REVIEW

The role of three-dimensional echocardiography for the clinical diagnosis and management of mitral valve disease

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Abstract: Echocardiography plays a central role in the characterization of the mitral valve (MV) morphology and function. In the past decade, the development of three-dimensional echocardiography (3DE) has revolutionized valvular imaging, becoming the technique of choice for an accurate evaluation of the MV anatomy and pathophysiology. Transthoracic and transoesophageal 3DE represent complementary imaging techniques to assess the complex MV apparatus in the beating heart, to plan interventions, to monitor transcatheter procedures (e.g. MitraClip, mitral valve balloon valvuloplasty, and paravalvular leak closure) and to assess the results of surgical repair. The aim of this article is to review the contribution of 3DE in evaluating the anatomy and function of the MV apparatus in a variety of MV diseases, highlighting the current clinical applications of this essential echocardiography technique.
Keywords: mitral valve, three-dimensional echocardiography, morphology, mitral regurgitation, mitral stenosis

Rezumat: Ecocardiografia a ocupat dintotdeauna un rol central în caracterizarea morfologiei și funcției valvei mitrale (VM). În ultimul deceniu, dezvoltarea ecocardiografiei tridimensionale (3D) a revoluționat imagistica valvulară, devenind modalitatea preferată pentru evaluarea cu acuratețe a anatomiei VM, indiferent de patologia evaluată. Ecocardiografia transtoracică și transesofagiană 3D reprezintă instrumente imagistice complementare utile pentru evaluarea funcției complexe a aparatului valvular mitral, precum și în planificarea managementului terapeutic. Acest articol își propune să prezinte rolul adițional al ecocardiografiei 3D pentru evaluarea diverselor patologii ale VM, subliniind aplicațiile clinice actuale și avantajele acesteia în raport cu ecocardiografia convențională.
Cuvinte cheie: valvă mitrală, ecografie tridimensională, morfologie, regurgitare mitrală, stenoză mitrală.

INTRODUCTION

The echocardiographic assessment of the mitral valve (MV) provides valuable insights into the aetiology and severity of the MV disease, which makes it essential to plan interventions, to guide and monitor transcatheter procedures, and to assess the results of surgical repair[1]. However, the MV is a complex three-dimensional structure that requires multiple views and complex mental reconstruction processes to figure out its anatomy using conventional two-dimensional echocardiography (2DE). Conversely, by using three-dimensional echocardiography (3DE), we can assess the non-planar mitral annulus (MA) and mitral leaflets, the complex subvalvular apparatus and their anatomical relationships with the surrounding structures, by virtually "dissecting" the beating heart using different cut planes[1].

Although cardiac magnetic resonance (CMR) has a higher spatial resolution than echocardiography, with the important advantage of non-invasiveness, its clinical use is limited due to increased acquisition time, costs, limited availability and lack of portability at the bedside or in the catheterization and operative rooms[2]. Multi-detector computed tomography, though

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used for MA anatomical assessment and spatial relationship to plan transcatheter interventions, has major limitations related to the inferior temporal resolution, radiation exposure, use of iodinated contrast, the impossibility of real-time imaging, flow assessment or regurgitation severity grading[3]. Accordingly, 3DE has emerged as the reference standard technique to assess MV morphology and function into clinical practice.

This review will address the applications of 3DE, providing an update on its current role for the diagnosis and clinical management of patients with various MV pathologies.

STEP-BY-STEP EVALUATION OF THE MITRAL VALVE MORPHOLOGY AND FUNCTION

The normal function of the MV requires the structural integrity of all the components of MV apparatus, which includes: leaflets, MA, chordae tendineae, papillary muscles (PMs), left ventricle (LV) and left atrium (LA), as well as their coordinated functional relationships during the cardiac cycle[4]. A previous study showed that 3DE gives additional information to 2DE MV morphological assessment in 36% of patients[5].

MV leaflets

Normal MV leaflets are thin and highly mobile structures, only partially visualized using tomographic techniques. 2DE allows the visualization of the MV leaflets only from the ventricular perspective. Conversely, 3DE allows the visualization of the whole anterior and posterior leaflets of the MV in the same cut plane, which can be rotated to display the MV either from the ventricular or the atrial (also called surgical) perspective (Figure 1). As a consequence, the echocardiographer does not need to imagine the actual anatomy of the MV from a limited number of tomographic views, but he/she is able to see an anatomically sound image of the MV in the beating heart. All derived views make it possible to obtain a detailed anatomical description of the MV (i.e. presence of calcifications, clefts, prolapses, attached masses, etc.)[6], and allow an easier pre-, intra- and post-procedural assessment compared with conventional 2DE imaging. Moreover, the „surgical view" of the MV by 3DE facilitates the communication between imaging expert, interventionalist and surgeon. Finally, real-time 3DE gives the unique advantage of a detailed functional assessment of the MV, which is essential to guide valvular interventional procedures. Using dedicated software, the 3D geometry of mitral leaflets and MA can be easily reconstructed and quantified (Figure 2)[7].

Subvalvular apparatus

The subvalvular apparatus, which includes the PMs and their chordae tendineae, is best appreciated using multiple longitudinal cut planes, allowing an optimal view of the PMs origin and of the chordal insertions on both PMs and MV leaflets. Chordal thickening, elonga-

