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Aortic Dilatation in Repaired Tetralogy of Fallot

Although the high prevalence of aortic root dilatation in adults with repaired tetralogy of Fallot (rTOF) is well established (1,2), evidence to guide clinical follow-up and decision making remains sparse.

We sought to define the features, determinants, and rate of progression of aortic dilatation in adults with rTOF using cardiovascular magnetic resonance (CMR).

We retrospectively identified adults with rTOF who had 2 interval CMR scans. Aortic dimensions were measured at sinus, sinotubular junction (STJ), and mid-ascending aortic level at both time points blinded to scan order and other clinical data. Dilatation was defined as diameter >2 SD larger than our published normal CMR aortic dimensions adjusted for age (3).

We retrospectively studied 110 patients (57 male; median age 30.9 years [interquartile range (IQR): 22.9 to 39.4 years]). One patient with aortic valve endocarditis requiring aortic valve surgery was excluded. Forty had a shunt prior to repair (median age at repair 4.5 years [IQR: 2.1 to 9.2 years]); 14 were repaired before 1 year of age; 9 had pulmonary atresia; 24 had right-sided aortic arch; and 11 were successfully treated for systemic hypertension. Twenty-nine patients (27%) had mild and 6 (5%) had moderate aortic regurgitation.

Seventy-six patients (69%) had aortic dilatation. Dilatation was present in 30 patients (27%) at sinus level, in 73 (66%) at STJ level, and in 24 (21%) at ascending aortic level. Thirty- five patients (31%) had normal aortic dimensions (**Figure 1A**). Patients repaired before 1 year of age were less likely to have aortic dilatation at any level compared with the remaining patients ($p = 0.001$).

Male sex and history of palliative shunt were independent predictors of aortic dilatation at any level ($p < 0.0001$ and $p = 0.023$, respectively) and were independent predictors of STJ dilatation ($p = 0.0001$ and $p = 0.033$, respectively). Male sex and pulmonary atresia were independent predictors of aortic sinus dilatation ($p = 0.008$ and $p = 0.0009$, respectively). Male sex, later repair, and pulmonary atresia were independent predictors of ascending aortic dilatation ($p = 0.008$, $p = 0.006$, and $p = 0.0004$, respectively).

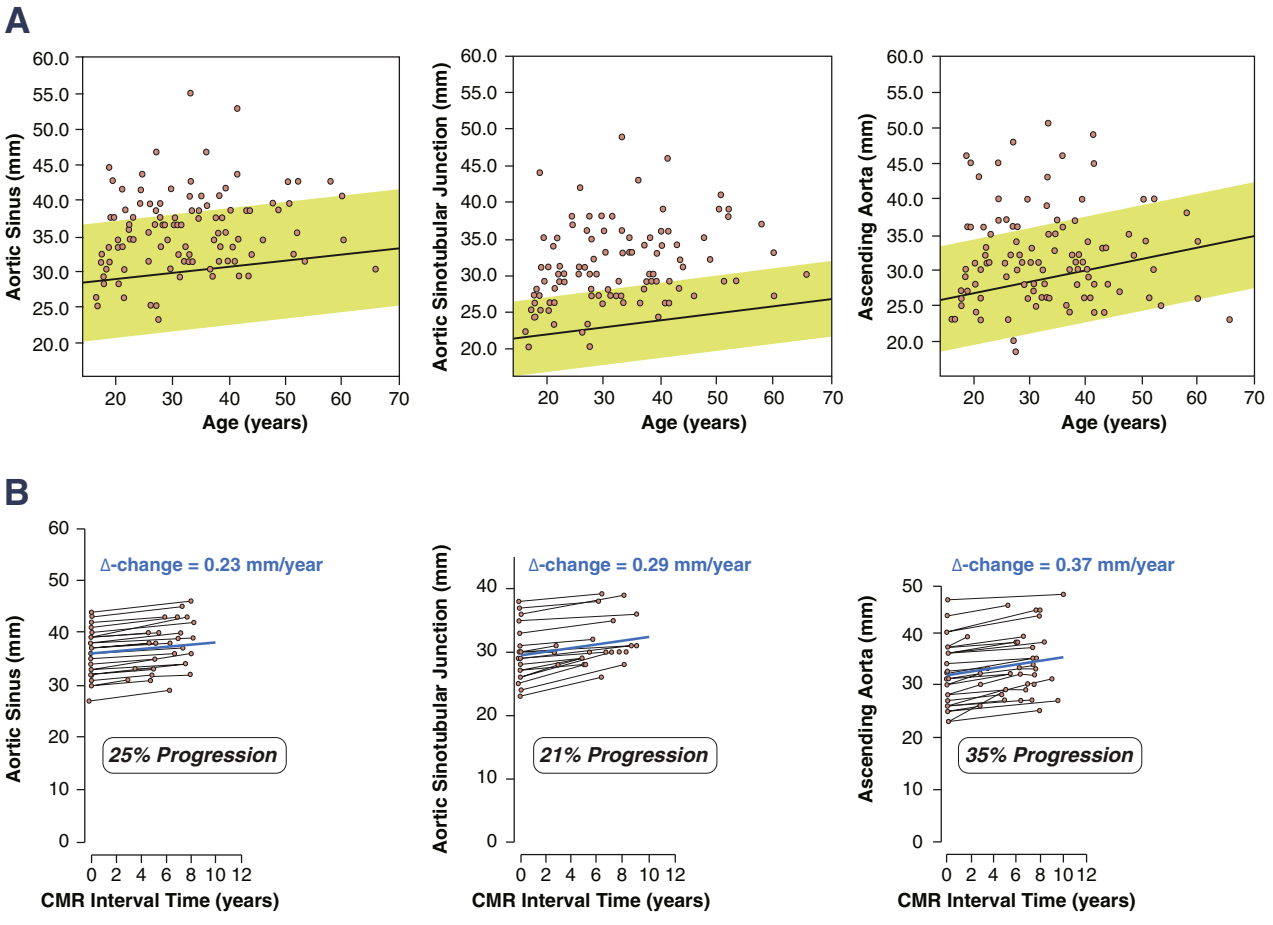
During a median interval of 6.3 (IQR: 5.1 to 7.6) years, aortic diameters increased in 47% patients (25% at sinus, 21% at STJ, and 35% at ascending aortic level) at rates between approximately 0.2 to 0.4 mm/year (**Figure 1B**). Even among patients with sinus diameter ≥45 mm at baseline ($n = 5$), there was no increase.

