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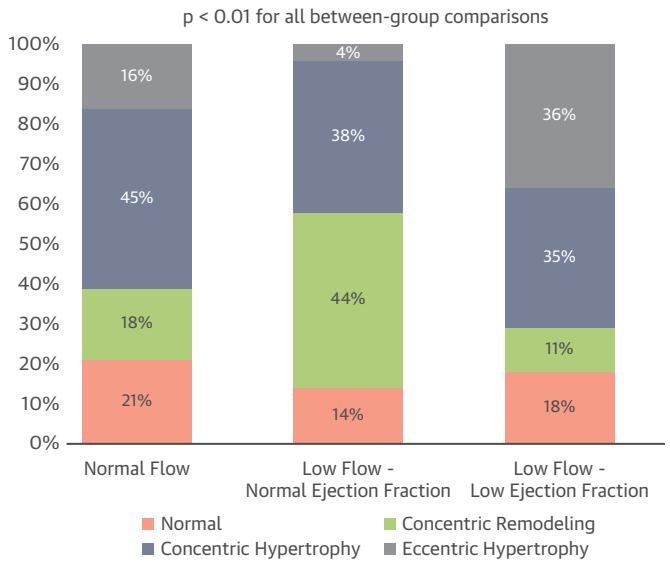
FIGURE 1 Flow Type Stratified by Left Ventricular Geometry



There were significant differences in geometric patterns between the different flow types, with overall p value <0.01 for association between flow type and geometry, and p < 0.01 for distributions within each flow type.

flow pattern and left ventricular geometry; 3) the different geometries in low flow-low EF aortic stenosis compared with normal flow are explained by clinical factors, whereas low flow-normal EF aortic stenosis has a strong independent relationship with concentric remodeling; and 4) concentric remodeling patients have lower flow and estimated plasma volume than those with other geometries. These findings suggest a potential pathophysiological role for volume underload, rather than increased peripheral impedance, in the development of low flow-normal EF severe aortic stenosis.

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Ventricular Response to Dobutamine Stress CMR Is a Predictor for Outcome in Fontan Patients

The Fontan operation is used to treat patients with a functional univentricular heart (1). Long-term complications include circulatory failure, thromboembolic events, arrhythmias, and death (1,2).

Cardiovascular magnetic resonance (CMR) using exercise or pharmacological stress might detect early dysfunction (3). Our aim was to evaluate the value of dobutamine-stress CMR to predict adverse outcome in patients with a Fontan circulation.

In earlier multicenter prospective studies, we obtained results of low-dose (7.5 μg/kg/min)

dobutamine-stress CMR, serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiopulmonary exercise testing (4). In the current study, the composite endpoint included events during follow-up after baseline CMR: cardiac death or reintervention, protein-losing enteropathy, and hospitalization or cardioversion/ablation for arrhythmias.

Time-to-event analyses (Kaplan-Meier method) and Cox proportional hazard regression analyses were performed to determine the predictive value for the endpoint. A p value <0.05 was required for the parameter to remain in the multivariable model.

Ventricular volumes were analyzed according to common practice and were indexed for body surface area (4). Changes in CMR parameters during stress were calculated as follows: parameter change = $\text{parameter}_{\text{stress}} - \text{parameter}_{\text{rest}}$.

Ninety-two patients were included, median age at stress CMR 11.5 (interquartile range [IQR]: 9.8 to 15.3) years, median time after Fontan completion 8.0 (IQR: 6.9 to 11.3) years. Thirty-one patients had a dominant right ventricle, 56 had a dominant left ventricle, and in 5 the dominant ventricle was undefined. The intra-atrial tunnel Fontan technique was used in 45, an extracardiac conduit in 42, and an atriopulmonary connection in 5 patients.

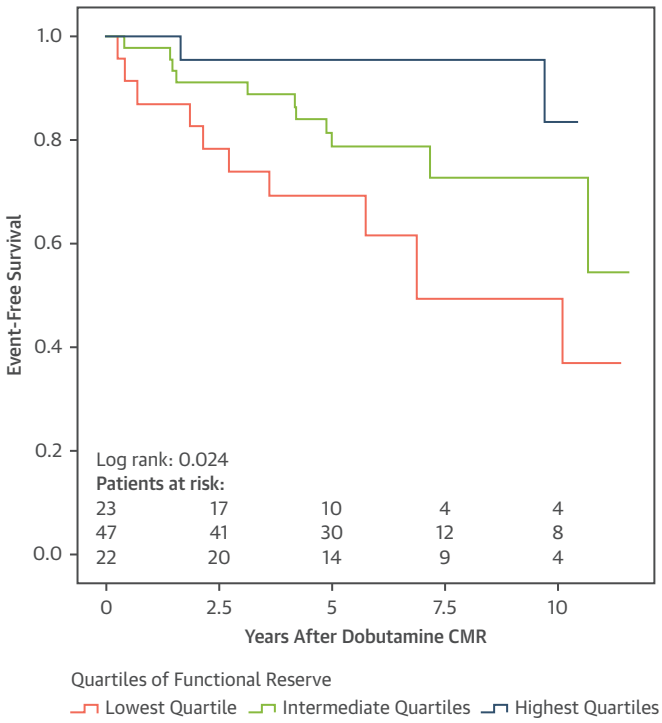
During dobutamine-stress, end-diastolic volume index (85 ± 21 vs. 73 ± 21 ml/m^2; p < 0.001) and end-systolic volume index (39 ± 16 vs. 26 ± 13 ml/m^2; p < 0.001) decreased and ejection fraction increased (55 ± 10 vs. 65 ± 10%; p < 0.001).

