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Echocardiographic Predictors of Mortality in Adults With a Fontan Circulation

Adults with univentricular physiology repaired with a Fontan-type procedure are at increased risk of premature death. We investigated echocardiographic indexes that are predictive of mortality in this setting because the prognostic utility of such imaging is not well characterized.

Adults who had undergone a Fontan procedure and had been seen at our institution since 2005 were screened. Exclusion criteria were Kawashima repair, pregnancy, ventricular outflow gradient >2.0 m/s, supraventricular arrhythmia during transthoracic echocardiogram, or paced ventricular rhythm. Follow-up continued until time of death, total cavopulmonary connection (TCPC) conversion, or most recent review.

Standard 2-dimensional and Doppler echocardiographic assessments were performed. In addition, systolic duration was measured from the onset to the end of atrioventricular (AV) valve regurgitation. Diastolic duration was measured from the end of AV valve regurgitation to the onset of the subsequent AV valve regurgitation signal. The AV systolic to diastolic duration ratio (S/D duration ratio) was then calculated.

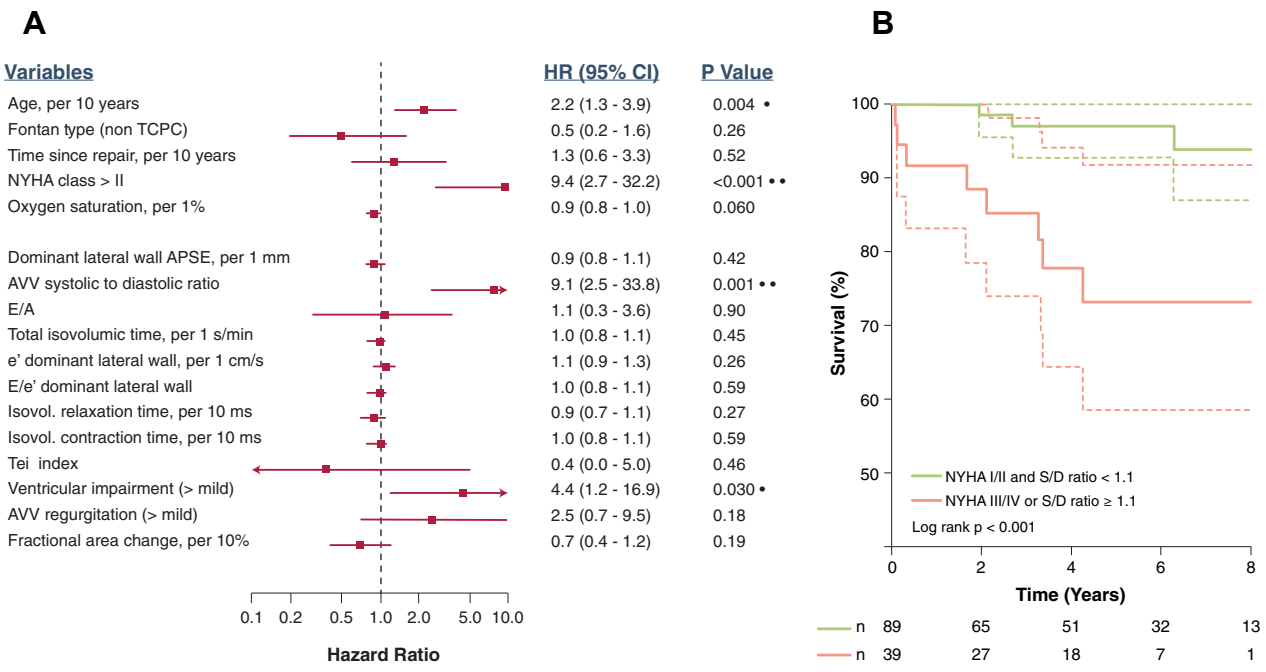
One hundred twenty-eight patients (64 men; median age 25 [interquartile range (IQR): 20 to 30] years; 107 [84%] with dominant left ventricle) were included. New York Heart Association functional class was I/II in 120 patients (94%) and III/IV in 8 (6%). Forty-eight had atriopulmonary connection (APC), and 80 had TCPC, of whom 16 had undergone an APC to TCPC conversion as an adult. Median follow-up was 4.2 years (IQR: 1.5 to 6.6 years). Overall, 75 patients (59%) had good systolic function by qualitative assessment. Thirty-eight patients (30%) had mild systolic impairment, 8 (6%) had moderate systolic impairment, and 7 (5%) had severe systolic impairment. One hundred eight patients (84%) had no AV valve regurgitation or mild AV valve regurgitation, and 20 (16%) had moderate to severe AV valve regurgitation.

