Pre-Fontan cardiac magnetic resonance predicts post-Fontan length of stay and avoids ionizing radiation

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Objective: Patients frequently undergo cardiac catheterization before the Fontan operation because of the limited echocardiographic windows in the region of the superior cavopulmonary connection and branch pulmonary arteries. Patients with obstruction to pulmonary blood flow are at increased risk for prolonged length of hospital stay after the Fontan operation. Cardiac magnetic resonance has unlimited imaging windows and can quantify both the branch pulmonary artery size and net flow distribution and thereby serve as a method for identifying patients at increased risk for prolonged length of stay.

Methods: We retrospectively reviewed 24 cardiac magnetic resonance studies of patients (mean age, 3.1 ± 1.0 years) referred before the Fontan operation. Cardiac magnetic resonance measured the cross-sectional area and flow to each branch pulmonary artery. Post-Fontan hospital course data were acquired from the medical record.

Results: Prolonged length of stay after the Fontan operation is observed among patients with one branch that is less than 25% of the total cross-sectional area (18.0 ± 5.5 vs 8.2 ± 3.8 days, $P = .01$) or with less than 40% flow to one branch (12.5 ± 6.9 vs 7.6 ± 1.5 days, $P = .04$). There is moderate correlation between the total branch pulmonary area and length of stay ($r = -0.75$).

Conclusions: Cardiac magnetic resonance noninvasively assesses the branch pulmonary area size and flow before the Fontan operation. These data predict which patients are more likely to experience a prolonged hospital course.

Video clip is available online.

The Fontan operation completes the process of converting a patient with a functional single ventricle from a circulation in parallel to a circulation in series. Investigators studying predictors of Fontan outcomes have considered the effect of many factors, including anatomic diagnosis, pulmonary artery size, ventricular size and function, and the presence of a reconstructed aortic arch.¹⁻¹² Patient characteristics that had been thought of as high risk for Fontan completion have been found to produce acceptable intermediate outcomes in the current era of improved perioperative care.¹³ However, there are still relatively few and at times conflict-

ing data regarding the effect of these factors on the hospital length of stay (LoS).^{7,10-12}

Before undergoing the Fontan operation, patients are commonly assessed with both noninvasive echocardiography and invasive diagnostic catheterization, with the occasional need for catheter intervention. Although noninvasive echocardiographic analysis might be sufficient to determine which patients will have a good outcome after the Fontan operation when unlimited echocardiographic windows are available, frequently the superior cavopulmonary connection and the branch pulmonary arteries (BPAs) are not adequately assessed.¹⁴

Cardiac magnetic resonance (CMR) provides quantitative measurements of the BPA size and flow distribution,¹⁵⁻¹⁷ ventricular ejection,¹⁸⁻²⁰ and cardiac index.^{21,22} With the exception of significant coil and stent artifacts, CMR provides unlimited imaging windows without the use of ionizing radiation. The purpose of this study was to investigate whether pre-Fontan CMR assessment can predict which patients will require a longer LoS.

MATERIALS AND METHODS

Patients

Twenty-four consecutive patients were referred for pre-Fontan CMR assessment on clinical grounds between April 2004 and September 2007 and have undergone Fontan completion. Their demographic data are described in Table 1.

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Abbreviations and Acronyms

AVV	= atrioventricular valve
AVVR	= atrioventricular valve regurgitation
BPA	= branch pulmonary artery
CMR	= cardiac magnetic resonance
EDV	= end-diastolic volume
ESV	= end-systolic volume
LoS	= length of stay
LPA	= left pulmonary artery
LV	= left ventricular
RPA	= right pulmonary artery
RV	= right ventricular

MRI Protocol

CMR studies are monitored by our cardiac anesthesia service. Studies are conducted while patients are spontaneously breathing. Patients are anesthetized with propofol and generally do not require intubation or paralytics. The core of the CMR protocol involves assessment of BPA size and flow distribution, cardiac index, and ventricular size and function. CMR data were also reviewed for ventricular morphology, atrioventricular valve regurgitation (AVVR), and aortic arch obstruction.

BPA Size and Flow Distribution

The BPAs were measured in 2 orthogonal dimensions, and the cross-sectional area was calculated from the linear measurements. For each BPA, the smallest cross-sectional area along the segment from the superior cavopulmonary connection to the origin of the upper lobe branch, including the central pulmonary artery portion under the arch, was used for data analysis. By using phase-contrast magnetic resonance, the fractional BPA pulmonary blood flow is calculated as follows:

$$\text{Fractional BPA pulmonary blood flow} = (\text{Net BPA flow} / \text{Net total pulmonary blood flow}) \times 100.$$

The single patient with a BPA endovascular stent was excluded from the BPA size and flow analysis.

