Evolving imaging techniques for the assessment of cardiac structure and function and their potential clinical applications

Shanks, M.

Author: Shanks, Miriam
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GENERAL INTRODUCTION AND OUTLINE OF THE THESIS

Novel echocardiographic modalities for the evaluation of the heart

For decades, echocardiography has been the first line modality for the diagnosis and management of many cardiac conditions. Recent development of new techniques for quantification of tissue motion and deformation has fundamentally altered the way echocardiography approaches the characterization of global and regional myocardial function. In addition, technological progress in 3-dimensional echocardiography has made it more accessible for routine clinical use, often providing superior accuracy and reliability over 2-dimensional echocardiography.

Echocardiographic imaging is ideally suited for the evaluation of cardiac mechanics because of its intrinsically dynamic nature. Several new, increasingly automated techniques for sophisticated analysis of cardiac mechanics have emerged over the past decades, including tissue Doppler imaging and 2-dimensional speckle tracking imaging. These techniques provide an unprecedented view of tissue motion and deformation on a region-by-region basis. These methods have been validated using sonomicrometry and tagged magnetic resonance imaging.[1, 2] A growing body of evidence suggests that myocardial deformation imaging provides incremental information in clinical settings, including assessment of myocardial ischemia and viability,[3, 4] detection of subclinical cardiac involvement in systemic diseases,[5-8] improving our understanding of heart failure with preserved ejection fraction,[9] assessment of different cardiomyopathies,[10-12] monitoring of response to therapy,[13-15] and evaluation of contractile function in valvular heart disease.[16-19] More recently, tissue Doppler imaging and 2-dimensional speckle tracking imaging have been successfully used for assessment of left atrial electromechanical properties and function as predictors of sinus rhythm maintenance after atrial fibrillation and for evaluation after percutaneous atrial septal defect repair.[20, 21]

Assessment of myocardial tissue mechanics by the novel imaging techniques may lead to more refined risk stratification, earlier diagnosis and management, and more sensitive monitoring of the response to treatment in patients with cardiovascular diseases.

Advances in the minimally invasive catheter based interventions increased the demands on accurate morphologic assessment of the cardiac structures. Over the last few decades, advances in 3-dimensional echocardiography have enabled real-time volumetric imaging of complex valvular anatomy, and displaying the images in unique perspectives previously only privy to surgeons. In addition, quantifications of chamber volumes and global functions from 3-dimensional datasets have superior accuracy and reproducibility over 2-dimensional echocardiography that often relies on erroneous geometric assumptions.[22] Lastly, 3-dimensional color Doppler echocardiography may allow more accurate quantification of the severity of valvular pathologies.

Together with multi-detector row computer tomography and magnetic resonance imaging, 3-dimensional echocardiography may become an integral part of cardiac multimodality imaging, with the goal to provide accurate data that lead to favorable outcomes and improved quality of life.

Deformation imaging: a measure of left ventricular myocardial performance beyond ejection fraction

Left ventricular myocardial function assessment with 2-dimensional echocardiography has traditionally been limited to volume-based evaluation of ejection fraction and visual estimation of regional wall motion, including thickening of the myocardial wall and inward movement of the endocardium. However, visual evaluation of wall motion only assesses radial deformation of the myocardium and it is known that myocardial contractility consists of thickening, shortening, and twisting of the left ventricle. Several imaging techniques have emerged over the past decades that allow quantitative assessment of myocardial function via image based analysis of local myocardial deformation, including tissue Doppler imaging and speckle tracking echocardiography. Various parameters of myocardial function can be measured by these techniques, including myocardial displacement, velocity, strain, strain rate, and rotation that provide more comprehensive characterization of left ventricular function. Unlike the traditional qualitative assessment of regional left ventricular function, myocardial deformation imaging offers the opportunity to quantify both the magnitude and timing of regional systolic and diastolic deformation.

Doppler imaging uses the phase shift between consecutive echoes for calculation of velocity. With tissue Doppler imaging, low-pass wall filter is used to display only low velocity signals originating from moving tissue and exclude high velocity signals originating from blood flow. By integrating the velocity over time, myocardial displacement can be calculated. However, both tissue Doppler derived velocity and displacement are subject to tethering and translational motion, therefore potentially underestimating or overestimating the magnitude of active myocardial contraction. On the other hand, strain and strain rate parameters reflect regional function independently of translational motion therefore providing information on active myocardial deformation (Figure 1). Strain describes the fractional change in the length of myocardial segment and is expressed as a percentage. Strain rate is the rate of change in strain and is usually expressed as sec^{-1}. The major limitation of tissue Doppler imaging is angle dependency. Therefore, image acquisition requires perpendicular alignment of the ultrasound beam with the direction of the myocardial motion in order to obtain accurate measurements. In addition, velocity components perpendicular to the beam remain undetected.