Twelve patients (9%) died during follow-up (age 37 [IQR: 29 to 45] years). Seven of those had APC, 3 had TCPC, and 2 had TCPC conversion. Eight deaths were due to heart failure, 2 were sudden, and 2 were due to liver failure. The results of univariable Cox regression analysis are shown in **Figure 1A**. When accounting for Bonferroni correction (significance $p < 0.003$), only functional class and S/D duration ratio remained significant predictors of death. Kaplan-Meier survival analysis is shown in **Figure 1B**. We performed post hoc analysis to assess whether atrioventricular S/D duration ratio correlated with other transthoracic echocardiogram measures of ventricular function. A significant correlation existed with subjective grade of ventricular function ($R = 0.32$; $p = 0.006$), fractional area change ($R = -0.25$; $p = 0.04$), and E/A ratio ($R = -0.23$; $p = 0.009$). Atrioventricular S/D duration ratio did not correlate with age ($R = -0.04$; $p = 0.7$) but had a strong correlation with heart rate ($R = 0.58$; $p < 0.0001$). On univariable analysis, S/D duration ratio corrected for heart rate remained a strong predictor (hazard ratio: 7.5; $p < 0.0001$), whereas heart rate was associated with a lesser hazard ratio (1.1; $p = 0.02$).

This study suggests that S/D duration ratio is an especially important prognostic marker in Fontan patients. Assessment of single-ventricular function with echocardiography, the mainstay of cardiac imaging in Fontan-palliated adults, is challenging. S/D duration ratio reflects global ventricular function and can be measured simply and consistently using continuous-wave Doppler assessment of the AV valve. This may be of particular significance in Fontan patients but has only been explored previously in a pediatric group with hypoplastic left heart syndrome at various stages of Norwood palliation (1), and tissue Doppler-derived S/D duration ratio has been reported not to correlate with magnetic resonance imaging-derived measures of systolic function in that setting (2). Tissue Doppler-derived indices that reflect motion in one wall might be less useful (because of dyssynchronous contraction) than continuous-wave Doppler-derived measurement in the setting of complex single-ventricle hearts.

Data investigating the relation between echocardiography and clinical outcomes in the Fontan circulation are scarce. Poor ventricular function and degree of AV valve regurgitation have been retrospectively associated with risk of death (3). In Fontan patients with protein-losing enteropathy, deceleration time <120 ms predicted mortality (4). Ghelani

FIGURE 1 Results



(A) Results of univariable Cox regression analysis for mortality. **(B)** Kaplan-Meier survival analysis showed patients with good functional class (New York Heart Association [NYHA] functional class I/II) and atrioventricular valve systolic to diastolic duration ratio below 1.1 have better survival compared to the remainder of the population (97% vs. 74% at 5 years, $p < 0.001$). APSE = annular plane systolic excursion; AVV = atrioventricular valve; CI = confidence interval; HR = hazard ratio; isovol = isovolumic; S/D ratio = systolic to diastolic duration ratio; TCPC = total cavopulmonary connection.

et al. (5) found that reduced systolic function and increased indexed ventricular volumes were associated with mortality; global circumferential strain was the strongest predictor of mortality and listing for transplant.

S/D duration ratio is an independent predictor of mortality in adults with a Fontan circulation. It is easily measurable, even in complex univentricular hearts, and should be incorporated into the routine assessment of ventricular function in these patients.

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