

REVIEW

The modern role of transoesophageal echocardiography in the assessment of valvular pathologies

Malgorzata Wamil MD PhD^{1,2}, Sacha Bull MA D.Phil³ and James Newton MRCP MD²

¹BHF Centre of Research Excellence, Radcliffe Department of Medicine, Oxford University, Oxford, UK

²Oxford Heart Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

³Department of Cardiology, Royal Berkshire Hospitals NHS Foundation Trust, Reading, UK

Correspondence
should be addressed
to M Wamil

Email
malgorzata.wamil@cardiov.ox.ac.uk

Abstract

Despite significant advancements in the field of cardiovascular imaging, transoesophageal echocardiography remains the key imaging modality in the management of valvular pathologies. This paper provides echocardiographers with an overview of the modern role of TOE in the diagnosis and management of valvular disease. We describe how the introduction of 3D techniques has changed the detection and grading of valvular pathologies and concentrate on its role as a monitoring tool in interventional cardiology. In addition, we focus on the echocardiographic and Doppler techniques used in the assessment of prosthetic valves and provide guidance for the evaluation of prosthetic valves. Finally, we summarise quantitative methods used for the assessment of valvular stenosis and regurgitation and highlight the key areas where echocardiography remains superior over other novel imaging modalities.

Key Words

- ▶ TOE
- ▶ valvular disease
- ▶ 3D echocardiography

Introduction

Over the past decade, advancements in transoesophageal echocardiography technology (TOE) have expanded the clinical applications of TOE beyond that of a purely diagnostic tool for assessing the valvular pathology. The latest TOE probes offer exceptional image quality and high resolution. The introduction of real-time 3D TOE transducers and hybrid imaging techniques have revolutionised its role as an excellent monitoring tool in the cath lab and in the peri-operative period. The use of 3D-capable transducers allows more complex data processing and measurements of curved areas of valvular structures as well as accurate visualisation of regurgitant jets. Real-time three-dimensional echocardiography is changing the practice of cardiology.

The development of interventional imaging has been mandated by rapid advances in the field of percutaneous procedures in the structural heart pathologies.

The echocardiographic assessment of patients undergoing transcatheter assessment differs from those of the routine evaluation of patients with native and prosthetic valves. TOE plays an essential role in the initial assessment, in the intra-procedural monitoring of device deployment and function and is the primary modality in the assessment of procedural complications and follow-up.

Here, we provide an overview of recommendations how to assess valvular pathologies using established transoesophageal 2D and 3D methods.

Current role of TOE in management of valvular heart disease

The significance of a systematic approach in performing every transoesophageal examination cannot be

emphasised strongly enough. The recent guidelines developed by the British Society of Echocardiography (BSE) provide a framework for performing a standardised TOE in any clinical settings (1, 2). This is particularly important when assessing valvular pathologies because the judgement of the severity depends on the assessment of size and function of both ventricles and concomitant pathologies, which may alter the physiology.

Mitral regurgitation

Mitral regurgitation (MR) is the most common cause of valvular regurgitation in the Western countries and is the best example how the introduction of 3D TOE has changed how we manage this disease.

MR classification

MR is classified as either primary (organic) or secondary (functional) in origin. Conventional 2D TOE requires multiple views of the mitral valve (MV) and use of the Doppler in defining the aetiology of MR. The best known classification of MR was proposed by Carpentier in the 1980s. It is based on the key differences in the leaflet motion. In type I, lesions are characterised by normal leaflet motion, and MR is a result of mitral annular dilatation or leaflet perforation (centrally directed jet). In type II, MR results from elongated or ruptured chordae allowing the affected leaflet to move beyond the coaptation line (jet is directed away from the prolapsing or flail leaflet). In type III, MR is a result of restricted leaflet motion and can be differentiated further into IIIa and b categories, which describe the type of restriction as either during both systole and diastole (rheumatic MR) or only in the systole as observed in ischaemic cardiomyopathy and caused by apical displacement of papillary muscles (jet directed towards the restricted leaflet). Examples of MV pathologies are shown in Videos 1, 2, 3, 4.

Echocardiographic assessment of MR

The European Association of Echocardiography (EAE) recommends transthoracic echocardiography (TTE) as the first line in the assessment of MR (3) and suggests that the complete examination should include analysis of aetiology of MR, the assessment of the mechanism and severity of MR and the likelihood of valve repair. Although frequently used in cases of severe MR, TOE is recommended peri-operatively and in cases when

Video 1

Example of 2D, 3D, Doppler assessment of MV prior to repair: example of P2 prolapse on 2D and 3D TOE.

View Video 1 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-1>.

Video 2

Example of 2D, 3D, Doppler assessment of MV prior to repair: example of P2 prolapse on 2D and 3D TOE.

View Video 2 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-2>.

Video 3

Example of 2D, 3D, Doppler assessment of MV prior to repair. View Video 3 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-3>.

Video 4

Example of 2D, 3D, Doppler assessment of MV prior to repair. View Video 4 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-4>.

TTE cannot give the definitive answer regarding the mechanism of regurgitation and the suitability for repair (3). According to the EAE TOE update from 2010 (4), essential views for MR analysis involve transgastric basal short axis view allowing localisation of the origin of the jet and visualisation of six scallops and two commissures, multiple mid-oesophageal views for systematic analysis of scallops, papillary muscles and chordae and colour Doppler assessment of the regurgitant jet and pulsed-wave Doppler of the upper pulmonary veins.

The echocardiographic assessment of the severity of MR is based on multiple parameters (vena contracta, PISA method and the analysis of pulmonary vein flow), which are described in detail in Table 1.

Pitfalls

It is important to note that general anaesthesia and sedation may significantly alter the loading conditions of the circulation and that this must always be taken into account when grading MR using TOE. A reduction in ventricular filling, systemic vascular resistance and blood pressure may all lead to a systematic underestimation of the degree of MR. Moreover, when judging the severity of MR and the suitability for repair or replacement, the LV response to the valve lesion must be assessed by taking into account the ejection fraction (<60%) and LV end-systolic diameter (>45 mm; less load dependent than end diastolic volume) (5). A recent large multicenter study

Table 1 Echocardiographic parameters used for the determination of the severity of valvular regurgitation as per EACVI (19) and the British Society of Echocardiography (BSE) guidelines.

