Clinical application of three-dimensional echocardiography: past, present and future

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Significant advances in three-dimensional echocardiography have made this modality a powerful diagnostic tool in the cardiology clinic. It can provide accurate and reliable measurements of chamber size and function, including the quantification of left ventricular mechanical dyssynchrony to guide patient selection for cardiac resynchronisation therapy. Furthermore, three-dimensional echocardiography offers novel views and comprehensive anatomic definition of valvular and congenital abnormalities, improving diagnosis and preoperative planning. In addition, it is extremely useful in monitoring the effectiveness of surgical or percutaneous transcatheter interventions. As its efficacy for more and more clinical applications is demonstrated, it is clear that three-dimensional echocardiography has become part of the routine clinical diagnostic armamentarium. In this article, we describe the development of three-dimensional echocardiography over the last decades, review the scientific evidence for its current clinical use and discuss potential future applications. (*Neth Heart J* 2009;17:18-24.)

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Echocardiography is the most clinically used diagnostic imaging modality in cardiac practice today, and with good reason. In addition to its noninvasive nature and time- and cost-efficiency, its bedside avail-

ability in the clinic, emergency ward and operating room is a major advantage. Furthermore, its uncomplicated use in children, pregnant women, and those with implanted pacemakers or defibrillators has set it apart from other closely competing imaging modalities, such as cardiovascular computed tomography (CT) and magnetic resonance imaging (MRI).

However, both M mode and two dimensional echocardiography (2DE) have their own limitations, mainly that quantitative measurements such as left ventricular (LV) volumes and ejection fraction (EF) are derived from assumptions of symmetrical LV geometry that are unreliable, especially in patients with ventricles that are dilated, aneurysmatic or with regional wall motion abnormalities. These assumptions as well as the inadvertent use of foreshortened views, and the conscious decision of many cardiology departments to rely on visual estimates of LV function and EF, despite the inherent subjectivity in interpreting two-dimensional (2D) data, probably account for the relative inaccuracy and poor reproducibility of these techniques. As important diagnostic, prognostic and therapeutic decisions rest upon this analysis, it is paramount that interobserver and intraobserver variability are reduced by developing and utilising accurate and reproducible echocardiographic quantification methods.

A significant development in this regard has been the introduction of three-dimensional echocardiography (3DE). Although the technology had a slow initial development with poor image quality and difficult and time-consuming acquisition and offline reconstruction techniques, through collaboration between clinical investigators and industry, great advancements in image acquisition and computer processing technology have been made to overcome these limitations. With the current state of technology, namely real-time 3D echocardiography, and the high ongoing pace of development, 3DE will become available for an expanding range of clinical applications.

Here, we review the development of 3DE from past to present, provide the scientific evidence for its clinical use and discuss its potential future applications.

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Three-dimensional echocardiographic techniques

The earliest 3DE techniques were dependent on the acquisition of multiple adjacent cross-sectional 2D images using either transthoracic (TTE) or transoesophageal (TEE) echocardiography, followed by volume rendering them into a 3D dataset. For this reconstruction to succeed the spatial and temporal relationships between images had to be registered, which required the transducer to be either moved along a fixed axis or tracked in space. From the first utilisation of 3DE in 1974 by Dekker et al.,¹ using a transducer attached to a mechanical arm, many methods have been applied to accomplish this, most notably an acoustic and magnetic locator. Improvements on these methods led to the so-called 'freehand' imaging,² allowing free movement of the transducer at a single or multiple acoustic windows and resulting in a three-dimensional wire-frame image. In symmetrical, aneurysmatic and even functionally single left ventricles these reconstructions led to accurate measurements of LV volume, mass and EF,³⁻⁶ as well as a new understanding of the shape and leaflet displacement of the mitral valve apparatus, subsequently changing the way mitral valve prolapse is diagnosed.⁷ These early methods, however, required cardiac and respiratory gating and were very complex with labour-intensive and time-consuming acquisition and offline reconstruction, in addition to being prone to artefacts and suffering from poor image quality.

Simultaneously with freehand imaging, a method of sequential 3D data acquisition was developed, based on the concept of the transducer moving in a pre-specified manner along a fixed axis, obviating the need to locate the transducer itself. Three modes of transducer movement can be used, namely a linear, a fan-like and, most popular, a rotational method. In time, both TTE and TEE probes became smaller in size with internal rotation of the transducer, controlled from the ultrasound machine itself. Both from a TTE and especially a TEE approach, good accuracy with strong correlation and agreement with different reference standards was found for measurements of LV volumes and EF with these techniques.^{8,9} In addition, improved

assessment of anatomy and function of valves was achieved through better detail (figure 1), as well as the first time use of 3D colour flow jets.¹⁰⁻¹³ With further advancements in technology, a transition from stepwise to continuous rotational scanning was achieved, offering the possibility of acquiring a complete 3D dataset within a single breath-hold of ten seconds. However, equal to freehand imaging there was still the necessity to interpolate between essentially multiple 2D images, making the technique sensitive to motion artefacts by involuntary movement of heart and lungs. Gating to the cardiac and respiratory cycles could minimise such artefacts but sometimes required long periods of acquisition time, especially in the presence of atrial fibrillation.