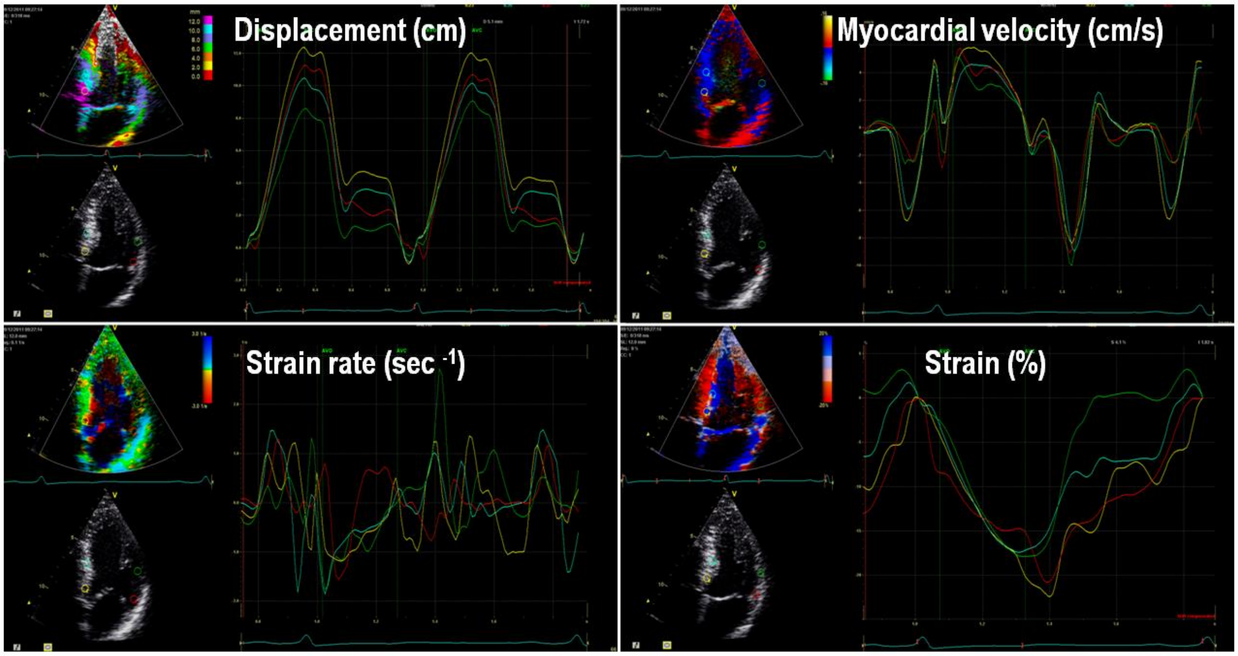

Figure 1. Tissue Doppler imaging. Color-coded tissue Doppler imaging provides local myocardial displacement information from which parameters of myocardial function such as velocity, strain and strain rate can be derived.

Speckle tracking imaging is a relatively new, angle independent technique used for evaluation of myocardial function.[23] Speckles are acoustic markers equally distributed within the myocardium that are seen in grayscale B-mode images. Blocks of speckles are tracked from frame to frame simultaneously in multiple regions within an image plane and provide local displacement information from which velocity, strain and strain rate are derived. In contrast to tissue Doppler imaging, strain and strain rate can be quantified in multiple directions within the imaging plane, including longitudinal, radial and circumferential directions (Figure 2). In addition, the helical nature of the heart muscle determines its wringing motion during the cardiac cycle, with the base and apex of the ventricle rotating in the opposite directions. Speckle tracking imaging allows for the measurement of the absolute apex-to-base difference in the left ventricular rotation, referred to as the net left ventricular twist angle (expressed in degrees) (Figure 2). The term torsion refers to the base-to-apex gradient in the rotation angle along the long axis of the left ventricle, expressed in degrees per centimetre.