Severe regurgitation	Quantitative parameters	Doppler parameters	Strong predictors	Haemodynamic consequences
Mitral	Organic MR VC width (cm) >0.7 R Vol (mL/beat) >60 RF (%) >50 EROA (cm ²) ≥0.40 Ischaemic MR R Vol (mL/beat) >30 EROA (cm ²) ≥0.20	Colour flow jet area: large central jet or eccentric jet adhering, swirling and reaching the posterior wall of the LA Mitral inflow: dominant E wave >1.5m/s Jet density, CW: dense, triangular, early peaking	Systolic flow reversal in pulmonary veins	LA and LV dilated
Aortic	VC width (cm) ≥0.6 Jet width/LVOT width: >65 R Vol (mL/beat): ≥60 RF (%): >50 EROA (cm ²): ≥0.30	Jet width in LVOT-colour flow: large in central jets, variable in eccentric jets Jet density, CW: dense Jet deceleration area (PHT, ms): steep <200	Holodiastolic flow reversal in the upper part of descending and in abdominal aorta	LA and LV dilated
Tricuspid	VC width (cm) >0.7 PISA radius (cm) >0.9 at a Nyquist limit of 28cm/s	Jet area, central jets (cm ²): >10 Jet density, CW: dense, triangular with early peaking	Systolic flow reversal in hepatic veins	RA, RV, IVC dilated
Pulmonary	VC width, EROA, R Vol not defined	Jet width ratio: >50–65% Jet size by colour Doppler: large with a wide origin, may be brief in duration Jet density, CW: dense, steep deceleration, early termination of diastolic flow Pulmonic systolic flow compared to aortic flow-PW: greatly increased	Systolic flow reversal in pulmonary arteries	RV dilated

CW, continuous-wave; ERO, effective orifice area; LA, left atrium; LV, left ventricle; PHT, pressure half time; PW, pulse-wave; RA, right atrium; RF, regurgitation fraction; RV, right ventricle; R Vol, regurgitation volume; VC, vena contracta.

showed a better survival rate in patients operated on before the LV end-systolic diameter reached 40 mm (6). As the LV response has been shown to be of prognostic significance, further research has focused on identifying more sensitive echocardiographic markers of subclinical LV dysfunction, such as longitudinal strain and tissue Doppler; although some studies suggest that they may be of some value, they have not yet entered routine clinical practice (7, 8).

Mitral valve repair

Mitral valve repair has been widely accepted as a preferential method of management of MR. This strategy is supported by better long-term outcomes as a result of

preservation of the chordal attachments, low rates of thromboembolism, no need for lifelong anticoagulation and very good durability. A recent meta-analysis showed that a strategy of early mitral valve repair in asymptomatic severe MR is superior when compared with a strategy of ‘watchful waiting’ (9). Although controversy remains, the guidelines suggest consideration of earlier intervention in cases suitable for repair (10, 11).

MV repair is feasible in 95% of patients with degenerative valve disease, 70% with rheumatic valve disease and 75% with ischaemic valve disease (12). Optimal results are anticipated in cases with isolated posterior leaflets (P2) prolapse, but is significantly reduced in cases of anterior commissural prolapse, multiple prolapsing scallops, severe mitral annular dilatation (>50mm), extensive MV calcification, large central

regurgitation jet and in other forms of primary MR secondary to endocarditis or rheumatic disease (3). Hence, the detailed echocardiographic assessment is crucial in the management of MR.

2D TOE had a transformative impact on the surgical treatment of mitral valve pathology in the 1980s enabling acquisition of high-quality views of the mitral valve allowing the repair strategy to be determined pre-operatively, the efficacy of the repair to be assessed, and immediately corrected post-operatively if necessary. Several decades later, advances in transducer technology have enabled acquisition of 3D and 4D anatomical imaging providing more detailed information relating to valve morphology and dynamics. The promise of these new technologies is to increase the precision of mitral valve diagnostics to tailor the repair plan to an individual's valve pathology. There is also hope that 3D and 4D TOE will be able to predict the outcome of a given repair technique using image-derived valve models as input to computational biomechanical analysis and by optimizing annuloplasty ring design.

Echocardiographic parameters of suitability for MV repair

There are no widely accepted criteria for establishing the suitability for MV repair, and the decision is based on the anatomical lesion and the experience of the surgeon. The echocardiographic report should include the degree

of MR and MS, the specific location of prolapsing or flail leaflet segments, the presence of leaflet perforation, calcification, excessive length and thickening of the leaflet and areas of normal leaflet mobility. The subvalvar apparatus should be assessed for the presence of torn chordae and chordal thickening. Additionally, the haemodynamic consequences of MR should be described as follows: the presence of a dilated left atrium with or without thrombus, the size and function of both ventricles and the presence of other significant valvular pathologies. Moreover, the surgeon should be alerted if there is a risk for systolic anterior motion of the MV with resultant left ventricle outflow obstruction after the MV repair.

Echocardiographic assessment for MitraClip

Percutaneous mitral valve edge-to-edge repair has evolved into a therapeutic option for high surgical risk patients with severe functional MR as well as insufficiency secondary to prolapse or flail leaflet (13). Several parameters (mostly derived from the Everest II trail (14, 15)), as defined in Table 2, can be assessed to predict the success of the procedure. Although very useful in the assessment of suitability for the procedure, the majority of centres will rely on a case-by-case assessment. The TOE should assess the MV morphology, the grade and the cause of the MR. The ideal valve morphology for a MitraClip procedure includes: degenerative or functional MR, no calcification in the grasping area, MVA >4cm², length of the posterior

Table 2 Echocardiographic analysis of the mitral valve prior, during and post Mitral Clip procedure using Everest criteria.

Echo assessment prior to Mitral Clip	
Mitral leaflet coaptation length and depth	>2 mm and <11 mm respectively
Gap between leaflets	<10 mm
Width of flail leaflet	<15 mm
Mitral valve opening area	>4 cm ²
Leaflet thickness	<5 mm
Considerable calcification of the mitral annulus	Not present
Marked restriction of posterior leaflet	Not present
Lack of primary or secondary chordal support	Not present
Several significant regurgitates jets	Not present
Procedural steps guided by echo during Mitral Clip	
The trans-septal puncture	3.5cm to 4cm above the plane of the mitral annulus
The advancement of the dilator though the interatrial septum	
The navigation of the clip-delivery-system in the left atrium towards the mitral valve	
The positioning of the device within the mitral leaflet zone of prolapse or coaptation defect	
The adjustment of perpendicularity of the clip into the left ventricle	
The grasping of the anterior and posterior leaflet by the clip and the closure of the clip	
Echo assessment post procedure Mitral Clip	
Reduction of the mitral valve regurgitation	
Exclusion of the mitral stenosis	

leaflet ≥ 10 mm, flail-gap < 10 mm and sufficient leaflet tissue for mechanical coaptation (16). On the other hand, perforated mitral leaflets, lack of chordal support, severe calcification in the grasping area and the presence of mitral stenosis especially rheumatic in origin makes the MR unsuitable for MitraClip. 3D TOE offers a remarkable benefit here allowing *en face* views of the MV from both LV and LA perspective. It provides a detailed description of the anatomy and function of the MV, the mitral valve apparatus and the structures in proximity to the MV (left atrial appendage and the aortic and tricuspid valves). Moreover, TOE plays a crucial role in guiding such key steps in MitraClip procedure as: (1) transeptal puncture, (2) introduction of guide catheter, (3) advancement of the delivery system, (4) positioning of the MitraClip and (5) grasping of the leaflets. There is a hope the combined methods using echocardiography and fluoroscopy fusion imaging will improve the success rate in the future.

