Canadian Journal of Cardiology 36 (2020) 1341–1343

Editorial

Echocardiographic Strain Imaging in the Systemic Right Ventricle: Early Clue for Late Decompensation

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See article by Woudstra et al., pages 1525–1533 of this issue.

Right ventricular (RV) systolic function is increasingly appreciated as a powerful determinant of patient outcome in a variety of conditions, including myocardial infarction, heart failure, valvular heart disease, pulmonary hypertension, and congenital heart disease.[1,2] Perhaps no other situation highlights the importance of RV systolic function more evidently than systemic RV (SRV), where the morphologic RV must support the systemic circulation. SRV occurs in mainly 3 congenital heart conditions: transposition of the great arteries corrected by a Mustard or Senning operation (TGA-MS), congenitally corrected TGA (CCTGA), and some Fontan patients. In patients with these conditions, chronic pressure overload on the RV, which is poorly suited to support the systemic circulation, leads to progressive dysfunction and subsequent complications, such as heart failure, arrhythmia, and death.[3]

Although assessing SRV function is crucial for patient management,[4] it is challenging to do so accurately due to the complex geometry of the RV. Anatomically, the RV comprises the inlet, the trabeculated apical myocardium, and the infundibulum, with circumferentially oriented superficial myocardial fibres and longitudinally oriented deep myocardial fibres responsible for systolic shortening in the 2 directions. In contrast to the ellipsoid left ventricle, the shape of the RV does not lend itself easily to the use of geometric formulae to estimate volumes and ejection fraction (EF). The gold standard for assessing RV size and function is cardiac magnetic resonance (CMR), which allows direct measurements of RV volumes and, as a result, more accurate estimation of the RV EF. Accordingly, CMR is the guideline-recommended imaging modality for the evaluation of SRV function.[4] However, the availability of CMR may be limited, and the technical feasibility may be challenging for patients with claustrophobia, cardiovascular implantable electronic devices, or irregular heart rhythms. In clinical practice, echocardiography remains the first-line modality for the assessment of RV function as it is widely available, relatively inexpensive, and portable at the point of care. Given the poor interobserver reliability of purely qualitative assessments of SRV function,[5] quantitative echocardiographic indices are recommended, including tricuspid annular plane systolic excursion, tissue Doppler-derived tricuspid lateral annular velocity, RV index of myocardial performance, 2-dimensional fractional area change, 3-dimensional RV EF, and global longitudinal strain (GLS).[6,7]

Among these indices, RV GLS by 2-dimensional speckle tracking has shown promise in the evaluation of patients with SRV. Speckle-tracking echocardiography is based on the tracking of natural acoustic markers on grey-scale images, has the advantage of being angle independent in contrast to Doppler-derived indices, and has been validated as a reliable method for myocardial strain imaging. RV GLS appears to correlate with CMR-derived RV EF in patients with SRV[8-10] and was shown to be impaired in patients with SRV compared with controls.[11] In earlier studies, impaired RV GLS was shown to be predictive of adverse clinical events in patients with TGA-MS.[8,11,12]

It is in this context that Woudstra et al.[13] sought to determine the predictive value of speckle-tracking echocardiography-derived indices among 60 participants in the Effect of Valsartan on Systemic Right Ventricular Function (VAL-SERVE) trial, which randomized patients with SRV to valsartan or placebo and which ultimately showed no benefit of valsartan with respect to change in RV EF, exercise capacity, or quality of life. In the VAL-SERVE trial, RV EF was evaluated by CMR or cardiac computed tomography (CT). In this substudy of VAL-SERVE, the following speckle-tracking echocardiography-derived indices were measured: RV GLS; mechanical dispersion, an indicator of electromechanical heterogeneity; and postsystolic shortening, an indicator of pathologic prolonged contraction or delayed relaxation. The primary outcome in this substudy was a composite of subjective (increase in NYHA class or diuretic dose) and objective (heart failure hospitalization, cardiac transplantation, and death) events. Fifteen patients reached the primary outcome over a median of 8.2 years. RV GLS, mechanical dispersion, and postsystolic shortening were all associated with event-free survival in unadjusted analyses. Neither RV GLS

Received for publication March 9, 2020. Accepted March 11, 2020.

