REVIEW

Recent advances in echocardiography for valvular heart disease [version 1; referees: 3 approved]

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Abstract

Echocardiography is the imaging modality of choice for the assessment of patients with valvular heart disease. Echocardiographic advancements may have particular impact on the assessment and management of patients with valvular heart disease. This review will summarize the current literature on advancements, such as three-dimensional echocardiography, strain imaging, intracardiac echocardiography, and fusion imaging, in this patient population.

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Introduction

The American Heart Association/American College of Cardiology Guidelines for the Management of Patients with Valvular Heart Disease[1] state that echocardiography (transthoracic [TTE] or transesophageal [TEE]) is the imaging modality of choice for the assessment of patients with valvular heart disease. Numerous less invasive therapies, such as percutaneous or transcatheter interventions, have recently been introduced for the treatment of structural heart disease. Many of these procedures require extensive multi-modality imaging guidance and have increased interest in advancements in echocardiography. Recent advancements in echocardiography are of particular relevance to valvular disease. This review will discuss the application of these new technologies to diagnose and manage various types of valvular heart diseases.

Three-dimensional echocardiography

The echocardiographic advancement that has had the most impact on the diagnosis of valvular heart disease is real time three-dimensional (RT3D) echocardiography. The advantages of three-dimensional (3D) imaging over two-dimensional (2D) imaging has been well described in the most recent societal guidelines: "Recommendations for cardiac chamber quantification by echocardiography in adults" update[2] and "Recommendations for image acquisition and display using 3D echocardiography"[3]. These guidelines review the significant data supporting the improved accuracy and reproducibility of 3D imaging for ventricular volumes and mass, as well as valvular morphology and function. Initially introduced in the year 2000, the continued improvement of 3D technology has led to its widespread availability and its growing utility, particularly for valvular heart disease[4].

Valve morphology

RT3D TEE has significantly changed the assessment of valvular pathology and has revolutionized patient selection not only for surgical repair but also for newer transcatheter procedures, discussed in a subsequent section.

RT3D TEE is not only more accurate than 2D techniques in identifying specific mitral valve pathology in the setting of complex disease but the diagnosis can be made more rapidly, which is of particular use in the intraoperative evaluation of patients undergoing mitral valve repair[5–9]. RT3D echo improves the accuracy and reproducibility of planimetry measurements of mitral valve area in the setting of rheumatic disease by ensuring on-axis imaging of the short-axis view[10–13]. This technology has also been integral to our understanding of the dynamic nature of the mitral valve complex in normal patients, as well as in primary and secondary mitral valve disease[14–18].

Recent RT3D TEE studies have shown a coupling of mitral and aortic valve dynamic anatomy. Mitral valve diseases may affect normal mitral-aortic coupling and aortic valve function; different patterns of abnormal mitral-aortic coupling are associated with different Carpentier types of mitral regurgitation[19]. Conversely, changes in aortic morphology may affect mitral valve function, particularly in the setting of aortic stenosis and calcification of the aortic-mitral fibrous continuity[20]. RT3D TEE has shown changes in mitral valve morphology following surgical aortic valve replacement[21] as well as transcatheter aortic valve replacement (TAVR)[22]. Notably, a decrease of tenting area predicted those patients whose mitral regurgitation improved following TAVR.

Aortic valve morphology as well as aortic root measurements are more accurate and reproducible with RT3D imaging. Inter-commissural distance and free leaflet edge lengths can be measured by 3D echocardiography and are used to choose the tube graft size in valve-sparing root operations[23]. Larger left ventricular outflow tract areas and calculated aortic valve dimensions and areas are obtained by RT3D TEE[24]. Planimetry of the aortic valve and left ventricular outflow tract area by RT3D has been shown to be accurate and reproducible[25–27] and may influence surgical decision-making in the setting of moderate-to-severe aortic stenosis[28]. With accurate measurement of the left ventricular outflow tract, geometric assumptions used in the continuity equation are avoided, resulting in more precise estimations of aortic valve areas using 3D echocardiography over traditional 2D methods.

