Chapter 5

Real-Time 3D Echocardiography in Percutaneous Balloon Mitral Valvuloplasty

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Additional information is available at the end of the chapter

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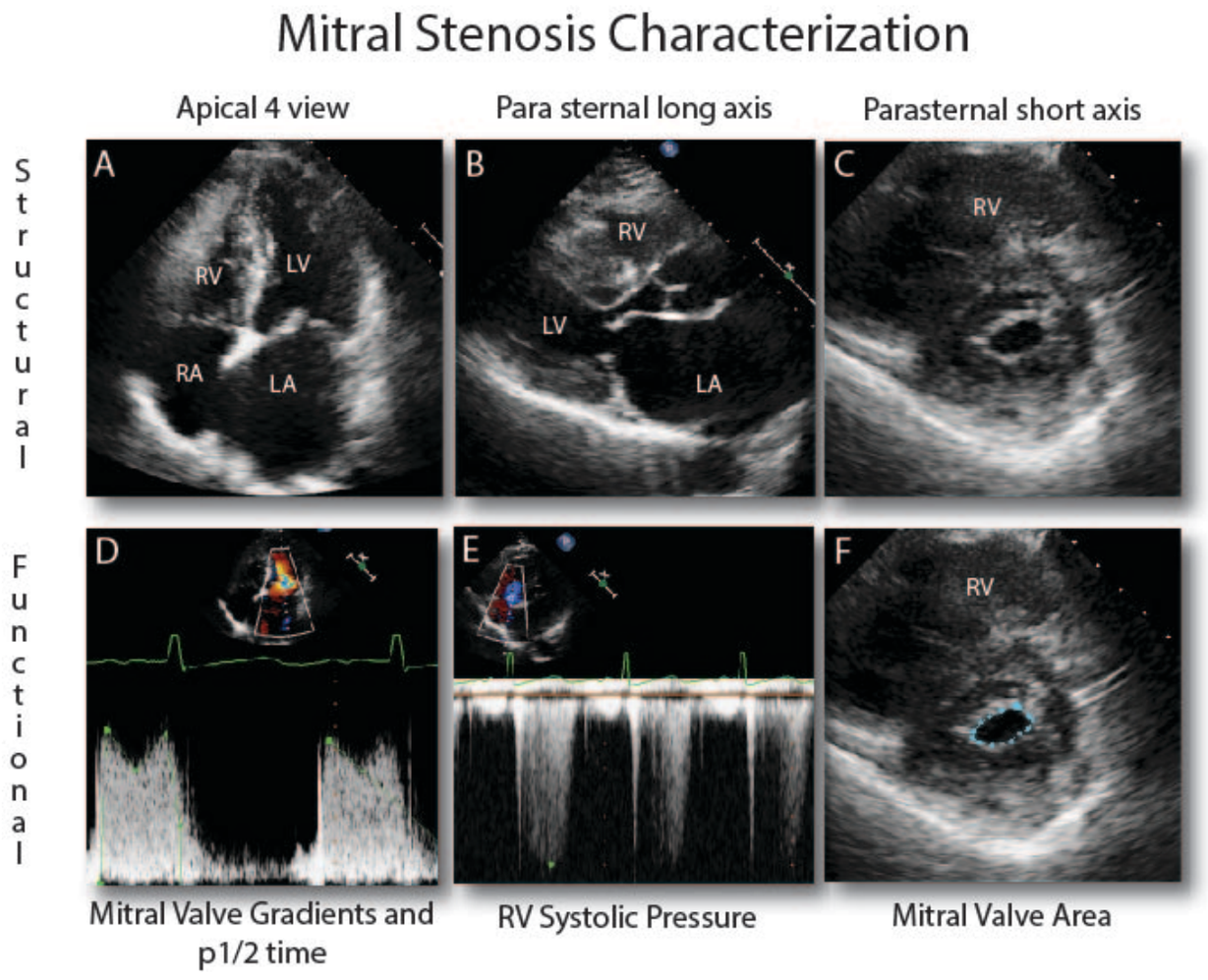
1. Introduction

Since Dr Kanji Inoue introduced the Inoue balloon catheter in 1984, percutaneous balloon valvuloplasty (PBMV) has become the treatment of choice for patients with symptomatic mitral valve stenosis and favorable valve morphology. PBMV is the preferred treatment for mitral stenosis as it is less invasive and provides longer-lasting results than closed commissurotomy. 1 PMBV is not suited for patients with mitral stenosis due to severe annular calcification or markedly degenerated valves. PBMV can be performed either an in antegrade fashion through a transseptal puncture or retrograde from the aorta to the mitral valve. Serial balloon dilations of the mitral valve using the self-centering Inoue balloon catheter (or alternatively, a standard valvuloplasty balloon catheter) are performed to physically split the mitral valve leaflet commissures and subsequently improve leaflet motion and hemodynamics. In successful cases, percutaneous balloon mitral valvuloplasty typically doubles the mitral valve area and decreases the mitral valve gradient by half. Splitting of the commissures is the principle mechanism that leads to improvement of hemodynamics and patient symptomatology.

The anatomy of the mitral valve is complex, and echocardiographic imaging plays a critical role in both the diagnosis and guidance of management of patients with mitral stenosis. Although Doppler hemodynamics and 2D transthoracic echocardiography are a mainstay in the echocardiographic assessment of mitral stenosis (Figure 1), real-time three-dimensional echocardiography (RT3DE) is an emerging imaging tool for not only the diagnosis of mitral stenosis (Figure 2), but also for the guidance of percutaneous balloon mitral valvuloplasty procedures in the catheterization laboratory.



RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium

Figure 1. Two dimensional and Doppler echocardiography in mitral stenosis. Traditionally 2D echocardiography has provided structural information regarding the morphology of the mitral valve in mitral stenosis. In addition chamber size, and ventricular function is assessed by echocardiography. Doppler methods provide hemodynamic functional information regarding the mitral valve in mitral stenosis. Peak and mean mitral valve gradients, pressure half time derived mitral valve area and systolic pulmonary pressure are usually recorded in these patients.

2. Diagnosis

Diagnosis of mitral valve stenosis commonly involves the use of 2D transthoracic echocardiography (2DE) to assess the severity of mitral disease, including mitral leaflet mobility, thickening, calcification and sub-valvular stenosis; as well as to exclude any contraindications to treatment, such us left atrial thrombus or significant mitral regurgitation.

