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NONINVASIVE DETECTION OF TRANSPLANT CORONARY ARTERY DISEASE WITH CONTRAST-ENHANCED CARDIAC MRI IN PEDIATRIC CARDIAC TRANSPLANTS

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Transplant coronary artery disease (TCAD) is the primary complication that limits long-term survival in pediatric heart transplant recipients. Surveillance for TCAD in pediatric recipients continues to depend upon recurrent invasive coronary X-ray angiography (1). Limitations of cardiac access due to previous cardiac catheterizations and surgeries in children can further complicate performance of coronary studies. Contrast enhanced cardiac magnetic resonance imaging (CE-CMR) has been used to identify arterial inflammation in Takayasu's arteritis (2) and coronary artery atherosclerosis (3). We hypothesized that there would be a difference in coronary wall signal intensity using CE-CMR in pediatric heart transplant recipients with angiographic evidence of TCAD and those who lack evidence of disease.

The Washington University human studies committee approved the study. All participants gave written informed consent. Inclusion criteria were: pediatric heart transplant recipient 10 years of age undergoing coronary angiography for routine TCAD surveillance; 12 months after transplantation; absence of thoracic metal (angiographic coils, etc.) and glomerular filtration rate ≥ 30 ml/min/1.73 m² measured by the modified Swartz formula. Healthy volunteers (controls) were also recruited for CE-CMR imaging. Subjects underwent CE-CMR within a median of 1 day (interquartile range, 1–15.5 days) of coronary angiography in a 1.5-T magnetic resonance scanner. CMR sequences and imaging parameters were identical to a method previously described (3) except field of view=240×240 mm, matrix=192×125, repetition time/echo time=5.7 ms/2.9 ms for coronary luminal imaging, number of slices=35, time delay from gadolinium injection (0.1 mmol/kg) to CE-CMR=10–15 min, and inversion time range=260–290 ms. For each individual, CE-CMR coronary artery wall segments were identified in the proximal left anterior descending (<2 cm from origin), left circumflex (<2 cm from origin), and right coronary artery (<1 cm from origin). A contrast to noise ratio (CNR) between the coronary wall signal (SI_{wall}) and aortic blood signal (SI_{blood}) was determined as (SI_{wall} - SI_{blood})/noise. CNR was re-measured in a subset of heart recipients (N=10) and controls (N=5) to assess reproducibility.

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Disclosure statement

None of the authors have any conflicts of interest to disclose.

Angiograms were interpreted by an experienced pediatric interventional cardiologist (DTB) blinded to the CE-CMR results.

Results are expressed as median, interquartile range (IQR) or mean $\pm$ standard deviation. Individual characteristics were compared using Kruskal Wallis (age), Mann Whitney U (years after transplant and LVEF); and independent T test (cardiac index). Analysis of variance with Games Howell post hoc test was used to compare coronary CNRs. Reproducibility was evaluated with Spearman's correlation coefficient (r_s).

Subjects were divided into 3 groups that differed by age ($p=0.008$): TCAD ($N=6$, median=18.8 years, IQR=16.5–20.3 years) and no TCAD ($N=23$, median=15.1 years, IQR=13.5–17.9 years); and 8 control subjects (median=13.3 years, IQR=12.2–15.4 years). TCAD compared to no TCAD subjects were longer transplant survivors (17.1 years, IQR=15.2–19.7 years vs 3.1 years, IQR=1.6–15.0 years; $p=0.008$); had lower cardiac index (2.85 ± 0.67 L/min/m² vs 3.47 ± 0.68 L/min/m², $p=0.041$); and lower LVEF (62.2%, IQR=60.6–70.9% vs 75.3%, IQR=70.4–78.8%; $p=0.008$). Myocardial scar was detected in only 2 TCAD and 0 no TCAD subjects. Enhancement of coronary arteries, especially in TCAD subjects, was observed (Figure 1). TCAD subjects exhibited a significantly greater coronary artery wall CNR than subjects with no TCAD (15.74 ± 13.30 vs 6.64 ± 5.55 , $p=0.015$) or controls (15.74 ± 13.30 vs 2.78 ± 1.92 , $p=0.001$, Figure 2). Coronary artery wall CNR for controls was less than that of heart recipients with no TCAD (2.78 ± 1.92 vs 6.64 ± 5.55 , $p<0.001$). The coronary wall CNR measurements had good reproducibility ($r_s=.913$, $p<0.001$).

This pilot study confirms that a significant difference in coronary enhancement intensity exists between pediatric heart transplant recipients with angiographically detectable TCAD and those without TCAD. Detection of TCAD in pediatric heart transplant recipients is important for selection of treatment that may range from initiation of mTOR inhibitors (4) to listing for retransplantation. CE-CMR appears to offer a noninvasive method to detect TCAD and linked ventricular dysfunction to guide the decision for retransplantation (5).

CE-CMR assessments may not be feasible in some pediatric heart recipients due to the presence of metallic stent, vessel coils, or severe renal insufficiency. Extension of CE-CMR imaging to infant and young children also may be problematic due to their higher resting heart rates. To avoid the need for sedation in this research study, we did not enroll children less than ten years of age.

Further studies with more patients will be needed to confirm these pilot observations and to elucidate whether changes in the magnitude of coronary wall enhancement is correlated with increasing severity and progression of TCAD.

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Figure 1. Coronary artery imaging. A pediatric heart recipient with angiographic TCAD of the left anterior descending artery (A) is shown with CMR coronary luminal imaging (B). CE-CMR imaging demonstrates gadolinium enhancement of the coronary wall (C).

Figure 2.

Coronary wall contrast to noise ratios (mean $\pm$ 95% confidence interval) for 8 controls, 23 heart recipients with no angiographic transplant coronary artery disease (no TCAD), and 6 heart recipients with angiographic transplant coronary artery disease (TCAD).