

Chapter 11

Summary

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Significant advances in three-dimensional echocardiography (3DE) have made this modality a powerful diagnostic tool in the cardiology clinic. Besides offering novel views and comprehensive anatomic definition of the heart itself, it can also provide accurate and reliable measurements of chamber size and function, including the quantification of left ventricular (LV) mechanical dyssynchrony to guide patient selection for cardiac resynchronization therapy. The recent introduction of 3DE speckle tracking (3DSTE) in particular has provided us with new opportunities for comprehensive evaluation of the LV, including chamber indices such as left ventricular volumes and ejection fraction, but also parameters directly assessing global and regional myocardial function such as strain and torsion. As its efficacy for more and more clinical applications is demonstrated, it is clear that 3DE has become part of the routine clinical diagnostic armamentarium.

The aim of the work presented in this thesis was to validate and evaluate the clinical applicability of the latest 3DE technology for quantification of the LV in four dimensions. For these purposes, the thesis was divided into three parts, namely quantitative assessment of chamber size and function (part 1), quantitative assessment of mechanical dyssynchrony (part 2), and finally a summarizing discussion and future perspective on the use of 3DE for quantification of the LV (part 3).

In part 1, chapter 2 covered a review on current use of 3DE for LV quantification, including methodology of acquisition and analysis, validation of its clinical application for assessment of LV volumes, ejection fraction, and dyssynchrony, and present limitations of the technique. It showed that in the last two decades the technology behind 3DE has greatly evolved, continually expanding its clinical applications. Ample evidence suggests that LV volumes and function measurements by 3DE have closer limits of agreement with magnetic resonance imaging (MRI) measurements as a reference method and better reproducibility than 2D echocardiography. Furthermore, it was postulated that further advancements in more automatic analysis of the LV with speckle tracking would enable fast online measurements that are accurate and reproducible and might ensure its integration into the routine echocardiographic examination.

In chapter 3, LV and left atrial chamber quantification by two different 3DE methodologies, namely direct volumetric and speckle tracking echocardiography, were compared to evaluate the interchangeability of their application in daily clinical practice. It was demonstrated that 3DE direct volumetric and speckle tracking methods give comparable results with equally good reproducibility, making interchangeable application a viable option in daily clinical practice.

In chapter 4, the reliability of LV volume and function measurements using 3DSTE was evaluated, including global and regional measurements of circumferential, longitudinal, and radial strain. Studied measures of reliability included intraobserver and interobserver reliability, as well as test-retest reliability, which is of vital importance for patient management and follow-up, including evaluation of treatment effect in clinical trials. Its results showed that 3DSTE is a reliable tool for routine evaluation of LV volumes and ejection fraction. Likewise, assessments of global and segmental circumferential strain demonstrated good reliability, whereas analysis by a single observer should currently still be recommended for longitudinal and radial strain due to moderate inter-observer and test-retest reliability.

In chapter 5, the accuracy of 3DE speckle tracking to assess LV volumes, ejection fraction, and global circumferential strain was evaluated in comparison to MRI as the reference technique in a group of healthy subjects. Furthermore, potential sources of differences between both techniques were investigated. Although 3DSTE-derived LV volumes were underestimated in most patients compared with MRI, measurement of LV ejection fraction revealed excellent accuracy. Measurements of circumferential strain were systematically greater with 3DSTE than MRI, which likely reflects various inter-technique differences that preclude direct comparability of their measurements. We postulated that, with the understanding of these intertechnique differences, further studies should establish normal reference values of 3DSTE-derived strain measurements in a larger healthy population and determine their added usefulness over current clinical standards of LV function assessment in different clinical scenarios.

In chapter 6, we evaluated the ability of a novel index based on area strain to reliably quantify global and regional LV function and accurately identify wall motion abnormalities using 3DE speckle tracking. It was concluded that area strain represents a promising novel automatic index that may provide an accurate and reproducible alternative to current echocardiographic standards for quantitative assessment of global and regional LV function. Furthermore, it seems to adequately identify regional wall motion abnormalities compared with the clinical standard of visual assessment by experienced echocardiographers.