To overcome these limitations a TTE online acquisition technique was developed by Von Ramm¹⁴ at Duke University in the early 1990s, which could acquire a pyramidal-like volume of data using a so-called sparse matrix array transducer. The individual piezoelectric crystals of a sparse array transducer are either dedicated to transmit or receive ultrasound and the elements are intermittently arranged in a grid, making it possible to steer the beam in multiple directions and thus obtain a three-dimensional full volume. For the first time a technique, later commercialised by Volumetrics® and now known as 'real-time' 3DE (RT3DE), offered near real-time three-dimensional images. Moreover, advantages such as considerably reduced acquisition time, the obviated need for respiratory and heart rate gating by linking to the cardiac cycle, and greatly reduced transducer size, all brought three-dimensional echocardiography closer to clinical use. However, a few limitations remained as image quality was still relatively poor and the dimensions of the 3D dataset volume limited.

Building on the strengths of RT3DE and significantly reducing its main disadvantage, namely poor image quality, Philips® Medical Systems introduced 'Live' 3DE. Contrary to the sparse array transducer used in Volumetrics® RT3DE, Philips® Live 3DE utilises a fully sampled (matrix) transducer with more than 3000 individual elements, which greatly enhances image quality. Increased computer processing power and hard drive capacity make it possible to process, store and analyse the data. While the acquisition of a full volume of the LV requires four cardiac cycles and gated capture, these limitations are acceptable since the time interval is relatively short. Online or offline analysis of LV volumes, mass, EF and mechanical dyssynchrony is fast and accurate. Above all, the potential to display live and anatomically correct images of every dynamic structure of the heart, while it is functioning and from any conceivable angle, is an unprecedented and crucial step in the adequate clinical evaluation of pathology and function. While transducer frequency and therefore image quality and depth are still relatively low compared with 2D images, advancements in

Figure 1. Multiplane 3D TEE rotational acquisition obtained in a patient with mitral stenosis during systole (A) and diastole (B).

application and computer technology are sure to provide improvements in the near future.

In 2007, Philips® introduced its new Live 3D TEE probe. It offers the same alternating use of 2D and live 3D features as its TTE counterpart, making it widely applicable. In contrast, however, the TEE probe also delivers superb image quality due to its closer proximity to the heart. In addition, it provides novel imaging perspectives, in particular of the heart's valves, allowing cardiologists and cardiac surgeons to diagnose and plan their treatment faster and more accurately. Finally, another true strength of live 3D TEE is the opportunity to monitor interventions in real-time and determine procedure outcomes so that if necessary, further repairs can be made before completing the procedure.

Evidence-based clinical application of three-dimensional echocardiography

Substantial evidence exists for the applicability of 3DE in several areas, including but not limited to the evaluation of ventricular size and function, quantification of mechanical dyssynchrony, assessment of regional LV wall motion at rest and during stress testing to detect ischaemic heart disease, as well as the evaluation of valvular and congenital heart disease. Although older 3DE techniques have shown their usefulness in the past, for present relevance primarily data on the clinical application of RT3DE and live 3DE are presented.

Analysis of chamber size and function

The clinical significance of quantitative analysis of ventricular volume and mass is well known for many cardiovascular diseases and their accurate and reliable measurement is therefore essential. While 2DE quantification techniques have limitations such as the need for geometric modelling and foreshortened views, these are absent in 3DE assessment of ventricular size and function. This theoretical advantage is validated in practice by numerous studies showing superiority of 3DE over 2DE in both accuracy and reproducibility of LV volumes and EF measurements when compared against the gold standard MRI.^{15,16} Similar results were reported for quantification of LV mass.¹⁷ An important additional value of 3DE is the potential to evaluate regional LV function based on segmental analysis of the 3D endocardial borders during the cardiac cycle (figure 2).¹⁸ The ability of 3DE to quantify segmental timing of endocardial systolic contraction, and thus detect and quantify LV intraventricular dyssynchrony, seems useful in predicting which patients will respond to cardiac resynchronisation therapy (CRT),¹⁹⁻²¹ although further studies are warranted.