Cardiac Index

Phase-contrast magnetic resonance acquisition was applied at the aortic valve for flow quantification and was indexed for body surface area. In patients who have a proximal reconstructive anastomosis of the great arteries without semilunar valve atresia, separate measurements of the native aortic and pulmonary valves were performed. The cardiac index was calculated as the sum of the 2 measurements. Phase-contrast magnetic resonance data analysis involved contouring regions of interest throughout all phases of the cardiac cycle. Forward, regurgitant (if applicable), and net flows were then automatically calculated from the resulting flow-time curves. The regurgitant fraction through a region of interest is defined as follows:

$$\text{Regurgitant fraction} = (\text{Reverse flow} / \text{Forward flow}) \times 100.$$

One patient, who woke during the study and could not be resedated, did not have an aortic phase-contrast magnetic resonance measurement for analysis.

Ventricular Volume Analysis

Cine short-axis imaging of the functional single ventricle was acquired from the base to the apex of the heart by using 8 contiguous slices ranging from 6 to 8 mm in thickness, depending on heart size. The ventricular sys-

TABLE 1. Characteristics of study patients

Parameters	Results
Age (y), mean $\pm$ SD (range)	2.7 $\pm$ 0.7 (1.5–5.2)
Male/female sex	13/11
BSA at CMR (m ²), mean $\pm$ SD (range)	0.59 $\pm$ 0.05 (0.47–0.67)
Cardiac anomaly (n = 24)	
Dominant, functional, single RV	n = 13
RV w/Norwood (HLHS, DORV/MA)	n = 11 (n = 10, n = 1)
RV w/normal aorta (single RV, unbalanced CCAVC)	n = 2 (n = 1, n = 1)
Dominant, functional, single LV	n = 7
LV w/Norwood (DILV/TGA)	n = 1
LV w/normal aorta (TA, DILV/TGA [S,L,L])	n = 6 (n = 5, n = 1)
Indeterminate ventricular morphology	n = 4
SCPC (n = 24)	
Age (y), mean $\pm$ SD [range]	0.5 $\pm$ 0.1 [0.3–0.7]
BDG (right bilateral)	n = 18 (n = 15, n = 3)
Hemi-Fontan	n = 6
Fontan (n = 24)	
Age (y), mean $\pm$ SD (range)	3.1 $\pm$ 1.0 (2–7.5)
Extracardiac conduit	n = 18
Lateral tunnel	n = 6
Fenestrations	n = 23

SD, Standard deviation; BSA, body surface area; CMR, cardiac magnetic resonance; RV, right ventricle; HLHS, hypoplastic left heart syndrome; DORV, double-outlet right ventricle; MA, mitral atresia; CCAVC, complete common atrioventricular canal; LV, left ventricle; DILV, double-inlet left ventricle; TGA, transposition of the great arteries; TA, tricuspid atresia; TGA(S,L,L), situs solitus of the atria with right ventricular outlet chamber to the left of the dominant morphologic left ventricle, aorta (arising from the right ventricular outlet chamber) to the left of the pulmonary artery (arising from the dominant left ventricle); SCPC, superior cavopulmonary connection; BDG, bidirectional Glenn; Hemi-Fontan, patch closure of the superior vena cava–right atrial junction and side-to-side anastomosis of the superior vena cava–right pulmonary artery junction.

tolic function analysis involved contouring the blood pool at end-diastole and end-systole at each level of the volume data set, thereby quantifying the end-diastolic volume (EDV) and end-systolic volume (ESV). The stroke volume is defined as the difference between the EDV and ESV, and the ejection fraction is defined as follows:

$$\text{Stroke volume} / \text{EDV} \times 100.$$

For the purpose of comparison, the patients were grouped into those with a dominant, functional single right ventricle (Video 1) versus those with a dominant, functional single left ventricle (Video 2). There were 4 patients with indeterminate ventricular morphology who were excluded from the right ventricle versus left ventricle analysis.

Atrioventricular Valve Regurgitation

The atrioventricular valve (AVV) regurgitant fraction was defined by using the following formula:

$$\text{AVV regurgitant fraction (\%)} = (\text{AVV regurgitant volume per heart beat} / \text{AVV inflow per heart beat}) \times 100$$

The AVV regurgitant volume is equal to the difference between the ventricular stroke volume (derived from cine magnetic resonance) and the cardiac output per heart beat (derived from phase-contrast magnetic resonance). In the absence of semilunar valve regurgitation, the AVV inflow is equal to the ventricular stroke volume.

