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REVIEW

Assessment of suitability for percutaneous mitral commissurotomy: a contemporary review of key anatomical criteria and predictive models

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The immediate result of percutaneous balloon mitral commissurotomy is largely determined by the anatomy of the mitral valve complex. Several scores and models have been developed to assess anatomical suitability for percutaneous balloon mitral commissurotomy. Although none has an optimal predictive power, these models look at the valvular apparatus from different perspectives bearing the potential for a complementary role.

Keywords mitral stenosis • balloon valvuloplasty • commissurotomy • echocardiography • anatomy • morphology • scores

Introduction

Rheumatic heart disease (RHD) remains a global burden, especially in low- and middle-income countries.[1,2] In high-income countries, RHD is frequent among some minorities[3] with a further dramatic increase in the incidence observed recently, in the context of increasing immigration from high-risk areas.[4] Currently, 40.5 million cases of RHD are estimated globally with over 306 000 attributable deaths per annum.[1,2]

The mitral valve (MV) is involved in most cases, with associated thickening, fibrosis, and calcification of the valvular complex resulting in progressive commissural fusion ultimately leading to mitral stenosis (MS). Standard treatment of rheumatic MS has gradually shifted from surgical approaches to percutaneous balloon mitral commissurotomy (PMC). *Figure 1* summarizes the natural history of rheumatic MS and the stages at which PMC is useful.

Echocardiographic evaluation of MV anatomy is the foundation of choosing suitable candidates for PMC who are likely to achieve commissural splitting and MV area (MVA) increase to >1.5 cm^2 without developing significant mitral regurgitation (MR). These criteria define 'good immediate result', and each component correlates with long-term clinical outcomes after PMC.[7] Although it is established that PMC is more suited to patients with less severe valvular deformity,[8] contemporary procedures are increasingly performed in candidates with 'unfavourable' clinical and anatomical features resulting in increased complications and reduced success rates.[9,10]

The increasing anatomical complexity of PMC candidates calls for a more refined approach to patient selection to achieve optimal outcomes. Many studies explored the approach to select the anatomy best suited for PMC, but none yielded a model with optimal predictive power.[8,11] In this review, we critically appraise the existing literature and explore ways in which these models can be reconciled for useful clinical application.

Key anatomical factors determining immediate PMC results

Several anatomical aspects of rheumatic MV pathology can influence the result of PMC and the following factors are key.

Leaflet disease

Valvular calcification

Unlike surgical commissurotomy, balloon dilatation may be unsuccessful in splitting a severely fibrotic/calcific commissure. Although less critical in determining the likelihood of commissural split, leaflet body calcification is a strong surrogate for possible commissural calcification,[12,13] which is often obscured on echocardiography. Bouleti *et al.*[14] compared patients with ($n = 314$, 31%) and without ($n = 710$, 69%) fluoroscopic MV calcification undergoing PMC using different techniques. Patients with valve calcification were older with a greater burden of comorbidities and had a smaller MVA and more severe MR at baseline. Good immediate result was more frequent in those without valvular calcification (93% vs. 80%,

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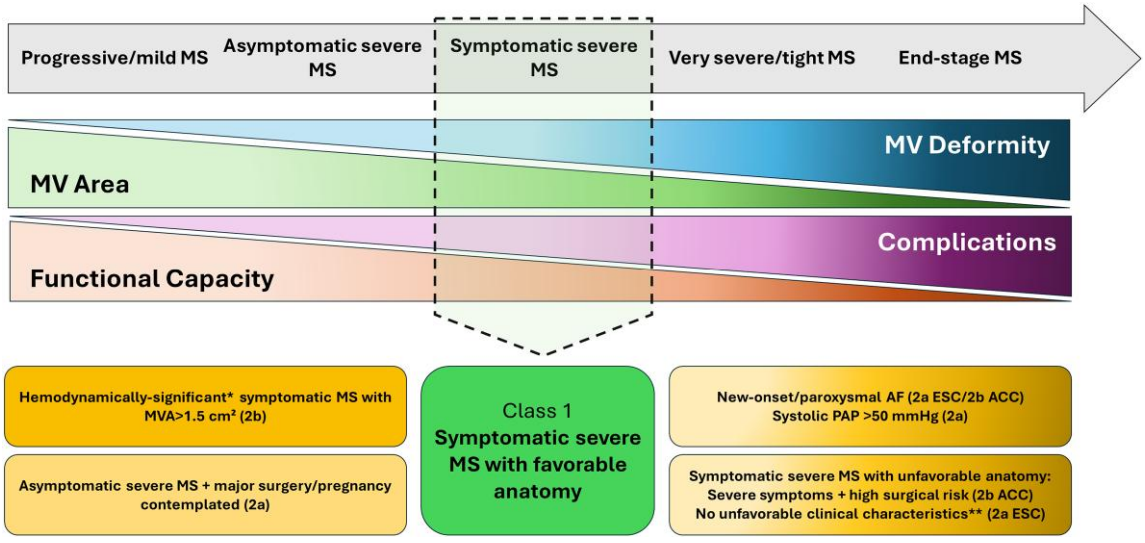