Timing of peak myocardial contraction can be obtained simultaneously from multiple segments within the imaging plane by both tissue Doppler imaging and speckle tracking imaging and has been used to assess synchronicity of left ventricular contraction (Figure 3).[24]

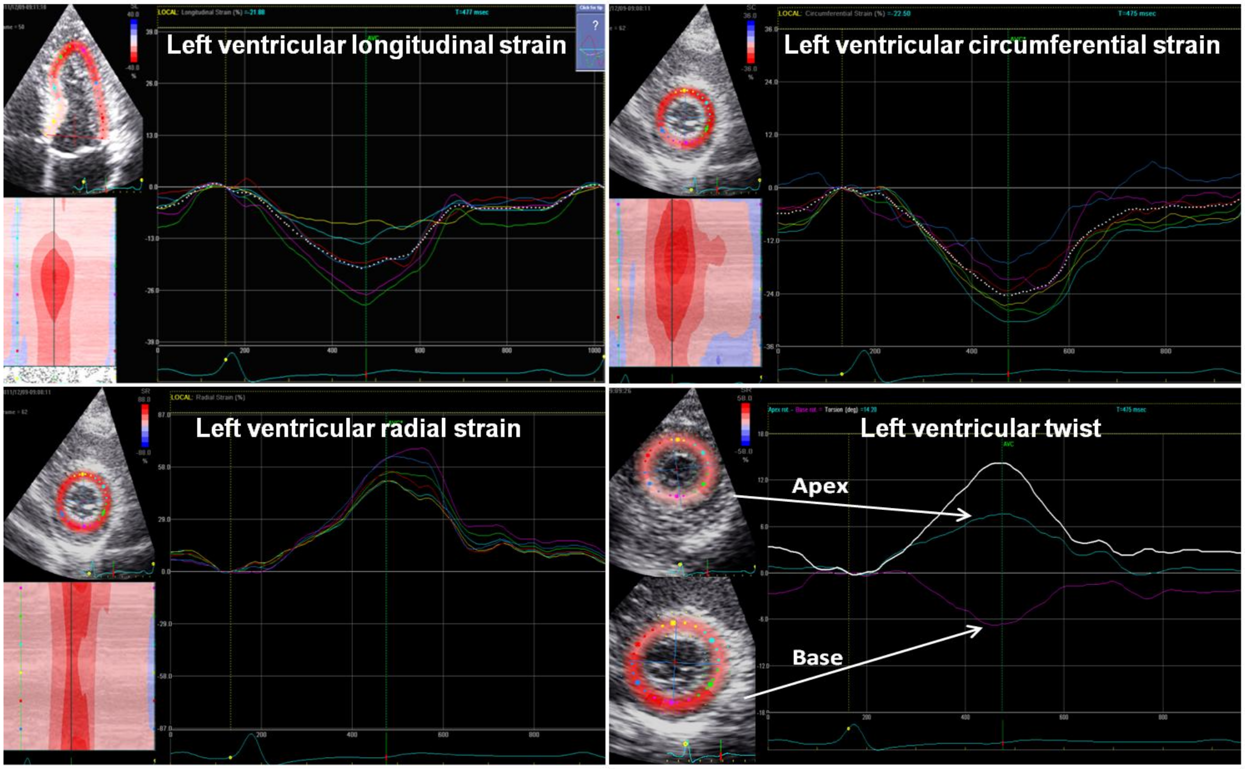

Figure 2. Myocardial deformation by speckle tracking imaging. Two-dimensional speckle tracking imaging enables assessment of myocardial deformation in multiple directions within the imaging plane including longitudinal, circumferential, and radial, and allows quantification of left ventricular twist.

