Role of modern 3D echocardiography in valvular heart disease

Takahiro Shiota

Department of Medicine, Heart Institute, Cedars-Sinai Medical Center and University of California, Los Angeles, Los Angeles, CA, USA

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Correspondence to
Takahiro Shiota, M.D.
Department of Medicine, Heart Institute, Cedars-Sinai Medical Center, 8700 Beverly Blvd, Los Angeles, CA 90048, USA
Tel: +1-310-423-6889
Fax: +1-310-423-8571
E-mail: takahiro.shiota@cshs.org

Three-dimensional (3D) echocardiography has been conceived as one of the most promising methods for the diagnosis of valvular heart disease, and recently has become an integral clinical tool thanks to the development of high quality real-time transesophageal echocardiography (TEE). In particular, for mitral valve diseases, this new approach has proven to be the most unique, powerful, and convincing method for understanding the complicated anatomy of the mitral valve and its dynamics. The method has been useful for surgical management, including robotic mitral valve repair. Moreover, this method has become indispensable for nonsurgical mitral procedures such as edge to edge mitral repair and transcatheter closure of paravalvular leaks. In addition, color Doppler 3D echo has been valuable to identify the location of the regurgitant orifice and the severity of the mitral regurgitation. For aortic and tricuspid valve diseases, this method may not be quite as valuable as for the mitral valve. However, the necessity of 3D echo is recognized for certain situations even for these valves, such as for evaluating the aortic annulus for transcatheter aortic valve implantation. It is now clear that this method, especially with the continued development of real-time 3D TEE technology, will enhance the diagnosis and management of patients with these valvular heart diseases.

Keywords: Echocardiography; Mitral valve; Aortic valve; Three-dimensional

INTRODUCTION

Echocardiography has been used to evaluate and diagnose patients with valvular heart disease for many years. New echocardiography methods with improved diagnostic accuracy have been proposed for over 40 years. In particular, 3-dimensional (D) echocardiography is now used clinically due to the development of the high-quality real-time transesophageal echocardiography (TEE). In general, 3D echocardiography allows visualization of cardiac structures such as the mitral valve (MV) from any spatial point of view. However, there are limitations to the currently available 3D ultrasound methods, especially the transthoracic version, due to its relatively low image quality and low time resolution. However, this method is widely used to evaluate valvular heart disease.

Herein, the author will discuss the clinical applications of 3D echocardiography for the mitral, aortic, and tricuspid valves (TVs) individually.

THE MITRAL VALVE

Among the four heart valves, 3D echocardiography, especially real-time 3D TEE, is most useful for the diagnosis and management of MV conditions.
MITRAL REGURGITATION

Mitral regurgitation (MR) is fundamentally classified as either organic or functional in etiology. Organic MR is usually caused by degenerative abnormalities, including valve prolapse and/or flail. Locating the prolapse and/or flail of the mitral leaflet (medial, central, and lateral) and its geometry is essential for selecting a surgical and/or transcatheter correction technique. However, 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 [1-12]. The superiority of transthoracic real-time 3D echocardiography over conventional 2D echo methods in analyzing the anatomy of MV in patients with MR has been reported multiple times since the introduction of transthoracic real-time 3D echocardiography [6,8-10,12,13].

The use of TEE has also been repeatedly reported to evaluate MV anatomy in patients with MR [1,2,5,11]. However, 3D TEE was not clinically accepted until user-friendly real-time 3D TEE was introduced circa 2007. In 2008, Sugeng et al. [11] reported clinical use of real-time 3D TEE in 211 patients. Excellent visualization of the MV (85% to 91% for all scallops of both MV leaflets, the interatrial septum 84%, left atrial appendage 86%, and left ventricle 77%) was observed. This real-time 3D TEE yields high-quality images of the MV (Fig. 1). Since these initial publications, many reports have described the use of real-time 3D TEE for imaging MV pathology [14-39]. For example, in 2013, we published a study on the superiority of real-time 3D TEE

Figure 1. Normal mitral valve imaged by 2-dimensional (D) echo (A, a long axis view in diastole; B, in systole) and real-time 3D transesophageal echocardiography (C, a view from the left atrium in systole; D, in early diastole; E, in late diastole). Arrows indicate each leaflet: lateral P1, middle P2, and medial P3. Ao, aorta; LA, left atrium; LV, left ventricle.
over 2D TEE for measuring the gap and width of a MV prolapse and flail [22]. As seen in this paper and many others, real-time 3D TEE provides a better overall perspective of the MV than 2D TEE, including the shape of the prolapse and the exact size and location of the MV, with the use of the so-called surgical view (Fig. 2). This specific view facilitates communication between echocardiologists and surgeons and interventionists.