Quantification of right ventricular (RV) volumes has always been extremely challenging, mainly because of the complex geometrical structure of the RV. As can be expected by its obviated need for geometric modelling, 3DE significantly improves accuracy and reproducibility compared with 2DE.^{22,23} Moreover, a

Figure 2. Measurement of LV volumes, ejection fraction and dyssynchrony. A cast of the LV is obtained using semi-automated endocardial border tracking from a full volume real-time 3D echo dataset (top left and right). Global and regional LV volumes can be calculated and plotted against time during the entire cardiac cycle. Besides end-diastolic and end-systolic volumes and ejection fraction, a comprehensive analysis of intraventricular mechanical dyssynchrony of the LV can be derived from regional volume curves (bottom right), which correspond to the standard 16 or 17 segments (bottom left).

Figure 3. RV analysis. Images from a full volume RV 3D dataset in sagittal (left), four-chamber (upper right), and coronal (lower right) views, allowing manual tracing and adjustments in all planes for each frame of the cardiac cycle.

recently developed specific 3D RV analysis tool by TomTec Imaging Systems® showed promising accuracy for analysing 3D RV echo data when compared with MRI (figure 3).²⁴

RT3DE can also have considerable clinical value in the evaluation of diastolic dysfunction through the measurement of left atrium (LA) volume (figure 4). As LA enlargement has shown to be an independent negative prognostic factor for survival in patients with myocardial infarction, congestive heart failure, and stroke, accurate assessment of LA volume is vital for making adequate therapeutic decisions. In this regard, multiple studies suggest that the accuracy of RT3DE is superior to 2DE.^{25,26}

Ischaemic heart disease

While diagnosis of myocardial ischaemia or infarction through regional wall motion abnormalities has always been routinely assessed by 2DE examination, few studies have been performed to determine the feasibility of 3DE for this evaluation.²⁷ Some data exist on the use of 3DE during dobutamine stress testing showing its feasibility.^{28,29} However, although 3DE eliminates many 2DE limitations, such as its operator dependency and limited number of cross-sections available for evaluation, the relatively low temporal and spatial resolution of 3DE are still critical limitations for clinical application. Besides the use of echo contrast, necessary improvements will largely depend on further advancements in transducer technology and computer processing. Future studies will have to show if 3DE has the potential to become an accurate and reliable diagnostic modality for ischaemic heart disease.

Contrast-enhanced three-dimensional echocardiography

Contrast enhancement can be recommended in patients with poor acoustic windows to improve endocardial border visualisation. Application of 3DE contrast enhancement for quantification of LV volumes and function has not only proven to be feasible, but also to be more accurate compared with non-contrast-enhanced 2DE or 3DE.³⁰ Similar results were found for contrast-enhanced 3D dobutamine stress echocardiography.^{29,31} Finally, contrast-enhanced 3DE allows rapid quantitative assessment of myocardial perfusion due to the benefit of capturing every conceivable imaging plane in a 3D dataset during a single contrast injection.³²

Valvular heart disease

2DE has always been the standard for evaluation of regurgitant or stenotic heart valves. However, the advantages of 3DE offering depth as an additional dimension and enabling unlimited view angles are of considerable value in the diagnosis and management of valvular heart disease. From its initial use, 3DE has been critical in providing new insights on the mitral apparatus and the pathophysiology of mitral stenosis

Figure 4. LA volume measurement. Volume is measured at ventricular end-systole just before opening of the mitral valve, including the LA appendage and excluding the pulmonary veins.

Figure 5. Mitral valve prolapse acquired with live 3D transoesophageal echocardiography. Arrows point to an extensive prolapse of P3 scallop of the posterior mitral leaflet which can be appreciated from an en face view, when the mitral valve is cropped from the left atrial side.

and regurgitation.^{7,33-35} Moreover, mitral valve area measurements by 3DE have shown lower intraobserver and interobserver variability compared with 2DE quantification measurements.³⁶ Although most studies were performed with TEE, evaluation of the mitral valve from a TTE approach was made possible with the development of the fully sampled matrix array transducer, yielding adequate reconstruction of the mitral valve in 70% of consecutive patients.³⁷ Over time the merit of 3DE in evaluating the mitral valve has led

Figure 6. Bicuspid aortic valve visualised and assessed with real-time 3D echocardiography from a trans-thoracic approach. The opening of the two individual leaflets (numbered) during systole creates a 'fish-mouth', which is characteristic for a bicuspid aortic valve (A). In addition, a fused raphe in the middle of one of the two leaflets can be appreciated (arrow) in systole (A) and diastole (B).

to a turning point, where many at present believe 3DE should be considered the new clinical standard for the assessment of mitral valve pathology.^{38,39} The arrival of the live 3D TEE probe and the encouraging first experiences with it only affirm these beliefs (figure 5).⁴⁰

In contrast, data on 3D imaging of the aortic valve are very limited (figure 6).^{41,42} In the presence of aortic valve pathology, acquisition of the valve is challenging in that drop-out artefacts frequently appear due to its thin or often heavily calcified leaflets. Although anecdotal evidence suggests that live 3D TEE provides easier and more accurate visualisation and assessment of the aortic valve,⁴⁰ future studies will have to determine its true value in this regard.