Prosthetic valve function can also be accurately assessed using RT3D TEE. With transcatheter solutions to bioprosthetic valve failure[29–31] and paravalvular regurgitation[32–34] RT3D TEE has become an important tool for intra-procedural guidance during percutaneous interventions. TEE can depict not only the relevant cardiac landmarks adjacent to the sites of paravalvular leaks but also wires, delivery catheters, and closure devices[35]. RT3D TEE imaging results in a more accurate localization of paravalvular defects and an estimation of the size of the defect that correlated better with surgical findings when compared with 2D TEE[36].

Quantification of valvular function

Three-dimensional color Doppler may overcome the limitations of 2D and standard Doppler measurements for quantifying regurgitation[3,37,38]. Studies have shown the feasibility of measuring the 3D vena contracta (narrowest portion of the regurgitant jet) on RT3D echocardiography to assess the severity of regurgitation for native regurgitant valve disease[37,39–41], as well as following surgical[42] or transcatheter interventions[43].

Calculation of regurgitant volume in native valvular disease using the proximal isovelocity surface area (PISA) method[44] has known technical limitations, primarily the geometric assumptions of PISA shape required to calculate effective regurgitant orifice area. Multiple studies have validated the use of single-beat RT3D echocardiographic color Doppler imaging allowing the direct measurement of PISA without geometric assumptions for aortic, mitral, and tricuspid regurgitation assessment[45–48].

Newer methods of determining relative flows within the heart make use of the velocity and direction of flow information which can be derived from color Doppler. Off-line software has been developed which uses 2D color Doppler images to determine the velocity, flow rate, and flow volume in any given region of the heart[49]. Extension of this technology to 3D color Doppler volume sets is now possible and allows rapid, accurate, and reproducible quantitation of relative stroke volumes[50,51]. Thavendiranathan *et al.*[51] used the velocity information encoded in the volume color Doppler data, targeting the appropriate region of interest by using the simultaneous 3D imaging of the mitral annulus and left ventricular outflow tract. Color Doppler velocity is multiplied by a known area of this cross-section (a voxel area), and the resulting spatially averaged flow rates are used to generate flow-time curves that resemble those obtained by magnetic resonance imaging. The temporal integration of the flow-time curve generates the stroke volume. There was excellent correlation between the automated measured mitral inflow and aortic stroke volumes, and magnetic resonance imaging stroke volume ($r = 0.91$, 95% confidence interval [CI], 0.83–0.95, and $r = 0.93$, 95% CI, 0.87–0.96, respectively, $P<0.001$) and very low interobserver variability. Automation of the measurement process allowed calculations of mitral inflow and aortic stroke volumes to be performed very rapidly. This methodology will likely become the standard for measurement of regurgitant volumes in the future.

Structural heart disease interventions

TAVR has become an acceptable alternative treatment for high-risk or inoperable patients with severe symptomatic aortic stenosis[52–55]. Three-dimensional echocardiography has been shown to improve sizing of the transcatheter valve[56–58]. RT3D TEE is comparable to computed tomography for annular assessment and prediction of paravalvular regurgitation due to oversizing[59,60], as well as measurement of coronary artery height[61]. RT3D TEE has been shown to provide superior spatial visualization and anatomic orientation, optimizing procedural performance, and RT3D TTE can be used to assess the severity of paravalvular regurgitation following TAVR[62]. Further study of this technique for quantifying regurgitant severity is warranted in addition to a unified scheme for grading paravalvular regurgitation following TAVR[63]. Newer devices, with features such as external skirts or the ability to reposition, may reduce the incidence of post-TAVR complication.

