Clinical Application of 3-Dimensional Echocardiography in the USA

Takahiro Shiota, MD, PhD

Three-dimensional (3D) echocardiography is one of the most promising methods for the diagnosis of cardiac disease. Left and right ventricular size and function are currently evaluated with 2D echocardiography. However, for unpredictable asymmetry of the chamber geometry, conventional 2D echocardiography cannot be used to accurately determine absolute chamber volumes and ejection fraction. As for valvular heart diseases, the 3D echo approach has proven to be the most unique, powerful, and convincing method for understanding the complicated anatomy of the valves and their dynamism. The method has been useful for surgical management, including robotic mitral valve repair. Moreover, this method has become indispensable for nonsurgical procedures such as edge-to-edge mitral valve repair. Color Doppler 3D echo has also been valuable to identify the location of the regurgitant orifice, and the severity and character of the valvular regurgitation. In addition, 3D echo is invaluable in the diagnosis and management of congenital heart disease and in certain other situations, such as evaluation of the aortic annulus for transcatheter aortic valve implantation or replacement. It is now clear that 3D echocardiography, especially with the continued development of real-time 3D transesophageal echo technology, will enhance the diagnosis and management of patients with heart diseases. (Circ J 2015; 79: 2287–2298)

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Echocardiography is now indispensable for clinical cardiology. For routine clinical purposes, 2-dimensional (2D) echocardiography is widely accepted for evaluating a variety of cardiac conditions. However, there is still uncertainty or inability to provide sufficient information on various cardiac conditions because of the inherent limitations of 2D echocardiography. 3D echocardiography was conceived as the ideal tool to overcome the limitations of conventional 2D methods. One of the most notable aspects that 2D echocardiography lacks is the ability to provide absolute chamber volumes, such as of the right ventricle (RV), without any mathematical assumptions. Another important limitation of 2D echocardiography is the lack of intuitive recognition of cardiac structures from any spatial point of view. Although the currently available 3D ultrasound methods suffer from relatively low image quality and low time resolution, especially for color Doppler, this method should be one of the ultimate goals of cardiac imaging. In light of the relatively recent development of real-time 3D transesophageal echocardiography (TEE), this new imaging ultrasound method has become a clinical standard for structural heart disease. Here, I will review published papers and comment on the clinically relevant issues of 3D echocardiography.

Left Ventricular (LV) Volume and Function

Absolute LV volumes and their dynamic changes during the cardiac cycle are indispensable and fundamental indices for assessing LV function in any cardiac disease. Routine 2D echocardiography is currently widely accepted and applied for evaluating LV size and function. Because the main reason for echocardiography is often to evaluate the LV ejection fraction (EF) and absolute LV size, the accuracy and reliability of this function are essential. For a normal LV, current 2D echocardiography is able to assess LV volume and EF without serious issues. However, in patients with abnormal LV cavity geometries, 2D echocardiography may not be accurate enough. The reason why 2D echocardiography is not able to provide accurate LV volume and function is the potential failure of the mathematical assumptions used for the 2D echocardiography method. 3D echocardiographic methods provide a unique ability to determine absolute LV volumes, stroke volumes and EF without any mathematical assumptions. The accuracy of 3D echocardiography for determining LV volumes and EF has been validated with magnetic resonance imaging (MRI) as an independent gold standard. Correlation of LV parameters, including LV volumes and EF, between 3D echocardiography and MRI are reportedly excellent.
Localized wall motion abnormality with abnormal regional stroke volume and EF is well visualized with 3D echo imaging (Figure 1). When the image quality improves with better time resolution, such an analysis of localized wall motion by 3D echocardiography may reveal the real efficacy of resynchronization therapy in patients. With currently available systems, 3D echocardiographic analysis in ischemic cardiomyopathy is not consistent with tissue Doppler imaging for the assessment of LV dyssynchrony. However, 3D global longitudinal strain is reportedly the most robust index for predicting future major adverse cardiac events in patients with asymptomatic severe aortic valve stenosis (AS) and preserved LVEF.