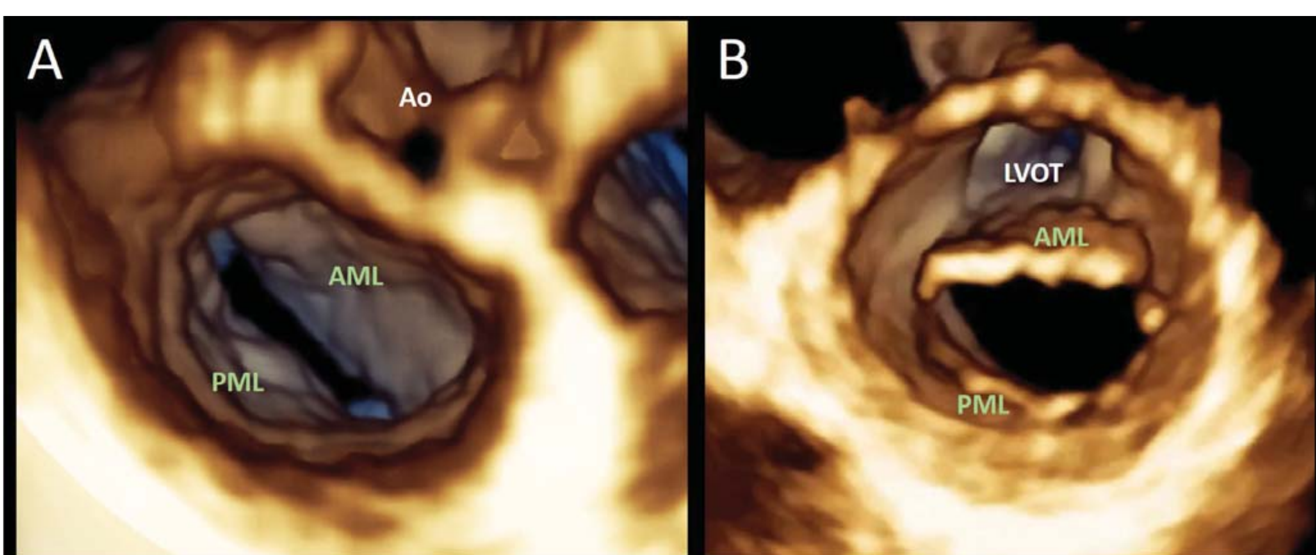

Figure 1. Transthoracic three-dimensional echocardiography assessment of mitral valve anatomy. The mitral valve can be seen from either the atrial (surgical view, panel A) or the ventricular perspective (panel B). The volume rendering display technique allows anatomically sound images and complete visualisation of the leaflets and surrounding structures.

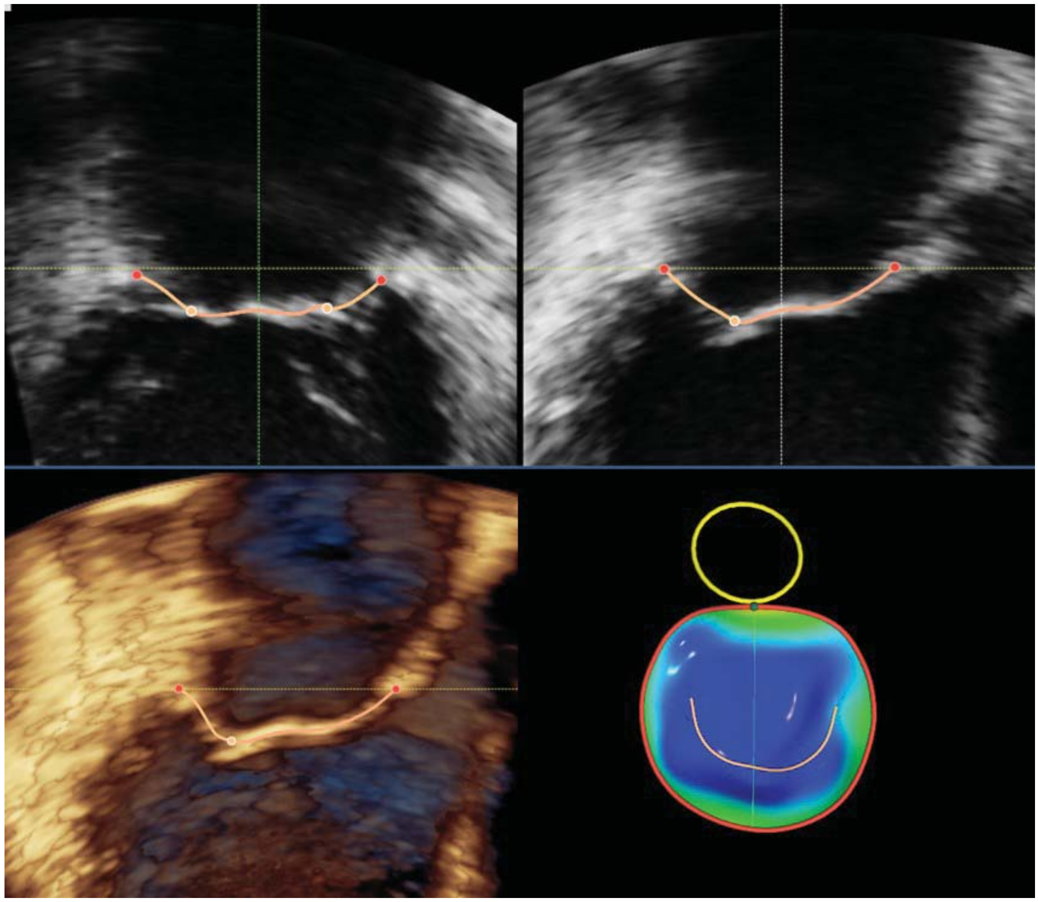

Figure 2. Transesophageal three-dimensional surface rendering display of the mitral valve. This display modality is obtained by semiautomated mapping of the leaflet surface and annulus contour in order to provide a quantitative analysis of the mitral valve annulus and leaflets using dedicated software packages.

tion or rupture are easily visualized using 3DE volume rendering display[1].

Mitral annulus

The MA is a pliable, non-planar, saddle-shaped structure that interconnects the MV leaflets with the LA and LV walls. The anterior part of MA is the most elevated point of the saddle, while the posterior part includes the lowest points of the saddle (near the medial and lateral commissures) and the posterior "horn"[8]. When viewed in cross-section, MA is D-shaped, with the straight border adjacent to the aortic valve[9]. The MA is also a highly dynamic structure, during the cardiac cycle: its area reaches a nadir in early systole, conversely its tenting height reaches its maximum at mitral valve closure[10,11]. Conventional 2DE diameters (i.e. anteroposterior and inter-commissural) are not suitable to provide reliable information about the complex 3D shape and function of the MA. Using commercially available dedicated software packages applied to 3DE data sets, a comprehensive assessment of the MA geometry and function is possible at the bedside for clinical purposes[12,13]. These measurements have important implications in selecting the optimal strategy for patients requiring MV surgical or interventional treatment.

Quantification of mitral regurgitation severity

Complementary to conventional 2DE and Doppler parameters, the use of 3D colour flow Doppler imaging may improve the quantification of MV regurgitation and help to guide transcatheter procedures by precisely identifying the origin of abnormal intracardiac flows[14-16].

3DE quantification has allowed to increase the diagnostic accuracy and reproducibility of the MR severity by integrating new parameters in its systematic approach. Planimetry of the vena contracta area and measurement of 3D effective regurgitant orifice area allow the evaluation of the functional and anatomical regurgitant orifice area, respectively (Figure 7)[17-19]. Both parameters are devoid of any geometrical assumption about the shape of the orifice and have been particularly useful in patients with eccentric regurgitant jets. Effective regurgitant orifice area and regurgitant volumes obtained from 3DE proximal isovelocity area were also reported to significantly increase the accuracy of MR severity quantification, but the method is available on a single echocardiography system[20-22]. Recently, updated American Society of Echocardiography guidelines on valvular regurgitations recommend the routine use of 3DE imaging for a comprehensive assessment of MR[23].

Assessment of LV and LA volumes and function

3DE proved to be more accurate than conventional 2DE to assess the LV and LA geometry and function[24-27]. In patients undergoing MV surgery, 3DE end-systolic LV volume was an independent predictor of postoperative LV dysfunction[28]. 3DE end-systolic LV volume provided additive prognostic value on top of M-mode end-systolic diameter and 2DE LV end-systolic volume. Finally, 3DE LA minimal volume is emerging as a predictor of adverse outcome in asymptomatic patients with severe organic MR[29].