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See page 1342 for disclosure information.

https://doi.org/10.1016/j.cjca.2020.03.013
0828-282X/

nor CMR/CT-derived RV EF showed a linear relationship with the outcome, and therefore both indices were dichotomized, with optimal cutoff values of -10.5% and 30%, respectively. After adjustment, only RV GLS $> -10.5\%$ and RV EF $< 30\%$ remained independently associated with event-free survival in multivariable analyses. A model combining RV GLS and RV EF significantly improved the predictive value over models including only one of the indices.

With this study, Woudstra et al. have added important insights into the potential value of RV GLS in improving risk stratification among patients with SRV, with results that span a significantly longer follow-up than earlier studies. Perhaps the most interesting and unexpected finding is the complementary value of RV EF and RV GLS in predicting outcome. It is important to note that in 25% of the included patients, RV GLS was measured approximately 1 year after inclusion into the study and CMR/CT measurement of RVEF. It is therefore possible that the added value of RV GLS could be in part due to the fact that this index was measured at a later time point in the patient's clinical evolution. It is also possible that this finding reflects the different aspects of RV function that are assessed by each approach. In response to a high-pressure circulation, longitudinal shortening of the SRV free wall diminishes, whereas circumferential shortening increases,[14,15] a contraction pattern that is opposite of what is observed in normal RVs and which more closely resembles the pattern in normal left ventricles. This pattern results in relatively preserved global RV EF until later overt deterioration and may suggest why a measure of RV EF encompassing both longitudinal and circumferential function may not detect early decreases in longitudinal function as would RV GLS. RV circumferential shortening was not assessed in the study by Woudstra et al. and would have provided additional insight into the pathophysiology behind the observed results.

Although it is understandable that patients with TGA-MS or CCTGA were pooled in this study to yield a larger cohort, the authors acknowledge that these groups may manifest significant morphologic and functional differences, and pooling them may have affected the results. Indeed, in an earlier study by Diller et al.,[11] RV GLS was associated with adverse events in the patients with TGA-MS but not in those with CCTGA, possibly reflecting inherent differences between the groups as well as heterogeneity within the CCTGA cohort.

The results of the study by Woudstra et al. contrast with the results of a recent prospective study of 86 patients with SRV over 5.9 years that included echocardiographic and serologic biomarkers.[16] The prognostic value of strain analysis was limited, with only RV septal strain and RV global circumferential strain but not RV GLS being associated with the secondary composite endpoint of all-cause mortality or arrhythmia. These discordant findings temper the reflex to integrate RV GLS for clinical decision making. It is also important to recall that in the VAL-SERVE substudy, RV GLS could not be analysed in 1 of 5 patients, suggesting that this technique may not be broadly applicable, though the rate of successful analysis may be higher with prospective image acquisition. Speckle-tracking echocardiography may be especially challenging in SRV. Poor acoustic windows related to the altered anatomic location of the SRV may reduce image resolution. As the SRV dilates, a wider sector is required to include the entire RV in an image, resulting in lower frame rates. Both of these limitations may render GLS analysis unfeasible. Furthermore, the value of serial assessment of RV GLS is also unclear. Finally, the place of RV GLS among other factors such as tricuspid regurgitation, subpulmonary LV function, clinical variables, and serologic biomarkers remains to be determined.

In conclusion, this study from the VAL-SERVE trial adds to the growing body of evidence for echocardiographic strain imaging to assess RV function and risk stratify patients with complex congenital heart disease. Further research is needed to address pertinent knowledge gaps surrounding the differential value of longitudinal and circumferential strain indices; the automation of strain measurements using artificial intelligence algorithms capable of filtering artefacts and interpolating speckles when image quality is suboptimal; and the actionable ramifications of detecting subclinical SRV dysfunction using strain imaging to guide clinical care and improve patient outcomes.

Funding Sources

Jonathan Afilalo is funded by CIHR and FRQ-S.

Disclosures

The authors have no conflicts of interest to disclose.

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