**RV Volume and Function**

RV size and function is currently evaluated by 2D echocardiography with a variety of parameters, including fractional area change, tricuspid annular plane systolic excursion, Tei index, and strain and the strain rate with speckle tracking. For determining absolute RV chamber volumes and stroke volumes, 3D imaging methods are even more important than for determining LV volume, because the RV chamber has a complex geometry (Figure 2). Thus, quite a few studies have used 3D echocardiography to determine RV volume, mass and function. In vitro models have been used to validate 3D echocardiography for determining RV volumes. Using real-time volumetric images of the RV in an animal model of RV volume overload, RV stroke volumes were determined by the use of parallel slices of the 3D volume. Good correlation and agreement were found between RV stroke volumes obtained by electromagnetic flow probes and meters and those obtained by the real-time 3D method (r=0.80). Shimada et al performed a meta-analysis on 23 studies including 807 subjects, which revealed underestimation of RV volume (P<0.00001) and EF (P=0.03) as compared with MRI values. Recently, single-beat 3D echocardiography has been introduced and is reportedly feasible and clinically applicable for RV volumetric quantification in acquired RV pressure or volume overload.

However, underestimation of MRI-derived LV volumes by 3D echocardiography has been consistently found. In a comparative study of the LV volume and EF determined by 3D echocardiography and by MRI, meta-analysis of 95 studies including 3,055 subjects revealed significant underestimation of LV end-systolic volume (−4.7 ml, P<0.0001) and end-diastolic volume (−9.9 ml, P<0.0001), whereas measurement for EF revealed excellent accuracy (−0.13%, P=0.41). A newly developed 3D speckle tracking method has also been used to determine LV volume and EF, and reportedly successful, although image quality is of great importance.
Valvular Heart Disease

Patients with valvular heart disease have been evaluated and diagnosed by echocardiography for many years. For over the past 40 years, new echocardiography methods have been proposed to improve the accuracy of the diagnosis of valvular heart diseases. In particular, 3D echocardiography has recently become a clinical tool, mainly thanks to the development of high-quality real-time 3D TEE.

Mitral Valve (MV)

Among the 4 heart valves, diagnosis of conditions affecting the MV has by far and away benefitted the most from the use of 3D echocardiography, particularly because real-time 3D TEE can show excellent images of the MV [Figure 3A]. Recognition of the MV’s anatomy as normal or abnormal is now easy for cardiologists performing real-time 3D TEE.

MV Regurgitation (MR)

MR is traditionally classified by etiology as either organic or functional. Organic MR is usually caused by degenerative abnormalities, including valve prolapse and/or flail. Location of the prolapse and/or flail of the mitral leaflet (medial, central or lateral) and its geometry is essential for determining surgical and/or transcatheter correction of MR. Conventional 2D echocardiography requires multiple views of the MV and mental reconstruction of the 3D image of the diseased structure. Many investigators have reported the usefulness of 3D echocardiography for visualizing, localizing and quantifying MV abnormalities in patients with MR.2,3,6–8 The superiority of transthoracic real-time 3D echocardiography over conventional 2D echo methods has been reported many times in studies analyzing the anatomy of the MV in patients with MR since the introduction of transthoracic real-time 3D echocardiography.41,43–47 However, clinical use of 3D echocardiography methods did not materialize until user-friendly real-time 3D TEE was introduced circa 2007. In 2008, Sugeng et al reported clinical use of real-time 3D TEE in 211 patients, with excellent visualization of the MV (85–91% for all scallops of both MV leaflets).2 Since those initial publications, there have been quite a few publications on the use of real-time 3D TEE in relation to MV pathology.48–73 In 2013, as an example, Izumo et al reported the superiority of real-time 3D TEE over 2D TEE for measuring the gap and width of MV prolapse and flail.56 As seen in this paper and many others, it is obvious that real-time 3D TEE can provide much better overall anatomic perspectives of the MV than 2D TEE, including the shape of the prolapse, and the exact size and location of the MV leaflets using the so-called surgical view [Figure 3B]. Importantly, this specific 3D view is helpful for echo cardiologists to communicate with surgeons and interventionists, or the heart team members.