THE ADDED VALUE OF 3DE IN MITRAL STENOSIS

Management of mitral stenosis (MS) patients relies on an accurate measurement of the mitral orifice area and a comprehensive assessment of MV complex anatomy (extent of leaflet thickening, commissural fusion, calcification, degenerative changes of subvalvular apparatus, etc.). Doppler-based methods for MV area assessment are heavily influenced by flow dependence, cardiac rhythm and rate, associated regurgitation, as well as the angle of insonation[4]. Planimetric MV area by 2DE frequently overestimates the actual residual orifice area, since there is no landmark to confirm that the parasternal short-axis 2DE view of the MV is obtained exactly at the level of the smallest MV area and oriented perpendicular to the MV opening axis[30]. 3DE has overcome these limitations by allowing to position the crop plane at the tips of the stenotic MV

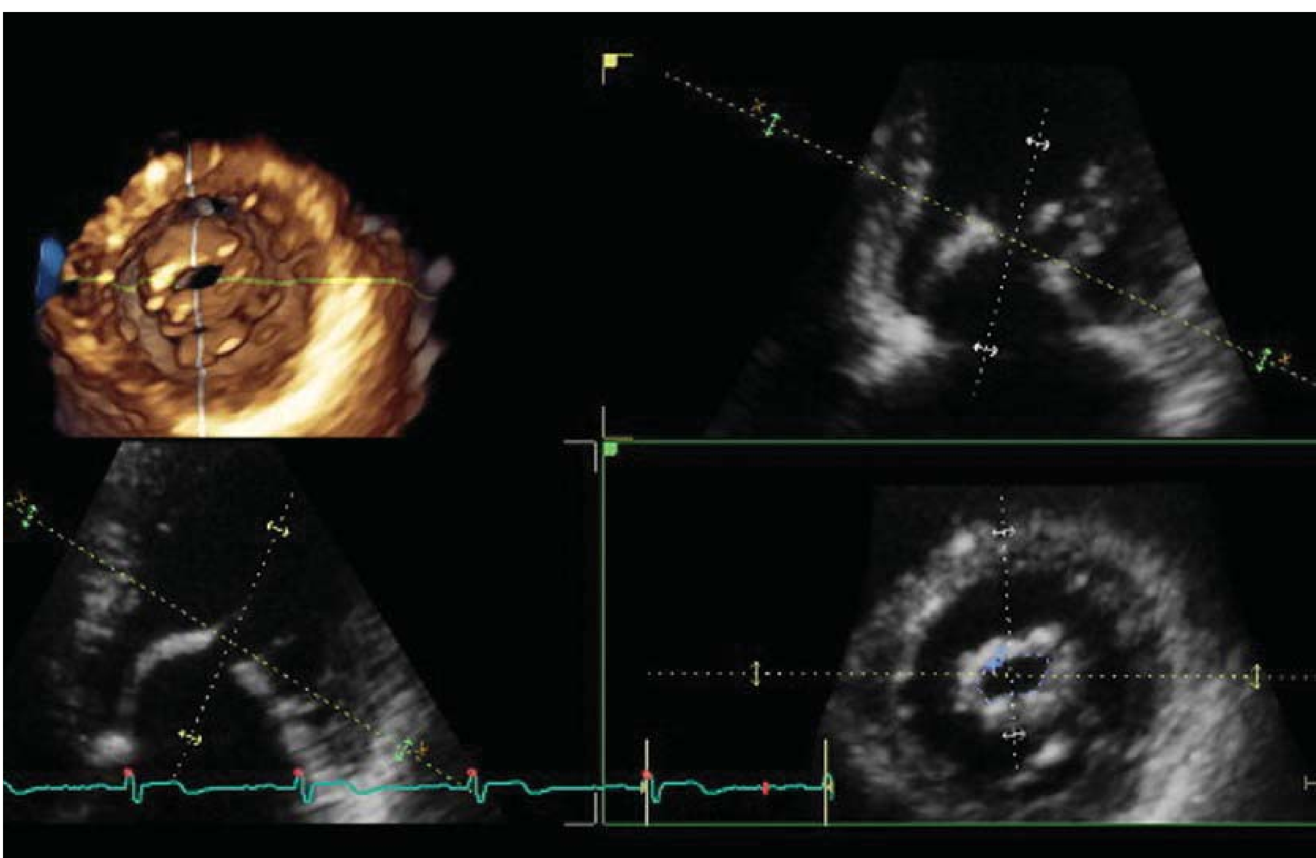

Figure 3. Transthoracic three-dimensional quantitation of rheumatic mitral stenosis severity. The cut plane of the three-dimensional dataset (green dotted line) is perpendicular to the opening direction of the mitral valve orifice, at the tip of mitral leaflets level, allowing an accurate planimetry of the smallest residual opening orifice.

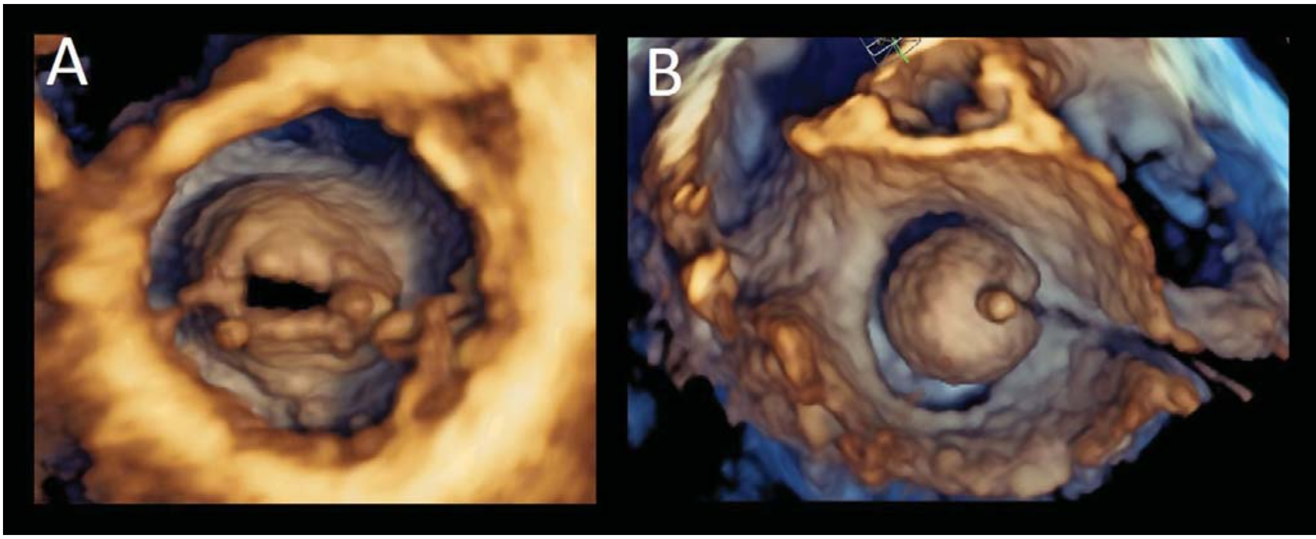

Figure 4. Mitral valve stenosis before and during balloon valvuloplasty. Transesophageal three-dimensional volume rendering visualization of the rheumatic mitral stenosis. The visualisation of the valve from the ventricular perspective (Panel A) allows to appreciate the leaflet morphology, the extent of fusion commissures and the area of the residual opening orifice. The same ventricular perspective can be used during the percutaneous mitral balloon valvuloplasty to monitor the procedure (Panel B).