Three-dimensional TEE may also improve procedural success and shorten procedure time for the MitraClip™ device (Abbott Vascular Structural Heart, Menlo Park, CA) (Figure 1)[64–66]. Altiok *et al.*[65] performed a structured analysis to compare information and guidance capability provided by RT3D TEE compared to 2D TEE and found 3D TEE advantageous in 9 of 11 steps of the percutaneous mitral repair procedure, including optimizing trans-septal puncture site, guidance of the clip delivery system, precise positioning of the clip delivery system simultaneously in anterior-posterior and lateral-medial direction, valvular regurgitation jet position, adjustment and visualization of the clip position relative to the valvular orifice, and assessment of remaining regurgitant jets[65]. Following MitraClip, assessment of residual regurgitation could also be assessed by 3D color Doppler[43]. A >50% reduction in regurgitant

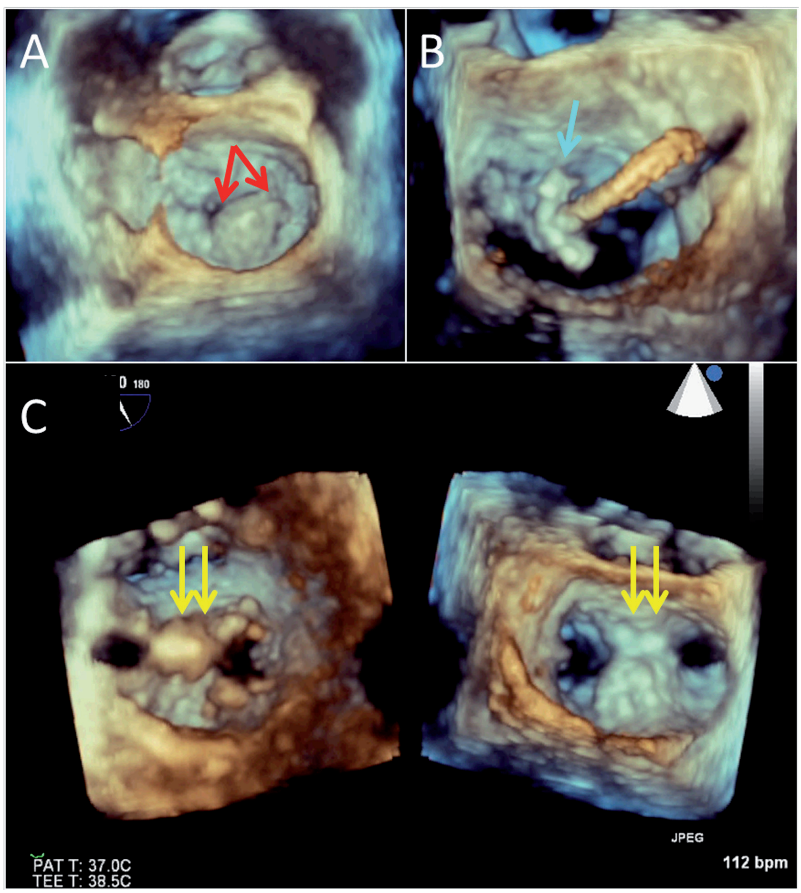

Figure 1. Three-dimensional echocardiography during a transcatheter mitral repair procedure. Panel A shows the baseline mitral valve morphology with a very large prolapsing and partially flail P2 (middle) scallop (red arrows). Panel B shows positioning of the MitraClip device (blue arrow). Panel C is a dual plane three-dimensional image (ventricular and atrial views) of the final, 2-clip (yellow arrows) resulting double orifice. There was trivial residual mitral regurgitation.

volume using the product of vena contracta areas defined by direct planimetry of RT3D color Doppler and velocity time integral using continuous-wave Doppler was associated with greater left atrial and ventricular remodeling.