In patients with MR, color Doppler capability, which was introduced in reconstruction 3D systems initially, then later in real-time 3D transthoracic and real-time 3D TEE, can provide 3D images of both the regurgitant flow jet [Figure 3C] and flow convergence.74–83 The location of the flow convergence zone or proximal isovelocity surface area (PISA) and its size can determine the location of the regurgitant orifice and the severity of the MR.82 Such information, especially the location of the regurgitant orifice, is critical for the choice of management in recent years; that is, whether to proceed with surgery vs. edge-to-edge clip procedure.84 For instance, for the edge-to-edge clip procedure [Figure 3D], MR originating from the anterior middle scallop/posterior middle scallop (A2/P2) is preferred to a commissural origin of MR according to the ongoing clinical mitral clip trial of Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COPAT) in the USA.

Also, color Doppler 3D echocardiography has demonstrated that the shape of the flow convergence zone is not a hemisphere in many conditions, such as in irregular or asymmetrically shaped orifices and also in patients with functional or ischemic MR.81,82–85 Matsunuma et al86 and other investigators87,88 have proposed more realistic geometric assumptions such as a hemi-ellipse and a hemi-ellipsoid for flow convergence zones to obtain more accurate estimates of regurgitant volumes.

In October 2013, edge-to-edge clip repair was accepted for surgically risky patients with severe degenerative MR in the USA. In the catheterization laboratory, real-time 3D TEE can assist with positioning of the clip on the MV orifice, the grasping of both MV leaflets [Figure 3D], and evaluation of the result, including visualization of any residual MR.83,90–91 At Cedars-Sinai Medical Center, 3D TEE is indispensable for the success of this procedure. We reported on the value of real-time 3D TEE for determining the unique shape, size and location of the atrial septal defect (ASD) created by septal puncture with the large catheter and its sheath (24F) used for the clip procedure.92

As for the postoperative evaluation of MV surgery, either repair or replacement, 3D TEE has proven to be important for visualizing the entire structure of the new artificial valve.93 In addition, color Doppler 3D TEE can delineate the location of any paravalvular MR, especially for transcatheter closure of the leak.93–96 In our study, color Doppler 3D TEE showed the exact location of the circumferential orifice of paravalvular regurgitation around the artificial MV and thus was able to effectively assist with transcatheter device closure procedure.96 Color Doppler 3D TEE also showed the exact location of residual MR after MV replacement in the Heart Institute, leading to immediate successful correction in the operating room [Figure 3E].

Mitral Valve Stenosis (MS)