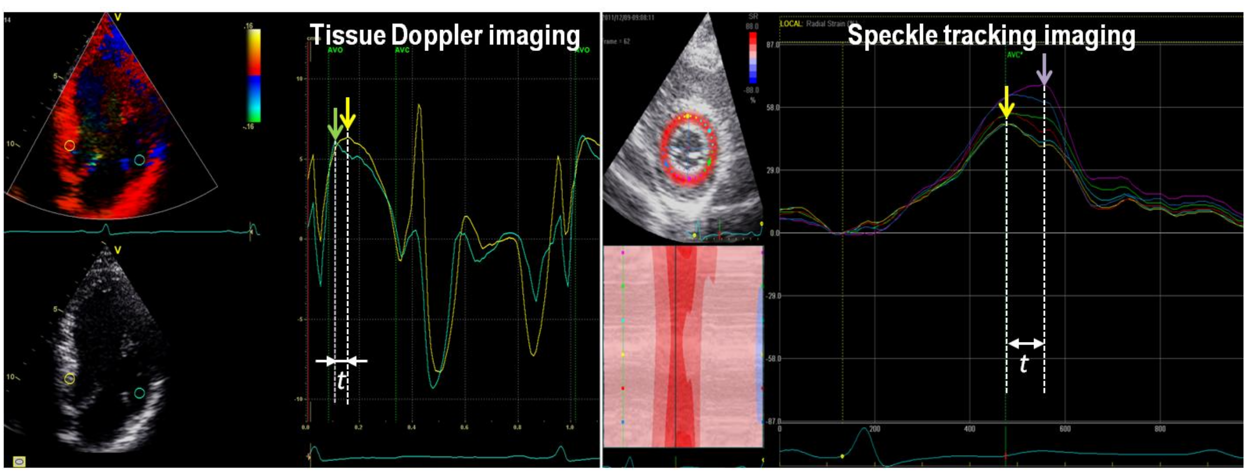

Figure 3. Left ventricular dyssynchrony assessment. Color-coded tissue Doppler imaging and speckle tracking imaging can be used for assessment of synchronicity of left ventricular myocardial contraction.

Three-dimensional echocardiography in the assessment of valvular structure and function

Three-dimensional echocardiography represents a major progression in the evolution of cardiac ultrasound imaging and has the potential to become essential in the assessment of valvular structure and function prior to the transcatheter based procedures and open heart surgeries. It has been shown to consistently provide excellent image quality of the mitral valve apparatus,[25] and is superior to 2-dimensional echocardiography in precise localization of the prolapsing scallops.[26] In the patients with mitral stenosis, direct planimetry by 3-dimensional echocardiography best agreed with mitral orifice area calculations derived from the invasive measurements.[27] Consequently, this approach has been suggested as the new standard for mitral valve orifice area measurements in patients with mitral stenosis.[28] Conventional Doppler echocardiographic methods for assessment of mitral regurgitation are limited by dependence on geometric assumptions, which can be overcome by the use of 3-dimensional volumetric color flow imaging. In contrast to 2-dimensional echocardiography, 3-dimensional color flow imaging enables unlimited image plane orientation allowing for a direct assessment of the size and shape of vena contracta area from en face view, which is then used for calculation of valvular regurgitant volume and fraction.[29] In addition, recently developed dedicated software has enabled advanced 3-dimensional rendering of the echocardiographic images of the valves, thus permitting quantitative off-line analysis of the mitral apparatus geometry which has further promoted an interest in improving characterization of the mechanics causing mitral regurgitation (Figure 4). The more complex the mitral lesion is, the more valuable 3-dimensional echocardiography is compared with 2-dimensional transesophageal echocardiography.[30]

Three dimensional echocardiography may improve accuracy during quantification of aortic stenosis severity by properly aligning the imaging planes during direct planimetry of the aortic valve orifice and left ventricular outflow tract, therefore eliminating the need for geometrical assumptions.[31]

These technical advances in 3-dimensional imaging technology may constitute an important step forward to promote further development of new minimally invasive surgeries or percutaneous therapeutic approaches for the valve disease. Moreover, the ability of 3-dimensional echocardiography to provide real-time imaging may be an invaluable tool for guiding the transcatheter based valve procedures, i.e. assisting in transseptal cannulation into the left atrium and guide the clipping of the opposing mitral leaflets with edge-to-edge technique,[32] providing more accurate quantification of the periprosthetic regurgitation in the balloon expandable transcatheter valves that often consists of multiple eccentric jets with crescent shape or circular orifices,[33] and monitoring for peri-procedural complications.

Therefore, the dissemination of these procedures will increase the demand on 3-dimensional assessment of the cardiac anatomy.