leaflets and its orientation to obtain an anatomically correct cross-section of the stenotic MV orifice (Figure 3)[31]. MV area planimetry by 3DE showed a strong correlation with the invasive area measurement (using Gorlin formula)[32] and represents the current gold-standard method for assessing MS severity by echocardiography[6,32]. Echocardiographic assessment of the MV is also essential to guide the type of intervention (percutaneous versus surgical) through validated risk scores[33,34]. Percutaneous mitral balloon valvuloplasty is the method of choice for patients with favourable MV anatomy or when open-heart surgery is contraindicated, with 3DE having a crucial role in guiding the procedure — device selection, balloon positioning, and inflation — and assessment of procedural success — MV area quantification by planimetry, extent of commissural opening, leaflet mobility, residual MR — (Figure 4)[35]. Additionally, 3DE TEE procedure guiding has the advantage of reduced exposure to radiation (particularly important in young patients or pregnant women with rheumatic MV disease)[36].

THE ADDED VALUE OF 3DE IN MITRAL REGURGITATION

Organic mitral regurgitation

The accurate description of the MV anatomy is critical before any treatment decision (surgical versus interventional, and repair versus replacement surgery) in patients with organic MR. Soon after the description of MV prolapse (MVP) by conventional echocardiography, degenerative MV disease prevalence was highly overestimated mostly due to the saddle-shape geometry of the MA and the false appearance of leaflets billowing using M-mode and 2DE[37,38]. By demonstrating the complex shape of the MA, 3DE has led to the reconsideration of the MVP definition as the leaflet displacement above the higher points of the MA[39]. Using the en face view of the MV from the atrial perspective, the echocardiographer can easily evaluate both MV leaflets and identify precisely the prolapsing scallops bulging into the LA. 3DE is particularly useful in cases of complex MVP, such as commissural lesions or multi-scallop prolapses (Figure 5)[40]. More than 10 years ago, the accuracy of 3D TTE and TEE in diagnosing MVP was described to be 95% and 97%, respectively[41], but with the latest development of the 3DE technology, nowadays it might be even higher. 3DE has been proved to be useful in both surgical planning and predicting MV repair outcome[42,43]. Systematic quantification of leaflets length, total surface area, and billowing volume is necessary to identify patients at risk for systolic anterior motion after MV repair[44].

Functional mitral regurgitation

Functional mitral regurgitation (FMR) is defined as mitral regurgitation in the presence of a structurally normal MV, developing as the consequence of regional/global LV dysfunction or LA dilatation, as in patients with chronic atrial fibrillation. Disregarding the aetio-

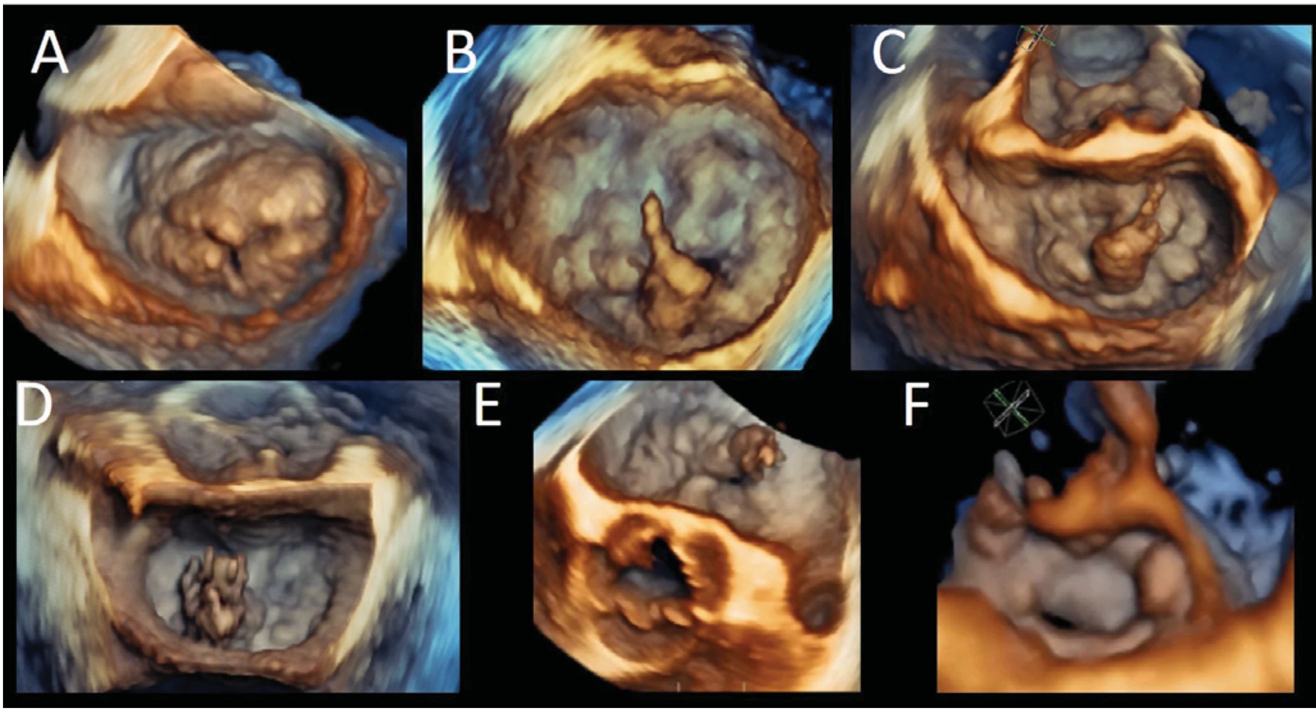

Figure 5. Three-dimensional volume rendering from the left atrial perspective (surgical view) of different forms of organic mitral valve disease. Barlow disease with associated posterior mitral leaflet cleft (Panel A); Barlow disease with P2 flail and chordal rupture (Panels B and C); papillary muscle rupture, bulging into the left atrium during systole, in a patient with fibroelastic deficiency (Panels D and E); medial commissural prolapse (Panel F).

logy, complex modifications occur at the level of the MA: dilatation, flattening and reduced dynamics[12,13,45]. In patients with LV enlargement, apical tethering of MV leaflets secondary to PM displacement and reduced trans-mitral pressure seems to be the main mechanism of FMR. The extent of MV distortion can be carefully assessed using 3DE by quantifying the geometry and function of the MA, the leaflet areas and tethering angles, tenting volume and maximal tethering area, as well as direct visualization of the MV subvalvular apparatus anatomy (Figure 6).