Predictors of aortic diameter increase at STJ level were older age, later repair, and right aortic arch. No predictors of aortic diameter increase at other levels were ascertained.

There were no aorta-related events during follow-up. Aortic regurgitation progressed from mild to moderate in only 2 patients without progressive aortic dilatation.

In conclusion, our data show that aortic dilatation is common, most frequently at STJ level (97% of patients with dilated aorta). Aortic dimensions increased in approximately 50% of patients during

FIGURE 1 **Aortic Diameters and Rate of Progression in 110 rTOF Patients Studied With CMR During Median Follow-Up of 6.3 Years**



(A) Patient aortic diameters against expected age-adjusted value illustrated by the **yellow zone** of 2 SD from our published mean. **(B)** Percentage of patients with aortic progression and the rate of diameter increase (**blue line** representing median progression) among patients that progress. CMR = cardiovascular magnetic resonance; rTOF = repaired tetralogy of Fallot.

a 6-year follow-up, most commonly in the ascending aorta, but with reassuringly low rates of progression.

Previous studies have reported aortic root dilatation in rTOF (1,2). We also found associated ascending aortic dilatation in 21% of the patients. Risk factors for aortic dilatation were similar to those previously reported (1,2) and are those that lead to increased volume overload of the aorta prior to repair. The combination of these with the intrinsically abnormal aortic vessel wall (4) may contribute to aortic dilatation. With earlier surgical repair, the importance of aortic dilatation may decrease.

We demonstrated a very low rate of aortic diameter progression comparable with known age-related increase in normal volunteers. Recent consensus recommendations suggest replacement of the ascending aorta when its diameter is at least 55 mm (5). Our data would not support a more aggressive approach or very frequent aortic assessment with CMR.

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CMR-Verified Regression of Cardiac AL Amyloid After Chemotherapy

Systemic light-chain (AL) amyloidosis is characterized by interstitial deposition of aggregated misfolded monoclonal immunoglobulin light chains in the form of amyloid fibrils. Cardiac involvement is the main driver of prognosis. Brain natriuretic peptides and echocardiography are currently the reference standards for assessing cardiac responses, but neither directly quantifies the amyloid burden. Cardiac magnetic resonance (CMR) is a sensitive tool for characterizing myocardial amyloid deposits: late gadolinium enhancement (LGE) shows a continuum of cardiac infiltration, from subendocardial LGE to transmural as the disease progresses (1). Native myocardial T1 and extracellular volume (ECV) measurements have been shown to track clinical disease in cardiac amyloidosis and improve diagnostic accuracy and patient stratification (2).

The aim of this study was to evaluate cardiac AL amyloidosis serially using CMR and ECV measurement. The study group comprised 31 consecutive patients diagnosed with cardiac AL amyloidosis (21 males [68%], age 61 ± 9 years) who underwent serial CMR evaluation with T1 mapping as well as comprehensive clinical assessment (electrocardiogram, echocardiogram, CMR, serum amyloid P [SAP] scintigraphy, and N-terminal pro-B-type natriuretic peptide [NT-proBNP] measurements) before and after chemotherapy in our center between 2011 and 2015. The clonal hematologic response was evaluated according to international consensus criteria (3). All subjects underwent CMR at 1.5-T (Avanto or Aera, Siemens Healthcare, Erlangen, Germany). T1 mapping was acquired using modified look-locker inversion recovery or the shortened modified look-locker inversion recovery sequence. Conventional 2-dimensional LGE was acquired with magnitude inversion recovery or phase-sensitive inversion recovery. ECV was measured as previously described (1). Regression in the cardiac amyloid burden was defined as a decrease in ECV by 2 SD. Changes in the visceral amyloid burden were assessed using serial SAP scintigraphy (4).

At baseline, the overall prevalence of LGE was 87%, with an average ECV of 54 ± 11%. The pattern of LGE was transmural in 29% and subendocardial in 58%; 4 patients (13%) had no LGE. The overall hematologic response rate was 61% and comprised complete response in 36%, very good partial response in 29%, and partial response or no response in 39% (3). Reduction in ECV attaining the CMR criteria for regression of amyloid occurred in 13 patients. The prevalence of regression was higher in patients with complete response/very good partial response (92%) versus patients in partial response/no response ($p < 0.01$) (**Figure 1**). The mass changed concordantly in 7 of the 13 patients (54%) whose amyloid regressed; the LGE pattern changed in 5 (38%). More than 30% reduction in NT-proBNP levels was present in 69% of patients with amyloid regression. Overall, regression of amyloid was associated with improvements in NT-proBNP, left ventricular mass, left atrial area, and diastolic function parameters. Regression of cardiac