Strain imaging

Recent American Society of Echocardiography Chamber Quantification guidelines strongly recommend routine assessment of ventricular systolic function by quantification of ventricular volumes and calculation of ejection fraction (EF)[2]. Cardiac mechanics, however, can now be assessed with the use of both tissue Doppler and speckle tracking for the measurement of myocardial displacement[67]. The measurement of myocardial deformation or "strain" is the fractional change in the length of a myocardial segment (expressed as a percentage of the baseline length). Strain rate is the rate of change in strain. The deformation of the myocardium is directional: lengthening would be represented by positive strain, and shortening by negative strain. Systolic strain can be measured along the anatomic coordinates of the cardiac chambers: longitudinal (negative strain), radial (positive strain), and circumferential (negative strain). The strengths and weaknesses of strain measurement have been well described[67]; however, the recent standardization of strain Digital Imaging and Communications in Medicine (DICOM) format will reduce inter-vendor variability which, along with improved software analysis and automation packages, will likely increase the clinical acceptability and use of this powerful technique.

Aortic valve disease

Numerous studies have shown the utility of strain imaging for assessing left ventricular function in aortic valve disease. In the presence of normal EF, increasing severity of aortic stenosis was associated with reduced global longitudinal strain (GLS)[68,69]. Subclinical improvement in global and regional systolic function by tissue Doppler and speckle strain also occurs following TAVR (Figure 2)[70–72]. In low flow, low gradient, severe aortic stenosis with normal EF, strain parameters improved following TAVR, even in the absence of significant change in EF[73]. Regional strain abnormalities in patients with severe aortic stenosis may be able to further sub-stratify patients with concomitant infiltrative diseases, such as amyloid as well as coronary disease. In patients with cardiac amyloid, relative apical sparing (with preserved apical longitudinal strain) was sensitive (93%) and specific (82%) in differentiating amyloid from controls, some of whom had severe aortic stenosis. In patients with moderate or severe aortic stenosis and concomitant coronary disease, on the other hand, worse apical and mid longitudinal strain parameters were predictive of significant coronary artery stenosis[74].

Because mortality is significantly associated with symptom development[75], strain has been postulated as a possible early marker of ventricular dysfunction in asymptomatic patients with severe aortic stenosis and thus may be a useful tool in determining the timing of intervention in this population. In fact, Carasso *et al.*[76] showed that longitudinal strain was low in asymptomatic patients with severe aortic stenosis with supernormal apical circumferential strain and rotation. In symptomatic patients, however, longitudinal strain was significantly lower with no compensatory circumferential myocardial mechanics. Other investigators suggest that, after adjusting for aortic stenosis severity and EF, only basal longitudinal strain (and not GLS) was an independent predictor of symptomatic status[77]. In fact, following TAVR, the improvement in GLS may be a result of basal and mid segment improvement only[78].

Strain imaging may be particularly useful in predicting outcomes in patients with severe aortic stenosis. In patients with low flow, low gradient, aortic stenosis with normal EF, a recent study showed both stroke volume index (≤35 ml/m^2) and GLS (>-15%) are independently associated with worse survival[79]. In patients with low flow, low gradient, aortic stenosis with reduced EF, GLS is independently associated with mortality and dobutamine stress GLS may provide incremental prognostic value beyond GLS measured at rest[80]. Three-dimensional GLS may be a better predictor of outcome compared to 2D strain[81]. Finally, Kusunose *et al.*[82] studied 395 patients with moderate-severe aortic stenosis (aortic valve area <1.3 cm^2) and found that GLS was an independent predictor of mortality in this population. A GLS >-12% was associated with the lowest survival[82].