Figure 1 The natural history of rheumatic MS and the stages at which PMC is useful. With disease progression from stage A (at risk of MS) to stage B (mild/progressive MS), valvular/subvalvular thickening, stiffening, amalgamation, and—eventually—calcification ensue. Commissural fusion simultaneously progresses resulting in orifice narrowing. The result is progressive left ventricular inflow obstruction and rise in left atrial (LA) pressure, which portends pulmonary venous congestion. Stages C and D correspond to severe asymptomatic and severe symptomatic MS, respectively. Left untreated, patients with severe symptomatic MS often develop complications, such as atrial fibrillation (AF), thromboembolism, and pulmonary hypertension (PH, leading to progressive right heart remodelling and tricuspid regurgitation, TR). End-stage MS is characterized by severe mitral orifice narrowing, advanced valvular deformity, huge LA dilatation, severe impairment of functional capacity, permanent AF, severe PH and/or right ventricular failure, and torrential TR. PMC is most useful at a sweat spot through this course, when MVA shows moderate–severe narrowing (1.0–1.5 cm^2), valvular/subvalvular pathology is mature (with bicommissural fusion) yet not severely deformed, symptoms have developed but are still mild–moderate, and complications are 'impending'. Before reaching this stage, PMC may be considered in symptomatic patients with MVA >1.5 cm^2 who display a disproportionate rise in transmitral gradient with exercise as well as in asymptomatic patients with MVA ≤1.5 cm^2 planned to undergo a major surgery or pregnancy. PMC can also be useful in patients with MVA ≤1.5 cm^2 in whom complications (e.g. PH or new-onset/paroxysmal AF) have already developed. Also, those with severe valvular deformity and orifice narrowing may still be offered PMC if surgical risk is high and no other clinical markers of poor PMC outcome are present. *Evidence of haemodynamically significant MS includes a pulmonary artery wedge pressure >25 mmHg or a mean MV gradient >15 mmHg during exercise. **Unfavourable clinical characteristics for PMC include old age, history of commissurotomy, New York Heart Association class IV, permanent AF, and severe pulmonary hypertension. The level of recommendation is based on the American (ACC) or the European (ESC) practice guidelines,[5,6] or their agreement.

$P < 0.001$) and increasing severity of calcification (from Grade 1, small, isolated nodule, through Grade 4, extensive deposit) was associated with a smaller final MVA (but not with increased post-procedural MR). In another report from the same group including PMC candidates with fluoroscopic calcification (Grade 1, 53%; Grade 2, 30%; Grade 3, 13%; Grade 4 4%), good PMC results were achieved in 85, 71, 77, and 64%, respectively ($P = 0.008$), and moderate–severe calcification (Grades 2–4) was an independent predictor of poor immediate result (OR: 2.1 [95% CI: 1.3–3.7]).[15]

More recently, Sarmiento *et al.*[16] explored the impact of echocardiographic calcification on outcomes of PMC using the Inoue balloon (Toray Industries, Tokyo, Japan). Calcification defined by the Wilkins score (*Table 1*) was mild (0–1 point) in 25% and moderate–severe (2–4 points) in 75%, and procedural success was achieved in 95.2 and 76.2% of these groups, respectively. Multivariable analysis identified moderate–severe MV calcification as an independent predictor of both poor immediate result and restenosis at 4 years.

Posterior leaflet length (posterior-to-anterior mitral leaflet ratio)

Mahfouz explored the impact of posterior-to-anterior mitral leaflet (PML/AML) length ratio on the outcome of PMC using the Multitrack double balloon (NuMED, Hopkinton, NY) in a young population (31 ± 6 years, $n = 106$) with mild valve deformity (Wilkins score 6.5 ± 1.2). PML/AML length ratio <1/2 was associated with a smaller final MVA and higher rates of new/worsening MR.[17] In a larger series ($n = 262$ Multitrack PMCs, Wilkins score ≤11), the same group found that PML/AML ratio was significantly higher in patients with favourable vs. unfavourable PMC outcome (0.62 ± 0.02 vs. 0.32 ± 0.03, $P < 0.01$).[18]

Commissural disease

Commissural fusion is a pre-requisite for commissurotomy, and the best theoretical mechanistic outcome of PMC is bicommissural splitting of completely fused commissures. To achieve this, symmetrical commissural disease (similar extent of thickening and fusion) with little resistance to dilatation (by fibrosis/calcification) is a hypothetical prerequisite. Indeed, percent gain and final MVA are much higher when both commissures are successfully split than when neither commissure could be split.[19,20] Moreover, 10-year rate of good functional results (survival without the need for mitral surgery or repeat dilation and New York Heart Association functional class ≤II) is significantly higher when both commissures are completely split than when either or both are not split.[20] Conversely, excessive commissural resistance diverting dilatation power to a leaflet body may result in significant tear and associated MR. Evaluation of commissural split is best achieved using 3D

Table 1 The Massachusetts General Hospital (Wilkins) echo score

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

Theoretical total score, 0–16, while a score of at least 2 (minimal thickening and limited mobility) is universal to rheumatic MS. A score of ≤8 indicates anatomical candidacy for PMC; a score of ≥10 indicates low PMC success rate.

