Right Ventricle in Pulmonary Hypertension
Echocardiography Strikes Back?
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Eight years ago, van Wolferen et al1 published a landmark article reporting the prognostic significance of cardiac magnetic resonance (CMR) imaging of the right ventricle (RV) in pulmonary arterial hypertension (PAH). A low stroke volume, RV dilatation, and impaired left ventricular filling assessed by CMR were independent predictors of mortality at a mean follow-up of 32 months. More importantly, further decrease in stroke volume, progressive RV dilatation, and further decrease in left ventricular end-diastolic volume at 1-year follow-up were the strongest predictors of later mortality. The editorial2 accompanying this article was titled as follows: Cardiac Magnetic Resonance in Pulmonary Arterial Hypertension: A Step in the Right Direction. Indeed, this was a promising time for CMR. It was expected that the traditional limitations of CMR, such as expense and suboptimal availability, would be eliminated with the increasing number of CMR devices in the hands of cardiovascular teams. With quick advances in the software used for CMR imaging, automated tracking of heart chamber contours seemed just a matter of time. This would lead to the wide use of CMR, potentially replacing transthoracic echocardiography for RV assessment in the clinical practice of pulmonary hypertension (PH).

See Article by Ryo et al

Since 2007, many important steps have been taken in the right direction in CMR-based research. We have learned about the disturbed systolic coronary flow in the pressure-overloaded RV,3 about the significant difference between longitudinal and circumferential RV systolic dysfunction in PH,4 about the difference in the performance of the apex and the base of the RV.5 Probably one of the most important CMR-based researches was aimed at solving an enigma related to the facts that the prognosis of patients with PAH remained poor and RV failure continued to be the leading cause of death, despite reducing pulmonary vascular resistance (PVR) with modern pharmacotherapy. A hypothesis emerged that reduction in PVR was not always followed by an improvement in RV function that was determined in PAH by more complex mechanisms than just afterload.6 This hypothesis was indirectly supported by a trial in which 76 patients with newly diagnosed PAH underwent baseline cardiac MRI repeated at 1 year. When measured at baseline, both RV ejection fraction and PVR were predictors of mortality. However, during the first 12 months, the changes in PVR correlated only moderately with the changes in RV ejection fraction ($R=0.330; P=0.005$). Moreover, the changes in RV ejection fraction were associated with survival (hazard ratio, 0.929; $P=0.014$), but the changes in PVR were not associated with survival (hazard ratio, 1.000; $P=0.820$). Although PVR decreased during medical therapy in 68% of patients, in one-fourth of those patients, CMR still showed a deterioration of RV function with poor clinical outcome. The authors concluded that RV function can deteriorate in patients with PAH, despite the apparently successful therapy as judged by the reduction in PVR. Such a deterioration of RV function was found to be associated with a poor outcome, irrespective of the trends in PVR.7

In this issue of Circulation: Cardiovascular Imaging, the study by Ryo et al8 suggests that the patients with such disadvantageous adverse RV remodeling may also be identified by state-of-the-art 3-dimensional (3D) echocardiography.

This is an important message because CMR has not become a standard to date for prognostic stratification in patients with PAH. This is despite the convincing evidence that CMR is more cost-effective than 3D echocardiography for RV morphological and functional assessment, at least for research purposes.9 Although several CMR-derived variables have now appeared among the potential treatment goals listed by experts at the last World Meeting on Pulmonary Hypertension held in Nice in 2013,10 it is unlikely that these will fight their way into routine clinical practice. This creates again opportunities for echocardiography. Indeed, although standard 2D transthoracic echocardiography has provided merely 3 potential treatment goals—preserved tricuspid annulus systolic excursion, normal right atrial area, and the absence of pericardial effusion—modern right heart echocardiography has potentially more to offer.11-20 Of note, in their study, Ryo et al did not follow this direction but limited the assessment to rather rudimental estimation of RV volumes, simply expecting better precision of the measurements assisted by 3D wall motion tracking when compared with traditional 2D echocardiography. Similar to CMR, this still required manual tracing of endocardial and epicardial borders. To improve resolution, 3D images were not acquired from single heart cycles in real life but were integrated sequentially from 4 to 6 consecutive heart cycles during breathhold. Despite those efforts, significant 15% dropout of technically unacceptable recordings represents one of the
important limitations of 3D approach to RV assessment. Nevertheless, the authors were able to, combining 3D echo and nonsimultaneous right heart catheterization data, identify patients whose RVs excessively dilated progressively, losing the ability to generate high systolic pressures. Different from the study by van Wolferen et al who used CMR, the most prognostically relevant variable found by Ryo et al with 3D echocardiography was end-systolic and not end-diastolic RV volume, indexed for body area.

There are several limitations and also some missed chances related to this publication. Most importantly, thickness and consequently the mass of the RV have not been taken into account in defining adaptive and maladaptive RV remodeling in increased afterload condition. This could have improved the prognostic significance of 3D echocardiographic findings. Based on estimated volumes, RV stroke could have been calculated and compared with its Doppler estimates derived from right and left ventricular outflow tracts. Stroke volume, correcting cardiac output by heart rate, was found to be particularly related to prognosis in CMR studies. Moreover, such assessment could also be used to better grade regurgitation fraction related to tricuspid insufficiency. Evaluation of RV wall strain has been limited by the authors to averaged global strain, not accounting for significant regional differences, particularly between longitudinal and radial/circumferential components. Interestingly, Ryo et al indirectly confirmed the earlier findings of Mauritz et al by pointing at poor sensitivity of longitudinal systolic events, such as tricuspid annulus systolic excursion, to differentiate between more advanced stages of adverse RV remodeling. Although initial stages of RV remodeling were indeed related to progressively decreasing longitudinal performance, it was the lateral dimension that became increased because of septal bulging into the left ventricle in more advanced stages of the disease.

In summary, echocardiography, and particularly 3D echocardiography, is re-emerging as an interesting source of prognostically relevant data in PH. It is unfortunate that the current study limited the measurements to few variables and thus failed to provide multivariate analysis identifying echocardiographic variables independently contributing to prognostic assessment. Clearly, without blinded adjudication of clinical end points, with lack of information on the types of PH ultimately diagnosed in the studied patients, and with echocardiographic cutoff values defined in part retrospectively based on adverse outcomes in individual cases, the trial cannot provide absolute criteria for therapeutic targets. This would still require prospective validation trial. So echocardiography should wait for a moment before it announces a strike-back to regain ground in the prognostic assessment and follow-up of patients with PH.

Disclosures

None.

References


**Key Words:** Editorials ■ echocardiography ■ heart ventricles ■ hypertension, pulmonary ■ magnetic resonance imaging ■ prognosis ■ stroke volume
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