Normal mitral valve area (MVA) is approximately 4-6 cm^2. Patients with symptomatic mitral stenosis typically have a valve area of less than 2.0 cm^2 and have severe mitral stenosis if the valve area is less than 1.0 cm^2.[2] (Figure 3) The narrowing of the mitral orifice creates a left atrioventricular pressure gradient (the hemodynamic hallmark of mitral stenosis), which in a

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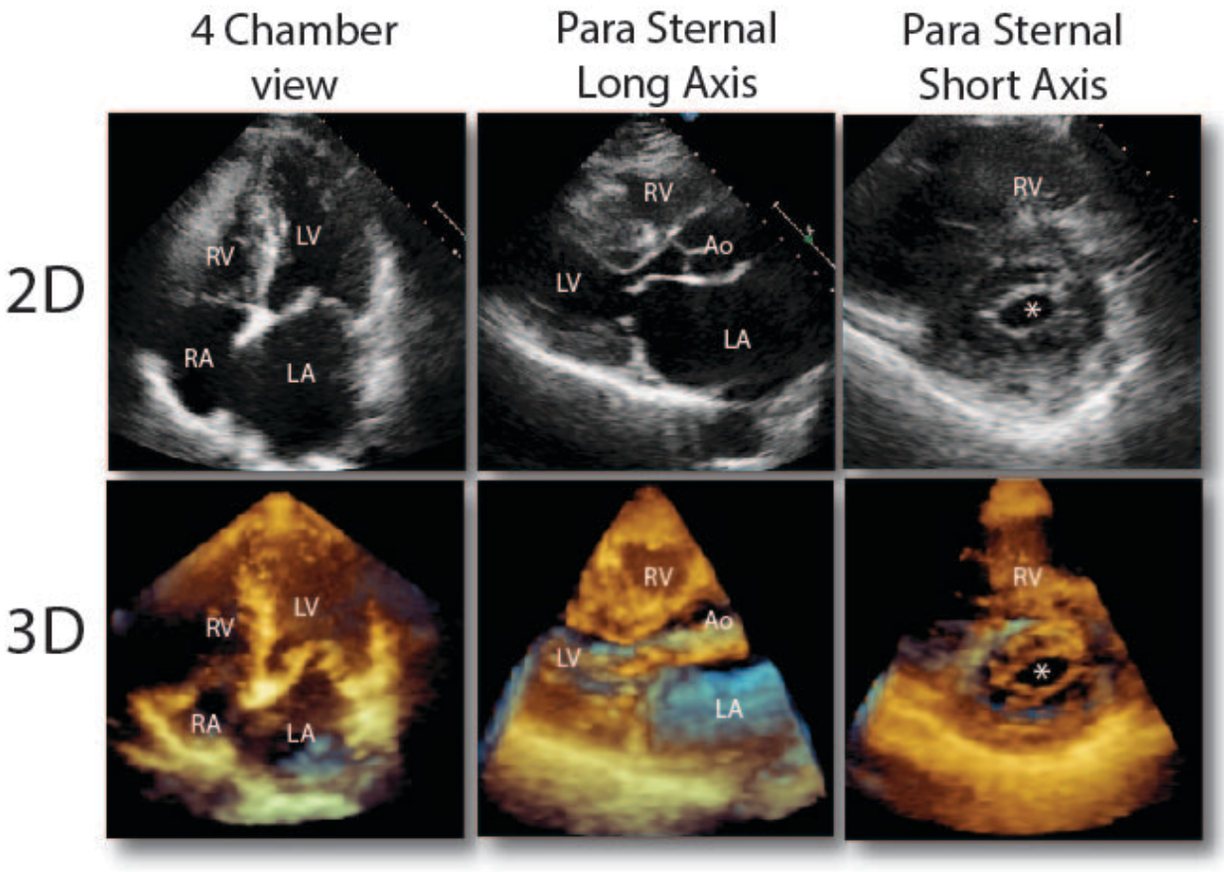

RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium; Ao: Aorta

Figure 2. Comparison of 2D and 3D transthoracic echocardiography in mitral stenosis. The most useful views to evaluate patients with mitral stenosis include the apical 4 chamber view as well as the parasternal long and short axis views. This figure illustrates the added value of 3D imaging in better characterizing the mitral valve apparatus. The third dimension increases the anatomic detail of the leaflets, commissures and subvalvular tissue.

normal functioning mitral valve is near zero. In the setting of hemodynamically significant mitral stenosis, patients can present with a constellation of symptoms that may include dyspnea, orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, poor exercise tolerance and/or palpitations.

3. Modalities used to evaluate the mitral valve

Various echocardiographic techniques can be used to measure mitral valve area, including pressure half-time (PHT), planimetry, continuity equation and proximal iso-velocity surface area (PISA). Each method has its own advantages and disadvantages.

Planimetry has shown to be more accurate when measuring MVA post PBMV compared to PHT, PISA or the continuity equation method.[3],[4] Planimetry involves the direct measurement of the mitral valve orifice and has correlated well with invasive anatomic measurement.[1] This method requires a considerable amount of expertise for reliability.