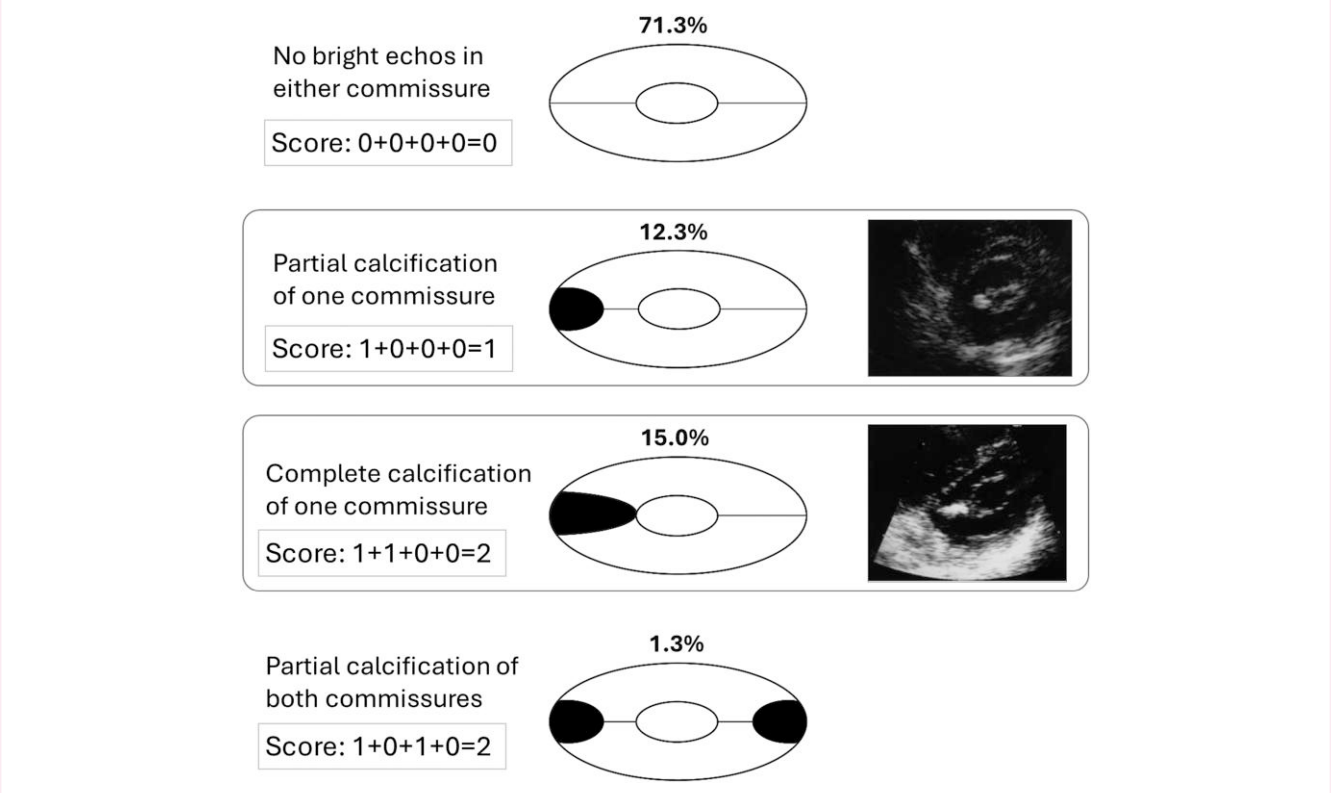

Figure 2 Commissural calcification grading and its frequency in a cohort of 300 PMC candidates.[24] Each half of the anterolateral (AL) and posteromedial (PM) commissures is scored for the presence of bright echos (calcification).

imaging, while 2D imaging underestimates the degree of commissural opening in a third of cases.[21]

Commissural morphology/fusion

In a small cohort of Inoue PMCs ($n = 30$) that assessed mitral commissural morphology for the likelihood of commissural splitting based on symmetry of remodelling and the presence of fibrosis/calcification in the parasternal short-axis (PSAX) view (see Supplementary data online, *Table S1*),[19] a good PMC outcome was achieved in 89% of patients in whom commissural splitting was deemed likely, but in none of the patients in whom it was deemed unlikely. In a larger series ($n = 72$),[22] Sutaria *et al.* utilized transoesophageal echocardiography (TEE) to assign each commissure a score reflecting the likelihood of