Mitral valve stenosis

The most common aetiology of mitral stenosis (MS) is rheumatic heart disease (17); the appearance of the valve is characterised by commissural fusion, chordal shortening and leaflet thickening and superimposed calcification contributing to the restriction of leaflet motion (18). Another pathognomonic feature of rheumatic MS is a hockey stick appearance of the anterior leaflet of the mitral valve caused by thickening of the leaflet tips. The transgastric two-chamber view is particularly helpful in the assessment of the subvalvular apparatus in more advanced cases when calcification of leaflets and annulus becomes

apparent. All these echocardiographic findings need to be taken into consideration when grading the severity of MS and making a decision regarding suitability for balloon mitral commissurotomy. In patients undergoing mitral valvuloplasty for MS, the Wilkin's scoring system is used to predict the outcome (19). Leaflet mobility, valve thickening, calcification, subvalvular thickening and commissural calcification or fusion are taken into account when predicting the outcome. Additionally, 3D echocardiography allows visualisation of the mitral valve from both the left atrial and the ventricular perspective and improves the ability to perform an accurate *en face* mitral valve planimetry by allowing positioning of the cropping lines parallel to the narrowest orifice of the MV (Fig. 1). Zamorano and coworkers also confirmed that the real-time 3D echocardiography is feasible, accurate and highly reproducible for estimating mitral valve area (MVA) in patients with rheumatic mitral stenosis when compared against gold standard, invasive Gorlin's method (20). The real-time 3D measurements had excellent inter- and intra-observer variability and provided the best inter-observer agreement for morphologic evaluation. Thus, this methodology has been recommended for the assessment of MVA immediately after balloon valvuloplasty.

Table 3 describes methods used for the estimation of the mitral valve area in native mitral stenosis on TOE and summarises the most important limitations associated with these methods. Reduction of mitral valve area below 2.5 cm^2 increases the atrioventricular pressure gradient to maintain adequate cardiac output and subsequently leads to the enlargement of the left atrium and atrial arrhythmias including atrial fibrillation and thus increases the risk of thromboembolism. Significant long-standing MS results

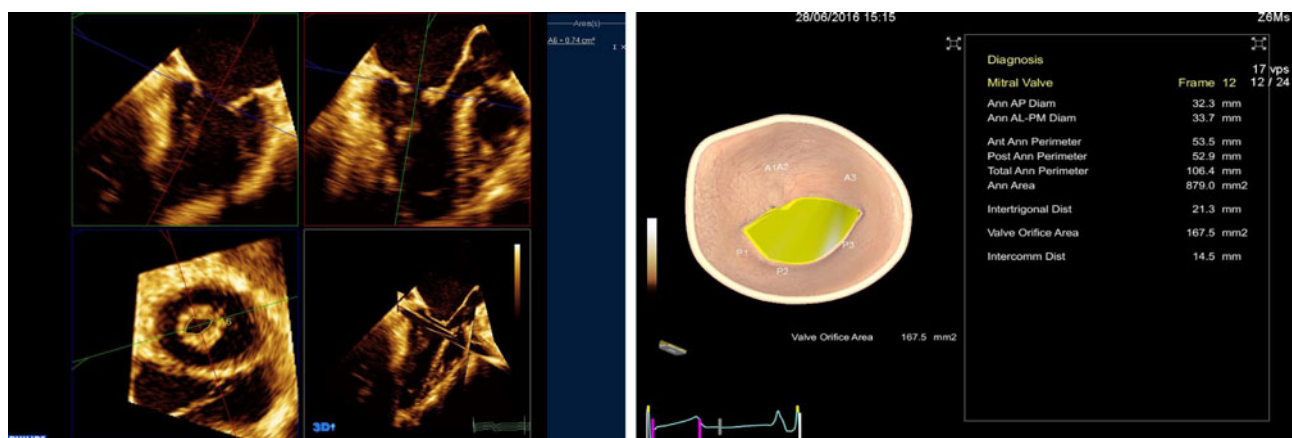


Figure 1

A transoesophageal 3D zoom image of the mitral valve showing severe mitral stenosis. QLAB (Philips Medical System) software was used for post-processing of the 3D dataset. The anatomical MV area (MVA) measures 0.7 cm^2 .

Table 3 Methods for calculating mitral valve area (MVA) in native mitral stenosis on TOE.

Method	How to perform	Points for consideration
Planimetry		
• by 2D	Tracing the mitral orifice obtained from the TG basal SAX view. Contour of the inner mitral orifice including commissures when opened	Direct measure of MVA, flow independent. Requires technical expertise to position the measurement plane on the mitral orifice
• by 3D	Performed from the mid-oesophageal view. The 3D dataset is cropped by an arbitrary plane, parallel to the MV annulus and then is planimeted using post processing software	3D TOE more accurate than 2D. Gold standard in the assessment of MS
Pressure gradient	Tracing the entire envelope of the CWD spectrum of mitral inflow, from the beginning of early diastolic flow (E wave) to the end of flow due to atrial contraction (A wave). Mean gradient from the traced contour of the diastolic mitral flow. Requires averaging values over 5–10 cycles in AF	Influenced by heart rate, cardiac output, and associated MR
Pressure half-time (P1/2)	$MVA (cm^2) = 220/P1/2$	Influenced by compliance of LA and LV. Severe AR underestimates severity of MS. Not accurate in diastolic dysfunction and AF
Deceleration time (DT)	$MVA (cm^2) = 759/DT (ms)$	The same limitations as for using P1/2 method
Continuity equation	$MVA (cm^2) = (CSA LVOT (cm^2) \times VTI LVOT) (cm) / VTI MV (cm)$	Independent from flow conditions. Multiple measurements required (source of errors). Not valid in severe AR and MR
Proximal isovelocity surface area (PISA)	$MVA = (PISA \times Velocity \text{ aliasing}) / \text{peak velocity transmitral}$	Technically difficult. Multiple measurements required. Angle correction is essential. Can be used in the presence of MR

3D, three dimensional; AF, atrial fibrillation; AR, aortic regurgitation; CSA, cross sectional area; CWD, continuous-wave Doppler; DT, deceleration time; MR, mitral regurgitation; MVA, mitral valve area; P1/2, pressure half-time; PISA, proximal isovelocity surface area; TG SAX view, transgastric short axis view; VTI, velocity time interval.

in pulmonary hypertension and subsequently right ventricular hypertrophy and enlargement. A common finding in that setting is functional tricuspid regurgitation due to right ventricular pressure overload. Thus, the echocardiographic evaluation of MS needs to consider all these haemodynamic consequences and exclude the presence of thrombus in the left atrial appendage (LAA). Another important point to note is the requirement of averaging 3–5 values for the assessment of mean pressure gradient when atrial fibrillation is present.