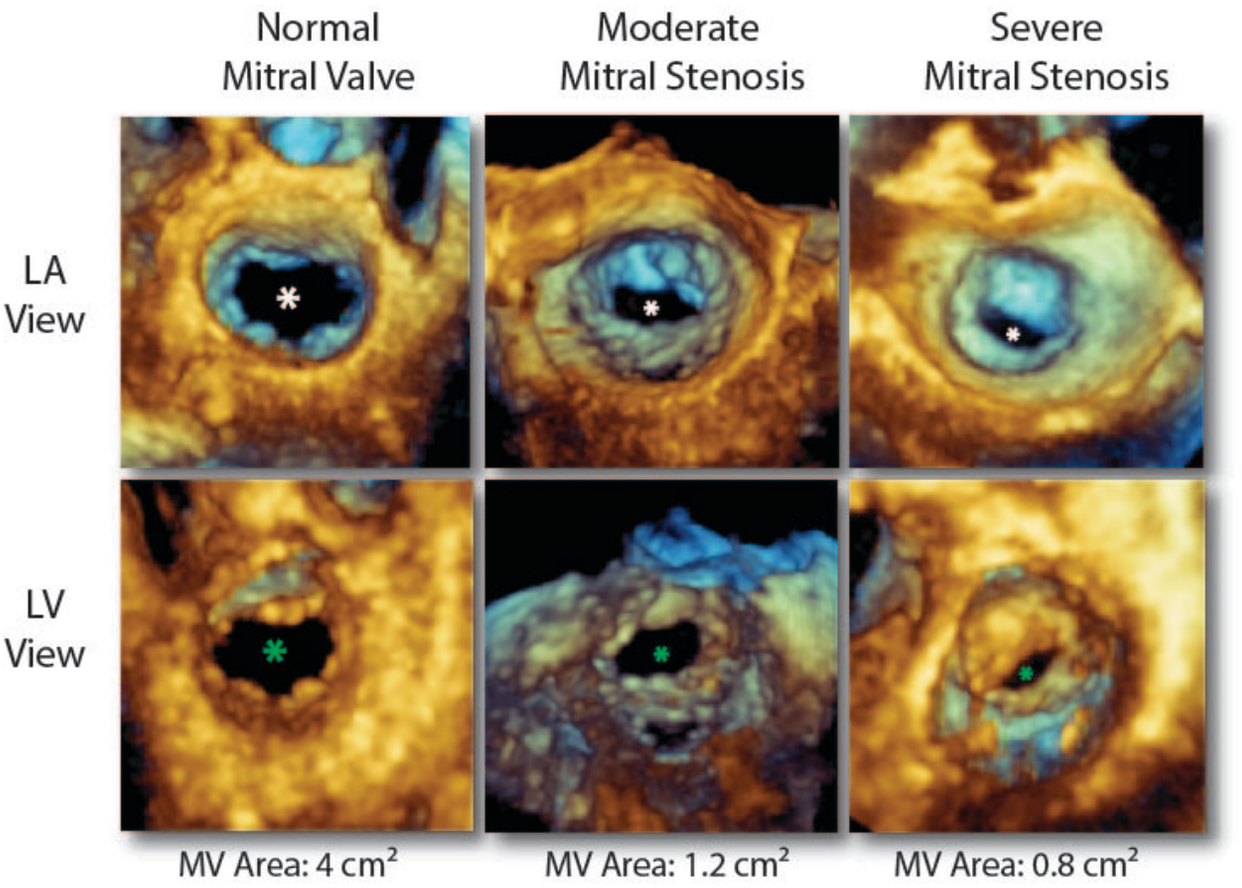

Figure 3. Normal mitral valve compared to mitral valves with moderate and severe mitral stenosis.The mitral valve orifice is seen from the left atrial side (LA view-white asterisk) and the left ventricular side (LV View- green asterisk) in a patient with a normal mitral valve (valve area 4cm^2, a patient with moderate mitral stenosis (valve area of 1.2 cm$^{2)}$, and in a patient with severe mitral stenosis (valve area of 0.8 cm^2).

The PHT method is easily performed, but is influenced by other concomitant valvular disease, such as aortic or mitral regurgitation, or by the dynamic hemodynamics seen post-PBMV.[4], [6],[7] In contrast, planimetry is not affected by hemodynamic variability, but is difficult because it requires technically challenging imaging views of the mitral orifice.

The PISA method requires many different imaging planes and variables to accurately calculate MVA and thus is very laborious. It can be however, used in the presence of mitral regurgitation dynamic flow changes.[7]

The continuity equation also involves the measurements of many variables, including size of the left ventricular outflow tract and mitral annulus. It also cannot be used in patients with atrial fibrillation or significant aortic or mitral regurgitation.

Planimetry has become the most reliable method for calculating mitral valve area and has been compared to the invasively derived Gorlin's formula, which by some is considered the gold standard for mitral valve area calculation.[2] However, real-time 3D echocardiography (RT3DE) may be a more accurate and feasible method for calculating MVA in patients being evaluated for PBMV.[6] Planimetry with 2DE relies on good echocardiographic technique and

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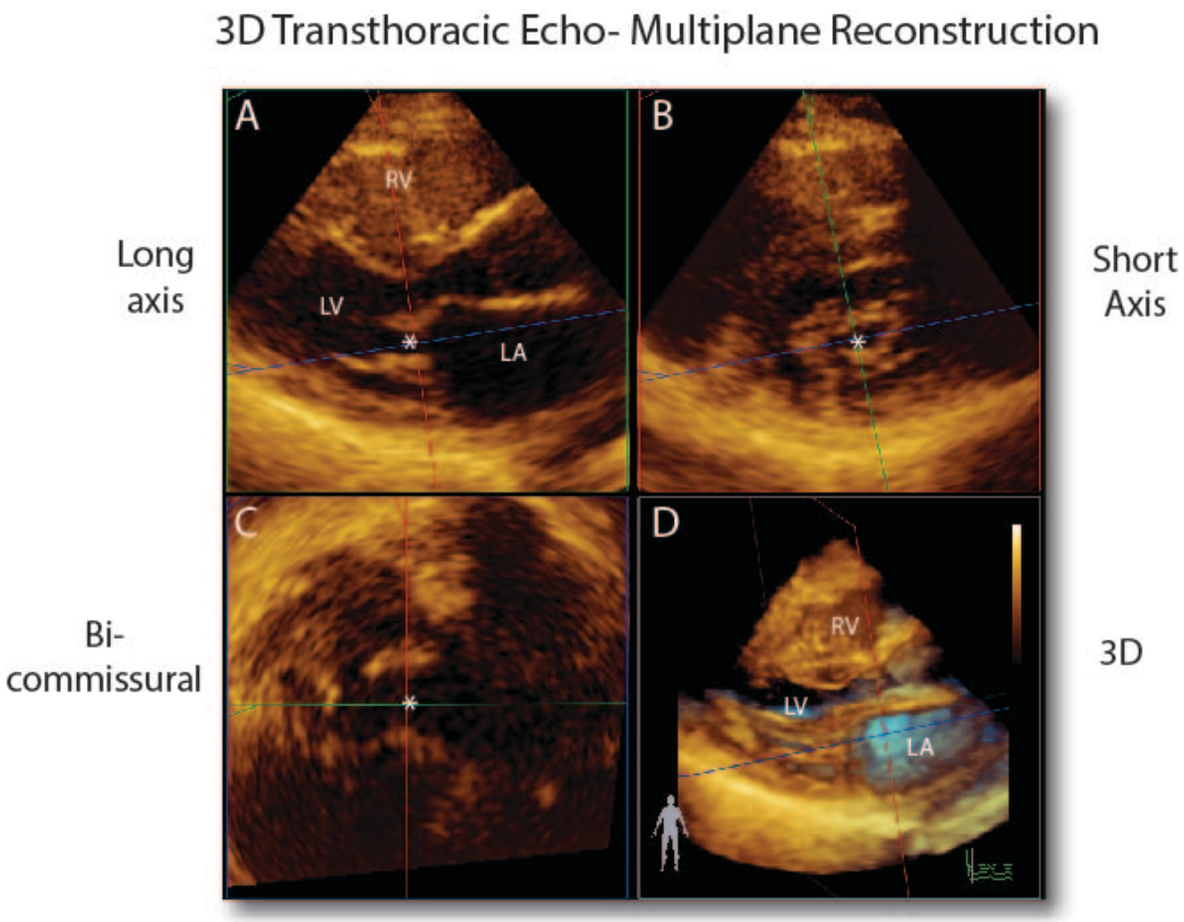
imaging windows in the parasternal short-axis plane to directly measure the mitral valve orifice. In contrast, RT3DE is not limited to a specific imaging plane and can image the mitral valve in several different planes, allowing for a recreation of a 3D image for precise tracing of the mitral valve orifice.(Figure 4) Even though poor imaging windows can affect both 2D and 3D echocardiography, RT3DE has been less affected by poor imaging windows compared to 2D.[8],[9] Real-time 3D echocardiography has been shown to be more accurate and reliable than 2DE planimetry for assessing MVA, severity of commissural fusion and extent of subvalvular disease.[8],[10] Real-time 3D echocardiography has also been shown to provide a more accurate and reliable MVA measurement in inexperienced echocardiographers using RT3DE compared to 2D echocardiography and nominally affected by mitral valve morphology and post-PBMV hemodynamic changes.[6],[8],[10]-[11]