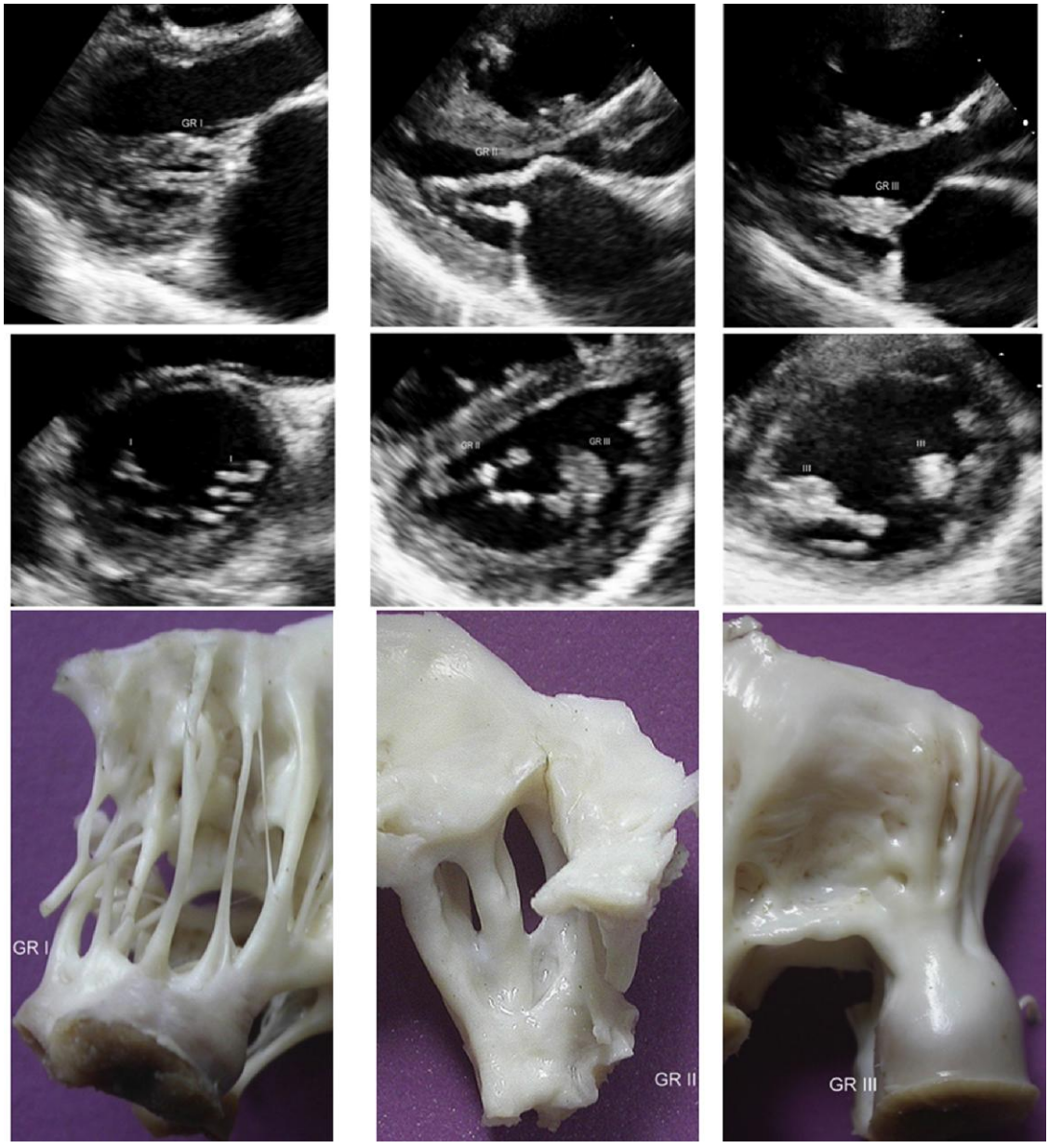

Figure 3 Echocardiographic [parasternal long- (upper panel) and short-axis (middle panel) views] and specimen (lower panel) images showing mild (Grade I), moderate (Grade II), and severe (Grade III) mitral subvalvular disease in left, middle, and right panels, respectively. The middle panel shows moderate (Grade II) disease of the posteromedial chordae and severe (Grade III) disease of the anterolateral chordae. Modified with permission from Bhalgat *et al.*[27]

effective splitting (high score indicating extensively fused, non-calcified commissures—bicommissural split likely, and low scores indicating either minimal fusion or resistant commissural calcification; range 0–4; see Supplementary data online, *Table S2*). A good outcome was achieved in 76% of patients with a commissure score 2–4 vs. 18% of patients with a score 0–1 (positive and negative predictive accuracy, 67 and 82%, respectively). However, the score did not correlate with the development of severe MR. Sancar *et al.*[23] published a report of 50 patients undergoing re-do PMC using the Inoue technique at a median interval of 11 years after initial PMC. Procedural success was achieved in 72%. The authors developed a 3D-TEE score that ranged from 1 (bicommissural fusion with no commissural calcification) to 6 (commissural calcification with no fusion; see Supplementary data online, *Table S3*). Compared with the Wilkins score, the 3D-TEE commissural score yielded a stronger relationship with re-do PMC success (>90% with score ≤3 and equally low for patients with scores 4–6).

Commissural calcification

Calcification of either commissure is present in 21% of all PMC candidates, in 44% of those with a total Wilkins score ≥10, and in 48% of those with Wilkins calcification grade ≥3.[12] In a study by Sutaria *et al.*[24] [$n = 300$, predominantly using the Inoue balloon ($n = 230$)], commissural calcification was assessed on the PSAX view. Each half

Table 2 Scores/models for the prediction of immediate results after percutaneous mitral balloon commissurotomy

Model, year of publication	No. of patients	Age[a]	PMC technique	Success definition	Parameters						
					Leaflets			Commissures		MVA	SVA
					Thickness	Mobility	Calcification	Calcification	Remodelling		
Point-based scores											
1. The MGH (Wilkins *et al.*[34]) echo score	22	57 [21–88]	SB/DB	MVA ≥ 1.0 cm^2, ΔMVA ≥25%, and LAP ≤ 10 mmHg	+	+	+				+
2. The commissural calcium (Reid *et al.*[35]) score	33	43 + 15	DB	MVA ≥1.5 cm^2	+	+		+			+
3. The calcification–subvalvular (Rifaie *et al.*[36]) score	50	36.4 ± 9	DB	MVA ≥ 1.5 cm^2, ΔMVA ≥50%, and ΔMR ≤1 grade			+	+			+
4. Revisited (Nunes *et al.*[32]) echo score	204	57 ± 16	Inoue/DB	MVA ≥ 1.5 cm^2, ΔMVA ≥50%, and ΔMR ≤1 grade		+			+	+	+
5. Real-time 3D echocardiography (Anwar *et al.*[25]) score	74	34.4 ± 5.9	Inoue	MVA ≥ 1.5 cm^2, ΔMVA ≥50%, and MR ≤ moderate	+	+	+				+
6. MR echocardiographic (Padial *et al.*[37]) score	62[b]	54 ± 14	DB/Inoue	Freedom from severe MR (≥3 + angiographic Sellers' grade)	+		+	+			+
Categorical schemes											
1. Nobuyoshi *et al.*'s[38] three-group model	106	53 ± 11	Inoue	Clinical success (symptomatic improvement)		+	+				+
2. Vahanian *et al.*'s[39] three-grade model	200	43 ± 16	SB/DB	MVA ≥ 1.5 cm^2 and MR ≤2+		+	+				+
3. Hung *et al.*'s[40] two-group model	219	43 [19–76]	Inoue	ΔMVA ≥50%			+				+
4. Iung *et al.*'s[28] three-group model	1514	45 ± 15	SB/DB/Inoue	MVA ≥ 1.5 cm^2 and MR ≤2+		+	+				+

+, this score has included this given parameter; DB, double balloon; LAP, left atrial pressure; MGH, Massachusetts General Hospital; MVA, mitral valve area; SB, single balloon; SVA, subvalvular apparatus disease.
[a]In years; mean ± standard deviation [range].
[b]Out of a total cohort of 566 patient, 31 patients with post-procedural severe MR were matched to 31 without severe regurgitation.