In patients with MR, color Doppler capability, which was initially introduced in reconstruction 3D systems, then later in real-time 3D transthoracic and real-time 3D TEE, can provide 3D images of regurgitant flow jets (Fig. 3) and flow convergence [40-48]. The location and size of the flow convergence zone or proximal isovelocity surface area (PISA) can determine the location of the regurgitant orifice and severity of MR [48]. Such information, especially on the location of the regurgitant orifice, is critical for selection of an appropriate treatment protocol; i.e., either surgery or the edge-to-edge clip procedure [49]. For instance, for the edge-to-edge clip procedure, A2/P2 MR is preferred for the commissural origin of MR in the ongoing clinical mitral clip trial, Clinical Outcomes Assessment of Percutaneous Treatment, in the United States.

Also, color Doppler 3D echocardiography has demonstrated that in many conditions the flow convergence zone is not hemispherical, such as for irregular or asymmetrical orifices, and in patients with functional or ischemic MR [47,50-53]. Multiple investigators have proposed more realistic geometric shapes for flow convergence zones, such as a hemiellipse or hemiellipsoid, to obtain more accurate regurgitant volumes [46,53,54].

The vena contracta (VC) area determined by color Doppler 3D echocardiography has been repeatedly found useful for quantitatively defining the MR severity [55-59]. These studies also noted a variety of VC shapes, including a curved VC, in functional MR patients (Fig. 4) [57]. Another recent study using 3D TEE demonstrated multiple VC shapes in a patient and added them together to determine MR severity [58]. The idea of 3D VC seems attractive because it is independent of geometric assumptions. However, the location

Figure 2. Mitral valve prolapse imaged by (A) 2-dimensional (D) transthoracic echocardiography (arrow) and (B) real-time 3D transesophageal echocardiography (arrows). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

Figure 3. Two types (A, one continuous jet; B, two separate jets) of functional mitral regurgitation jet clearly distinguished by color Doppler 3-dimensional transesophageal echocardiography.

Figure 4. Difference in the shape of vena contracta from degenerative mitral valve disease (Ac) and functional mitral valve disease (Bc) delineated by color Doppler 3-dimensional transesophageal echocardiography.
and size of VC from the PISA to the distal jet may vary depending on the operator and cutting the VC in the exact plane in 3D space is difficult, especially when the jet is quite eccentric. In addition, the cutoff value of the VC area for severe MR has not been firmly established. Practically, therefore, one may prefer the size of the PISA when it is appropriately imaged with proper Nyquist limits to the 3D VC for determining MR severity. Both methods can be used together with classic regurgitant jet imaging to increase accuracy.

As mentioned above, edge-to-edge clip repair was approved for high-risk surgical patients with severe degenerative MR in the United States in October 2013. In the catheterization laboratory, 3D TEE can assist the positioning of the clip on the MV orifice, grasping of both MV leaflets, and evaluating the result, including visualization of the residual MR (Fig. 5) [60-63]. At the author’s institution, 3D TEE is indispensable for the success of this procedure. We reported previously the value of real-time 3D TEE for determining the unique shape, size and location of the atrial septal defect created by septal puncture with the large catheter and its sheath (24 F) used for the clip procedure [64].

Regarding postoperative evaluation of MV repair or replacement, 3D TEE has been shown to facilitate visualization of the entire structure of the new artificial valve [65]. In addition, color Doppler 3D TEE can delineate the location of the paravalvular MR, especially useful for transcatheter closure of the leak [65-68]. In our study, color Doppler 3D TEE showed the exact location of the circumferential orifice of paravalvular regurgitation around the artificial MV, thus assisting the transcatheter device closure procedure [66]. Fig. 6 shows a case of postoperative residual paravalvular MR. Color Doppler 3D TEE showed the exact location of the residual MR, which allowed immediate successful surgical correction (Fig. 6).