The asterisks represent the mitral valve orifice from each of the 3 orthogonal planes. RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium

Figure 4. Multiplane reconstruction of the mitral valve apparatus in mitral stenosis. 3D echocardiography can be presented in a volume rendition form (panel D) or in a simultaneous multiplane rendition (panels A, B and C). From the long axis plane (panel A) one can choose the tips of the leaflets to obtain the true minimal mitral valve orifice area, as depicted in panel B. Panel C represents an orthogonal view at the bi-commissural level, a view that is not obtainable from 2D echo alone.

4. Patient selection

Favorable patients for percutaneous balloon mitral valvuloplasty are typically evaluated through calculation of the echocardiographic Wilkin's score (Figure 5). It is the most widely used prognostic score to determine a favorable PBMV outcome. It is derived non-invasively by echocardiography using four variables, valve leaflet mobility, thickening, calcification and degree of sub-valvular thickening. The Wilkin's score assigns a value from 1 to 4 for each category, with a higher value indicating more extensive disease. A patient is considered a good candidate for PBMV if they have a total score of ≤ 8 and the absence of severe mitral regurgitation. An optimal patient is associated with a high level of procedural success and low complication rate. Patients with scores > 8 have an increased risk for adverse outcomes and should be considered for surgical management.[12] However, even in unfavorable candidates percutaneous balloon valvuloplasty is often still the first treatment of choice in experienced centers.

Grade	Mobility	Thickening	Calcification	Subvalvular disease
1	Highly mobile with only leaflet tips restricted	Leaflets near normal in thickness (4-5mm)	A single area of increased echo brightness	Minimal thickening just below the mitral leaflets
2	Leaflet mid portions and base portions have normal mobility	Midleaflets normal, considerable thickening of margins (5-8mm)	Scattered areas of brightness confined to leaflet margins	Thickening of chordal structures extending to one of the chordal length
3	Valve continues to move forward in diastole, mainly from the base	Thickening extending through the entire leaflets (5-8mm)	Brightness extending into the mid portions of the leaflets	Thickening extended to distal third of the chords
4	No or minimal forward movement of the leaflets in diastole	Considerable thickening of all leaflet tissue ("/>8-10mm)	Extensive brightness throughout much of the leaflet tissue	Extensive thickening and shortening of all chordal structures extending down to the papillary muscle

Adapted from Wilkins et al.[12]

Table 1. Mitral Valve Anatomy Scoring Using the Wilkin's Score

Iung and Cormier also developed a scoring system to evaluate mitral valve anatomy in a less complex way. In addition, the Cormier scoring system also factors in chordae length, a feature not included in the more traditional Wilkins score. Interestingly, however, neither the Wilkins or Cormier scoring systems address the issue of commissure disease, such as fusion and extent of calcification. Inadequate leaflet splitting and the development of mitral regurgitation can be related to severe commissural disease.[14]-[16] Identifying the degree of commissural disease can help to predict poor patient outcomes. Because of the potential importance of commissural disease in PBMV outcomes, there is interest in incorporating this variable into a new, RT3DE-derived mitral stenosis scoring system.[9]

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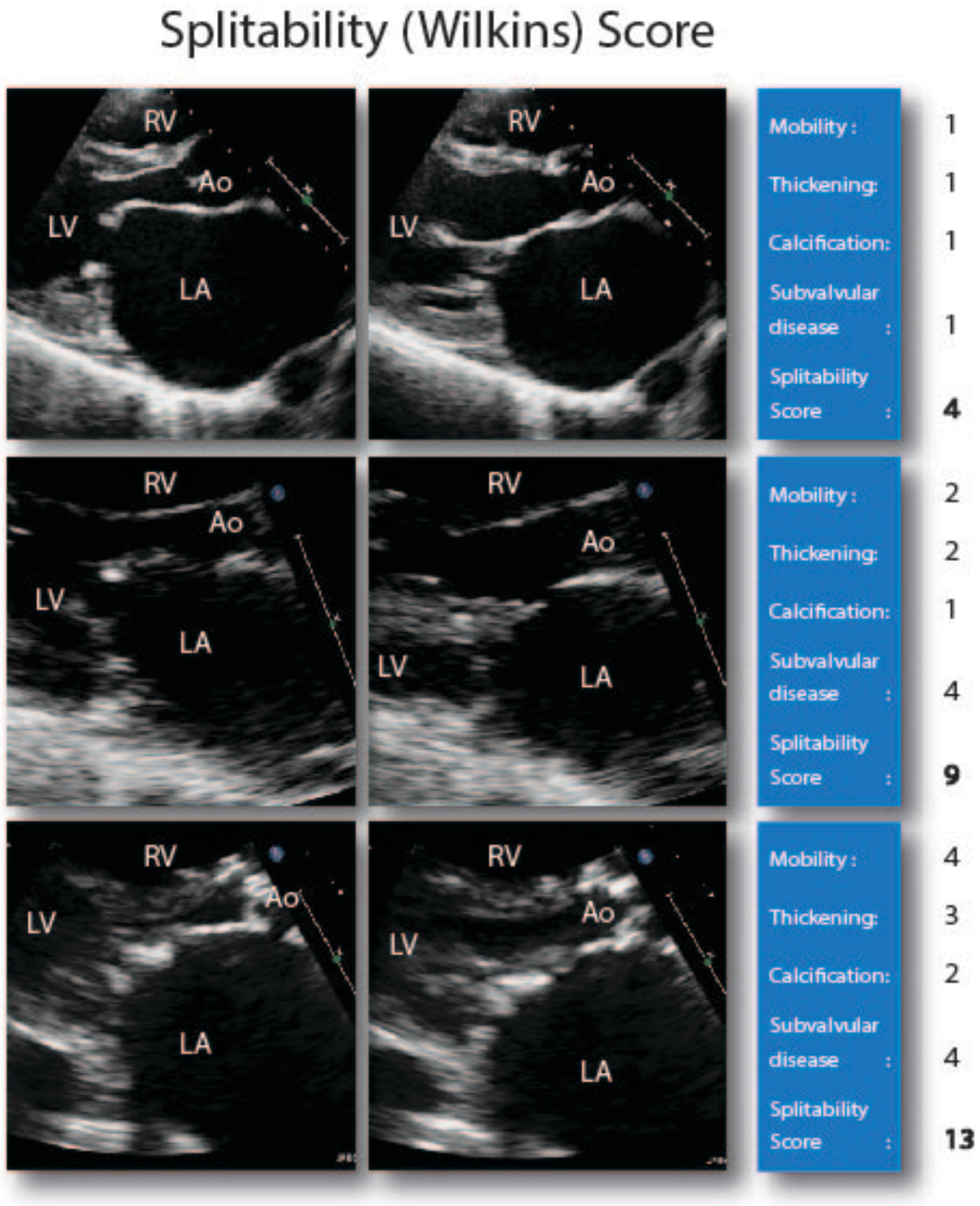

RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium; Ao: Aorta

Figure 5. Splitability scores obtained in three patients with mitral stenosis. Diastolic frames are depicted to the left and systolic frames to the right. The upper panels are from a patient with a Splitability score of 4, which would make him a good balloon valvuloplasty candidate. The middle panels are from a patient with a score of 9 which would make him a borderline candidate for valvuloplasty. The lower panels are from a poor candidate for balloon valvuloplasty with a score of 13.

Echocardiographic Grade	Mitral valve anatomy
1	Pliable non-calcified anterior mitral leaflet and mild subvalvular disease (i.e., thin chordae 10mm long)
2	Pliable non-calcified anterior mitral leaflet and severe subvalvular disease (i.e., thickened chordae < 10mm long)
3	Calcification of mitral valve of any extent, as assessed by fluoroscopy, whatever state of the subvalvular apparatus.

Adapted by Iung B et al.[13]

Table 2. Cormier Score

When compared to 2DE, real-time 3D echocardiography allows for superior visualization of the mitral valve and sub-valvular anatomy. (Figure 2) Specifically, real-time 3D echocardiography allows for better resolution of mitral leaflet thickening and annular calcification and enhanced anatomic detail of chordal thickening and separation.[9] Commissural separation, a key determinate of PBMV success is also better assessed by RT3DE.[10] Finally, leaflet calcification, including distribution of calcium is better visualized with RT3DE. This is important because leaflet calcification is a strong predictor of commissural splitting. The presence of calcification also can help predict adverse outcomes such as embolic stroke or conduction abnormalities.[9]

1. Persistent left atrial or left atrial appendage thrombus
2. Severe mitral regurgitation
3. Massive or bicommissural calcification
4. Severe concomitant aortic valve or severe tricuspid regurgitation or stenosis
5. Severe concomitant coronary artery disease requiring bypass surgery

Adapted from ACC/AHA 2006 Guidelines for the management of valvular heart disease.[17]

Table 3. Contraindications to percutaneous balloon mitral valvuloplasty

Contraindications to PBMV are listed in Table 3. However, with the advancement of technique and imaging, even "unfavorable" candidates are often considered for PBMV as first line treatment in experienced centers. Other patient factors such as age, presence of severe pulmonary hypertension, atrial arrhythmia, history of prior commissurotomy, smaller valve area, presence of mitral regurgitation, NYHA class IV and surgical risk help determine those patients best suited for PBMV.[13],[18],[19]

5. Immediate and late results

The successful splitting of the commissures is the primary determinant of procedural success. A mitral valve gradient that decreases to 50% pre-PBMV gradient and a mitral valve area that

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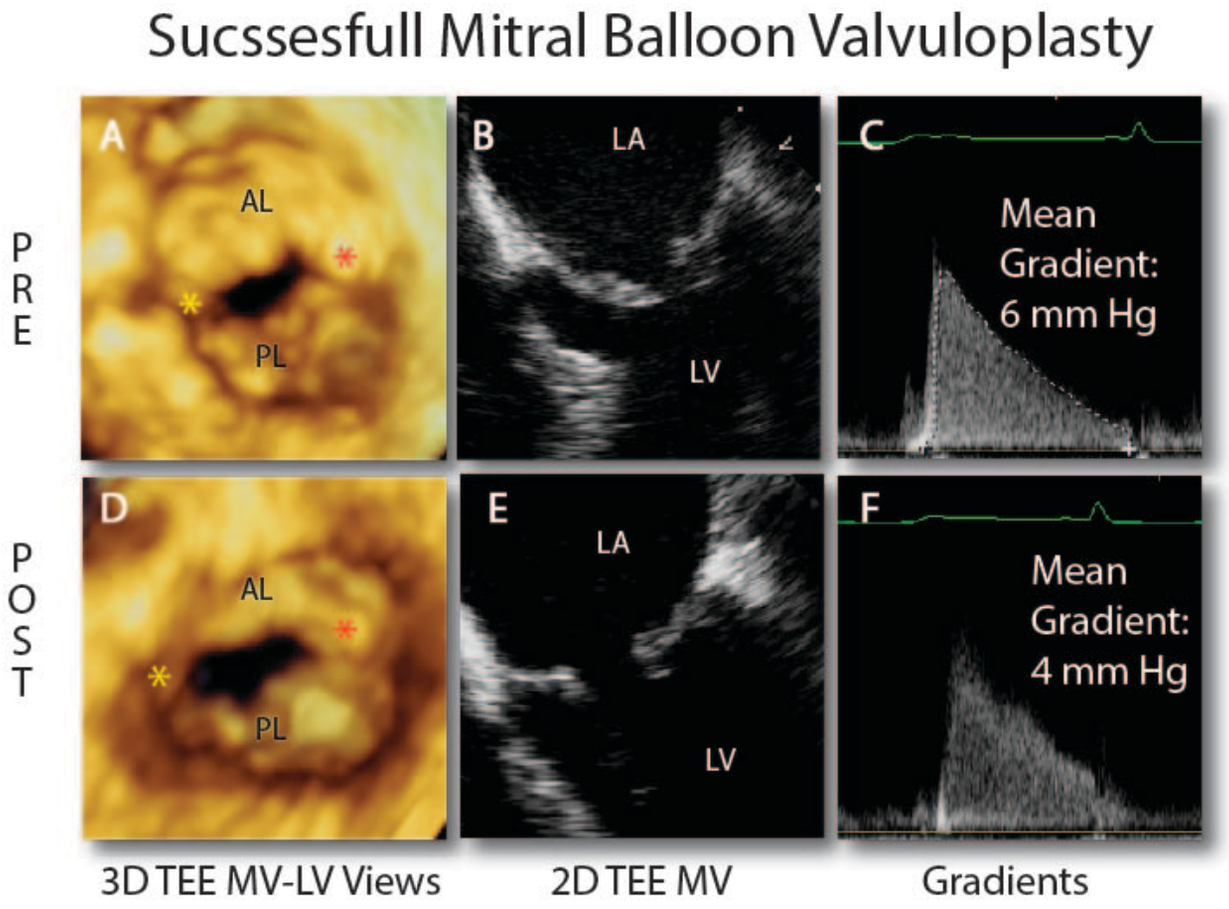
roughly increases by 100% or > 1.5cm² without significant mitral regurgitation are hemodynamic criteria used to gauge success.[20] Other, often unmeasured variables such as exercise capacity, pulmonary pressures, left atrial pressure and cardiac output also increase respectively.