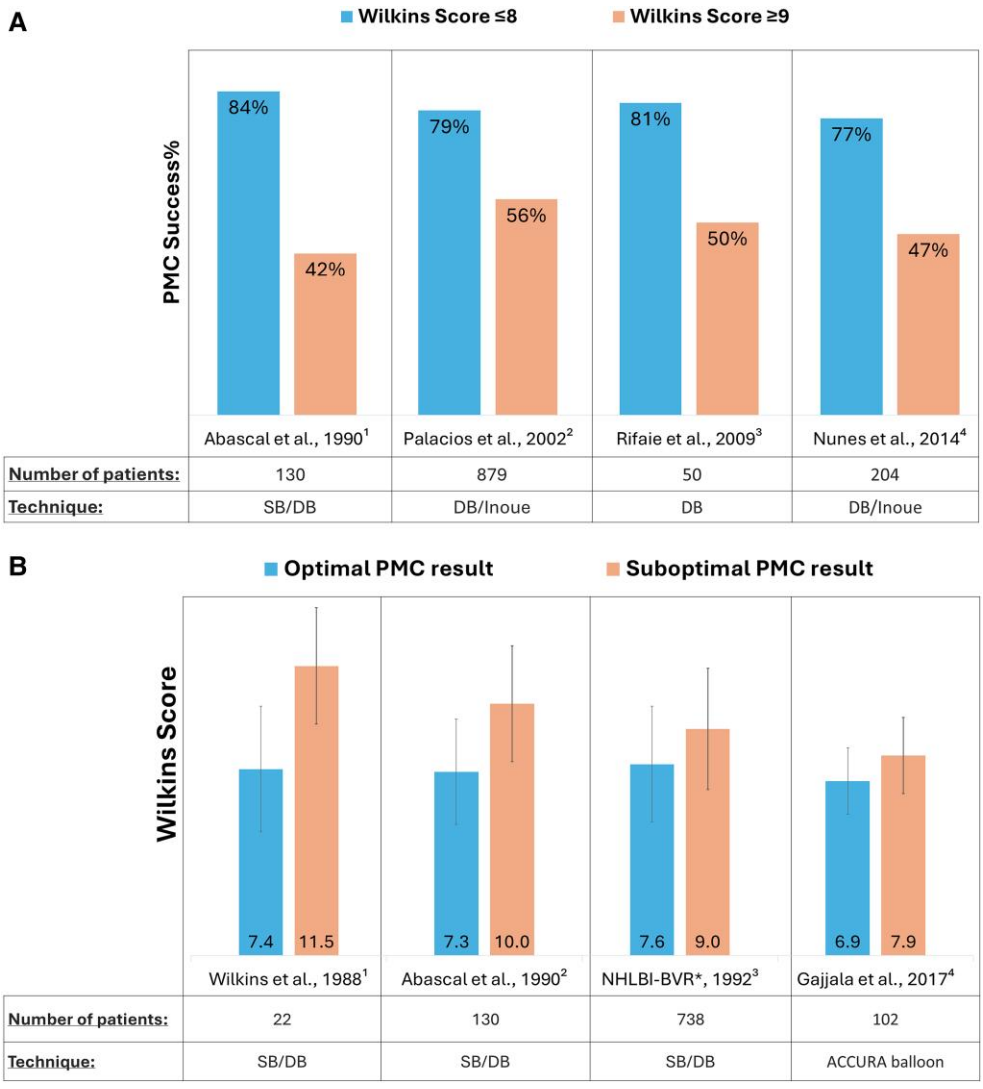

Figure 4 (*A*) PMC success rates in patients with high vs. low Wilkins score. DB, double balloon; SB, single balloon. [1]Successful PMC: final MVA ≥ 1.5 cm^2 + MVA increase ≥25%. [2]Successful PMC: final MVA ≥1.5 cm^2 or ≥50% MVA increase and MR ≤2+. [3]Successful PMC: increase ≥50% of MVA with final MVA ≥1.5 cm^2 and increase of MR severity by ≤1 grade. [4]Successful PMC: increase ≥50% of MVA or final area ≥1.5 cm^2 and ≤1 grade increment in MR. (*B*) Wilkins score (bars and numbers at their base = mean; thin line with whiskers = standard deviation) in patients with optimal vs. suboptimal PMC results. [1]Successful PMC: MVA ≥ 1.0 cm^2 + MVA change ≥25% and mean left atrial pressure (LAP) ≤10 mmHg. [2]Successful PMC: MVA ≥ 1.5 cm^2 + MVA change ≥25%. [3]Successful PMC: MVA ≥1.5 cm^2. [4]MVA > 1.5 cm^2 + MVA change ≥50 with ≤1 grade increment in MR. *National Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry.

commissure (inner and outer halves) with a high-intensity bright echo was given a score of 1 (total commissural calcification score range 0–4; *Figure 2*) and calcification grades 0, 1, 2, and 3 were observed in 214, 37, 45, and 4 patients, respectively. Commissural calcification predicted the achievement of MVA >1.5 cm^2, especially in patients with a Wilkins score ≤8 (67% vs. 46% in commissural calcification 0/1 vs. 2/3).

The study by Dreyfus *et al.*[13] ($n = 464$, Inoue technique) classified the location of valvular calcification (leaflets vs. commissural) and scored the degree of calcification for each commissure as absent, mild, moderate, or severe. Group 1 ($n = 261$) had no leaflet or commissural calcification; Group 2 ($n = 141$) had leaflet calcification with absent/mild commissural calcification; and Group 3 ($n = 62$) had at least one commissure with moderate/severe calcification (54 also had calcification of the leaflet body). The frequency of final MVA ≥1.5 cm^2 (93% vs. 85% vs. 77%), complete opening of at least one commissure (92% vs. 94% vs. 84%), and overall good immediate results (88% vs. 78% vs. 73%) varied significantly between the three groups. Beyond predicting the immediate result of PMC, Cannan *et al.*[12] found that the presence of commissural calcification portends a lower survival and a higher incidence of MV replacement at intermediate term after PMC.