Aortic regurgitation

The recommendations from the European Association of Cardiovascular Imaging (EACVI) regarding echocardiographic assessment of aortic regurgitation (AR) suggest that the echo report should include information about the aetiology, the type of dysfunction and the likelihood of valve repair (21). The assessment of the

morphology and dimension of the aortic root is also mandatory. 3D echocardiography can provide better delineation of the valvular morphology including the description of the cusp pathology (redundancy, restriction, cusp height to indicate likely adequacy of coaptation, pliability, thickness and integrity) and commissure variations (fusion, splaying, attachment site and alignment) (22). The classification system, similar to Carpentier classification system for MR, has been developed to describe the mechanism of AR, guide repair techniques and allow long-term follow-up. The key in understanding the aetiology of AR is the distinction between the intrinsic disease of the aortic cusps (calcific, rheumatic, myxomatous, congenital, infectious or traumatic) and the conditions that affect predominantly aortic annulus such as annular dilatation, aortic dissection and aneurysmal disease.

The grading of the severity of AR is based on parameters described in detail in Table 3. Briefly, the vena contracta, proximal isovelocity surface area (PISA)

method and assessment of flow reversal in descending aorta are used. Colour jet area is affected by the aortic and LV diastolic pressure gradient and LV compliance and therefore is only weakly correlated to the degree of AR; colour should therefore only be used for the detection and initial visual assessment of AR (21). 3D assessment of the vena contracta can be used to provide a measure of the actual regurgitation orifice area (23).

The guidelines recommend the use of the PISA method for the assessment of both central and eccentric jets as it provides valuable quantitative assessment of regurgitation severity as effective orifice area (EROA) and regurgitant volume (R Vol) (Table 3). Overall, the single most significant determinant of the severity of AR is the measurement of the diastolic flow reversal in the descending and abdominal aorta (24). Lastly, it is worth noting that CMR plays an increasingly important role in the assessment of AR, as it can provide accurate *in vivo* quantification of the regurgitation using flow mapping (25), assessment of LV function and precise information about the anatomy of the thoracic aorta.

Aortic stenosis

Management of patients with aortic stenosis (AS) relies on accurate diagnosis of the cause and stage of the disease process. The advantage of using TOE is that it offers greater confidence of aortic valve morphology and greater accuracy for planimetry of AVA at valve tips especially in patients with poor transthoracic echocardiography (TTE) windows. One of the limitations of using TOE is that it can be quite difficult to get a pressure gradient across the AV in some patients. Thus, TTE remains the mainstream technique for the assessment of patients with AS. Significantly, 2D TOE offers greater accuracy of the LVOT diameter measurement for the continuity equation and 3D TOE also allows a biplane assessment from the long-axis view to guide a short-axis slice level with the smallest orifice in funnel-shaped valves.

According to the EAE guidelines, the following parameters should be measured to assess the severity of AS: AS jet velocity, mean transaortic gradient and valve area by continuity equation (utilizing velocity–time integrals) (26). Haemodynamic severity is best characterised by the high transaortic maximum velocity (or mean pressure gradient). However, some patients with AS have a low transaortic volume flow rate due to either left ventricular systolic dysfunction

with a low left ventricular ejection fraction (LVEF) or due to a small hypertrophied left ventricle with a low stroke volume. In the recent guidelines published by the American Heart Association, symptomatic severe AS has been divided into three categories: (1) high-gradient AS, (2) low-flow/low-gradient AS with reduced LVEF and (3) low-gradient AS with normal LVEF or paradoxical low-flow AS (10). Especially the last category of severe AS poses a diagnostic and management challenge, and guidelines stress that interventional management could be considered in that group of patients only if clinical, haemodynamic and anatomic data support valve obstruction as the most likely cause of symptoms, and the data were recorded when the patient was normotensive. Hence, a careful approach should be undertaken when evaluating these patients with echocardiography. Loading conditions influence velocity and pressure gradients; therefore, measurements of valve stenosis should always be interpreted in the clinical context.

Imaging before, during and after transcatheter aortic valve implantation

Assessment of aortic valve anatomy, morphology and severity of aortic valve stenosis is crucial in the pre-

Video 5

The role of TOE in monitoring TAVI procedure: Siemens 3D TOE root analysis demonstration. View Video 5 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-5>.

Video 6

The role of TOE in monitoring TAVI procedure: 2D TOE showing preparation and deployment of the AVR during the TAVI procedure. View Video 6 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-6>.

Video 7

The role of TOE in monitoring TAVI procedure: colour Doppler confirming good result post TAVI procedure (TG view). View Video 7 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-7>.

Video 8

The role of TOE in monitoring TAVI procedure: colour Doppler confirming good result post TAVI procedure (MO LAX view). View Video 8 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-8>.

Video 9

The role of TOE in monitoring TAVI procedure: 2D showing normally functioning AVR. View Video 9 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-9>.

Video 10

The role of TOE in monitoring TAVI procedure: aortic valve pre- and post- TAVI procedure. View Video 10 at <http://movie-usa.glencoesoftware.com/video/10.1530/ERP-16-0034/video-10>.

procedural evaluation of candidates for transcatheter aortic valve implantation (TAVI). TOE plays an important role in the assessment of the presence of bicuspid aortic valve and extensive calcification at the commissures and the tips of leaflets, which could increase the risk of complications during the TAVI procedure. For TAVI purposes, aortic annulus is measured in the aortic long-axis at the mid-oesophageal view from the hinge point of the right coronary cusp to the commissure between left and non-coronary cusp (Videos 5, 6, 7, 8, 9, 10). The diameters of the sinus of Valsalva, sinotubular junction and ascending aorta are also measured. 3D TOE has been shown to provide better assessment of the annular size in those patients whose annulus is not circular. 3D TOE-guided prosthesis sizing has been proved to lead to implantation of larger prostheses than when 2D assessment was used (27). When the accuracy of 3D TOE measurements of aortic annulus was assessed against CT and MRI, it underestimated the size of the annulus and showed greater variability than MRI (especially when correlated with increasing calcium burden) (28).