THE ADDED VALUE OF 3DE IN MV ENDOCARDITIS

Although 2DE has a good sensitivity in diagnosing MV vegetations due to its high temporal and spatial resolution, the limited number of views is often insufficient to understand the complexity of the lesion (size, ori-

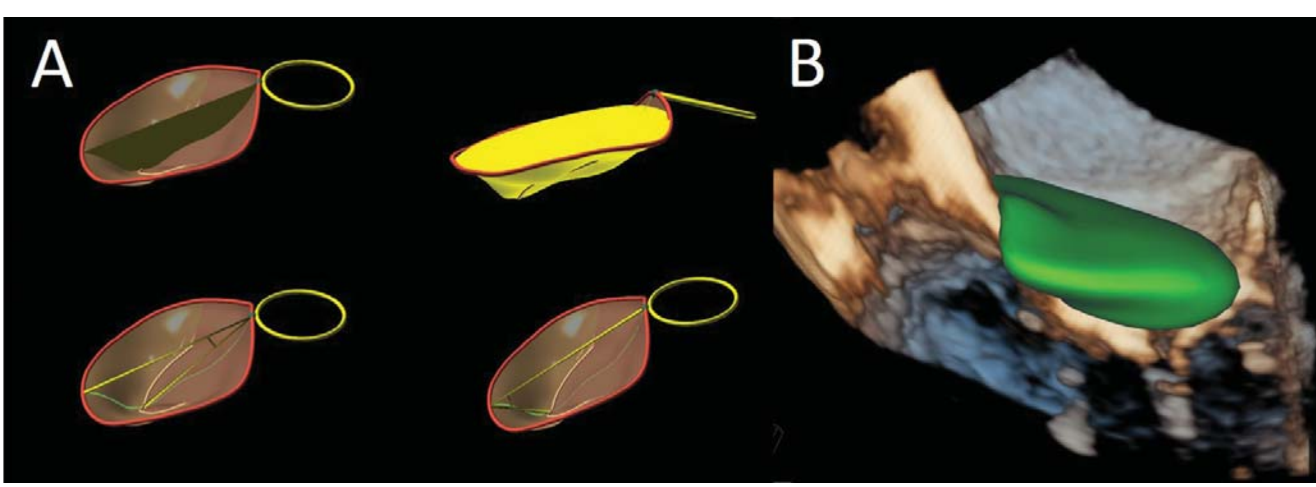

Figure 6. Functional mitral regurgitation. Three-dimensional reconstruction of the mitral annulus tenting area, volume, anterior and posterior mitral leaflets angles (Panel A) and automatic quantification of the tenting volume (Panel B).

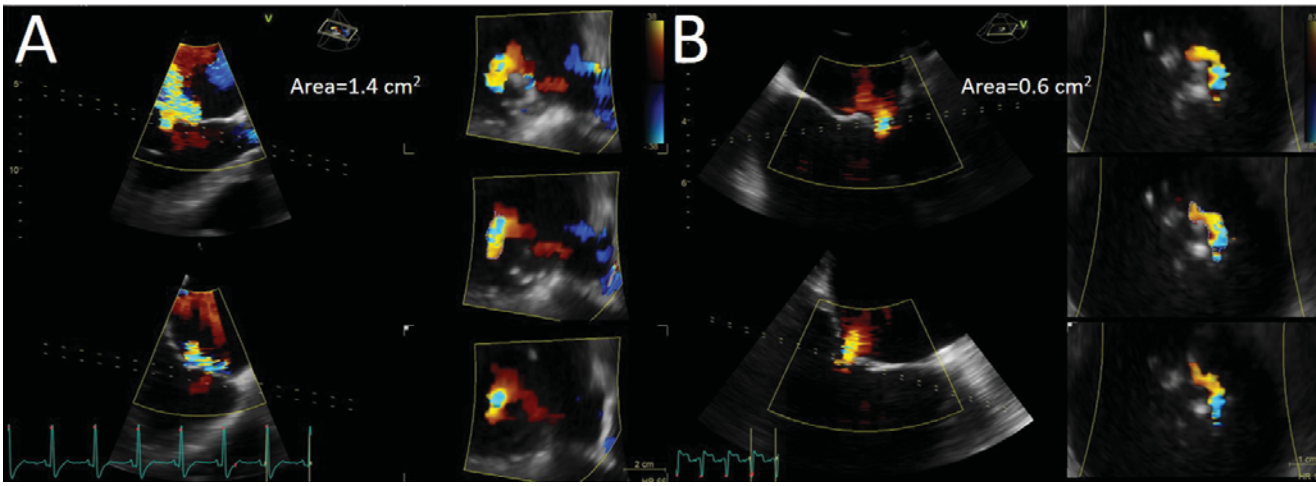

Figure 7. Three-dimensional colour flow data set showing the origin of mitral regurgitation jet. Multiple slicing of the proximal part of the jet (dotted lines) allows the identification of the smallest vena contracta area planimetry. Two different cases, with different orifice shapes and sizes, are illustrated. (A) and (B).

gin, the involvement of other structures etc.) and their functional impact. 3D TEE is the preferred technique in patients with clinical suspicion of MV endocarditis to exclude or confirm the diagnosis and to identify complications (Figure 8).

THE ADDED VALUE OF 3DE IN MITRAL PROSTHESES

3DE (particularly 3D TEE) is pivotal to assess MV prosthesis normal function (Figure 9) and to evaluate for potential complications: endocarditis, thrombosis, dehiscence, paravalvular leaks, etc. (Figure 10 and 11). Localisation, size, and mobility of the prosthetic masses are essential information in evaluating the risk of embolization and the proper management strategy. Prosthetic dehiscence or paravalvular leaks are accurately assessed using 3D colour Doppler imaging and 360° rotation around the prosthetic ring, providing critical information for management decision.

