Ventricular Inefficiency in Repaired Tetralogy of Fallot Assessed with 4D Flow MRI

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Target Audience: Those with interest in congenital heart disease, cardiopulmonary physiology and 4D flow MRI.

Background: Repaired Tetralogy of Fallot (rTOF) is frequently complicated by right ventricular (RV) and occasionally biventricular dysfunction leading to poor long-term outcomes. Conventional monitoring with CMR to measure RV volumes and function does not always reflect performance status or predict success following repair of pulmonic insufficiency in patients with rTOF. Additionally, reduced left ventricular ejection fraction (LVEF) has been shown to be one of the strongest predictors of mortality in patients with rTOF. Ventricular kinetic energy (KE) measurements provide a novel method of monitoring cardiac function and may provide a more robust and earlier predictor of declining RV and LV efficiency than current standard measurements of RV and LV size and function. Our purpose was to evaluate the following: (1) feasibility of calculating RV kinetic energy (KERV) and LV kinetic energy (KELV), (2) ventricular-vascular coupling with 4D Flow MRI and (3) to assess differences between rTOF and healthy volunteers.

Materials and Methods: Ten subjects with rTOF and 9 healthy volunteers were scanned according to an IRB-approved and HIPAA-compliant protocol. Radially undersampled 4D flow MRI using Phase Contrast Vastly Undersampled Isotropic Projection Reconstruction (PC VIPR) was performed on clinical MRI scanners (GE Healthcare, Waukesha, WI) after administration of gadolinium based contrast agents. PC VIPR parameters: FOV = 260-320 mm³, isotropic 1.3 mm spatial resolution, TR/TE = 8.8-10.9/2.8-3.7 ms (1.5T), and 6.2-3.7/2.0-2.2 ms (3.0T). Venc = 400-400 cm/s, scan time: 9-17 minutes using retrospective and prospective ECG gating. Post processing was conducted using Mimics (Materialise, Leuven, Belgium) for dynamic segmentation, Ensight (CEI, Apex, NC) for visualization, and customized Matlab (The MathWorks, Natick, MA) routines to measure KE RV, KE LV, main pulmonary artery flow (QMPA), KE LV, and aortic flow (QAO) throughout the cardiac cycle. The KE of a voxel of blood was calculated as \( KE = \frac{1}{2}mv^2 \), where the mass \( m \) represents the voxel volume multiplied by the density of blood (1.025 g/ml) and the velocity \( v \) of each voxel was determined from 4D Flow MRI. KE RV and KE LV were determined from the sum of the KE of the voxels within the segmented RV or LV, respectively, at each phase of the cardiac cycle. The directionality component of velocity was not considered. Differences in peak systolic and diastolic KE RV and KE LV in addition to the QAO/KE RV and QMPA/KE LV ratios (a measure of ventricular-vascular coupling) between groups were assessed using the Wilcoxon rank-sum test.

Results: Three distinct KE RV and KE LV peaks were observed in all subjects. Peak systolic (p=0.0002) and diastolic (p=0.0002 peak 1, p=0.0003 peak 2) KE RV were higher in rTOF than in healthy volunteers (Fig. 2A). The QAO/KE RV ratio was lower in rTOF than in healthy volunteers (p=0.0002). Peak systolic (p=0.0004) and diastolic (p=0.0002 peak 1, p=0.0008 peak 2) KE LV were higher in rTOF than in healthy volunteers (Fig. 2B). The QAO/KE LV ratio was lower in rTOF than in healthy volunteers (p=0.0002) (Fig. 2C).

Discussion: Time-resolved KE RV and KE LV were measured in rTOF and healthy volunteers using 4D flow MRI (PCVIPR). KE RV and KE LV were higher and QAO/KE RV and QMPA/KE LV ratios were lower in rTOF than in healthy volunteers, indicative of greater inefficiency in RV and LV function to generate the same cardiac output. Previous studies suggest interventricular interactions are responsible for left ventricular dysfunction in rTOF. Future studies are needed to determine if changes in KE RV and KE LV provide earlier evidence of ventricular dysfunction and the need for re-intervention than standard CMR measurements. In addition, future studies could demonstrate a closer relationship of KE RV and KE LV with exercise performance and capacity than standard CMR measurements.

Summary: These preliminary results are remarkable for the significant dysfunction of both the RV and LV in patients with rTOF. When compared to normal volunteers, this analysis shows that there is substantial energetic expenditure by the RV and LV in these patients, without a corresponding ability to generate pulmonary or systemic flow. Quantification of the amount of wasted ventricular work in these patients with rTOF.