At the time of the procedure), we rely heavily on echo evidence of bicommissural splitting, which is best seen with RT 3D TEE (Figure 6). The reason for this is that patients undergoing PMBV are usually under general anesthesia, or heavily sedated, which dramatically impacts the hemodynamics through the valve. An anatomic endpoint, as opposed to a hemodynamic endpoint, is what is generally used to assess the efficacy of the PMBV.

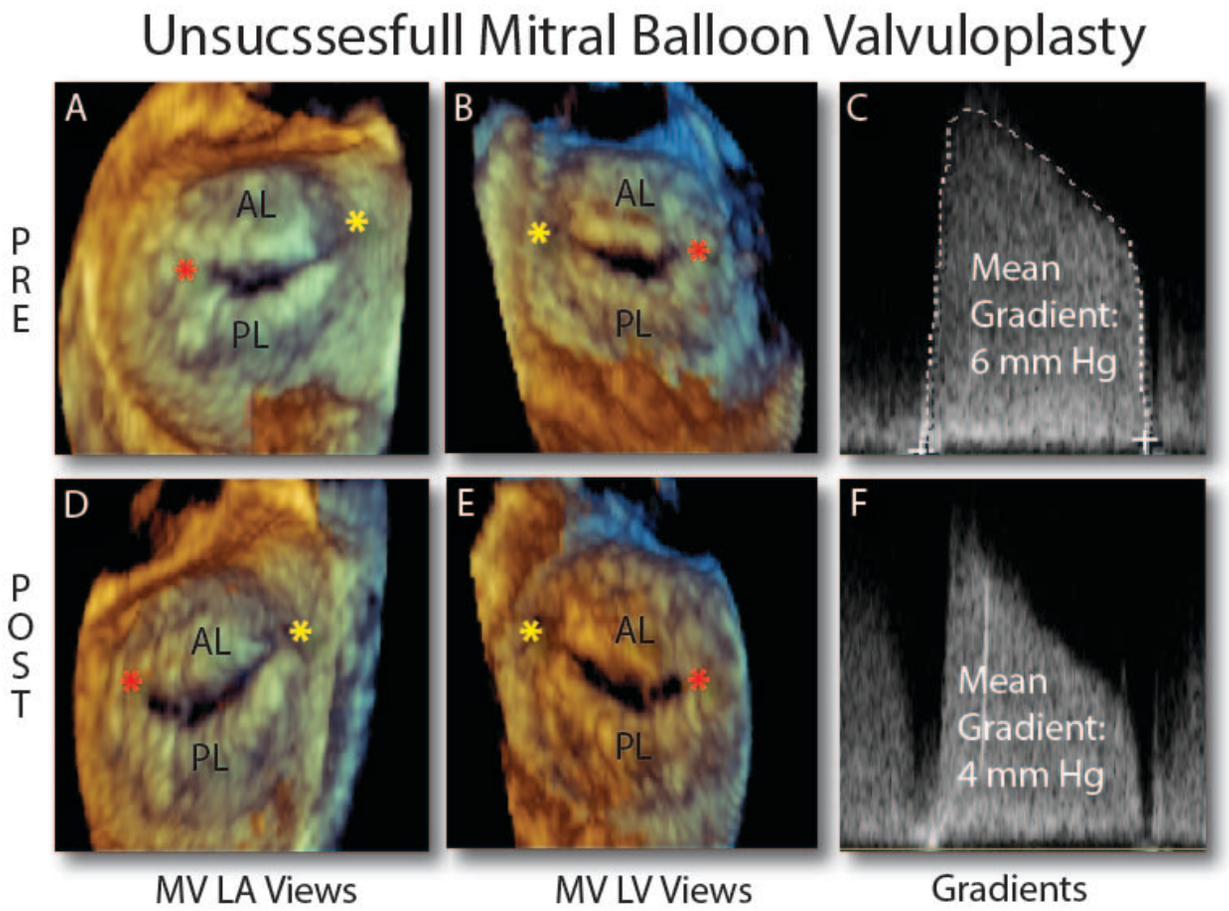


Yellow asterisk: lateral commissure; red asterisk: medial commissure.

Figure 6. Panels A and D depict the mitral valve orifice as seen from the LV. Note the commissural fusion and the small mitral orifice in the pre procedure image (Panel A). In panel D, were the commissures are now split and the arealof the mitral orifice has increased. Panels B and E illustrate the 2D TEE views of the mitral valve pre and post procedure. Note the increased leaflet distance post procedure. Panels C and F illustrate the transmitral Doppler gradients pre and post procedure. The pre-procedure gradients had already diminished under general anesthesia and the post procedure gradients showed only a mild drop despite good bi-commissural splitting. This is not uncommon to see in the immediate post procedure studies and is probably related to decreased left atrial compliance, therefore to gage procedural success; we rely mostly on the 3D visualization of the mitral orifice size and commissural splitting.