TOE is used to guide the following steps during TAVI: the aortic valve crossing, balloon dilatation and positioning and deployment of the prosthesis (Videos 5, 6, 7, 8, 9, 10). The mid-oesophageal short-axis view is usually used to visualise the catheter position at the cusp level during procedure, and deep transgastric views are used to image the prosthetic aortic valve after implantation. It also plays a crucial role in the early assessment of the result and complications of the procedure. It can define the severity and location of paraprosthetic regurgitation, which occurs in 5–20% of patients undergoing TAVI and is associated with a 2.0- to 2.5-fold increase in mortality. Other potential complications, which could be identified by TOE include: cardiac tamponade, LV failure, severe aortic regurgitation, new mitral regurgitation, aortic dissection or occlusion of the coronary ostia.

Pulmonary valve

Pulmonary regurgitation

The echocardiographic assessment of pulmonary regurgitation (PR) includes integration of data from imaging of the PV and RV and Doppler measures of regurgitation severity (Table 1). Methods used for the quantification of valvular regurgitation have not been established for estimating the grade of the PR. Additionally, the PV and the RVOT can be difficult to assess with echocardiography due to the location of the valve behind the sternum. Hence, CMR has recently emerged as a 'gold standard' method for the assessment of the PV and RVOT as it can not only visualise the PV but also accurately quantify the regurgitation and RV volumes and function (25).

Percutaneous pulmonary valve implantation

Percutaneous pulmonary valve implantation (PPVI) is a treatment for PR associated with residual RVOT lesion after repair of congenital heart disease (pulmonary atresia, ventricular septal defect, Tetralogy of Fallot, absent pulmonary valve, Truncus arteriosus, Rastelli-type repair of transposition and after Ross operation). Echocardiography plays an important role in the assessment of PR, the degree RV dilatation and dysfunction, RV systolic pressure from the tricuspid regurgitant jet and the RVOT gradient calculated from the velocity across the RVOT. Not infrequently transthoracic echocardiographic assessment of the RVOT and pulmonary valve are superior to TOE given the anterior location of the structures involved. Typically a multimodality approach with echo, CMR and biplane cine-angiography are required to prepare for the procedure. Similar to other interventional procedures, TOE can be used to guide the balloon positioning, the valve deployment and in the assessment of pressure gradients across RVOT to determine the success of the valve placement, although frequently it is performed under fluoroscopic control only.

Pulmonary stenosis

Pulmonary stenosis is almost always congenital in origin and echocardiography together with CMR plays important role in the assessment of these pathologies. The particular attention should be taken to exclude the RVOT obstruction from the right

ventricular hypertrophy mimicking pulmonary stenosis in selective cases. Direct planimetry of the valve cannot be performed because TOE does not allow visualisation of the pulmonary valve *en face*. Assessment of the right ventricle size and function are important in grading the severity of pulmonary stenosis. Quantitative assessment is mainly based on the transpulmonary pressure gradient. Other methods have not been validated in pulmonary stenosis.

Tricuspid valve

Tricuspid regurgitation (TR) is a common finding in asymptomatic patients. The most common cause of TR is impaired valve coaptation caused by dilatation of the RV or of the tricuspid annulus due to left-sided heart disease such as congenital heart defects, and cardiomyopathy, which can lead to pulmonary hypertension (29). For the TOE assessment of TR, the following views should be obtained: 4-chamber view, RV inflow–outflow view at the mid-oesophageal level and transgastric RV inflow and tricuspid short-axis views. Assessment of TR severity is, in principle, similar to MR and has been summarised in the Table 1. Systolic flow reversal in the hepatic veins is the strongest single predictor of the severity of TR (30). Importantly, the absence of systolic flow reversal does not rule out severe TR. Blunted systolic hepatic flow can be seen in abnormal RA and RV compliance, AF and elevated RA pressure. When describing severe TR, the echocardiographer should include in the report the assessment of RA and RV, IVC and hepatic veins and the presence of the systolic bowing of the interatrial septum towards the LA.

Tricuspid stenosis is the least common of the valvular stenosis, and the evaluation of TS is done using the CW Doppler method as described for MS.

A roadmap for evaluation of prosthetic valves

Approximately 290,000 prosthetic heart valves are implanted each year worldwide, and this number is estimated to triple to over 850,000 by 2050 (31). The specific flow pattern and imaging features of prosthetic heart valves pose major challenges for the Doppler echocardiographic assessment of structure and function. Consequently, a comprehensive approach that integrates several semi-quantitative and quantitative parameters

