Comparison Between Echocardiography and Cardiac Magnetic Resonance Imaging in Predicting Transplant-Free Survival After the Fontan Operation

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Adverse outcomes increase in frequency as patients after Fontan operation approach adulthood. Cardiac magnetic resonance (CMR) imaging–derived parameters have been shown to predict death/transplant; however, limited data are available on the usefulness of echocardiography in risk stratification. We conducted a retrospective, single-center review of records of patients after Fontan operation with an echocardiogram and CMR within 1 year of each other. The primary end point was time to all-cause mortality or listing for transplant. Of the 127 eligible patients, there were 12 end points (9%; 10 deaths and 2 listing for transplant). Median age was 16.8 years (interquartile range 12 to 23.1) with a median follow-up of 3.8 years (interquartile range 2.6 to 5.7). Among clinical parameters, protein-losing enteropathy had the strongest association with the outcome. Among echocardiographic variables, global circumferential strain showed the strongest association (hazard ratio 1.3 per unit change, 95% confidence interval 1.1 to 1.5, p value 0.001, C-index 0.81), whereas among CMR variables indexed ventricular end-diastolic volume showed the strongest association with the outcome (hazard ratio 1.04 per 10 ml/BSA$^{1.3}$ increase in volume, 95% confidence interval 1.02 to 1.06, p value 0.001, C-index 0.82). Cox proportional hazards analysis revealed echocardiography and CMR models to each individually have a higher predictive ability than the clinical model; however, in direct comparison, neither technique was superior. In conclusion, both echocardiography-derived circumferential strain and CMR-derived ventricular end-diastolic volume index are associated with transplant-free survival in patients after Fontan operation. Echocardiography and CMR parameters have higher discriminative ability than clinical variables. Although neither imaging technique is superior in this cohort, both introduce important factors for risk stratification. **(Am J Cardiol 2015;116:1132–1138)**

The Fontan circulation is the final physiological state achieved after a series of palliative procedures in patients with functional single ventricles. Perioperative morbidity and mortality have significantly decreased in children after the Fontan surgery; however, adverse outcomes are increasingly frequent as they approach adulthood.[1,2] Several clinical risk factors have been associated with poor survival in this population. Protein-losing enteropathy (PLE) occurs in ~3% to 15% of patients after Fontan operation, with high mortality.[3–5] Patients with diminished exercise capacity, portal hypertension, systemic oxygen desaturation, and with functional single right ventricles have also been identified to have a higher risk of death.[6–8] Despite routine interval imaging follow-up with echocardiography and/or cardiac magnetic resonance (CMR) examinations, there is limited knowledge about associations between imaging parameters and adverse outcomes, such as death or need for transplantation.[9–12] We recently demonstrated that CMR-derived indexed ventricular end-diastolic volume (EDV_i) independently predicted death and transplantation in patients late after the Fontan operation and added incremental value over clinical variables alone.[13] Myocardial strain measured by echocardiography has been studied in patients after Fontan operation, but there are no data on its utility in predicting adverse outcomes.[14–16] The goal of this study was to compare the echocardiographic and CMR parameters associated with death or transplantation in patients after the Fontan operation.

Methods

We conducted a retrospective, single-center study of patients after Fontan operation who had both an echocardiogram and a CMR performed at Boston Children's Hospital within 1 year of each other from January 1, 2005, to June 30, 2013. A minimum of 1 year of clinical follow-up after the latter of the 2 studies, or occurrence of the primary end point defined subsequently, was required for inclusion. Patients were excluded if there was a catheter or surgical intervention between echocardiogram and CMR or if images were inadequate for ventricular size and function

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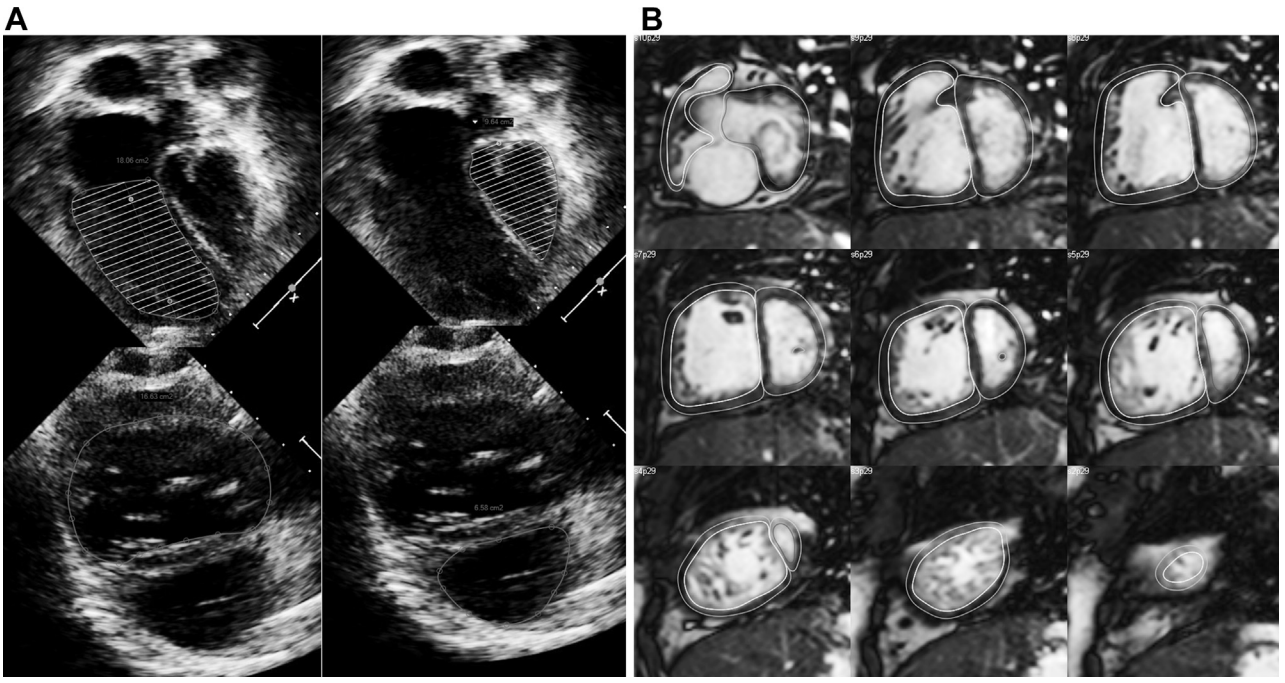