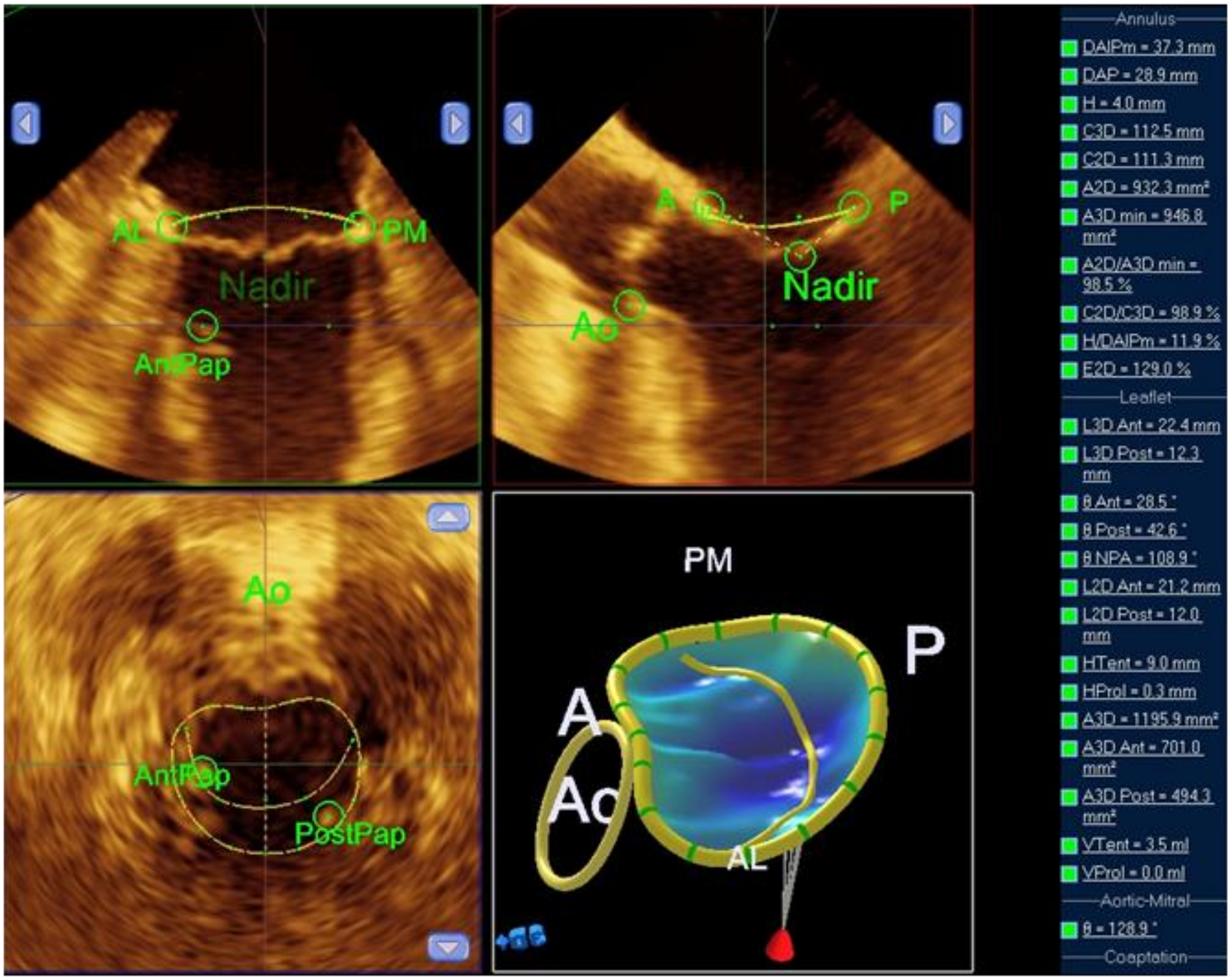

Figure 4. Quantitative assessment of mitral valve morphology. Mitral valve quantification software used for off-line post-processing of 3-dimensional echocardiography images is capable of providing additional volumetric information on the mitral valve morphology otherwise unavailable with most other imaging modalities.

Objectives and outline of the thesis

The objectives of this thesis were to study the clinical applications of the novel echocardiographic imaging modalities in the patients with cardiovascular diseases.

Part I focuses on the evaluation of the novel parameters of myocardial function in the common cardiac conditions using 2-dimensional speckle tracking imaging and tissue Doppler imaging. In patients with ischemic heart disease, changes in the left ventricular myocardial mechanics and their incremental prognostic value for the cardiovascular outcomes are described. In addition, the mechanical properties of the left ventricle in heart failure patients, their role in predicting outcome, and their changes with therapy are explored.

Part II explores the role of the novel imaging modalities in the assessment of the cardiac anatomy and valvular function. Advanced clinical applications of 3-dimensional echocardiography in various cardiac conditions are described in **Part IIA**. The accuracy and clinical feasibility of the assessment of the mitral valve geometry from 3-dimensional images using dedicated mitral valve quantification software that is comparable to the multi-row detector cardiac tomography measurements was demonstrated in **Chapter 6**. In addition, 3-dimensional echocardiography was evaluated for its accuracy for quantification of mitral regurgitation, using magnetic resonance imaging as gold standard (**Chapter 7)**. The role of multimodality imaging in the emerging transcatheter aortic valve implantation procedures is discussed in **Part IIB**, including its usefulness in pre-procedural screening, procedural guidance and post-procedural follow-up.

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