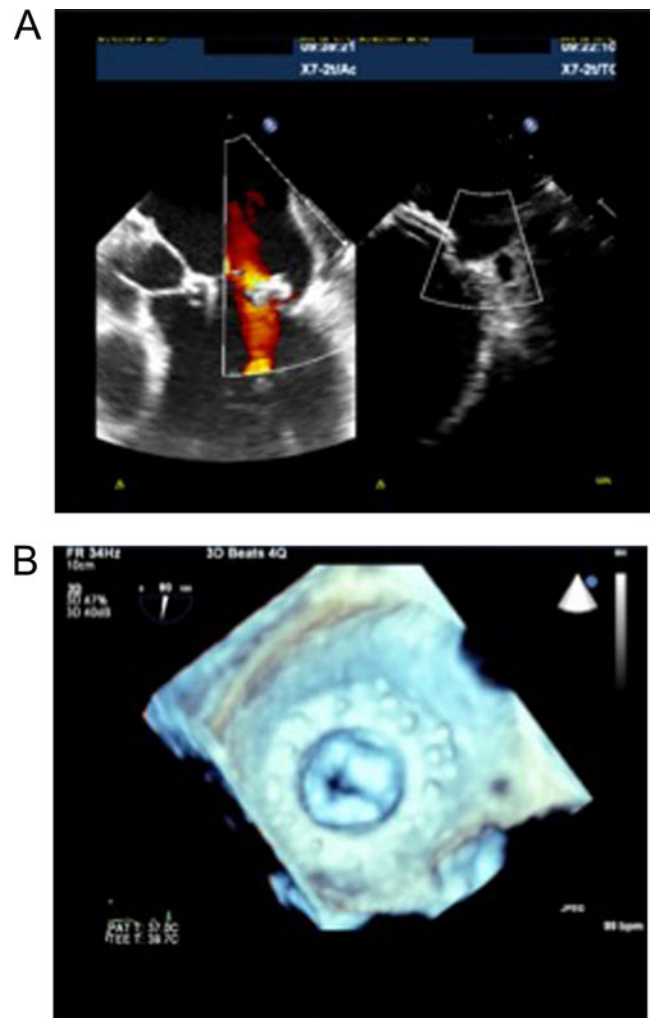


Figure 2

An approach to echocardiographic assessment of a prosthetic valve. A complete TOE examination of the prosthetic valves includes the following steps. Firstly, 2D imaging of the structure and the motion of leaflets or occlude should be recorded. The calcification on the leaflets or abnormal echo densities on the various components of the prosthesis and the valve sewing ring integrity and motion should be evaluated. Secondly, the measurement of trans-prosthetic gradients and valve effective orifice area (EOA) needs to be recorded. Thirdly, the location (central versus paravalvular) and severity of regurgitation should be assessed. Lastly, such supportive parameters as left ventricular size and systolic function and systolic pulmonary arterial pressure should be evaluated. Examples of the failing prosthetic valves: (A) 2D views: before and after closure of the paraprothestic mitral valve leak; (B) 3D 'en face' view of a severely stenotic mitral valve bio-prosthesis.

obtained from multiple views of valve is necessary to assess the prosthetic valve dysfunction (Fig. 2).

By design, almost all prosthetic valves are obstructive. The guidelines suggest that the first postoperative transthoracic echocardiography should be performed 3–12 weeks after surgery (when the haemodynamic status has stabilized and the chest wound has healed),

as the baseline for further follow-up and monitoring of the complications (32). Patients with bioprosthetic valve should be screened by TTE every year after 5 years after their valve implantation. For mechanical valves, routine annual echocardiography is not indicated unless there is high clinical suspicion of complications (32). Prosthesis-patient mismatch (PPM) occurs when the valve EOA of a normally functioning prosthesis is too small in relation to the patient's body size, and thus, cardiac output requirements, resulting in abnormally high postoperative velocities and gradients (33). To identify the PPM, the EOA of the prosthesis is divided by the patient's body surface area. Severe PPM is identified when indexed EOA $\leq 0.65 \text{ cm}^2/\text{m}^2$ for aortic and $\leq 0.9 \text{ cm}^2/\text{m}^2$ for mitral prostheses.

Pathologic obstruction of the prosthetic valve may be caused acutely by thrombosis or endocarditic vegetations or by chronic processes such as pannus formation or calcific degeneration of bioprosthetic valve leaflets (structural valve degeneration). To identify the prosthetic valve stenosis, the EOA measured in the patient needs to be compared with the normal reference value of EOA for the model and size of prosthesis that has been implanted (BSE EchoCalc app, (32)). Assessment of severity of prosthetic regurgitation is more complex than in native valves, due to the high prevalence of paravalvular regurgitation and complex, eccentric and irregular jets. Additionally, most of the mechanical prostheses have normal patterns of so-called 'washing jets', which are short in duration, narrow and symmetrical. TOE plays an important role in the detection and localisation of prosthetic regurgitation and in demonstrating the surrounding anatomy.

Quantitative methods, such as the proximal isovelocity surface area (PISA), are often not feasible when assessing regurgitation in prosthetic valves due to the problems with applying these methods in situations with complex and multiple jets (11). As an alternative, in such cases we can use the Doppler method estimate of the regurgitant volume. This is done by calculating the difference between the stroke volume measured in the right ventricular outflow tract or at the mitral annulus.

Percutaneous repair of the paravalvular leak

Percutaneous repair of the paravalvular leak (PVL) is an alternative for patients at high operative risk for redo valve replacement. Echocardiographic assessment is essential in patient selection and helps to exclude such contraindications to the percutaneous leak closure such as active infection, valve instability and intra-

cardiac thrombus. Although 2D TOE is used in the initial assessment of the paravalvular regurgitation, 3D echocardiography with multiplane reconstruction is superior in all stages of peri-procedural management. In particular, real-time 3D colour plays an important role in the assessment of procedural success. The clock face is commonly used to describe the location of the PVL. The nomenclature of medial, lateral, anterior and posterior location is also commonly used to characterise the position. TOE allows description of the orifice shape and some assumptions about the size of the PVL, which is essential in the choice of the closure device. TOE guidance is necessary in using the transeptal system and in the deployment of the device. At the end of the procedure, TOE should show mobile valve leaflets and unobstructed structures in proximity to the device.

The role of TOE in management of patients with endocarditis

The high spatial and temporal resolution of the TOE probe allows evaluation of thin and highly mobile structures; TOE is therefore a key imaging modality in assessment of infective endocarditis. It allows the detailed description of size, attachment site and mobility of vegetations and the consequences of infective endocarditis such as abscess and fistula formation in the peri-valvular area, pseudoaneurysms, perforations and chordal rupture. TOE is mandated in assessing prosthetic valves for suspected endocarditis (34). 3D TOE may be superior to 2D imaging in endocarditis because it is able to clearly delineate components of both mechanical and bioprosthetic valves; furthermore, 3D imaging overcomes the challenge of acoustic shadowing commonly seen in 2D imaging of prosthetic valves. 3D echocardiography, with its ability to provide a comprehensive anatomical assessment of the entire valve, is better in distinguishing between a vegetation and the suture material. The *en face* view is particularly helpful in identifying the valve dehiscence, fistulas and paravalvular leaks as complications of infective endocarditis. It is, however, important to note that due to its higher frame rate, 2D echocardiography is more reliable than 3D when assessing small and very mobile vegetations.

Stroke complicates about 10% of cases of infective endocarditis and represents one of the most severe complication associated with an increased morbidity and mortality (35). Infection of prosthetic valves,

mitral valve and due to aggressive bacteria, such as *Staphylococcus aureus*, is associated with the highest risk of embolization (36). Most stroke-related infective endocarditis happens in the initial phase of disease (36, 37) and thus, an echocardiogram is mandatory in all cases where there is a high clinical suspicion of infective endocarditis. Both the size and mobility of the vegetation have been associated with an increased risk of embolism. Most emboli are fragments of vegetations, and the risk of embolization increases with large vegetations (>10mm).