FIGURE 1. Comparison of hospital length of stay for patients with differential size and flow characteristics. Patients with one branch pulmonary artery (BPA) that had an area of less than 25% of the total cross-sectional area (CSA) were compared with patients with BPAs that both had areas greater than 25% of the total CSA. Patients with one BPA that received less than 40% of the total flow were compared with patients with BPAs that both received greater than 40% of the flow. Both comparisons show a significant difference. Error bars depict the standard deviation.

Aortic Arch Obstruction

Aortic arch adequacy was determined by means of direct measurement with gadolinium magnetic resonance angiographic analysis (n = 22) and bright-blood static axial images (n = 24). In circumstances in which there was clinical concern for residual aortic arch obstruction, such as Norwood reconstruction, off-axis cine imaging of the aortic arch was used for further delineating arch morphology and identifying flow turbulence (Videos 3 and 4).

Pre-Fontan Echocardiographic Analysis and Catheterizations

Pre-Fontan echocardiograms and, where available, cardiac catheterizations were reviewed for assessment of the superior cavopulmonary connection and BPA anatomy, ventricular function, AVVR, and aortic arch obstruction.

Hospital Course

The medical record was reviewed for determination of the surgical procedure, complications, and LoS. The LoS was defined as days of hospitalization within the first 30 days after the Fontan operation.²³ There were 2 patients who were discharged and subsequently readmitted for treatment of infection. One patient had an isolated wound infection, and the other presented with mediastinitis (fever, wound degeneration, and an associated effusion) and required a prolonged readmission because of parental noncompliance with antibiotic treatment. For both patients, their LoSs were calculated on the basis of their initial hospitalization.

Statistical Analysis

Standard descriptive statistics using means with ranges and standard deviations were used to describe the patient demographics. The 2-tailed, 2-sample Student's *t* test was used to compare the LoS, cardiac index, percentage left pulmonary artery (LPA) size, and percentage LPA flow data between patient groups dichotomized by ventricular morphology and the presence of Norwood reconstruction. Patients were also dichotomized by percentage size and flow to one branch of the pulmonary artery, and the 2-tailed, 2-sample Student's *t* test was used to compare differences in LoS. A power regression was used to examine the relationship between the total indexed BPA size and the LoS. All statistical analysis was performed with Microsoft Excel software (Microsoft, Redmond, Wash).

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the article as written. The study was approved by the Institutional Review Committee of The Children's Hospital of Philadelphia.

RESULTS

Hospital Course

All 24 patients underwent the Fontan operation. There were no deaths. The mean LoS was 10 days, the median was 8 days, the mode was 5 days, and the range was 4 to 25 days. In 22 of the 24 patients, the primary postoperative issue specifically noted in the medical record was diuretic therapy for pleural effusions, which accounted for the LoS. The mean discharge oxygen saturation for all patients was $86.4\% \pm 3.4\%$, with a range of 77% to 94%. There was 1 patient with cyanosis caused by arteriovenous malformations and 1 patient with a moderate pericardial effusion.

BPA Size/Flow Distribution and LoS

The mean right pulmonary artery (RPA) cross-sectional area measured $1.0 \pm 0.4 \text{ cm}^2/\text{m}^2$, and the mean LPA cross-sectional area measured $0.6 \pm 0.3 \text{ cm}^2/\text{m}^2$. The mean RPA versus LPA flow distribution measured 59.6% versus $41.4\% \pm 19.6\%$.

Patients were dichotomized by differential BPA size and flow. Patients with one BPA accounting for less than 25% of the total cross-sectional area, patients with one BPA accounting for less than 40% of the total net BPA flow, or both remained in the hospital significantly longer (Figure 1). There was moderate correlation between the total (RPA plus LPA) cross-sectional area and LoS. Patients with a total cross-sectional area of less than 1.5 cm^2 experienced a non-linear increase in LoS (Figure 2).

LoS, Cardiac Index, Percentage LPA Size, and Percentage LPA Flow

When dichotomized by ventricular morphology, it was found that patients with the dominant ventricle having left ventricular (LV) morphology had a shorter LoS and higher cardiac index compared with patients with dominant ventricles of right ventricular (RV) morphology. There was no difference in percentage LPA size or percentage LPA

FIGURE 2. Power regression comparing the total cross-sectional area of the right pulmonary artery (RPA) and left pulmonary artery (LPA) with length of stay (LoS). Note that at less than 1.5 cm², the LoS increases in a nonlinear fashion.

flow between LV and RV morphologies. When dichotomized by the presence of Norwood reconstruction, patients without Norwood reconstructions had a shorter LoS. However, there was no significant difference in cardiac index, percentage LPA size, or percentage LPA flow (Figure 3).