MITRAL STENOSIS

Mitral stenosis (MS) is usually caused by rheumatic MV
disease. Fusion of the commissure is the major cause of the stenosis. Conventional 2D echocardiography has been widely used to determine the smallest valve area. However, 2D echocardiography can only minimally visualize the entire MV and the subvalvular apparatus, resulting in erroneous measurement of the smallest valve area. Three-dimensional echocardiography has been reported to be superior to conventional 2D echocardiography for determining the smallest area and visualizing morphological abnormalities [6,29,32,69-78]. In an early study, 3D echocardiography provided accurate and highly reproducible measurements of the mitral valve area (MVA) and was easily performed via an apical approach [70]. In another study, a real-time 3D echocardiographic system was used for MV planimetry [72]. This was reportedly more accurate than the Gorlin method for measurement of the valve area. The authors concluded that 3D echo planimetry may be a better reference method than the Gorlin method in terms of assessing the severity of rheumatic MS [72]. The recently introduced real-time 3D TEE yields striking images of MS in patients (Fig. 7) [79]. Not only the stenosis but also the shape, location, and anatomical abnormalities of the MV leaflets, such as heavy calcification, are visualized intuitively. In a clinical study of 43 patients with rheumatic MV stenosis, 3D TEE allowed excellent assessment of commissural splitting and leaflet tears not seen on 2D echocardiography [80]. Additionally, in 63 consecutive patients with rheumatic MS, valve area assessment using the flow convergence (or PISA) method with a newly developed single-beat real-time 3D color Doppler echocardiography was reportedly feasible in a clinical setting and more accurate than the conventional 2D PISA method [79]. This new type of real-time 3D TEE seems clinically feasible and useful with and without color Doppler.

APPLICATION OF 3D ECHOCARDIOGRAPHY FOR BALLOON MITRAL VALVULOPLASTY

Application of 3D echocardiography for mitral valvuloplasty has also been reported [80-83]. In one of these studies, an old type of reconstruction 3D TEE enabled visualization of the MV, allowing visualization of commissural splitting and leaflet tears not seen on 2D echocardiography [80].

Thanks to the recent development of relatively high quality transthoracic real-time 3D echocardiography, improvement of valve area and changes in valve geometry after balloon valvuloplasty were reported in a clinical study [81]. In this study, transthoracic real-time 3D echo, instead of multiplane TEE 3D reconstruction, was employed to measure the valve area in 29 patients with rheumatic MS who underwent balloon valvuloplasty [81]. The authors concluded that transthoracic real-time 3D echocardiography is a feasible and accurate technique for measuring the MVA in patients with rheumatic MV stenosis [81]. In another study, real-time 3D echocardiography improved visualization of valvular anatomy and provided a unique assessment of the extent of commissural splitting [84].

Anwar et al. [85] proposed a new score system based on real-time transthoracic 3D echocardiography that was feasible and highly reproducible for the assessment of MV morphology in patients with MS. According to this study, the score system can provide incremental prognostic information in addition to the Wilkins score [85].

More recently, real-time 3D TEE showed its superiority for evaluating the efficacy of mitral valvuloplasty due to its higher-resolution MV images compared to the old-type reconstruction 3D TEE and transthoracic real-time 3D echocardiography [86].

Figure 7. Three-dimensional transesophageal echocardiography images of a stenotic mitral valve (A) from the left atrium and (B) from the left ventricle. Arrows indicate severe calcifications.
THE MITRAL ANNULUS

Real-time 3D echocardiographic methods have been used to evaluate non-planarity and area changes in the mitral annulus in animals and humans [87-98]. Extracted 3D images obtained with multiplane TEE can also be used to evaluate non-planarity and area changes of the mitral annulus in patients with an annuloplasty ring [99,100]. The saddle-shaped geometry of the mitral annulus has been repeatedly reported and confirmed by 3D echocardiography, and its assessment of mitral annular size and function in control subjects and patients with cardiomyopathy was reportedly accurate and well correlated with magnetic resonance imaging (MRI) findings [101]. Three-dimensional echocardiography allowed quantitative analysis of not only the annulus geometry but also the valve tethering or tenting in ischemic cardiomyopathy and idiopathic cardiomyopathy [91,94,102,103]. In one recent study of real-time 3D TEE, the mitral annulus in functional MR was significantly larger, rounder, and flatter, and dilated further and became more flattened at late systole, compared to controls [95]. Considering the clinical importance of annuloplasty for managing such patients with MR, detailed geometric evaluation should be performed to 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 postoperatively. A 16.3% reduction in the mitral annular area was observed. The anterior annulus underwent a greater reduction in length compared to the posterior annulus, which suggested mechanical compression by the prosthetic valve [98].

THE AORTIC VALVE

Considering its 3D structure, the aortic valve may prove to be one of the most important applications of 3D echocardiography [104-107].