Late re-stenosis is defined as a valve area < 1.5cm² or a > 50% decrease of initial increase in valve area post- PBMV.[21] Patients with optimal anatomy (Wilkin's score ≤ 8) have a re-stenosis rate nearly 15% less for the same time frame of those with non-optimal anatomy.[20]

Favorable long-term results are directly correlated to desirable baseline valve anatomy and good immediate results of PBMV.[18] Favorable patients with Wilkin's scores < 8 have less re-stenosis as those with scores > 8.[20],[22] In addition, several clinical factors have been shown to influence late PBMV results: NYHA functional class III-IV, age ≥ 70 years atrial fibrillation, and suboptimal valve morphology after the procedure.[18] Unsuccessful balloon commissurotomy (Figure 7) and incomplete commissural splitting is associated with a higher post-procedure mitral gradient and smaller post-PBMV valve area.



Yellow asterisk: lateral commissure; red asterisk: medial commissure
AL: anterior leaflet; PL: posterior leaflet

Figure 7. Panels A and D depict the mitral valve orifice as seen from the LA. Note the commissural fusion and the small mitral orifice in the pre procedure image. In panel D, post procedure, the commissures are not splitted and the area of the mitral orifice has not increased. Panels B and E illustrate the views of the mitral valve from the left ventricle with similar findings.. Panels C and F illustrate the transmitral Doppler gradients pre and post procedure showing no significant drop in mean transmitral pressures

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Event-free survival; Table 4, has been shown to be as high as 90% in 5 years or longer after the procedure.[23]

Study	(n) patients	Age (yrs)	Follow-up (yrs)	Event –free Survival (%)
Fawzy et al.[24]	520	31	17	31±
Iung et al.[18]	1024	49	10	56±
Palacios et al.[26]	879	55	12	33±
Ben-Farhat et al.[25]	654	34	10	72±
Song et al.[23]	402	44	9	90*
Fawzy [28]	547	31	10	88
Cohen [27]	136	59	5	51*

*Survival without intervention

± Survival without intervention in NYHA I or II

Table 4. Event Free Survival

6. Procedural complications

Rates of success of PBMV can exceed 95% in experienced centers to less than 60% in patients with unfavorable mitral valve anatomy.[20] A direct relationship exists between the experience of the interventional cardiologist performing the procedure and the incidence of procedural complications.[29] Most of the complications of the procedure including, mitral regurgitation, tamponade and a suboptimal improvement in mitral valve gradient are most often related to unfavorable mitral valve anatomy (represented by elevated Wilkin's scores).[7],[12] In contrast, patients with Wilkin's scores < 8 have a low rate of complications (< 2%), less re-stenosis and more than a 90% chance of procedure success.[20]

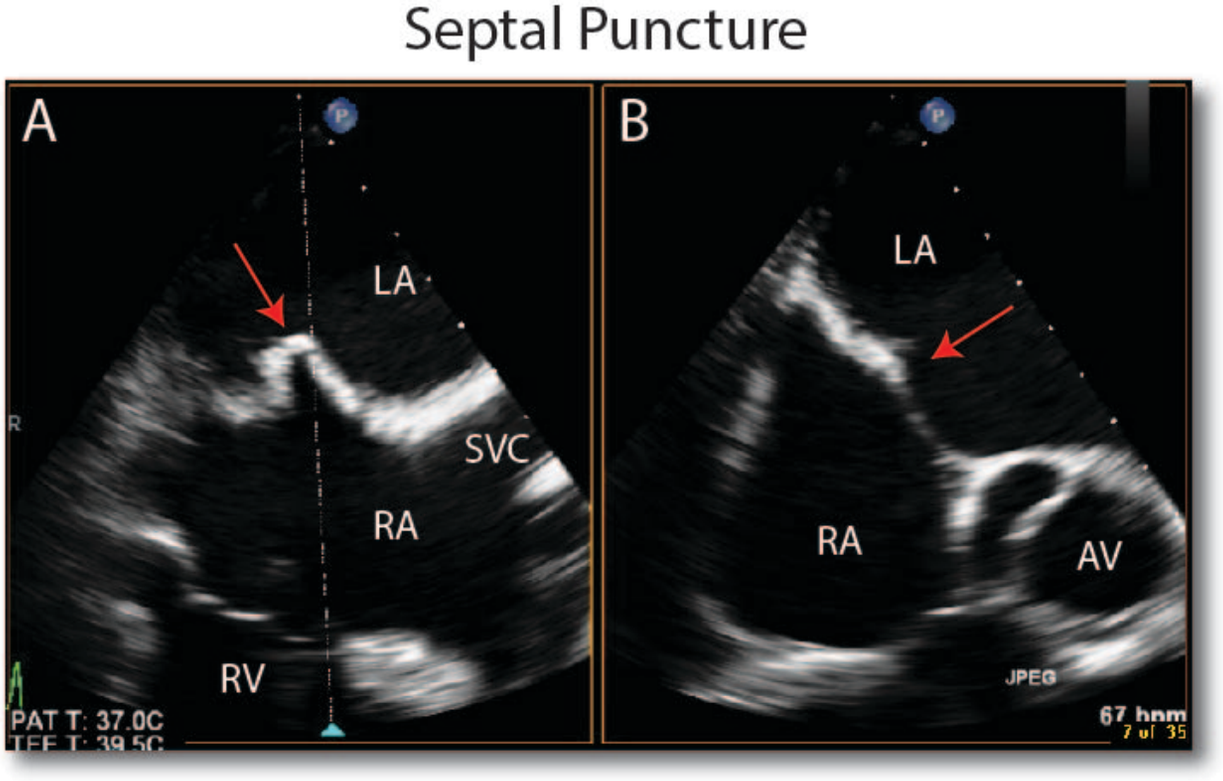
7. Mitral regurgitation

While mild mitral regurgitation is a common outcome following PBMV and is an understandable consequence of commissurotomy, acute severe mitral regurgitation is fortunately a rare complication that develops when the balloon commissurotomy produces a leaflet(s) tear, damages the sub-valvular compartment and/or causes chordae rupture. This may require emergent surgical correction.[19],[27] Severe mitral regurgitation is most often seen in patients with severe orifice narrowing, severely diseased leaflets and significant sub-valvular disease.[20]

The Brockenbrough procedure creates an iatrogenic inter-atrial septal defect, which usually carries no hemodynamic significance. However, hemo-pericardium can occur with perforation of adjacent structures by the Brockenbrough needle with an incidence of 2.0 %.[20] Manipulation of the catheter in the mitral valve position can lead to an unintended perforation of the left atrium, left atrial appendage, pulmonary veins, ventricular wall or apex, or aortic root. These complications can be readily avoided using real-time 3D echocardiography, which can promptly identify a pericardial effusion and help guide catheterization equipment in intracardiac structures.