Ventricular Volume Analysis

Volume data from cine magnetic resonance demonstrated that patients with RV and LV morphologies had no significant differences in EDV. However, stroke volume and ejection fraction were higher in patients with LV morphology, which was associated with a significantly smaller LV ESV

compared with RV ESV. No significant differences in EDV, ESV, or stroke volume were found when comparing patients with Norwood reconstructions with patients with normal aortas. The difference in ejection fraction reached significance when the data were analyzed according to whether a patient had a Norwood reconstruction versus a normal aorta. (Figure 4).

AVVR and Aortic Arch Assessment

Ventricular stroke volume data (from cine magnetic resonance) and aortic valve flow data (from phase-contrast magnetic resonance) were available in 19 patients for quantification of AVVR. Seventeen (89%) of 19 patients had AVV regurgitant fractions of less than 10%. Two (11%) of 19 patients had an AVV regurgitant fraction of between 10% and 21%. The CMR aortic arch assessment in all patients did not reveal any significant coarctation thought to require further intervention.

Pre-Fontan Echocardiographic Data

In 10 (42%) of the 24 patients, echocardiographic analysis correctly identified that the superior cavopulmonary connection and the BPAs were unobstructed. Because of limited echocardiographic windows, the superior cavopulmonary connection and at least one of the BPAs could not be adequately assessed in 6 and 12 patients, respectively. In one instance the limitation of echocardiography was attributed to the patient being nonsedated, and a second patient could not be properly assessed because of an artifact produced by a pulmonary artery stent.

FIGURE 3. Comparison of hospital length of stay, cardiac index, left pulmonary artery area divided by total cross-sectional area (% LPA Size), and left pulmonary artery flow divided by total flow (% LPA Flow) for different patient groups. Patients with right ventricular morphology (RV) were compared with patients with left ventricular morphology (LV), and patients who underwent Norwood reconstructions were compared with patients with normal aortas. P values are shown for each comparison. NS, Nonsignificant P values. Error bars depict the standard deviation.

FIGURE 4. Comparison of volumetric data between patients with right ventricular morphology (RV) and patients with left ventricular morphology (LV) and between patients who underwent Norwood reconstructions and patients with normal aortas. *P* values are shown for each comparison. NS, Nonsignificant *P* values. Error bars depict the standard deviation.

Catheterization Data

There were 12 Pre-Fontan cardiac catheterizations. Of the 12 Pre-Fontan catheterizations, 3 were interventional. All 3 interventions were balloon angioplasty of one of the BPAs. Two of the interventional catheterizations were performed before CMR, and one was performed after CMR demonstrated RPA stenosis. Nine of the 12 catheterizations were diagnostic and did not alter the patient's clinical course. No patient who underwent catheterization after CMR had new findings that led to a catheter intervention or an altered surgical approach.

There was one diagnostic catheterization performed in the immediate post-Fontan period (postoperative day 7) for determination of the cause of cyanosis. The patient was known to have arteriovenous malformations diagnosed by means of preoperative catheterization. No new diagnostic data were derived, and no intervention was performed. The patient was discharged on postoperative day 12.

DISCUSSION

In the present study we found that CMR measurements of the BPA sizes and flows are predictive of a patient's LoS after the Fontan operation. We demonstrate that small BPAs with a significant differential in size or flow distribution are associated with a prolonged LoS. Many studies have concentrated on the effect of small BPAs on Fontan operation-related mortality.^{1-7,12,13} It has been shown that even patients thought to have a contraindication to the Fontan operation because of small BPAs can safely undergo the procedure.^{4,13}

Our investigation of BPAs is unique in several ways. First, using precise CMR measurements from tomographic

images (rather than cardiac catheterization angiographic projection images), our analysis, as presented in Figure 1, emphasizes differential size (and flow) between the 2 lungs rather than absolute cross-sectional area. Our data suggest that the differences in cross-sectional area (and pulmonary blood flow) between the 2 lungs might be as important as the total available pulmonary vascular tree. This finding is consistent with the fact that although patients with a single lung can survive the Fontan operation, they are at increased risk for morbidity and mortality.²⁴

Second, by using phase-contrast magnetic resonance, this is the first study to demonstrate the effect of BPA differential flow on LoS. Investigating differential flows is important because BPAs might appear to be of normal caliber without stenosis but still have a significantly altered flow distribution.