MS is usually caused by rheumatic MV disease. Fusion of the commissures is the major cause of the stenosis. Conventional 2D echocardiography has been widely used to determine the smallest valve area; however, this imaging method is limited for visualizing the entire MV and the subvalvular apparatus, resulting in erroneous measurements of the smallest valve area. 3D echocardiography has been reported as superior over conventional 2D echocardiography for determining the smallest area and visualizing the morphological abnormalities.41,63,66,99–103 In an early study, 3D echocardiography provided accurate and highly reproducible measurements of the MV area that could easily be performed from an apical approach.100 In another study, real-time 3D echocardiographic system was used for MV planimetry,102 which was reportedly more accurate than the Gorlin method for measuring valve area. Those authors concluded that we should keep in mind that 3D echo planimetry may be a better reference method than the Gorlin method for assessing the severity of rheumatic MS.102 Recently introduced real-time 3D TEE has demonstrated striking images of MS in patients.109 Not only the severity of the stenosis but also the shape, location and anatomic abnormalities of the MV leaflets, such as heavy calcification, are visualized in a most intuitive way. In a clinical study of 43 patients with rheumatic MS, 3D TEE allowed excellent assessment of commissural fusion and valve area planimetry.105 According to a recent clinical study, 3D TEE should be considered for accurate valve area assessment, especially in patients with a large left atrium and large angle.
Figure 3. (A) Normal mitral valve imaged by 2D echo (Upper panels) and real-time 3D transesophageal echocardiography (Lower panels). (B) Mitral valve prolapse (middle scallop, P2; arrows) imaged with real-time 3D TEE. (C) Two types (1 continuous jet (Left) and 2 separate jets (Right)) of functional mitral regurgitation jet clearly distinguished by color Doppler 3D TEE. (D) Real-time 3D TEE images of a MitraClip (red arrows, Left panel viewed from the left atrium, Right panel from the left ventricle). A2/P2 area was clipped. (E) Residual mitral regurgitation immediately after surgical mitral valve replacement (a tissue valve). (Upper panel) 2D TEE image. (Lower panel) Color Doppler 3D TEE image demonstrating the exact location of the residual MR (arrow), which could assist in second pump correction of the MR. AO, aorta; AP, appendage; AV, aortic valve; LA, left atrium; LAA, left atrium appendage; LV, left ventricle; MV, mitral valve; TEE, transesophageal echocardiography.
between the lines of the true MV tip and the echo beam-to-the tip.22

Additionally, in 63 consecutive patients with rheumatic MS, valve area assessment using the flow convergence (or PISA) method by the newly developed single-beat real-time 3D color Doppler echocardiography was reportedly feasible in the clinical setting and more accurate than the conventional 2D PISA method.108 This new-type real-time 3D TEE with and without color Doppler appears to be clinically feasible and useful.

**Mitral Annulus** Daimon et al and other investigators have reported the usefulness of 3D echocardiographic methods for evaluating non-planarity and area change of the mitral annulus as well as leaflet tenting, in both animals and patients.110–121 Extracted 3D images obtained by multiplane TEE were able to be used in the evaluation of non-planarity and area change of the mitral annulus in patients with an annuloplasty ring.122,123 The saddle-shaped geometry of the mitral annulus has been repeatedly reported and confirmed with the use of 3D echocardiography, and assessment of mitral annular size and function in control subjects and patients with cardiomyopathy was reportedly accurate and correlated well with MRI.124 Not only the annular geometry, but also valve tethering or tenting in ischemic cardiomyopathy and idiopathic cardiomyopathy have been quantitatively analyzed by 3D echocardiography.114,117,125,126 In a recent study using real-time 3D TEE, the mitral annulus in functional MR patients was significantly larger, rounder and flatter, and dilated further and became more flattened in late systole than in controls.118 Considering the clinical importance of annuloplasty for managing such patients, detailed geometric evaluation may improve surgical results. Real-time 3D TEE showed that in 35 patients undergoing elective surgical aortic valve replacement, the mitral annulus underwent significant geometric changes immediately after the surgery; in fact, a 16.3% reduction in the mitral annular area was observed. The anterior annulus underwent a greater reduction in length compared with the posterior annulus, which suggested the existence of mechanical compression by the prosthetic valve.121

**Aortic Valve**

Considering its 3D structure, assessment of the aortic valve may prove to be one of the most important applications of 3D echocardiography (Figure 4).127–130

**Aortic Valve Regurgitation (AR)** AR is caused by abnormalities such as bicuspid aortic valve, senile degenerative (calcification) valve, and rheumatic valve disease and also by aortic annular dilation such as in Marfan syndrome and annular ectasia. In addition, a new type of AR has recently drawn the attention of cardiologists, interventionalists and surgeons, through the development of transcatheter aortic valve replacement (TAVR). AR post-TAVR is often paravalvular in nature and its severity can be difficult to determine, as Mihara et al recently reported.131 3D echocardiography, especially real-time 3D TEE, together with simultaneous color Doppler multiple 2D views, is particularly important for the prevention and diagnosis of this type of AR.131–133 In general, the role of 3D echocardiography in AR evaluation, including post-TAVR AR, is probably 2-fold: detailed anatomical assessment of the valve and leakage location and size, on the one hand, and quantitative evaluation of the severity of AR on the other.134 3D echocardiography, especially real-time 3D TEE, has a true advantage over 2D echo for visualizing aortic valve anatomy in detail.135 Shibayama et al reported that real-time 3D TEE can reveal characteristic anatomic differences between type I (annular dilation) and type II (prolated) AR.135