AORTIC VALVE REGURGITATION

Aortic regurgitation (AR) is caused by valvular abnormalities such as a bicuspid aortic valve, senile degenerative (calcification) valvular disease, and rheumatic valve disease and also by aortic annular dilations such as Marfan syndrome and annular ectasia. In addition, another new type of AR has recently drawn the attention of cardiologists, interventionists, and surgeons due to the development of transaortic valve replacement (TAVR). AR post-TAVR is paravalvular in nature, and its severity is often difficult to determine. Three-dimensional echocardiography, especially real-time 3D TEE, is particularly important for the prevention and diagnosis of this type of AR [108,109]. In general, the role of 3D echocardiography in AR evaluation, including this post-TAVR AR, is probably twofold: providing detailed anatomical assessment of the valve and leakage location and size, and quantitative evaluation of the severity of AR [110].

Three-dimensional echocardiography, especially re-

Figure 8. Three-dimensional transesophageal echocardiography images of normal aortic valve in a cardiac cycle (A, diastole; B, early systole; C, mid-systole).
al-time 3D TEE, has an advantage over 2D echo methods for visualizing the aortic valve anatomy in depth (Figs. 8 and 9) [111]. We reported that real-time 3D TEE could reveal characteristic anatomical differences between type I (annular dilation) and type II (prolapsed) AR [111].

As for AR severity, quantitative assessment of AR with 2D echocardiography remains challenging. A recent clinical study in 32 patients with AR reported the accuracy of 2D transthoracic echocardiography (TTE) for AR quantification, using 3D three-directional velocity-encoded (VE)-MRI as the reference method. With color Doppler TTE, the 2D area was calculated using PISA. From the 3D TTE multiplanar reformation data, the 3D area was calculated using planimetry of the VC. Regurgitant volumes were obtained by multiplying the 2D and 3D area by the velocity-time integral of the AR jet, then compared with those obtained using VE-MRI. For the entire population, the 3D TTE-derived regurgitant volume was highly correlated to the VE-MRI-derived regurgitant volume ($r = 0.94$ and $-13.6$ to $15.6$ mL per beat, respectively). In contrast, the 2D TTE-derived regurgitant volume showed a modest correlation and large limits of agreement with the VE-MRI ($r = 0.70$ and $-22.2$ to $32.8$ mL per beat, respectively). The investigators concluded that AR regurgitant volume quantification using 3D TTE is accurate, and is particularly advantageous over 2D TTE in patients with eccentric jets [112]. However, AR volume quantification is not often required in a clinical setting. Thus, 3D echo quantification as reported above may be impractical in many cases.

AORTIC VALVE STENOSIS

Aortic stenosis (AS) is either congenital (usually bicuspid) or acquired (degenerative calcific valve). The normal aortic valve area is ~3 to 4 cm$^2$. In this current aging population, degenerative calcific aortic valve stenosis is the most commonly detected by conventional 2D echocardiography. In one clinical study on AS, 3D echocardiographic methods for planimetry of the aortic valve area showed good agreement with the standard TEE technique in patients with AS [106]. Also, 3D planimetry methods were at least as good as standard TEE and had better reproducibility [106]. The authors concluded that 3D aortic valve planimetry is a novel non-invasive technique that provides an accurate and reliable quantitative assessment of AS [106]. However, the image quality of the aortic valve with TTE is often suboptimal, which may hinder measurement of 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 [113,114]. We reported better agreement between the
continuity aortic valve area and planimetry area with the use of real-time 3D TEE than with conventional 2D echocardiography [114]. The advantage of 3D over 2D echocardiography is evidenced by the ability of the 2D plane to search for the smallest valve area in the 3D space (Fig. 10) [114].

THE AORTIC ANNULUS

The geometry and size of the left ventricular outflow tract (LVOT) or the aortic annulus has become the focus of 3D computed tomography (CT) and echo research because of the development of TAVR and its residual AR. Greater than mild paravalvular AR after TAVR is reportedly a poor prognostic indicator. 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 or LVOT where the new aortic valve will be placed. Three-dimensional imaging techniques, including 3D echocardiography, can demonstrate that the shape of the annulus is not circular, but oval. Thus, 3D methods, including CT and 3D TEE, should be used to evaluate the aortic annulus area because 2D imaging techniques provide only a sagittal view, which may underestimate it [109,114-117]. In conjunction with this, assessment of LVOT stroke volume with 3D echocardiography is more accurate than that by the conventional 2D continuity method [107,114]. Thus, 3D echocardiography is highly recommended over 2D echo for determining the LVOT area [114].