Twenty-three patients developed an event, a median 3.1 (IQR: 1.5 to 5.7) years after baseline CMR. These events were death (n = 1), cardiac reoperations (n = 7), out-of-hospital cardiac arrest (n = 1), hospitalization/ablation for arrhythmias (n = 7), pacemaker implantation (n = 5), extracardiac conduit-conduit stenting (n = 1), and coiling collaterals (n = 1). Protein-losing enteropathy was not noted.

Age at baseline CMR was similar for the event and nonevent groups. There was no significant difference in the presence of moderate to severe atrioventricular valve regurgitation, present in 30% of the event group versus 29% of the nonevent group, p = 0.895. There was no significant difference in peak Vo_2 (event group: 34.4 [IQR: 24.8 to 39.4] ml/min/kg; p = 0.66; n = 72), predicted Vo_2 peak (event group: 77.5% [IQR: 57.7 to 88.3]; p = 0.14; n = 72), or NT-proBNP (event group: 13.7 [IQR: 8.2 to 47.8] pmol/l; p = 0.18; n = 83) at baseline for the event versus the nonevent group.

Patients who developed an event had a lower increase in ejection fraction during stress (functional reserve [FR]) and a higher ventricular wall mass, compared with the nonevent group (FR: 6 ± 7 vs. 11 ± 6%; p = 0.002, mass 73 ± 23 vs. 57 ± 16 g/m^2; p < 0.001). We found no relation between right ventricle/left ventricle dominance or moderate and severe atrioventricular valve regurgitation and stress response.

FIGURE 1 Kaplan-Meier Curve for Event-Free Survival for Functional Reserve



Kaplan-Meier curve for event-free survival for functional reserve (FR). CMR = cardiac magnetic resonance imaging.

In Figure 1, the event-free survival for the different quartiles of FR is shown. The event-free survival was better for the patients in the highest quartile of FR (≥14%) (log rank: 0.024). In the lowest, intermediate, and highest quartiles, respectively 10, 11, and 2 patients developed an event.

In univariable analysis age at CMR and Fontan, right ventricle morphology, (log transformed) NT-proBNP, peak Vo_2, end-diastolic volume, end-systolic volume, stroke volume, ejection fraction, and moderate and severe atrioventricular valve regurgitation were not found to be predictive for the composite study endpoint. In multivariable analyses with the significant predictors from the univariable analysis, FR (hazard ratio [HR]: 0.86%; 95% confidence interval [CI]: 0.79 to 0.93; p < 0.001) and ventricular mass (HR: 1.04 g/m^2; 95% CI: 1.02 to 1.07; p = 0.001) were predictive for the

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study endpoint. There was no significant correlation (r = -0.069; p = 0.510) between ventricular mass and FR.

In this study we have demonstrated, using a composite endpoint derived of common outcomes in Fontan patients, that patients with a Fontan circulation with a good ventricular response to dobutamine stress have a lower risk of developing cardiac events during follow-up. The relation between stress CMR parameters and hard outcome measures has only been reported in congenital heart disease in adults (3). Because none of the other previously identified predictors (end-diastolic volume index >125 ml/m^2, peak Vo_2, NT-proBNP) (1,2,5) related to outcome in our young patients, who could be considered at relatively low risk, we think stress CMR parameters, particularly FR, may be useful early markers for outcome in Fontan patients.

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Comparison of [^{18}F]-FDG and [^{18}F]-NaF Positron Emission Tomography on Culprit Carotid Atherosclerosis

A Prospective Study

The application of positron emission tomography (PET) with different radioisotopes in atherosclerosis can detect various pathological cascades within atheroma (1). The 2-deoxy-2-[18F]-fluoro-D-glucose (FDG) ligand was the first radioisotope introduced in atherosclerosis study that measures inflammation activity (1). Recently, 18-F NaF ligand representing calcification activity within atheroma showed superior efficacy for detecting culprit coronary vessel when compared with the FDG ligand (2). We performed both FDG and NaF PET for stroke patients with carotid stenosis to determine whether NaF is also superior to FDG for detecting culprit atheroma.

The study protocol was approved by the institutional review board of Chung-Ang University Hospital. Twenty patients with acute ischemic stroke or transient ischemic attack with carotid artery stenosis >50% on brain computed tomography angiography were prospectively enrolled after providing written informed consent. We excluded patients with active cancer or autoimmune disease, uncontrolled diabetes mellitus with blood glucose more than 11 mmol/l at admission, and renal dysfunction with estimated glomerular filtration rate <45 ml/min/1.72 m^2. The culprit (+) group consisted of individuals with a culprit carotid lesion, defined as a carotid stenosis that was ipsilateral to ischemic lesions in the absence of another embolic source. All other individuals were deemed to have a nonculprit carotid lesion, composing the culprit (-) group.

When a patient was stabilized, FDG and NaF PET imaging were performed on separate days by the same protocol (median time after stroke: 17 days). After fasting for 8 h, 259 to 370 MBq (7 to 10 mCi) of FDG or NaF was injected intravenously. Approximately 60 min after the injection, PET images were acquired at 5 min/bed for the head and 1 min/bed from the skull base to the proximal thigh right after computed tomography scan (120 kVp, 50 mA). The maximum standardized uptake value at the carotid level where the atheroma was largest was selected and divided by standardized uptake value of aortic blood to derive the maximum target-to-blood ratio.