Data concerning the impact of commissural calcification on the development/worsening of MR are conflicting. Commissural calcification (*per se*) could not predict the incidence of MR grade ≥3 in the study by Dreyfus *et al.*[13] Sutaria *et al.* were also unable to document a relationship between commissural calcification (assessed by transthoracic[24] or TEE[22]) and the development of post-procedural MR. On the other hand, the 3D echocardiography study by Anwar *et al.*[25] identified valvular calcification (especially commissural) as the most important

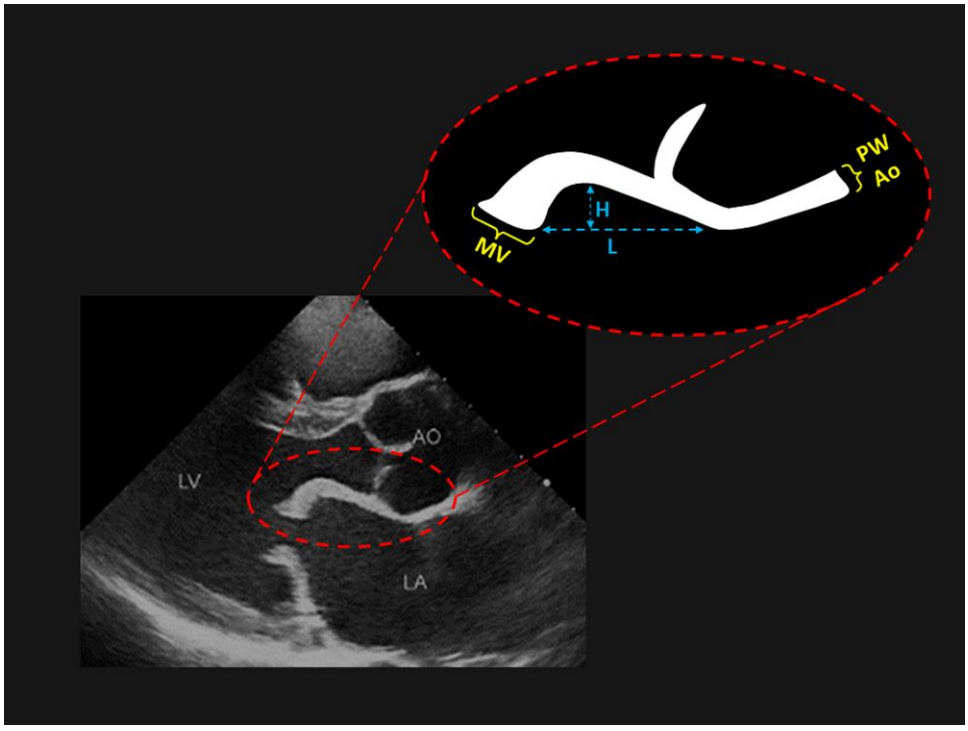

Figure 5 Assessment of AML motion and thickness from parasternal long-axis view (Reid *et al.*[35]). The slope of leaflet motion is calculated as AML doming height (*H*) divided by its length (*L*). AML thickness ratio is calculated as AML tip thickness divided by thickness of posterior aortic wall (PWAo).

predictor of significant post-procedural MR compared with other valvular/subvalvular characteristics.

Subvalvular apparatus disease

Based on theoretical assumptions and clinical observations, deformity of the subvalvular apparatus (SVA; amalgamation and contracture) is a strong predictor of PMC outcome.[8,11] In an early report of 38 patients by Chen *et al.*,[26] a final MVA >1.5 cm^2 was achieved in only 1/4 patients with grade IV subvalvular disease (extensive thickening with no apparent chordal separation) and in 33/34 patients with less severe subvalvular abnormalities. On multivariable analysis, subvalvular disease was independently related to final MVA and increasing MR. Age correlated significantly with MV calcification and thickening, but not with subvalvular disease. In a more recent larger report by Bhalgat *et al.*[27] ($n = 356$ patients, Inoue technique), the two SVAs (anterolateral and posteromedial) were assessed individually, and severe pathology was defined as fused chordae appearing as a single, thick chord below the commissure. The SVA score was I, II, or III, if neither, one, or both SVAs had severe disease, respectively (*Figure 3*). The SVA score was III in 41/43 patients with failed PMC (29 with severe MR) and in all 14 patients with inadequate dilatation.

Pre-procedural MVA

A smaller pre-procedural MVA has been identified as an independent predictor of the immediate result of PMC using different techniques and in different patient cohorts.[28–32] The relationship with PMC result was consistent when baseline MVA was represented as a categorical (≥1.25, 1.25–1.00, 1.00–0.75, and ≤0.75 cm^2),[28] a binary (MVA above vs. below 1.0 cm^2),[30,32] or a continuous parameter.[32]

Notably, across the spectrum of valve deformity [from mild deformity (Wilkins score ≤8) to significant valvular calcification], baseline MVA remained an independent predictor of PMC outcome.[14,33]

Multiparametric models involving different valve components

Several anatomical models and scores have combined different parameters of valvular and subvalvular anatomy to predict PMC outcome. *Table 2* groups these models according to their concept and summarizes their component parameters and the characteristics of their derivation/validation cohorts.

Point-based scores

The Massachusetts General Hospital (Wilkins) echo score

In 1988, Wilkins *et al.*[34] published outcomes of the first 22 patients undergoing PMC at the Massachusetts General Hospital, Boston, 11 of whom experienced a suboptimal result. Analysis of leaflet mobility, valvular and subvalvular thickening, and leaflet calcification (each graded from 0 to 4, *Table 1*) yielded an echocardiographic score ranging from 0 to 16 [a score of at least 2 (minimal thickening and limited mobility) universal to rheumatic MS]. The mean total echocardiographic score was 9.4 ± 3.1, significantly lower in those with an optimal result (7.4 ± 2.5, range 4–11 vs. 11.5 ± 2.3, range 9–16; $P < 0.001$]. Among 18 clinical, echocardiographic, and haemodynamic variables, the Wilkins score was the best predictor of immediate PMC outcome.[34] In a separate report (also published in 1988), the same group concluded that their score could not predict an increase in MR after PMC.[41]

The larger-scale validation published by the same group in 1990 represents the foundation evidence underpinning the Wilkins

Table 3 University of Southern California commissural calcium score (Reid et al.[35])

Morphologic feature	Definition	Score[a]
Leaflet restriction	H/L ratio	
Mild	≥0.45	0
Moderate	0.26–0.44	1
Severe	<0.25	2
Leaflet thickening	MV/PWAo ratio	
Mild	1.5–2.0	0
Moderate	2.1–4.9	1
Severe	≥5.0	2
Subvalvular disease		
Absent–mild	Thin, faintly visible chordae	0
Moderate	Areas of increased density equal to endocardium	1
Severe	Thickened chordae with areas denser than endocardium	2
Commissural calcification		
Absent	Homogenous density of MV	0
Unicommissural	Increased density of either AL or PM commissure	1
Bicommissural	Increased density of both AL and PM commissures	2

H, height of doming of mitral valve; L, length of dome of mitral valve; MV, mitral valve; PWAo, posterior wall of aorta.
[a]A combined leaflet restriction/thickening score >2 indicates low PMC success rate.

