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EDITORIAL COMMENT

Diastolic Right Ventricle Dysfunction in Repaired Tetralogy of Fallot

Is it Time for 4D-Flow-MRI Parameters?

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Tetralogy of Fallot (TOF) is one of the most frequent cyanotic congenital heart diseases.[1] Although there has been drastic clinical and surgical improvement in the diagnosis and treatment of TOF, the management and the risk stratification of this population in still challenging. Actually, residual defects, such as pulmonary regurgitation and/or pulmonary stenosis, and tricuspid regurgitation led to a progressive right ventricle (RV) overload, systolic and diastolic dysfunction, exercise intolerance, and arrhythmias. The term *right ventricular restrictive physiology (RVRP)* has been used to describe the phenomenon of end-diastolic forward flow (EDFF) in the pulmonary artery and interpreted as a pattern of RV diastolic function in interpreted as a possible reduced right ventricle diastolic compliance.[2] RVRP is traditionally diagnosed by Doppler echocardiography as forward flow in the pulmonary artery in late diastole (EDFF) coincident with premature opening of the pulmonary valve during atrial systole with, therefore, a direct flow passing to the pulmonary artery in late diastole.[2] RVRP was also evaluated by cardiac magnetic resonance (CMR), mainly as a presence of EDFF on phase-contrast CMR. RVRP has been reported to prolong the postoperative recovery[3,4]; however, its impact at long-term follow-up is controversial.[3] This calls into question whether the EDFF always reflects diastolic dysfunction and if EDFF may have multiple causes.[4] A hypothesis of 2 main phenotypes of EDFF has been proposed[3]: 1) early-onset, "primary" EDFF with smaller RV; and 2) late-onset, "secondary" EDFF. Moreover, previous studies including a recent metanalysis found no significant associations of EDFF with typical markers of restrictive filling of the RV, including right atrium dimensions.[3,4] Therefore, the evaluation of RV diastolic function in repaired tetralogy of Fallot (r-TOF) is still challenging.

The 4-dimensional (4D)-flow CMR sequence is moving from a research tool to clinical applications especially in congenital heart disease patients, including patients with r-TOF.[5,6]

In this issue of *JACC: Asia*, Zhao et al[7] explored novel 4D Flow-MRI parameters, in particular, biventricular kinetic energy (KE) and flow components in a cohort of both pediatric and adult r-TOF with and without EDFF. They demonstrated higher RV KE parameters, encompassing global, peak systolic, systolic, diastolic, peak E-wave, and KE discordance in a r-TOF cohort of patients in comparison with a healthy group. KE is defined as the work needed to accelerate a given mass (blood) from rest to its stated velocity.[6] Because KE reflects ventricular performance, it might be a potential early marker of ventricular dysfunction.[3] They found higher RV kinetic energy normalized to end-diastolic volume (KEiEDV) in r-TOF consistent with previous studies.[8] Sjöberg et al[8] found RV diastolic peak KE to be higher in r-TOF in comparison with the control group, but the difference was most pronounced in patients without EDFF; however, in the cohort of Zhao et al,[7] the peak E-wave KEiEDV was increased in patients with EDFF, and diastolic KEiEDV was not significantly different. This could be attributable to several factors: the population study characterization, the different significance of peak E-wave KEiEDV and diastolic peak KE, and also that KE was indexed by EDV for the Zhao cohort

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and by the stroke volume for the Sjöberg cohort. This highlights the need for a consensus to standardize 4D flow-MRI parameters. Another hypothesis is that EDFF did not reflect the same physiopathology pattern in the 2 cohorts. Zhao et al[7] also demonstrate different flow components between r-TOF and healthy subjects.

Flow components were evaluated using particle trace analysis to visualize biventricular blood flow.[9,10] The volume at end-diastole was divided into 4 functional flow components: direct flow (blood that enters and exits the ventricle within the same cycle), retained inflow (blood that enters the ventricle but does not exit during the same cycle), delayed ejection flow (blood that had remained in the ventricle from the cycle before and is ejected during the current cycle), and residual volume (blood that is stagnant in the ventricle, not entering nor exiting during the cycle).

They demonstrated a reduced RV direct flow and increased delayed ejection flow and residual volume, which agreed with their previous study.[11] However, the reduced RV direct flow was less pronounced in the pediatric population patients with EDFF and not significantly different in patients with and without EDFF in the adult population. These results, if confirmed by larger studies, may help our understanding of the remodeling of the RV over time and perhaps also of the significance of EDFF.

In summary, beyond the results of Zhao et al,[7] this study should encourage further research with 4D-flow CMR novel parameters to improve the knowledge on ventricular flow in patients with r-TOF. 4D-flow CMR has the potential to revolutionize our understanding of complex dynamic cardiovascular relationship[12] and may improve noninvasive evaluation of RV diastolic function in r-TOF. Multiple 4D-flow CMR parameters have been evaluated in r-TOF.[5,6,12] However, a few studies evaluated the RV flow components in r-TOF. Flow components are gaining interest in the evaluation of LV and RV diseases. A decrease in direct flow volume and KE at end-diastole has been hypothesized to detect LV dysfunction even in subtle or subclinical LV remodeling,[13] with a good reproducibility in particular for flow components as a proportion of the EDV.[14] In healthy subjects, direct flow contributes to a larger portion of the RV diastolic volumes than the direct flow of the LV[15] and may be of high importance when assessing RV diastolic function.[16] Moreover, 4D flow-CMR may be helpful for a tailored interpretation of EDFF in r-TOF. The study of flow components by 4D-flow CMR particle tracing is already feasible. However, there are still many limitations, such as spatio-temporal resolution of the CMR data, computation time, lack of proof of clinical value, and possible suboptimal settings.[6,17]

Future developments of the technology, optimal parameter settings, standardized parameters, and larger studies are still needed to better exploit this unique technology.

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