Future perspectives in TOE

Until relatively recently, an important limitation of 2D echocardiography was that the images generated of the pathology and surrounding anatomy were sometimes difficult to interpret. High-quality, real-time 3D TOE allows visualisation of complex valvular anatomy from any spatial point. This characteristic has so far proven beneficial to an array of procedures, including surgical management of mitral valve repair (including robotic mitral valve repair); nonsurgical mitral procedures such as edge-to-edge mitral repair; transcatheter closure of the paraprothetic leaks and evaluation of aortic annulus for transcatheter aortic valve implantation. Real-time 3D TOE also offers an important additional dimension in the echocardiographic evaluation of prosthetic valves. Moreover, 3D or even 4D printing has promised to revolutionise the management of valve disease as printing of highly personalised replacement valves may be possible based on the 3D echo images acquired in the future, thus eliminating problems with poorly fitted prosthesis.

Another approach, which is gaining increased popularity, is hybrid cardiac imaging, which uses the principle of combining images obtained with two different imaging modalities to improve diagnostic accuracy. The majority of cardiac hybrid imaging is done by fusion of static rather than dynamic images, most commonly with CT/SPECT images. Currently, only the combination of transoesophageal echocardiography with fluoroscopy allows real-time image fusion of high-quality moving images for improved diagnostic accuracy during structural heart disease interventions. Future developments in hybrid imaging may include fusion techniques to combine CT, nuclear, CMR or TOE images, which may further enhance the diagnostic power of TOE.

Conclusion

In this review, we described both established and new 2D and 3D TOE techniques in the management of valvular heart disease. By summarising current guidelines and highlighting areas that remain controversial, we hope we provided a comprehensive overview of the modern and yet evolving role of TOE in general cardiology.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this review.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Author contribution statement

M W wrote the paper, S B revised the paper for intellectual content and J N assisted with revisions and contributed the figures for the paper.

Acknowledgements

M W acknowledges support from the BHF Centre of Research Excellence, Oxford, UK.

References

- Sharma V, Alderton S, McNamara H, Steeds R, Bradlow W, Chenzbraun A, Oxborough D, Mathew T, Jones R, Wheeler R, *et al*. 2015 A safety checklist for transoesophageal echocardiography from the British Society of Echocardiography and the Association of Cardiothoracic Anaesthetists. *Echo Research and Practice* **2** G25–G27. (doi:10.1530/ERP-15-0035)
- Wheeler R, Steeds R, Rana B, Wharton G, Smith N, Allen J, Chambers J, Jones R, Lloyd G, O'Gallagher K, *et al*. 2015 A minimum dataset for a standard transoesophageal echocardiogram: a guideline protocol from the British Society of Echocardiography. *Echo Research and Practice* **2** G29–G45. (doi:10.1530/ERP-15-0024)
- Lancellotti P, Moura L, Pierard LA, Agricola E, Popescu BA, Tribouilloy C, Hagendorff A, Monin JL, Badano L, Zamorano JL, *et al*. 2010 European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *European Journal of Echocardiography* **11** 307–332. (doi:10.1093/ejehocard/jeq031)
- Flachskampf FA, Wouters PF, Edvardsen T, Evangelista A, Habib G, Hoffman P, Hoffmann, R, Lancellotti P, Pepi M & for the European Association of Cardiovascular Imaging Document reviewers: Donal E & Rigo F 2014 Recommendations for transoesophageal echocardiography: EACVI update 2014. *European Heart Journal – Cardiovascular Imaging* **15** 353–365. (doi:10.1093/ehjci/jeu015)
- Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, Flachskampf F, Hall R, Lung B, Kasprzak J, *et al*. 2007 Guidelines on the management of valvular heart disease: The Task Force on the Management of Valvular Heart Disease of the European Society

