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[1,2,4]. Additionally, reduced left ventricular ejection fraction (LVEF) has been shown to be one of the strongest predictors of mortality in patients with rTOF[2]. 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[3]. Our purpose was to evaluate the following: (1) feasibility of calculating RV kinetic energy (KE_{RV}) and LV kinetic energy (KE_{LV}), (2) ventricular-vascular coupling with 4D Flow MRI and (3) to assess differences between rTOF and healthy volunteers.

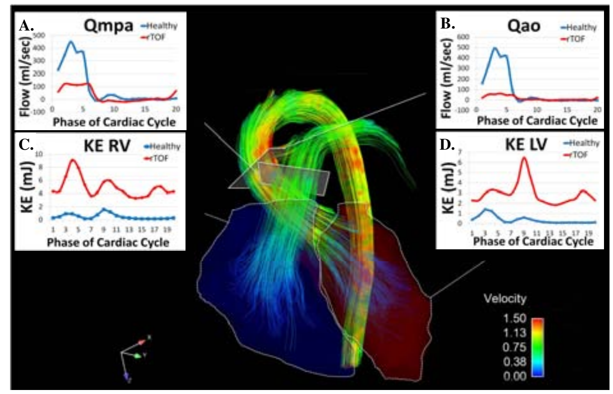

Figure 1: 4D Flow MRI was used to calculate flow and KE. [A-B] Flow in main pulmonary artery (mpa) and Aorta (ao) during a cardiac cycle in a sample healthy volunteer and rTOF. [C-D] KE_{RV} and KE_{LV} in the same healthy volunteer and rTOF. Note the high KE and low Qao and Qmpa of the rTOF patient.

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 mm^3, 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= 40-400 cm/s, scan time: 9-17 minutes using respiratory and retrospective 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}, main pulmonary artery flow (Q_{MPA}), KE_{LV}, and aortic flow (Q_{AO}) throughout the cardiac cycle. The KE of a voxel of blood was calculated as $KE = 1/2mv^2$, 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 Q_{MPA}/KE_{RV} and Q_{AO}/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 Q_{MPA}/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 Q_{AO}/KE_{LV} ratio was lower in rTOF than in healthy volunteers (p= 0.0002) (Fig. 2C).

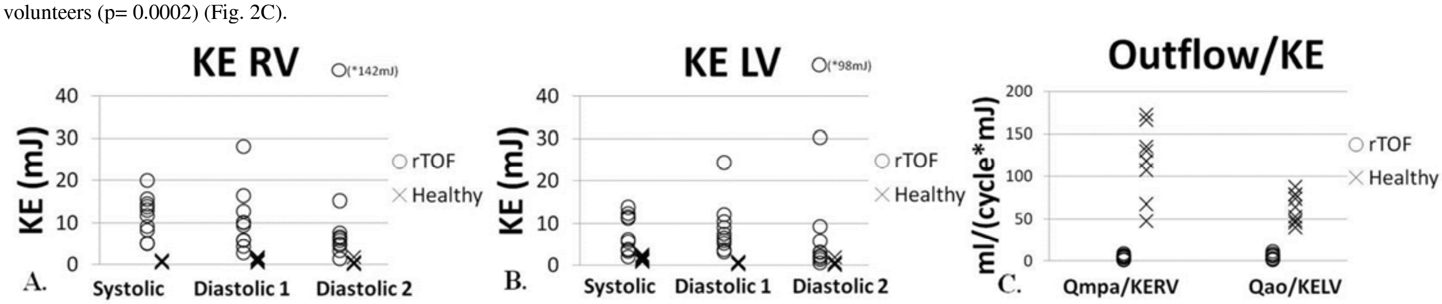

Figure 2: [A] KE_{RV} comparison between rTOF and healthy volunteers. Differences in KE_{RV} peak systolic (p=0.0002) and diastolic (p=0.0002 peak 1, p=0.0003 peak 2) are statistically significant. [B] Differences in peak systolic (p=0.0004) and diastolic (p=0.0002 peak 1, p=0.0008 peak 2) KE_{LV} are also statistically significant. [C] Ratios of ventricular KE and outflow. Q_{MPA}/KE_{RV} was significantly lower in rTOF than healthy volunteers (p=0.0002). Q_{Ao}/KE_{LV} was also significantly lower in rTOF than healthy volunteers (p=0.0002).

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 Q_{MPA}/KE_{RV} and Q_{AO}/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 energy 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 is a new observation in these patients with rTOF.

References: [1] Khalaf A et al, *Pediatr Cardiol* 34:1206-1211(2013). [2] Ordovas KG *et al, J Magn Reson Im.* 35:79-85(2012). [3] Carlsson M, *et al, Am J Physiol Heart Circ Physiol* 302: H893-H900(2012). [4] Francois CJ, *et al. J Cardiovasc Magn Reson* 14(1):16(2012).