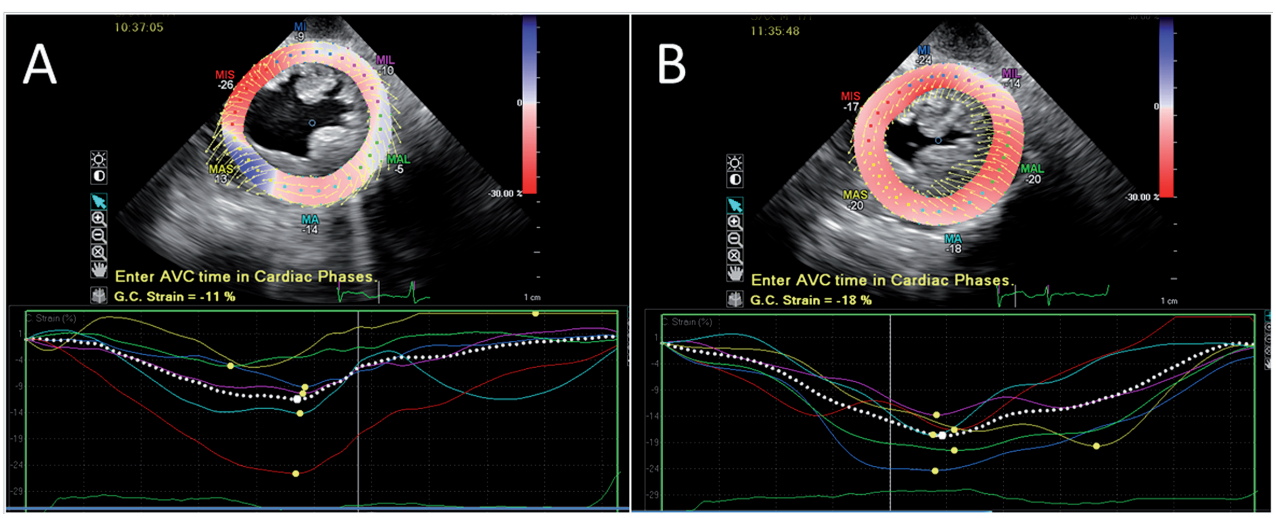

Figure 2. Strain imaging during transcatheter aortic valve replacement (TAVR). Panel A shows a global circumferential strain (GCS) of -11% prior to TAVR. Panel B shows a GCS of -18% following TAVR. This represents an improvement (greater shortening) in ventricular mechanics.

Deformation characteristics have also been studied in patients with aortic regurgitation[83–87]. In a prospective study of young patients (<18 years old) with aortic regurgitation, the only significant predictor of progression of disease on multi-variable analysis was GLS (*P*=0.04, cut-off value of >-19.5%, sensitivity of 77.8%, specificity of 94.1%, and area under the curve of 0.89)[83]. Prospective studies of adult patients have also shown that strain parameters by speckle-tracking could detect early myocardial systolic and diastolic dysfunction, and lower strain values were associated with disease progression in medically managed patients, or impaired outcomes in surgically treated patients[85]. A systolic radial strain rate of <1.82/sec was a good predictor of postoperative left ventricular dysfunction[86]. Finally, in a prospective study, 60 patients with chronic aortic regurgitation were followed for 64 months and global longitudinal strain (four-chamber view only) was an independent predictor of mortality (hazard ratio 1.313, 95% CI 1.010-1.706, *P*=0.042)[87].

Mitral valve disease

Chronic mitral regurgitation is associated with complex left ventricular adaptive remodeling, eccentric hypertrophy, and, eventually, reduced EF. Current guidelines recommend intervening on severe, asymptomatic mitral regurgitation in the setting of reduced EF because of a high incidence of persistent or worsening dysfunction[88]. In chronic severe degenerative mitral regurgitation, numerous studies have shown that a reduced baseline GLS signifies a maladaptive preload-related change that is associated with a reduction in left ventricular EF immediately after mitral valve repair[89–91]. A GLS cutoff of >-19.9% was a strong independent predictor of long-term left ventricular dysfunction and may become an appropriate indication for intervention in the setting of normal EF[90].

