	0.48 ± 0.39	0.41 ± 0.25
P value		.63		.5		.32		.21		.76

APRI, AST to platelet count ratio index; *eGFR*, estimated glomerular filtration rate; *IHT*, isolated heart transplantation; *ND*, not detected; *TB*, total bilirubin.
The pre-IHT and post-IHT time point values comparison using the paired 2-tailed Mann–Whitney *U* test with a *P* value <.05 taken as significant.

Table II. Paired blinded liver biopsy scores

Patient	METAVIR fibrosis score	Central vein fibrosis	Sinusoidal fibrosis	Sinusoidal dilatation
1-pre	2	0	0	3
1-post	2	1	3	1
2-pre	3	0	2	2
2-post	2	1	3	1
3-pre	2	1	3	2
3-post	1	1	2	1
8-pre	3	1	3	1
8-post	2	1	3	2

METAVIR: 0, no fibrosis; 1, portal fibrosis expansion without septa; 2, focal bridging; 3, extensive bridging; 4, cirrhosis.
Central vein fibrosis: 0, absent; 1, perivenular expansion.
Sinusiodal fibrosis: 0, absent; 1, present in 1 liver zone (perivenular, midzonal, periportal); 2, present in 2 liver zones; 3, panlobular, present in all zones.
Sinusoidal dilatation: 0, absent; 1, present in perivenular zone; 2, present in perivenular and mid zones; 3, panlobular, present in all zones.