In part 2, chapter 7, a critical appraisal of the current literature on the feasibility and reproducibility of dyssynchrony assessment by 3DE was given, providing clinically useful reference values in healthy subjects and heart failure patients, and examining its accuracy in predicting response to cardiac resynchronization therapy (CRT) by means of a comprehensive meta-analysis. It demonstrated that 3DE is a feasible and reliable tool for assessment of LV dyssynchrony and may have additional value to current selection criteria for accurate prediction of response to CRT. In addition, we postulated that these findings support a prospective multicenter randomized controlled trial to evaluate the

usefulness of LV dyssynchrony assessment using 3DE in selecting patients for this therapy.

In chapter 8, the comparability of LV dyssynchrony assessment by tissue Doppler imaging and 3DE was studied in patients with a wide range of LV function and different causes of cardiomyopathy. In addition, the ability of both techniques to predict response to CRT was evaluated and compared. In patients with normal to impaired LV function and different etiologies of cardiomyopathy, tissue Doppler imaging and 3DE derived dyssynchrony indices showed only a moderate correlation. Depending on the severity of LV dysfunction, marked differences between techniques were found for the presence of mechanical dyssynchrony when current cutoff values were applied, making interchangeability of these techniques uncertain. However, the sensitivity and specificity of 3DE to predict clinical response as well as reverse remodeling was superior to tissue Doppler imaging, which suggests that the assessment of mechanical dyssynchrony by 3DE might be an appropriate alternative for accurate prediction of the response to CRT.

In chapter 9, the comparability between regional LV volume curves obtained with 3DE and circumferential strain curves obtained by MRI tagging for assessment of LV dyssynchrony was evaluated in patients eligible for CRT. The results demonstrated high cross-correlations between regional MRI derived LV circumferential strain and real-time 3D-echocardiography derived regional LV volume. However, regional differences in time delay between the curves were found, leading to discrepancies in the quantification of mechanical dyssynchrony. This could mainly be ascribed to the poor correlation between regions with little or positive circumferential strain (dyskinesia or “bulging”) and the accompanying regional volume curves, and is probably inherent to the calculation method of regional LV volume. Therefore, it was postulated that both modalities might represent different measures of mechanical dyssynchrony.

Finally, in part 3, chapter 10, a general discussion was provided, in which the present work was critically evaluated and placed in the context of current literature. In addition, the future of echocardiographic LV quantification was discussed, including current technological limitations of 3DE that warrant improvement as well as potential areas for further research. It was concluded that quantification of global and regional LV function has significantly improved in the last few decades with regards to accuracy and reproducibility. Moreover, advances in echocardiographic technology have made it possible to quantitatively assess not only LV volumes and ejection fraction but all LV mechanics, including 3D strain and its components, area strain, as well as rotation, twist, and torsion in all four dimensions. However, these promising novel parameters of global and regional LV function will need further validation and strenuous testing in prospective studies to gain acceptance for general clinical application. Finally, further improvements in temporal resolution and image quality, as well as the possibility of a wider sector angle for adequate acquisition of severely dilated ventricles often present in heart failure patients would greatly enhance LV dyssynchrony assessment and provide the opportunity for more comprehensive evaluation

of diastolic LV function beyond mere left atrial volume measurement, i.e. assessment of diastolic strain-rate and untwisting.

In summary, the work presented in this thesis described the development of 3DE over the last decades, provided the scientific evidence for its current clinical use in LV chamber quantification and discussed its potential future applications. The findings demonstrated that 3DE is an accurate and reliable clinical tool for quantification of LV volumes and ejection fraction, regardless of whether direct volumetric and speckle tracking algorithms are used. Furthermore, 3DE assessment of LV strain may provide us with more robust, quantitative information on global and regional myocardial function than current echocardiographic standards. Finally, assessment of mechanical dyssynchrony with 3DE may be useful in selecting patients for CRT. Future research into these and other topics and further technological advancements towards reliable fully automated echocardiographic assessment of global and regional LV function will reaffirm the position of echocardiography as the clinically most applicable imaging tool for LV quantification.