Intra-cardiac echocardiography

Although TEE imaging is well established and provides exceptional images, particularly for intra-procedural guidance, it most commonly requires general anesthesia and may be associated with intermittent obstruction of fluoroscopic viewing[92]. With the current move toward conscious sedation for structural heart disease interventions, intra-cardiac echocardiography (ICE) may be an acceptable alternative in some patients with no other adequate intra-procedural imaging options. Evidence that ICE guidance can improve safety and outcome of interventional procedures is still lacking; however, ICE imaging for paravalvular leak closure has been reported to be feasible and advantageous[32,93]. A reduction in contrast use has also been reported with 2D ICE when used in TAVR (Figure 3)[94]. The recently introduced AcuNav® V catheter (Siemens Inc. Mountain View, USA) represents the only commercially available RT3D ICE system. The 10F catheter carries a matrix transducer providing a 22° × 90° real-time volume image. This small volume represents the main limitation, particularly in near field applications, such as structural heart disease interventions.

Fusion imaging

Combining images from two or more different imaging techniques, or fusion imaging, has been accomplished most recently with real-time echocardiography and fluoroscopy[95–97]. This technology, which co-registers the TEE probe position with the intervention table and the angulation of the fluoroscopy C-arm, allows for relatively accurate placement of the TEE image onto the fluoroscopic image. This integration eliminates the need for two different image display monitors and the mental integration of two very different imaging datasets by the operator of structural heart disease interventions.

The ability to define targets on echocardiographic images (whether 2D or 3D), and co-register these targets onto the fluoroscopic images, should improve guidance of structural heart disease interventions (Figure 4). This technology has been shown to be safe and feasible

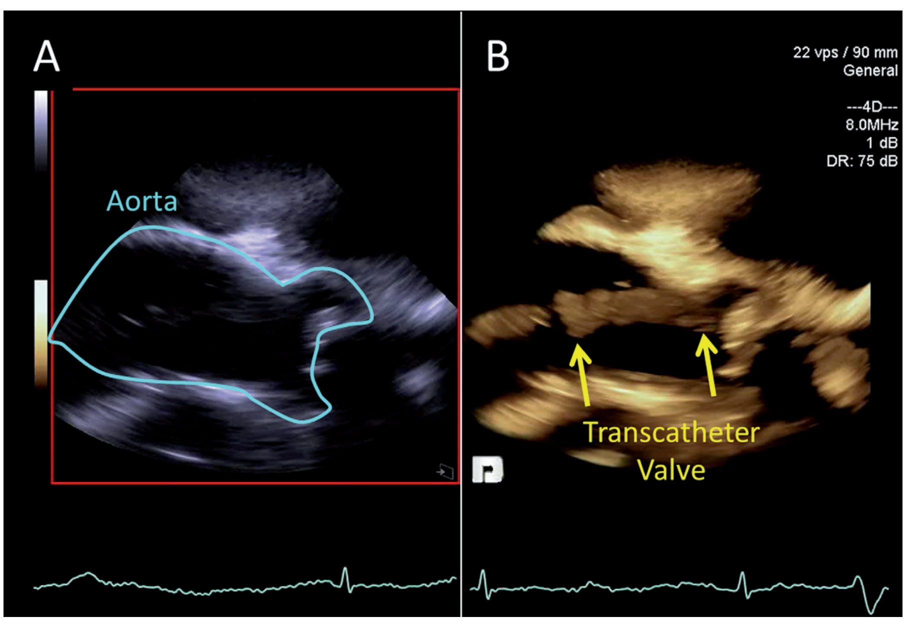

Figure 3. Intra-cardiac echocardiography (ICE) during transcatheter aortic valve replacement (TAVR). Panel A is the two-dimensional ICE image with panel B showing the simultaneous three-dimensional volume during positioning of the transcatheter aortic valve (yellow arrows).