Figure 1. Ventricular volume measurements by echocardiography and CMR imaging. *(A)* Measurement of ventricular volumes by echocardiography using modified biplane Simpson's method. *(B)* Measurement of ventricular volume using short-axis stack of CMR images.

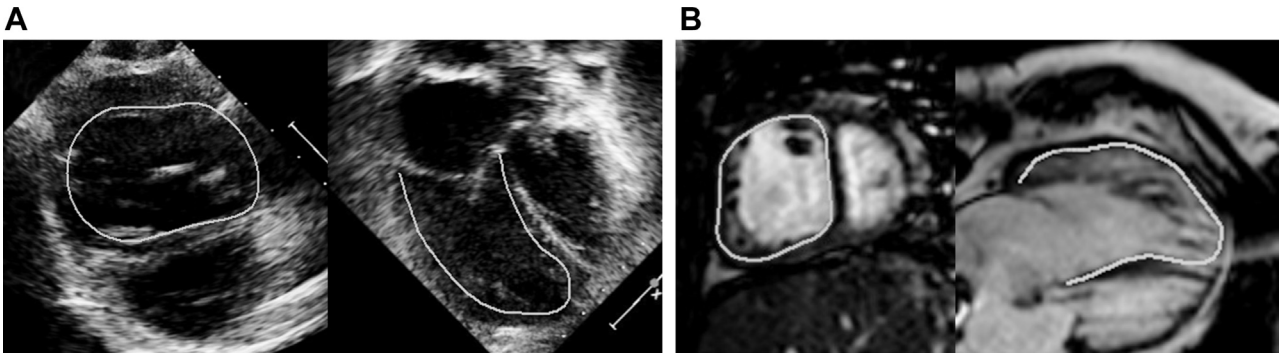

Figure 2. Ventricular strain measurements by echocardiography and CMR imaging. *(A)* Echocardiogram-based measurements of circumferential and longitudinal strain. *(B)* Circumferential and longitudinal strain measurements using CMR.

measurements or speckle tracking (in at least 1 echocardiographic view). If multiple sets of echocardiograms and CMR examinations met inclusion criteria, the oldest available study was used for analysis. The Boston Children's Hospital Committee on Clinical Investigation approved this study and waived the requirement for informed consent.

The primary end point was a composite of all-cause mortality or listing for heart transplantation. Dates of listing for cardiac transplantation, transplantation, or death were confirmed against the New England Organ Bank and the Social Security Death Index databases. For survival analyses, follow-up was measured from the date of echocardiogram to either the end point or the last known follow-up date with documented transplant-free survival.

Patient medical records were reviewed for the following clinical variables: date of birth, gender, age and body surface area (BSA) at testing, cardiac anatomy, and type of Fontan surgery. Ventricular morphology was classified as left ventricular, right ventricular, or mixed (eg, unbalanced atrioventricular canal), according to previously published criteria.[2] Ventricular type was classified as mixed if both ventricles had a CMR-derived EDV z-score greater than −4. Recorded co-morbidities included sustained ventricular tachycardia (VT), significant atrial arrhythmia (documented atrial flutter, fibrillation, or other supraventricular tachycardia), successful resuscitation after cardiac arrest, history of cerebrovascular accident, seizures, and PLE. Diagnosis of PLE was made based on review of notes written by patients' primary attending cardiologists.

All echocardiograms were obtained using Phillips IE33 machines (Philips Healthcare, Best, The Netherlands) using S8/S5/X5 transthoracic probes. Echocardiograms were reviewed by a single observer (SJG) for the following: aortic regurgitation grade, atrioventricular valve regurgitation grade, qualitative assessment of systolic function, and presence or absence of a Fontan fenestration. EDV and