Congenital heart disease

MRI has always been the modality of choice for evaluation of right and single ventricular function. Unfortunately, MRI has many limitations such as its contraindication for patients with pacemakers, those suffering from claustrophobia, and the need for anaesthesia and ventilation for adequate imaging in many paediatric patients. Not only are most of these limitations absent or avoidable during echocardiographic examination, at the same time the intrinsic nature of 3DE makes it an ideal technique for the evaluation of the complex anatomic relationships present in congenital heart disease. An important advancement in this regard has been the development of smaller transducers, allowing intercostal placement of the probe, even in small children. In addition, with the use of 3DE an examination might be completed faster compared with 2DE, hence reducing the need for sedation in paediatric patients. 3DE has been applied in the evaluation of various congenital defects such as atrial, ventricular and atrioventricular septal

defects,^{43,44} but also congenital valvular and vascular abnormalities.⁴⁵⁻⁴⁷ Furthermore, studies have shown that 3DE can provide additional information when compared with 2DE, which might be useful in the diagnosis and management of the individual patient with congenital heart disease.^{45,48}

Contrary to the general emphasis that is placed on quantification of LV size and function, accurate and serial assessment of the RV is at least as essential for adequate management in patients with congenital heart disease, especially where surgical planning and postoperative evaluation are concerned. Many studies have shown that 3DE quantification of LV and RV volumes correlates well with MRI in patients with congenital heart disease.^{24,49,50}

Future directions for three-dimensional echocardiography

It is clear that 3DE has become part of routine clinical application in a complementary role to 2DE and, with further technological advancements, has the potential to assume its place as principal echocardiographic imaging technique in the future. An important development in this regard is the capability of the new live 3D TEE probe to perform not only 3D, but also 2D and colour Doppler imaging, and to switch between these different modes with just the push of a button. Coupled with fast acquisition, easy navigation through the 3D volume dataset and the ability to view the structures of the heart from any plane, the time to complete an echocardiographic examination will likely be significantly reduced with further experience. In addition, the image quality of the recent live 3DE is far superior compared with prior 3DE techniques.

However, to further enhance the quality and expand the clinical applications of 3DE some limitations will still need to be overcome. First of all, both temporal

and spatial resolution will need to improve for optimal image quality. Concerning range, wider angle acquisition is indispensable for adequate visualisation of severely enlarged ventricles often seen in the growing population of patients with heart failure. At the same time the benefits of acquiring a complete 3D dataset in merely one single heart beat are very appealing, since acquisition time will decrease and artefacts due to irregular heart rate, respiration and patient movement are concurrently eliminated.

In addition to new developments in hardware technology, advancements in dedicated software technology for processing, storage, display and analysis are crucial for various clinical applications. An important step forward will be the evolvement from semi-automated to fully automated border detection and chamber quantification. Another example is 3D stress echocardiography, which will greatly benefit from the automatic registering and subsequent rendering of standard cut planes for wall motion analysis. With the additional benefit of fast and easy manual rotation through the complete 3D dataset, potentially even the smallest of wall motion abnormalities can be appreciated. Ultimately, as accuracy and reliability of automated quantification methods are validated, the need for offline analysis will disappear. This will greatly benefit 3DE application in general, but particularly its use in the critical care unit and during interventions in the catheterisation laboratory and operating theatre, where reaching rapid but accurate diagnoses and management decisions is paramount.

Additional clinical applications will likely include quantification of myocardial strain and strain-rate through 3DE speckle tracking, selection of patients eligible for CRT through assessment of interventricular mechanical dyssynchrony, and an in-depth assessment of diastolic dysfunction in patients with heart failure or atrial fibrillation. Finally, researchers and industry alike are showing great interest in the development of 'fusion imaging', a technique which combines different modalities, consequently benefiting from both their individual advantages. It is not inconceivable that fusion of 3DE images with either CT or MRI, thus combining the higher temporal resolution of the first with the exceptional spatial resolution of the latter, might have a comparable impact on cardiac imaging as PET-CT has had in oncology.

Conclusions

In the last two decades the technology behind 3DE has greatly evolved, continually expanding its clinical applications. With the prospect of incorporation in official guidelines, considering the overwhelming and indisputable evidence that 3DE is superior to 2DE in the assessment of LV size and function, as well as the quantification of mitral valve area in mitral stenosis, its routine application in these clinical situations is strongly advocated. With further technological advancement, continued scientific research and increasing clinical

experience, 3DE will be able to fully assess the heart in anatomy and function, establishing its position as the clinically most applicable diagnostic imaging tool in the future.

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