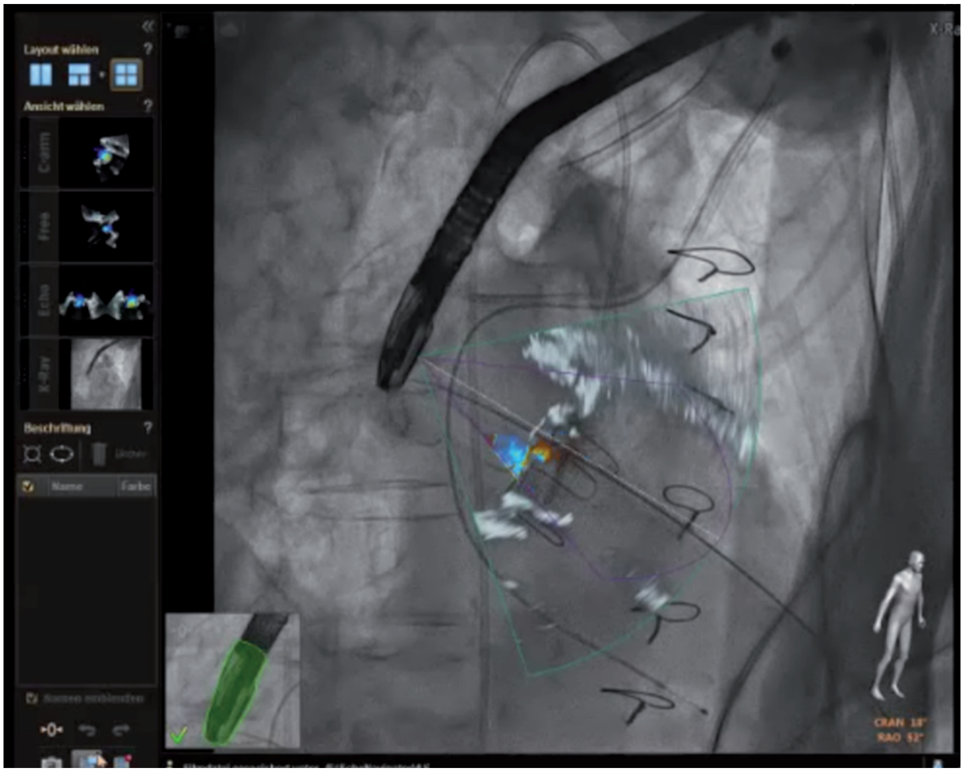

Figure 4. Hybrid/fusion imaging during paravalvular regurgitation closure. After coregistration of the transesophageal echocardiographic probe with the fluoroscopic image, the two images can be fused to allow a more comprehensive understanding of anatomy. Localizing the regurgitant orifice on transesophageal echo imaging can then be translated to the corresponding position on the fluoroscopic image.

for the transcatheter mitral repair procedure with the MitraClip™ device (Abbott Vascular Structural Heart, Menlo Park, CA) and shows a trend towards reduction of fluoroscopy and procedure time[98].

Conclusion

Echocardiography is the primary imaging modality for the diagnosis and management of patients with valvular heart disease. Improvement in surgical outcomes and advances in interventional techniques require further refinements in echocardiographic imaging. Three-dimensional echocardiography, strain imaging, intracardiac echocardiography, and fusion imaging have significant application in advancing our understanding of pathophysiology and anatomy, as well as the diagnosis and management of patients with valvular heart disease.

Abbreviations

2D, two-dimensional; 3D, three-dimensional; confidence interval, CI; EF, ejection fraction; GLS, global longitudinal strain; ICE, intra-cardiac echocardiography; PISA, proximal isovelocity surface area; RT3D, real time three-dimensional; TAVR, transcatheter aortic valve replacement; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

Competing interests

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This review by Dr. Hahn from Columbia University covers major areas of the topic (recent advances in echocardiography in valvular heart disease) and is well written. With this, readers can appreciate her daily clinical experiences with new modalities such as three dimensional color Doppler echocardiography. In addition, recent major publications, including her own, are well chosen for the educational purpose.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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