Review of: "Defining the reference range for right ventricular systolic strain by echocardiography in healthy subjects: A meta-analysis"

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The meta-analysis “Defining the reference range for right ventricular systolic strain by echocardiography in healthy subjects” reports the pooled means and lower limits of normal (LLN) of right ventricular (RV) systolic strains in 4439 healthy subjects from 45 studies. It defines thresholds for abnormal, borderline and normal, two- (2D) and three-dimensional (3D) right ventricular global (RVGLS), free wall (RVFWLS) and interventricular septal wall (IVSLS) longitudinal strains. Authors also note that, in meta regression, important factors associated with RV systolic strains were RV fractional area change (FAC) and vendor software.

The subject is of interest as the right ventricular function has recently emerged as an independent predictor of morbidity and mortality in multiple cardiovascular affections. Despite growing interest for RV function, its evaluation remains challenging. The current recommendations for cardiac chamber quantification of the ASE/EACVI favours a multiparametric approach, while cardiac magnetic resonance (CMR) derived ejection fraction (EF) remains the gold standard[1]. Yet, echocardiography is more readily available, and speckle tracking echocardiography (STE) is emerging as a new reliable tool for the assessment of RV mechanical changes[2]. However, the use of RV strain is still limited in clinical practice, mainly due to the lack of standardized normal values. This meta-analysis is trying to address this issue, deriving normal values from pooled data of RV strain measurements in healthy subjects.

Overall, literature search is well described and the quality of data collection and analysis is good. Eligibility criteria and reasons for study exclusion are clearly listed. However, the clinical applicability of the normal values from this meta-analysis is questionable. Indeed, there are still a number of unresolved issues to take proposed thresholds at face value. Although most of these issues are adequately discussed by the authors, we found interesting to emphasize obstacles remaining in the way to use RV strain in the clinical setting.

The major problem is the considerable heterogeneity of mean and LLN strain values across studies, especially as subgroup sensitivity analysis failed to explain this variability. Some may be related to difficulties inherent in data acquisition and strain measurements. The accuracy of RV systolic strain differs depending on operator experience and image quality. The meta analysis does not report information about the echocardiographic protocols of included studies, although the acquisition of RV focus views is far from being a common practice. It should be stated whether specific RV images were acquired prospectively for the study, or if strain was measured retrospectively from routine echocardiographic examinations. Also, while strain is highly dependent of image quality, frame rate was not reported in all studies. Standardization of image acquisition of RV focus views should be a first step to homogenize reference values for RV strain.

Also questioning the quality of image acquisition, we are surprised that only FAC and not TAPSE was associated with RV strain in the meta regression. In previous work, TAPSE was found to be highly correlated with RV strain (r = −0.547 to −0.83) while RV-FAC generally showed weaker correlation (r = −0.213 to −0.73) and was found to have high interobserver and intraobserver variability.[3] Furthermore, several studies showed sex and age differences in strain, also not confirmed in the meta regression.[4,5]

Most important brake to the implementation of strain measurements with standardized reference values is the high intervendor variability. The fact that vendor software was one of the few parameter affecting strain in the meta regression highlights this issue. Although it has been repeatedly mentioned in the literature, it seems no effort is made from vendors to homogenize their techniques. Hence, universal reference values applicable independently of the software seem unrealistic at this point.

We also believe no conclusion should be drawn for 3D strain based on so few data. The authors states that 3D strain techniques are currently less robust than 2D because of wider 95% confidence interval of the LLN. This might be more related to the small number of studies (3) and subjects (N=140) involved in analysis of 3D strain than to the reliability of the technique.

To conclude, although this meta-analysis was correctly conducted and well written, with extensive discussion of limitations, authors might overstate their findings when they interpret the results. They say “pooled LLN for RVGLS was -16.4% (-17.3%, -15.5%), meaning that RVGLS less negative than -15.5% would be abnormal, between -17.3% and -15.5% borderline, and more negative than -17.3 normal. We obtained this reference range for RVGLS, RVFWLS and IVSLS measured by both 2D- and 3D speckle-tracking echocardiography.” As stated above, we believe no conclusion should be drawn on 3D strains given the small number of healthy subjects involved. More importantly, we doubt that, at this point, reference values should be used independently of vendor softwares. Lack of standardization of echocardiographic protocols for the acquisition of RV images, and high intervendor variability remain major obstacles in the applicability of universal reference ranges for RV strain in daily practice.

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