Finally, in Figure 2 we display the value of correlating total cross-sectional area with LoS. This power regression demonstrates that at approximately 1.5 cm², the LoS increases in a nonlinear fashion. This critical value has never been reported in the Fontan literature.

Moreover, this is the first study to use CMR for measuring ventricular size, function, and cardiac index in patients undergoing the Fontan operation. When indexed for body surface area, our cine data suggest that dominant ventricles with either RV or LV morphologies have similar EDVs. However, the RV ESV is significantly greater than the LV ESV, resulting in a relatively lower RV stroke volume and RV ejection fraction. Phase-contrast magnetic resonance measurement of the cardiac index confirms the cine data, showing that the cardiac index in patients with RV morphology was significantly lower than that seen in patients with LV morphology. In our study population we found that

patients with RV morphology had a prolonged LoS after the Fontan operation compared with that seen in patients with LV morphology (12.7 vs 5.3 days, $P < .01$). Quantification of ventricular function is especially important to measure in light of the recent report of Hosein and colleagues,¹² which argued that preoperative ventricular function is predictive of early and late Fontan outcome. Furthermore, we did not find significant differences in pulmonary artery size or flow among patients with RV and LV morphologies as a means of explaining their differences in LoS. Rather, these differences appear to be associated with ventricular function and cardiac index. Although patients with a Norwood reconstruction had a prolonged LoS (12.4 vs 7.7 days, $P = .05$), there were no differences in percentage LPA size, percentage LPA flow, EDV, ESV, or cardiac index to explain this finding.

Future Directions

It has been argued that in the context of excellent imaging windows, noninvasive echocardiographic analysis can be used reliably to determine whether a patient can safely undergo the Fontan operation without confirmation with diagnostic cardiac catheterization.¹⁴ However, frequently echocardiographic windows are limited and the imaging data are inadequate for assessment of the superior cavopulmonary connection and BPAs. Therefore many patients would require diagnostic pre-Fontan catheterization based on echocardiographic data alone.

In this retrospective study we demonstrate the broad capacity of CMR to assess patients before the Fontan operation. CMR can quantify BPA size/flow, ventricular function, cardiac index, AVVR, and residual coarctation. We include a subpopulation analysis of the available echocardiographic and catheterization data. In half of our patients, at least one of the BPAs could not be adequately assessed echocardiographically. Furthermore, of the 12 pre-Fontan catheterizations, 9 were diagnostic, and none had new findings that led to a catheter intervention or an altered surgical approach. Of note, there was one patient in whom CMR identified RPA stenosis, which led to interventional balloon angioplasty.

Currently, diagnostic catheterization remains the standard of care among many pediatric cardiologists for pre-Fontan assessment.²⁵ There is clearly a need for physicians taking care of these complex patients to develop a methodology toward standardizing pre-Fontan assessment. This is an imperative issue to address in light of recent studies demonstrating that children exposed to ionizing radiation from diagnostic imaging are at increased risk of future malignancies.^{26,27} Given our experience that most pre-Fontan catheterizations are purely diagnostic in nature, it is logical that, where available, CMR should ideally serve as the initial screening tool for pre-Fontan assessment and as the basis for referring patients for interventional catheterization. Therefore we

advocate for a larger prospective study to determine whether CMR can replace routine invasive diagnostic catheterization for pre-Fontan assessment.

Study Limitations

The major limitation of this study is its retrospective nature. A prospective study in which all patients undergo both CMR and catheterization is necessary to more completely compare the efficacy and safety of CMR versus diagnostic catheterization. In contrast to other post-Fontan outcome studies, this study population is fairly uniform and represents pre-Fontan patients who have all been assessed in the current surgical era at a single center. The only major exception to this with respect to surgical technique is that 25% of the patients underwent a lateral tunnel instead of an extracardiac conduit Fontan operation. The RV versus LV morphology volume and function data are limited by the relatively small sample sizes and the fact that these comparisons were univariate analyses. Further investigation is warranted to confirm these suggested findings. Finally, the subpopulation analysis comparing CMR and catheterization might be limited because it is possible that other institutions have different pre-Fontan interventional catheter strategies, resulting in more referrals to interventional catheterization and less purely diagnostic catheterizations.

CONCLUSION

In conclusion, quantitative CMR measurements of BPA size and flow in pre-Fontan patients predict LoS after the Fontan operation. CMR suggests that pre-Fontan patients with a dominant ventricle of RV morphology have lower ejection fractions and cardiac indexes compared with patients with LV morphology. Finally, CMR is an excellent imaging tool for assessment of the cavopulmonary connection and BPAs in patients undergoing the Fontan operation.

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