Regarding the subaortic membrane, multiplane analysis of 3D datasets is reportedly a sensitive and accurate method for delineation of morphological details of discrete sub-AS, adding to information gained from 2D echocardiography [118]. Recently, we reported the value of real-time 3D TEE for evaluating dynamic changes in the LVOT in both the subaortic membrane and in obstructive hypertrophic cardiomyopathy (Fig. 11) [119].

THE TRICUSPID VALVE

Assessment of TV size and function plays an important role in a number of disease states. However, all three TV leaflets (septal, anterior, and posterior) cannot be visualized in one cross-sectional view using either transthoracic or transesophageal 2D echocardiography. In contrast, 3D echocardiography allows visualization of the entire TV from any perspective (Fig. 12). This capability significantly improves our understanding of the pathophysiological mechanism underlying various TV diseases.

TRICUSPID VALVE REGURGITATION

Causes of tricuspid regurgitation (TR) may be classified into two major categories, primary and secondary, as in MR. The former is caused by an anatomical abnormality of the TV itself while the latter is caused not by the valve itself, but by abnormalities of the surrounding or supporting structures, such as tricuspid annular dilation and/or RV dilation and dysfunction and pulmonary hypertension. Two-dimensional echocardiography is widely used to evaluate the cause and severity of TR. However, its clinical utility is far from perfect.

Three-dimensional echocardiography has been reported to be advantageous over 2D echocardiography...
for evaluation of the anatomical abnormalities of the TV and the location of the TR orifice. Primary TR is caused by a variety of anatomical abnormalities that can be better visualized using 3D than 2D echocardiography, including an apically located leaflet in Epstein disease, or a thickened and restricted leaflet in carcinoid syndrome [120-126]. One important finding with 3D echocardiography is lead-derived TR related to a pacer/device. Multiple publications have reported the usefulness of 3D echocardiography for detecting the location of the lead and its relationship to significant TR [127-129]. In one of these studies, 45 of 100 patients showed device-lead TV leaflet interference. The septal leaflet was the most commonly affected (n = 23). On multivariate analysis, the preimplantation VC width and the presence of an interfering lead were independently associated with postdevice 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 [127].

One of the causes of secondary or functional TR is reportedly dilation of the tricuspid annulus, which can be determined using 3D echocardiography [130]. In another clinical 3D echocardiographic study of 54 patients with various degrees of functional TR, its severity was determined based mainly on septal leaflet tethering, septal-lateral annular dilatation, and the severity of pulmonary hypertension [131].

THE TRICUSPID ANNULUS

The geometry and size of the tricuspid annulus have been investigated using 3D echocardiography [101,102,130-133]. We found that a normal tricuspid annulus has a unique 3D geometry (Fig. 13) [130]. With the 3D geometric concept, a new annuloplasty ring for a tricuspid annulus was developed and used in patients with severe TR (Fig. 12) [134]. Short term results with this new annuloplasty ring appear to be satisfactory [135]. Three-dimensional
echocardiography has been valuable not only for understanding complicated cardiac structures but also for developing new strategies, such as this new annuloplasty ring, for treatment of patients.

INFECTIVE ENDOCARDITIS

The current diagnostic protocol for endocarditis does not include 3D echocardiography, mainly because 2D echocardiography, especially 2D TEE, is fully capable in this regard. The author admits that 3D TEE is less sensitive than 2D TEE for detecting small vegetations due to its lower image quality. However, the shape, location, and extension of the endocarditis findings, including vegetations, perforations, and abscesses, are evaluated with greater accuracy and in more detail than with conventional 2D echocardiography (Figs. 14 and 15) [26,65,136-138]. It is almost impossible to image the entirety of a complicated mobile vegetation with 2D echocardiography. In contrast, 3D echocardiography, especially real-time 3D TEE, facilitates visualization of the full extension and motion of the complicated vegetation in one view from any desired angle (Fig. 15). As a result, the maximum size of the vegetation was underestimated by 2D TEE as compared to 3D TEE (a mean difference of 3.2 mm) in our recent study [138].

In summary, 3D echocardiography has been shown to be useful for clarifying complicated valvular anatomy. In particular, real-time 3D TEE has reduced the technical and quality problems of previous 3D echocardiography and has resulted in widespread use of 3D echocardiography in patients with valvular heart disease.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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