- of Cardiology. *European Heart Journal* **28** 230–268. (doi:10.1093/eurheartj/ehl428)
- 6 Tribouilloy C, Grigioni F, Avierinos JF, Barbieri A, Rusinaru D, Szymanski C, Ferlito M, Tafanelli L, Bursi F, Trojette F, et al. 2009 Survival implication of left ventricular end-systolic diameter in mitral regurgitation due to flail leaflets: a long-term follow-up multicenter study. *Journal of the American College of Cardiology* **54** 1961–1968. (doi:10.1016/j.jacc.2009.06.047)
 - 7 Agricola E 2004 Pulsed tissue Doppler imaging detects early myocardial dysfunction in asymptomatic patients with severe mitral regurgitation. *Heart* **90** 406–410. (doi:10.1136/hrt.2002.009621)
 - 8 Kim MS, Kim Y-J, Kim H-K, Han J-Y, Chun H-G, Kim H-C, Sohn D-W, Oh B-H & Park Y-B 2009 Evaluation of left ventricular short- and long-axis function in severe mitral regurgitation using 2-dimensional strain echocardiography. *American Heart Journal* **157** 345–351. (doi:10.1016/j.ahj.2008.10.004)
 - 9 Goldstone AB, Patrick WL, Cohen JE, Aribeano CN, Popat R & Woo YJ 2015 Early surgical intervention or watchful waiting for the management of asymptomatic mitral regurgitation: a systematic review and meta-analysis. *Annals of Cardiothoracic Surgery* **4** 220–229. (doi:10.3978/j.issn.2225-319X.2015.04.01)
 - 10 Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, et al. 2014 2014 AHA/ACC Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* **129** e521–e643. (doi:10.1016/j.jtcvs.2014.05.014)
 - 11 Vahanian A, Alferi O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, Borger MA, Carrel TP, De Bonis M, Evangelista A, et al. 2012 Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *European Journal of Cardio-Thoracic Surgery* **42** S1–S44. (doi:10.1093/ejcts/ezs455)
 - 12 Deloche A, Jebara VA, Relland JY, Chauvaud S, Fabiani JN, Perier P, Dreyfus G, Mihaileanu S & Carpentier A 1990 Valve repair with Carpentier techniques. The second decade. *Journal of Thoracic and Cardiovascular Surgery* **99** 990–1001; discussion 1001–1002.
 - 13 Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, et al. 2011 Percutaneous repair or surgery for mitral regurgitation. *New England Journal of Medicine* **364** 1395–1406. (doi:10.1056/NEJMoa1009355)
 - 14 Alqoofi F & Feldman T 2009 Percutaneous approaches to mitral regurgitation. *Current Treatment Options in Cardiovascular Medicine* **11** 476–482. (doi:10.1007/s11936-009-0050-4)
 - 15 Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, Whitlow PL, Gray W, Low R, Herrmann HC, et al. 2009 Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. *Journal of the American College of Cardiology* **54** 686–694. (doi:10.1016/j.jacc.2009.03.077)
 - 16 Wunderlich NC & Siegel RJ 2013 Peri-interventional echo assessment for the MitraClip procedure. *European Heart Journal – Cardiovascular Imaging* **14** 935–949. (doi:10.1093/ehjci/jet060)
 - 17 Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, Tornos P, Vanoverschelde JL, Vermeer F, Boersma E, et al. 2003 A prospective survey of patients with valvular heart disease in Europe: the Euro heart survey on valvular heart disease. *European Heart Journal* **24** 1231–1243. (doi:10.1016/S0195-668X(03)00201-X)
 - 18 Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, Iung B, Otto CM, Pellikka PA, Quiñones M, et al. 2009 Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *European Journal of Echocardiography* **10** 1–25. (doi:10.1093/ejehocard/jen303)
 - 19 Wilkins GT, Weyman AE, Abascal VM, Block PC & Palacios IF 1988 Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. *British Heart Journal* **60** 299–308. (doi:10.1136/hrt.60.4.299)
 - 20 Zamorano J, Cordeiro P, Sugeng L, Perez de Isla L, Weinert L, Macaya C, Rodríguez E & Lang RM 2004 Real-time three-dimensional echocardiography for rheumatic mitral valve stenosis evaluation: an accurate and novel approach. *Journal of the American College of Cardiology* **43** 2091–2096. (doi:10.1016/j.jacc.2004.01.046)
 - 21 Lancellotti P, Tribouilloy C, Hagendorff A, Popescu BA, Edvardsen T, Pierard LA, Badano L, Zamorano JL & Scientific Document Committee of the European Association of Cardiovascular Imaging 2013 Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. *European Heart Journal – Cardiovascular Imaging* **14** 611–644. (doi:10.1093/ehjci/jet105)
 - 22 Muraru D, Badano LP, Vannan M & Iliceto S 2012 Assessment of aortic valve complex by three-dimensional echocardiography: a framework for its effective application in clinical practice. *European Heart Journal – Cardiovascular Imaging* **13** 541–555. (doi:10.1093/ehjci/jes075)
 - 23 Fang L, Hsiung MC, Miller AP, Nanda NC, Yin WH, Young MS, Velayudhan DE, Rajdev S & Patel V 2005 Assessment of aortic regurgitation by live three-dimensional transthoracic echocardiographic measurements of vena contracta area: usefulness and validation. *Echocardiography* **22** 775–781. (doi:10.1111/j.1540-8175.2005.00171.x)
 - 24 Tribouilloy C, Avinée P, Shen WF, Rey JL, Slama M & Lesbre JP 1991 End diastolic flow velocity just beneath the aortic isthmus assessed by pulsed Doppler echocardiography: a new predictor of the aortic regurgitant fraction. *British Heart Journal* **65** 37–40. (doi:10.1136/hrt.65.1.37)
 - 25 Myerson SG 2012 Heart valve disease: investigation by cardiovascular magnetic resonance. *Journal of Cardiovascular Magnetic Resonance* **14** 7. (doi:10.1186/1532-429X-14-7)
 - 26 Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, Iung B, Otto CM, Pellikka PA & Quiñones M 2009 Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *Journal of the American Society of Echocardiography* **22** 1–23; quiz 101–102. (doi:10.1016/j.echo.2008.11.029)
 - 27 Gripari P, Ewe SH, Fusini L, Muratori M, Ng AC, Cefalù C, Delgado V, Schalijs MJ, Bax JJ, Marsan NA, et al. 2012 Intraoperative 2D and 3D transesophageal echocardiographic predictors of aortic regurgitation after transcatheter aortic valve implantation. *Heart* **98** 1229–1236. (doi:10.1136/heartjnl-2012-301998)
 - 28 Tsang W, Bateman MG, Weinert L, Pellegrini G, Mor-Avi V, Sugeng L, Yeung H, Patel AR, Hill AJ, Iazzo PA, et al. 2012 Accuracy of aortic annular measurements obtained from three-dimensional echocardiography, CT and MRI: human in vitro and in vivo studies. *Heart* **98** 1146–1152. (doi:10.1136/heartjnl-2012-302074)
 - 29 Badano LP, Muraru D & Enriquez-Sarano M 2013 Assessment of functional tricuspid regurgitation. *European Heart Journal* **34** 1875–1885. (doi:10.1093/eurheartj/ehs474)
 - 30 Gonzalez-Vilchez F, Zarauza J, Vazquez de Prada JA, Martín Durán R, Ruano J, Delgado C & Figueroa A 1994 Assessment of tricuspid regurgitation by Doppler color flow imaging: angiographic correlation. *International Journal of Cardiology* **44** 275–283. (doi:10.1016/0167-5273(94)90292-5)
 - 31 Yacoub MH & Takkenberg JJ 2005 Will heart valve tissue engineering change the world? *Nature Clinical Practice Cardiovascular Medicine* **2** 60–61. (doi:10.1038/ncpcardio0112)
 - 32 Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, et al. 2009 Recommendations for evaluation of prosthetic valves with

- echocardiography and doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *Journal of the American Society of Echocardiography* **22** 975–1014; quiz 1082–1084. (doi:10.1016/j.echo.2009.07.013)
- 33 Pibarot P & Dumesnil JG 2000 Hemodynamic and clinical impact of prosthesis-patient mismatch in the aortic valve position and its prevention. *Journal of the American College of Cardiology* **36** 1131–1141. (doi:10.1016/S0735-1097(00)00859-7)
- 34 Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, Dulgheru R, El Khoury G, Erba PA, Iung B, *et al.* 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *European Heart Journal* **36** 3075–3128. (doi:10.1093/eurheartj/ehv319)
- 35 Cabell CH, Pond KK, Peterson GE, Durack DT, Corey GR, Anderson DJ, Ryan T, Lukes AS & Sexton DJ 2001 The risk of stroke and death in patients with aortic and mitral valve endocarditis. *American Heart Journal* **142** 75–80. (doi:10.1067/mhj.2001.115790)
- 36 Thuny F, Di Salvo G, Belliard O, Avierinos JF, Pergola V, Rosenberg V, Casalta JP, Gouvernet J, Derumeaux G, Iarussi D, *et al.* 2005 Risk of embolism and death in infective endocarditis: prognostic value of echocardiography: a prospective multicenter study. *Circulation* **112** 69–75. (doi:10.1161/CIRCULATIONAHA.104.493155)
- 37 Dickerman SA, Abrutyn E, Barsic B, Bouza E, Cecchi E, Moreno A, Doco-Lecompte T, Eisen DP, Fortes CQ, Fowler VG Jr, *et al.* 2007 The relationship between the initiation of antimicrobial therapy and the incidence of stroke in infective endocarditis: an analysis from the ICE Prospective Cohort Study (ICE-PCS). *American Heart Journal* **154** 1086–1094. (doi:10.1016/j.ahj.2007.07.023)

Received in final form 16 December 2016

Accepted 17 January 2017

Accepted Preprint published online 17 January 2017