THE ADDED VALUE OF 3DE IN CONGENITAL MITRAL VALVE DISEASE

Congenital abnormalities of the MV include both stenotic and regurgitant lesions (Figure 12) and the

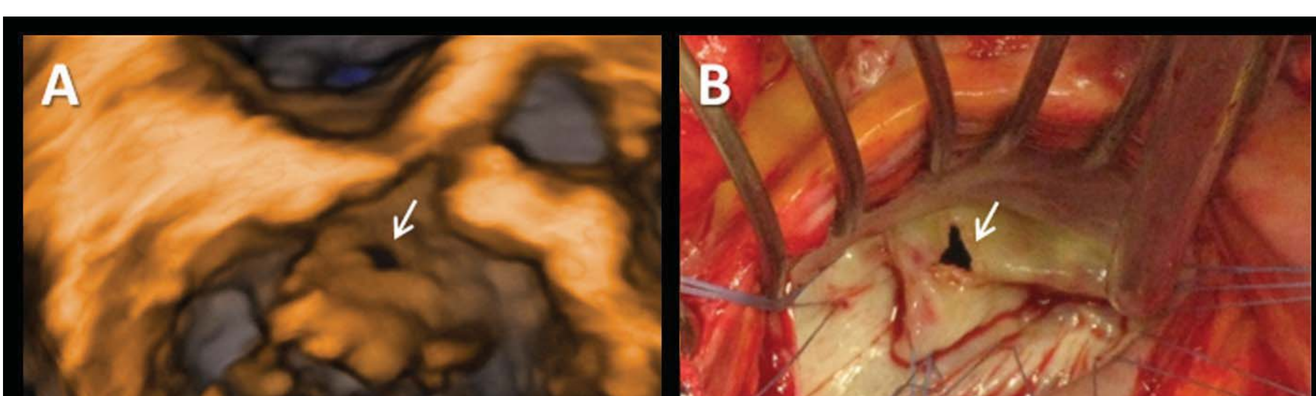

Figure 8. Anterior mitral leaflet perforation (arrow) complicating native aortic valve endocarditis. Transthoracic three-dimensional volume rendering (Panel A) and intra-operative (Panel B) views.

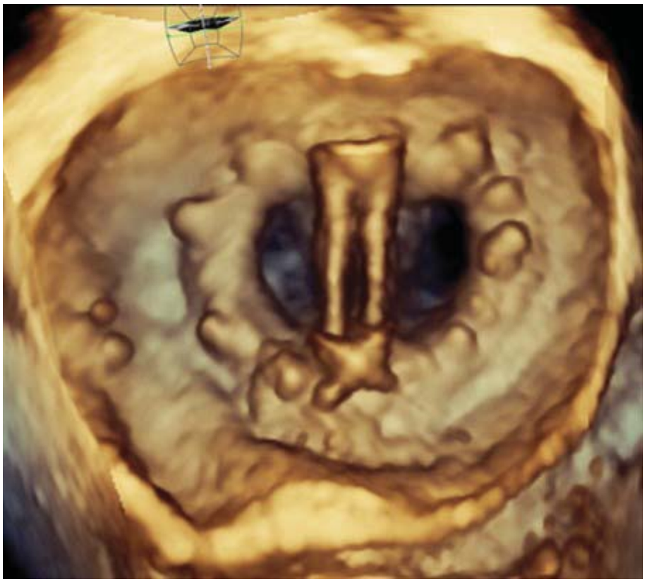

Figure 9. Three-dimensional transesophageal volume rendering of a mechanical prosthesis visualised from the surgical view for morphological and functional characterization.

advantages of the 3DE in defining the anatomy of defects and quantifying their haemodynamic implications are similar as described before. The wide range of options to post-process the 3D dataset (cropping, rotation etc.), the multiple displaying modalities (volume rendering, tomographic multi-slices), as well as the unique perception of depth offered by 3DE are pivotal in the process of understanding the complexity of congenital abnormalities[46,47]. A recent study addressing the prevalence of MV cleft in a population with significant MR, using 3DE, has shown a 3.3% of isolated MV cleft in this population[48], a considerably higher percentage compared with previous results based on 2DE (0.07% for isolated posterior mitral leaflet cleft and unknown for isolated anterior mitral left cleft), these results being representative for the increased accuracy of 3DE compared to 2DE in evaluating complex MV diseases[49].

THE ADDED VALUE OF 3DE IN MITRAL VALVE STRUCTURAL INTERVENTIONS

For the past decade, several percutaneous transcatheter procedures addressing MV pathologies have emerged as alternatives to traditional surgical therapy in high-risk patients. Newer interventional therapies for MV disease – as edge-to-edge repair, annuloplasty,

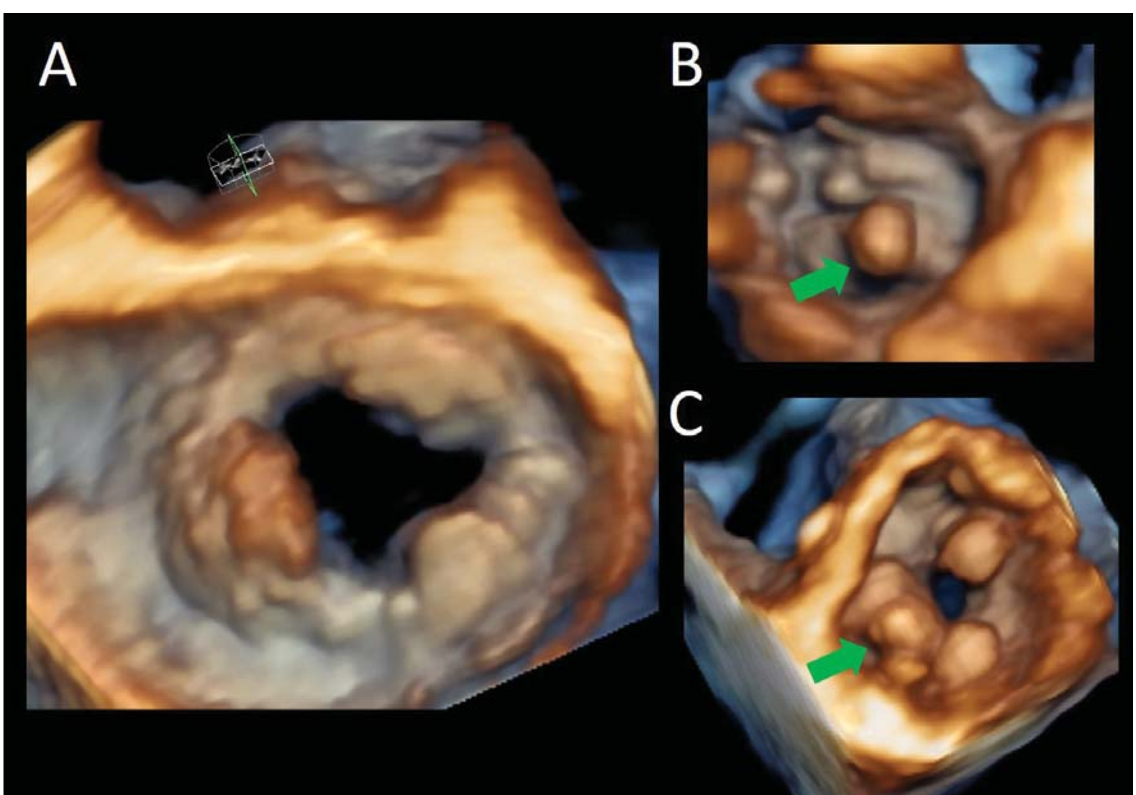

Figure 10. Mitral prosthesis masses. Three-dimensional volume transesophageal volume rendering from the surgical (panelA) and ventricular (Panels B and C) views of a mitral bioprosthesis with signs of degeneration (calcifications, green arrows) and a thrombotic mass (red arrow, between 7 and 10 o'clock).