8. Procedural guidance and assessment of results

Currently, real-time 3D trans-esophageal echocardiography (RT3DTEE) is often used in the catheterization laboratory to guide the various steps involved in performing a PBMV procedure,[30] (Figures 8 and 9) as the guide-wires, catheters and devices used during the procedure may not be readily apparent when using 2D trans-esophageal echocardiography. RT3DTEE,



LA: left atrium; RA: right atrium; SVC: superior vena cava; AV: aortic valve

Figure 8. transeptal puncture is usually the first step in the mitral valve balloon valvuloplasty. Transesophageal echocardiography now plays a central role for guiding this procedure. Simultaneous biplane imaging is the preferred TEE guiding mode. Panel A depicts a bicaval view with the Brockenbrough needle tenting (red arrow) the interatrial septum at the level of the fossa ovalis. In panel B the same is illustrated from an orthogonal view at the level of the aortic valve.

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particularly presented in the x plane format, can effectively visualize the precise location of the tenting of the septum during septal puncture, thereby increasing the safety of this critical step.[31] Moreover, real-time 3DTEE can more accurately assess MVA and mitral regurgitation before and after valvuloplasty, compared to 2DE. RT3DTEE allows for imaging the valve during balloon dilation, "en face" and possibly avoiding leaflet damage by stepwise balloon over-dilatation by visualizing commissural splitting and leaflet tears immediately after balloon dilation.[31] 3D TEE is also useful to help determine whether the balloon is free of the chordal stuctures prior to inflation. RT3DTEE can accurately determine when optimal MVA balloon dilatation has been achieved and the procedure can be successfully completed.

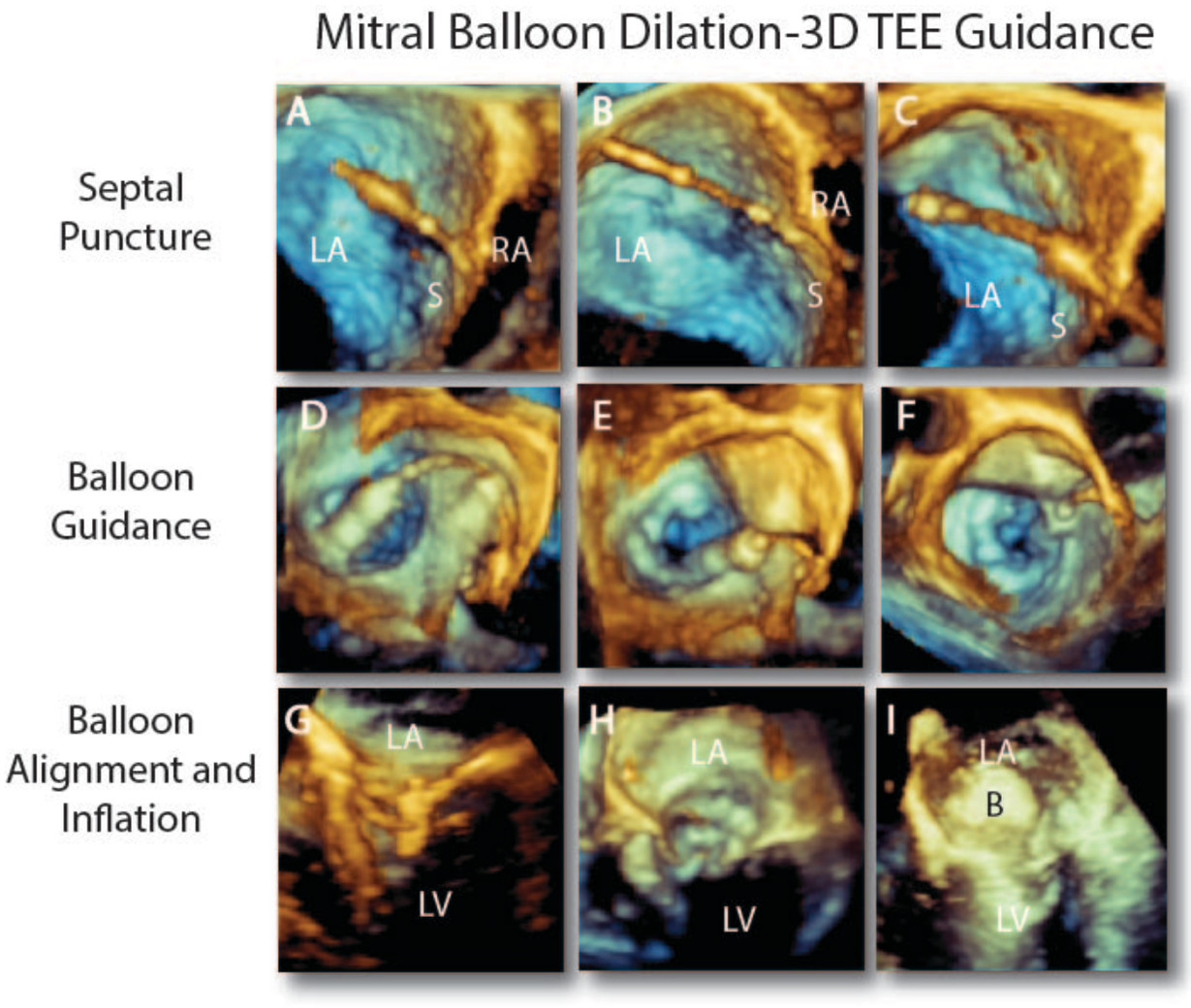

Figure 9. Three D TEE guidance is now commonly used to assist with all the phases of mitral balloon valvuloplasty. In panels A, B and C septal puncture is accomplished and the catheter is advanced through the inter-atrial septum (S) from the right atrium (RA) to the left atrium (LA). In panels D, E and F the balloon is guided to the mitral orifice and finally through the mitral valve into the left ventricle. In panels G and H the balloon is aligned to the long axis of the left ventricle (LV) and in panel I the balloon is inflated.

9. Conclusion

Percutaneous balloon mitral valvuloplasty has become the first line of treatment in individuals with symptomatic rheumatic mitral stenosis.

Echocardiographic imaging plays a pivotal role in both the diagnosis of mitral stenosis as well as the guidance of catheter-based procedures (e.g., PBMV) used in treatment. With the advancement of ultrasound imaging real-time 3D echocardiography supplements current 2D technology and offers an advantage over conventional echocardiography for the evaluation of patients being considered for percutaneous balloon mitral valvuloplasty. With the large number of factors that play a role in determining patients suitability for PBMV as well the risk for poor outcomes, further defining patient anatomy with advanced imaging such as real-time 3D echocardiography should improve both short and long-term outcomes.

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