As for AR severity, quantitative assessment with 2D echo remains challenging. A recent clinical study in 32 patients with AR reported the accuracy of 2D and 3D transthoracic echocardiography (TTE) for AR quantification, using 3-directional velocity-encoded MRI (VE-MRI) as the reference method. The investigators concluded that AR regurgitant volume quantification using 3D TTE was accurate, and its advantage over 2D TTE was particularly evident in patients with eccentric jets.136 However, in clinical settings, 3D echo quantification of AR volume as reported above may not be very accurate and/or necessary. Additionally, for closing aortic paravalvular leaks, it is imperative to identify the location of the leak.137 3D TEE is truly useful for this purpose, as with the device closure of MV paravalvular leak mentioned before.138–142 Fortunately, newer types of TAVR valves such as the Sapien 3 have been developed, with successful reduction of paravalvular AR.

**Aortic Valve Stenosis (AS)** The cause of AS is either congenital (usually bicuspid) or acquired (degenerative calcific valve). The normal aortic valve area is approximately 3–4 cm². In our aging population, degenerative calcific AS is most commonly detected by conventional 2D echocardiography. In one clinical study, 3D echocardiographic methods for planimetry of the aortic valve area showed good agreement with the standard TEE technique in patients with AS.129 Also 3D planimetry methods were at least as good as standard TEE and had better reproducibility.129 The authors concluded that 3D aortic valve planimetry is a novel non-invasive technique.
that provides an accurate and reliable quantitative assessment of AS.\textsuperscript{129} However, the quality of the images of the aortic valve with TTE is often suboptimal, which may cause difficulty in measuring the smallest valve area. TEE is certainly superior to TTE in this regard. Multiple publications have reported the usefulness of 3D TEE, especially real-time 3D TEE for this purpose.\textsuperscript{143,144} Saitoh et al reported better agreement between the continuity-derived aortic valve area and planimetry area with the use of real-time 3D TEE than with conventional 2D echocardiography.\textsuperscript{144} The advantage of 3D echocardiography over 2D echo is clearly recognizable when the 2D plane can search for the smallest valve area in the 3D space.\textsuperscript{144}

**Aortic Annulus** The geometry and size of the LV outflow tract (LVOT) and the aortic annulus have become the focus of 3D CT and echo research because of the development of TAVR and its associated residual AR. Greater than mild paravalvular AR after TAVR is reportedly a sign of poor prognosis. Thus, proper sizing of the aortic annulus is necessary for the success of TAVR. CT and 3D echocardiography, especially real-time 3D TEE, have contributed to the analysis of the shape and size of the aortic annulus and LVOT where the new aortic valve is being placed. 3D imaging techniques, including 3D echo, have demonstrated that the shape of the annulus is not circular, but oval. Thus, 3D methods, including CT and 3D TEE, should be used to evaluate aortic annulus area, because 2D imaging techniques provide only a sagittal view, which may underestimate them.\textsuperscript{133,144-147}

**Tricuspid Valve (TV)**
Assessment of the TV’s size and function plays an important role in a number of clinical disease states. However, all 3 TV leaflets (septal, anterior and posterior) cannot be visualized in the same cross-sectional view using either transthoracic or transesophageal 2D echocardiography. In contrast, 3D echocardiography can demonstrate the entire TV from any perspective (Figure 5). This capability significantly improves our understanding of the pathophysiological mechanism underlying various TV diseases.