Table 4 Calcification–subvalvular score (Rifaie et al.[36])

	Score[a]
Leaflet/commissural calcification	
No calcification	0
Mild leaflet calcification (localized to leaflet margins)	2
Extensive leaflet calcification (extending to leaflet bodies, sparing commissures)	4
Uni/bicommissural calcification	6
Subvalvular disease	
No subvalvular involvement	0
Mild thickening (<half of chordal length)	2
Moderate thickening (≥half of chordal length)	4
Severe thickening (whole chordae and papillary muscle)	6
Total score	0–12

[a]A score of >4 predicts poor outcome.

score.[42] This study included 130 patients who underwent the procedure between 1985 and 1988 using single- ($n = 28$) or double-balloon technique ($n = 102$), with a score of 7.3 ± 2.1 in those with a good result (MVA increased by ≥25% to ≥1.5 cm^2) vs. 10.0 ± 2.3 in those with a suboptimal result ($P < 0.0001$). A score of 8 conferred the optimal combination of sensitivity and specificity [sensitivity 72%, specificity 73%, positive predictive value (PPV) 84%, and negative predictive value (NPV) 58%]. Among 73 patients with a score ≤8, 84% had a good result, whereas a suboptimal outcome was observed in 58% of 57 patients with a score ≥9. Correlation of the change in MVA with total score was weak ($r = -0.40$) with substantial data scatter, with a stronger correlation with valvular thickening alone ($r = -0.47$).

A larger-scale validation from the National Heart, Lung, and Blood Institute Balloon Valvuloplasty Registry including 738 patients was published in 1992.[43] Patients with a lower score (≤8) had slightly greater increase in MVA (1.0 ± 0.7 vs. $0.85 + 0.6$ cm^2, $P = 0.004$), and regression analysis identified the echo score as an independent predictor of a final MVA > 1.5 cm^2.

Evidence of validity of this score in PMC using the Inoue technique has been less consistent. In the initial US experience,[44,45] no correlation was observed between the Wilkins score and MVA gain. However, a later report from the North American Multicenter Inoue Registry[46] demonstrated that patients with severe valvular/subvalvular deformity (Wilkins score ≥10, mean score 11.7 ± 1.5) had a lower final MVA (1.5 ± 0.5 cm^2) and lower likelihood of optimal outcome (64%) than observed in the entire cohort (1.8 ± 0.6 cm^2 and 74%, respectively). Out of this cohort with severe valve disease, 31% required MV replacement or re-do PMC and 13% died at 23 ± 11 months, suggesting adverse long-term outcomes.

In a large series involving different PMC techniques (double-balloon, $n = 695$; Inoue, $n = 237$),[29] patients with a score ≥9 ($n = 278$) were older, more symptomatic with more comorbidities and a higher grade of MR at baseline. Procedural success rates (90–29%) and final MVA (2.2–1.4 cm^2) were progressively lower in patients with increasing Wilkins score, and a score ≥9 was an independent predictor of procedural failure.

In a contemporary cohort,[32] PMC was successful in 77% of those with a Wilkins score ≤8 vs. 47% of those with a higher score and unsuccessful in all 7 patients with a very high score (≥12).

In summary, the Wilkins score was generated from a small series but underwent subsequent extensive validation, demonstrating undisputed predictive value for both early and late PMC outcomes but considerable overlap between those with and without good immediate results. Many patients with a high score still undergo successful PMC, but long-term outcome remains impaired (*Figure 4*).

The University of Southern California commissural calcium (Reid) score

Based upon their initial double-balloon PMC experience, Reid *et al.*[35] constructed a score comprising AML motion and thickness (*Figure 5*), chordal thickness, and commissural calcification (*Table 3*). While severe leaflet motion restriction and/or severe thickening were determinants of final MVA, the extent of subvalvular disease and commissural calcification were not. Classified by a combined score for leaflet motion and thickness (each scored 0–2), a final MVA ≥1.5 cm^2 was achieved in 96% of patients with a score of 0–2 but in only 29% with a score of 3–4. Leaflet motion was the most decisive echocardiographic parameter in multivariable analysis.

The calcification–subvalvular (Rifaie) score

In a series of 50 relatively young patients undergoing double-balloon PMC at Ain Shams University, Cairo, Egypt,[36] the total Wilkins score (as well as mobility and thickening grades) did not differ in patients with optimal vs. suboptimal outcome. Nevertheless, calcification and subvalve disease grades were significantly higher in patients with a suboptimal result. A model comprising leaflet/commissural calcification (score 0, 2, 4, or 6) and subvalvular disease (score 0, 2, 4, or 6;