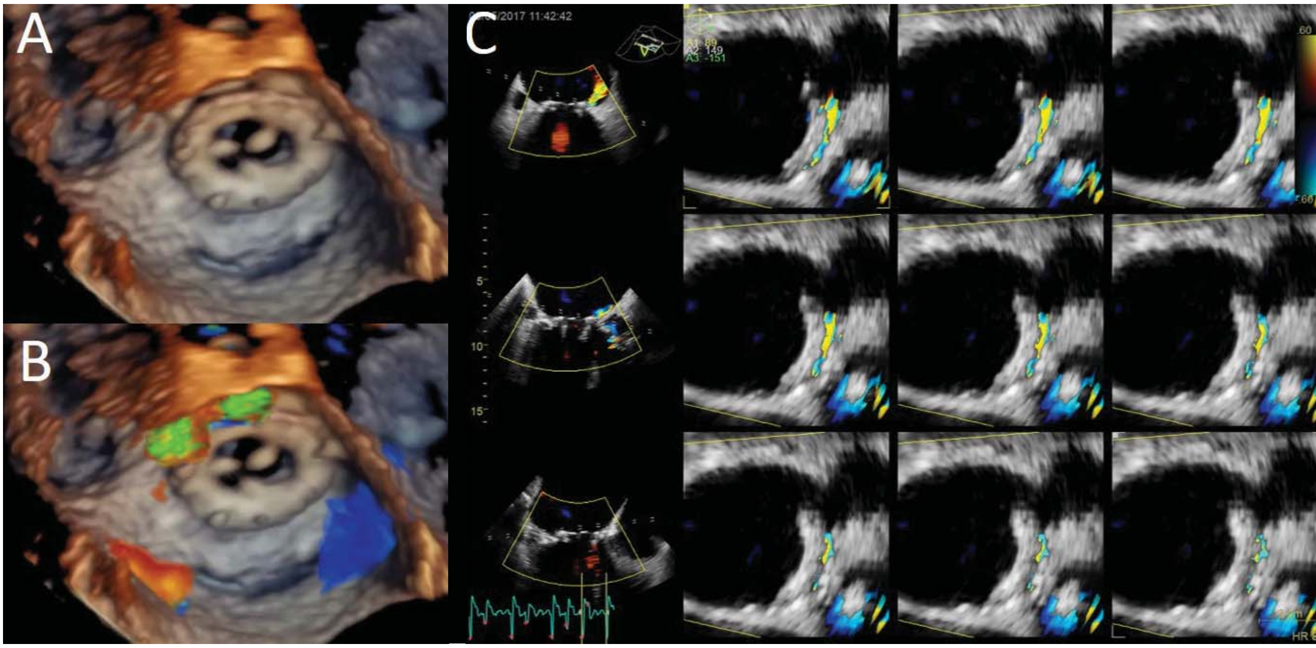

Figure 11. Mitral periprosthetic regurgitation. Three-dimensional transesophageal volume rendering (Panel A) and colour flow acquisition (Panel B) showing anterolateral periprosthetic regurgitation (between 10-12 o'clock). Multi-slice display to allow planimetric quantitation of the regurgitant orifice (Panel C).

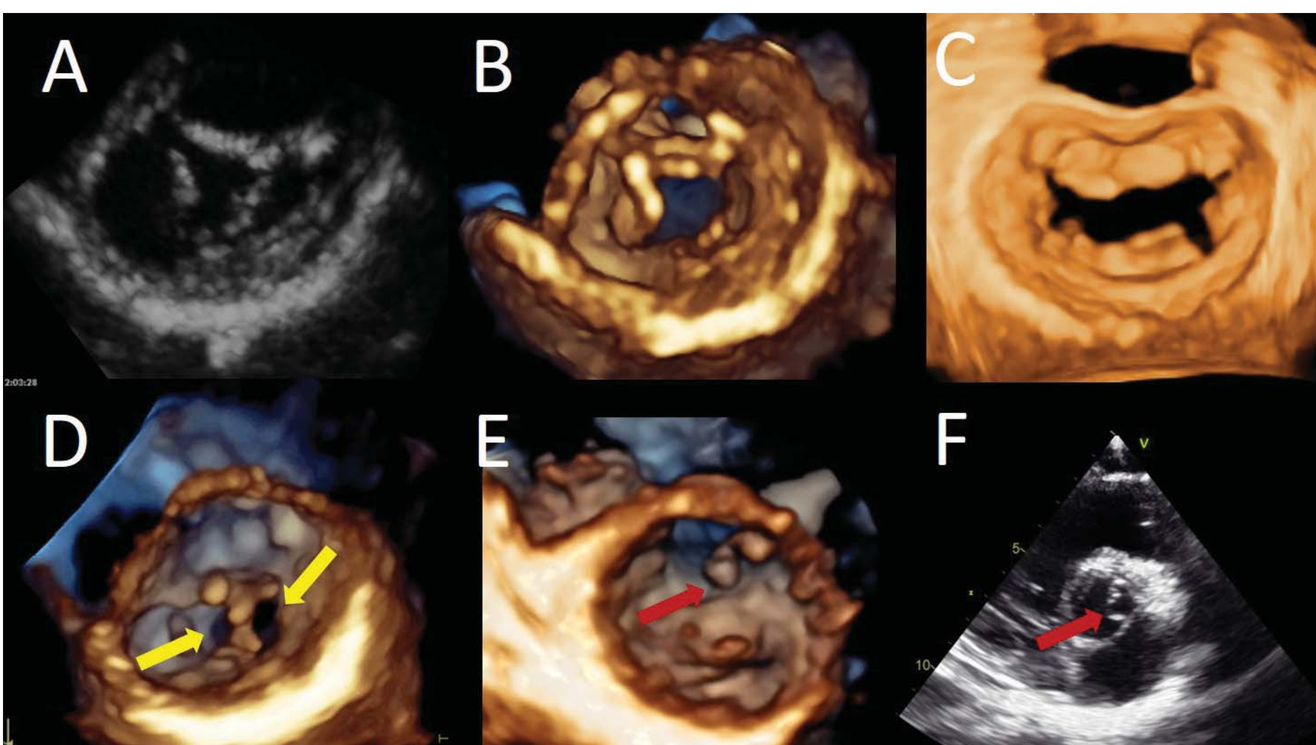

Figure 12. Congenital mitral valve diseases. Two-dimensional short axis view (Panel A) and three-dimensional transthoracic volume rendering of an anterior mitral leaflet cleft from the ventricular perspective (Panel B) in a patient with an incomplete atrio-ventricular canal. Surgical view of the mitral valve showing posterior mitral leaflet cleft, between P2 and P3 scallops (Panel C). Three-dimensional transthoracic volume rendering from the ventricular side showing a double orifice mitral valve - yellow arrows - (Panel D). Transthoracic three-dimensional volume rendering from the ventricular view (Panel E) allowing an accurate identification of the anatomy and localisation of the accessory tissue (red arrow). Two-dimensional transversal cut plane obtained from a transthoracic three-dimensional data set using an intermediary plane between the levels of the aortic valve and the mitral valve to visualise accessory mitral valve tissue (Panel F).