**Tricuspid Valve Regurgitation (TR)** Causes of TR may be classified into 2 major categories; namely, primary and secondary, similar to MR. The primary type is caused by the organic abnormality of the TV itself whereas secondary TR is caused not by the valve itself, but by a surrounding or supporting structural abnormality such as tricuspid annular dilation and/or RV dilation and dysfunction and pulmonary hypertension. 2D echocardiography is widely used to evaluate the cause and severity of TR, but its clinical capability is far from perfect.

3D echocardiography has been reported to be advantageous over 2D echo for evaluation of the anatomic abnormalities of the TV and the location of the TR orifice. Primary TR is caused by a variety of anatomic abnormalities that can be better visualized by 3D echocardiography than by 2D echo, including the apically located leaflet in Epstein disease, or the thickened and restricted leaflet in carcinoid syndrome.\textsuperscript{148-154} One important finding with 3D echocardiography is pacer-/device-related lead-derived TR. Multiple publications have reported the usefulness of 3D echocardiography for detecting the location of the lead and its association with significant TR.\textsuperscript{155-158} In one of those studies, 45 of 100 patients showed device lead TV leaflet interference. The septal leaflet was the
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most commonly affected (n=23). On multivariate analysis, pre-implantation vena contracta width and the presence of an interfering lead were independently associated with post-device TR. Additionally, the presence of an interfering lead was the only factor associated with TR worsening, increasing the likelihood of developing moderate or severe TR. The authors concluded that lead-leaflet interference as seen on 3D echocardiography is associated with TR after device lead placement, suggesting that 3D echocardiography should be used to assess lead interference in patients with significant TR.

Fukuda et al used 3D echocardiography to reveal that one of the causes of secondary or functional TR was dilation and flattening of the tricuspid annulus. In another clinical 3D echocardiographic study of 54 patients with various degrees of functional TR, septal leaflet tethering, septal-lateral annular dilatation, and the severity of pulmonary hypertension were the main determinants of TR severity.

Congenital Heart Disease

3D echocardiography methods, including 3D TEE, have been reported as powerful tools for evaluating congenital heart diseases.

In an early study, real-time transthoracic 3D echocardiographic measurements of the maximum dimension, maximum circumference, and maximum area of the ASD agreed well with the sizing balloon in the catheterization laboratory. Live/real-time 3D TEE can visualize an ASD with better imaging quality than transthoracic 3D echocardiography (Figure 6) and can assist in and confirm the successful closure of the ASD, demonstrating the clinical feasibility of this echo method. Thus, applications of real-time 3D TEE on the interatrial septum and/or ASD (Figure 6) and devise closure have been reported repeatedly. 3D TEE showed greater values for the maximal ASD size than did 2D echo because 3D echo can visualize the entire shape of ASD clearly whereas 2D echo cannot. When considering percutaneous closure of an ASD, it is critical to know the location, size and dynamic motion of the ASD relative to other cardiac structures such as the coronary sinus, inferior and superior venae cavae and the aorta. As for patent foramen ovale, Tanaka et al described its unique tunnel geometry revealed by real-time 3D TEE (Figure 7).
As for ventricular septal defect (VSD), the older type of volume-rendered 3D echocardiography provided excellent visualization of both experimentally created defects and in 25 patients with VSD. In the LV en face projection, the position, size, and shape of VSDs can be accurately determined. Thus, Kardon et al predicted that precise imaging by 3D echocardiography may be beneficial for surgical and catheter-based closure of perimembranous and singular or multiple muscular VSDs. Real-time transthoracic 3D echocardiography was successfully used to evaluate various congenital heart diseases. A total of 75 patients with suspected congenital heart defects were examined using real-time transthoracic 3D echocardiography. The investigators concluded that unique region-oriented views obtained from the 3D data set could be acquired quickly and have the potential to enhance understanding of complex cardiac anatomy. Real-time 3D TEE can project the en face view of a VSD (Figure 8), which may assist with its transcatheter occlusion.

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References


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