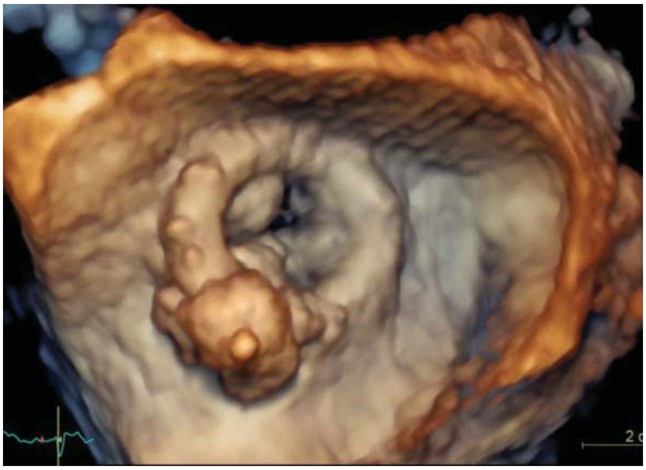

Figure 13. Transesophageal three-dimensional surgical view of the mitral biological prosthesis after perivalvular leak closure showing the final (posterolateral) position of the plug.

chordal implantation or transcatheter mitral valve replacement (TMVR) – rely on real-time visualization of the MV in the beating heart using echocardiographic guidance as the leaflet are not visible at fluoroscopy and MV diseases are often associated to limited degenerative calcification[50]. Delivery catheters, devices, and target structures can be visualized in one single view using 3D TEE, optimizing the transseptal puncture, the steering of the catheters towards the MV and proper positioning of the device in relation to MV anatomy[51]. TEE visualization of the MV during interventions can guide the prosthesis to reach its final position, assess the success of repair, and allow quantification of the residual regurgitation.

Intraprocedural guidance of MV repair with MitraClip system is primarily based on 2DE and 3DE, with limited utility of fluoroscopy[52]. 3DE TEE plays a leading role in all the procedural steps for MitraClip implantation: transseptal puncture, device positioning, proper leaflet grasping and post-deployment evaluation of the results (residual MV orifice area and MR reduction, difficult to assess given the double – or even triple – MV orifice and the subsequent multiple regurgitation jets) and possible complications (iatrogenic interatrial defect)[53].

Artificial chordal implantation is another option for patients with degenerative MV disease and TEE 3DE plays a major role in patient selection, identifying the site of implantation (site of prolapse), the number of chords needed, as well as the appropriate chordal length. During the procedure, TEE is useful in checking the LV site of puncture, excluding subvalvular apparatus entrapment by the delivery catheters, ensuring adequate grasping of the desired scallop(s) and adaptation of neochordae length according to the real-time evaluation of the MR severity[36].

With regard to TMVR, 3D TEE is of major importance for pre-procedural anatomical assessment of the MA and to identify the landmarks used for valve deployment (trigons, aorto-mitral continuity etc.), for characterization of the landing zone – essential in selecting the most appropriate device based on their specific characteristics –, for intraprocedural guidance, confirmation of proper device position, MV prosthesis functional assessment and procedure-related complications[3,51,54]. For valve-in-valve TMVR, 3D TEE has an additional role in assessing the presence of inter-device regurgitation (between the transcatheter device and surgical bioprosthesis), with guidance for further balloon post-dilatation in case that multiple jets are evident around the circumference of the newly implanted valve[53].

MV paravalvular leak is associated with increased morbidity and reoperation has increased mortality risk, making transcatheter closure a good option in patients with significant regurgitant volume or haemolysis (Figure 13)[55]. 3D TEE is the preferred imaging modality for pre-procedural evaluation of the orifice shape and size (planimetric area), for peri-procedural guidance – including the use for additional devices –, post-procedural evaluation of the results and follow-up[56].

Newly developed technologies that synchronize multimodality imaging – fusion imaging – may increase diagnostic accuracy and procedural precision in transcatheter MV repair and replacement[5]. Of particular importance is echocardiographic and fluoroscopic imaging fusion (i.e. EchoNavigator system, Philips Healthcare), which facilitates procedural guiding in MV repair by providing depth perception and demonstrating the relationship between devices and surrounding structures - 2DE and 3DE images superimposed on fluoroscopic projection – as well as visualizing the regurgitant jet on the fluoroscopic silhouette and allowing the selection of the ideal device position[57,58]. Moreover, fusion imaging has the potential to enhance the safety of the procedures and to reduce the fluoroscopy and procedure times[52].

LIMITATIONS OF 3DE AND FUTURE PERSPECTIVES

Traditionally, 3DE was subject to artefacts related to inaccurate gain settings, the inability of the patient to hold respiration and the presence of arrhythmias.

Moreover, high-quality transthoracic 3D data sets are greatly dependent on a good acoustic window and the experience of the echocardiographer. 3D TEE images are easier to obtain, real-time acquisitions being often sufficient for an accurate diagnosis due to the reduced 3D volume acquisition and high spatial resolution. However, the new 3D technology allowing single-beat acquisitions at high frame-rate has overcome most of the previous limitations, and the automated software packages for MV geometry assessment requiring only minimal manual intervention have made 3DE easier to learn and more reproducible.

Another limitation of 3DE is the lack of tissue characterization. Since the different colors of the images are coding the depth of the structure from the transducer and not the tissue characteristics, differentiating intracardiac masses (calcifications, tumor versus thrombus or endocarditis versus thrombus) is challenging by 3DE only. Moreover, due to the lower spatial resolution, small structures (such as vegetations) appear larger in 3DE than in 2DE images, a limitation that can be overcome by displaying 3D datasets as longitudinal or transversal 2D slices.

CONCLUSION

The advent of 3DE has changed completely the way the MV is evaluated by echocardiography and opened a new era in the transcatheter treatment of MV diseases. Application of 3DE in the evaluation of MV contributes with essential anatomical and functional information, independently of the clinical indication, and should be the technique of choice whenever a complex MV lesion is suspected. The systematic training in 3DE acquisition and interpretation appears to be pivotal in the near future for physicians dealing with patients with MV diseases.

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