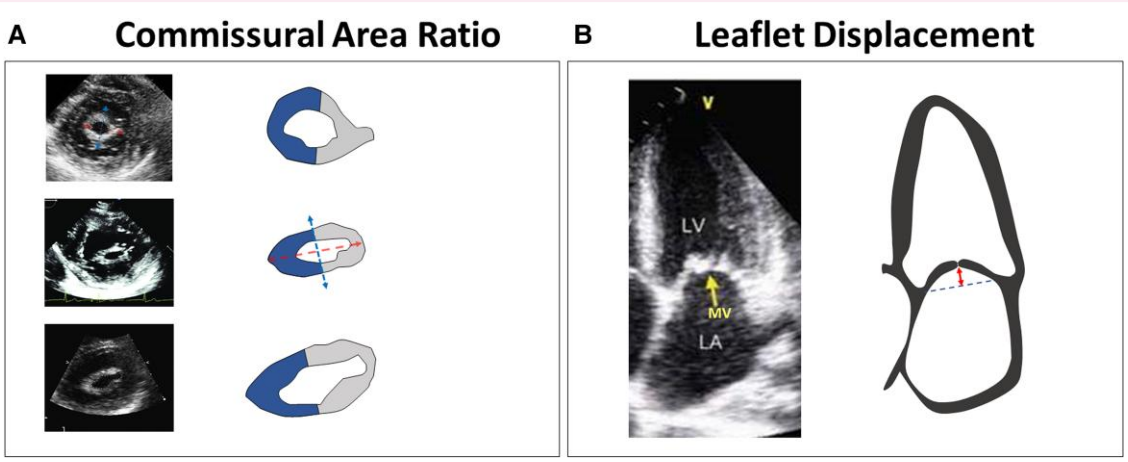

Figure 6 Commissural area ratio and leaflet displacement components of the revisited echo score (Nunes *et al.*[32]). (*A*) The commissural area ratio is measured from the PSAX view by tracing the inner and ventricular (outer) margins of the leaflets and the area between the two tracings divided by a vertical line (dashed vertical double-head arrow) at the midpoint of the transverse diameter of the outer tracing (dashed transverse double-head arrow). The commissural area ratio is the ratio between the leaflet areas on either side of this vertical line. (*B*) Apical displacement (doming height) of the leaflets (diastolic apical four-chamber view) from the mitral annulus to the midpoint between MV leaflet tips.

Table 5 The revisited echo score (Nunes *et al.*[32])

Echocardiographic variables	Prevalence (%)	OR[a]	Score points
MVA ≤ 1 cm^2	36	2.73	2
Maximum leaflet displacement ≤12 mm	35	3.40	3
Commissural area ratio ≥1.25	37	3.10	3
Subvalvular extensive thickening	18	3.23	3

Risk groups for PMC outcome: low (score 0–3), intermediate (score 5), and high (score 6–11). Scores of 1, 4, 7, and 10 are not possible.
[a]Odds ratio of inadequate PMC result.

Table 6 RT3DE score (Anwar *et al.*[25])

	Leaflets					
	Anterior leaflet			Posterior leaflet		
	A1	A2	A3	P1	P2	P3
Thickness (0–6)	0–1	0–1	0–1	0–1	0–1	0–1
Mobility (0–6)	0–1	0–1	0–1	0–1	0–1	0–1
Calcification[a] (0–10)	0–2	0–1	0–2	0–2	0–1	0–2

	Subvalvular apparatus		
	Proximal third	Middle third	Distal third
Thickness (0–3)	0–1	0–1	0–1
Separation[b] (0–6)	0–1–2	0–1–2	0–1–2

Total score: 0–31 points; mild MV involvement defined as <8 points, moderate involvement as 8–13 points, and severe MV involvement as ≥14 points.
[a]A higher weight given to commissural/juxta-commissural calcification.
[b]Normal separation = distance >5 mm (0); partial separation = distance <5 mm (1); and absence of separation (2).

Table 4) was associated with suboptimal result independent of the total Wilkins score and other clinical factors. At a cut-off value of >4, this score outperformed the Wilkins score (≥9) in predicting suboptimal result (sensitivity 87% vs. 60%; specificity 83% vs. 74%; PPV 68% vs. 50%; NPV 94% vs. 81%). Furthermore, an optimal outcome was achieved in 81% vs. 50% of patients with low vs. high Wilkins score and in 97% vs. 26% of patients with low vs. high calcification–subvalvular score.

The revisited (Nunes) echo score

Nunes *et al.*'s[32] study included derivation and validation cohorts of patients undergoing PMC to develop a model that predicts immediate and long-term outcomes. In the derivation cohort ($n = 204$, performed at the Massachusetts General Hospital 2000–2011), the Wilkins score was intermediate–high in 39% and PMC unsuccessful in 38%. Multivariable analysis identified baseline MVA, the maximal leaflet excursion from the annulus in diastole (doming height), commissural area ratio (a metric of asymmetrical remodelling; *Figure 6*), and subvalvular thickening as the most significant predictors of PMC result. A point-based score including these four parameters (*Table 5*) yielded three groups: low (score 0–3), intermediate (score 5), and high (score 6–11), with suboptimal outcomes in 16.9, 56.3, and 73.8%, respectively. The new score significantly improved reclassification of subjects with unfavourable PMC results, with a net reclassification improvement of 45.2% in comparison with the Wilkins score [even higher (76.8%) in patients with intermediate Wilkins score (9–11)].

In a younger validation cohort ($n = 121$), baseline MVA was smaller but with less severe valve deformity. The total Wilkins score did not predict immediate PMC outcome, while the new score classified 102 patients as low risk, 11 as intermediate risk, and 8 as high risk, with suboptimal PMC outcome in 11.8, 72.7, and 87.5%, respectively.

Commissural area ratio (OR 1.23 [1.07–1.41] per 10% increment) and subvalvular thickening (OR 2.71 [1.31–5.58]) were significant

Table 7 The echocardiographic MR score (Padial et al.[37])

Variable	Score
I. AML thickening	
Even, near-normal thickness (4–5 mm) or only one thick segment	1
Even fibrosis/calcification (no thin segments)	2
Uneven fibrosis/calcification (thinner segments >5 mm thick)	3
Uneven fibrosis/calcification (thinner segments ≤5 mm thick)	4
II. PML thickening	
Even, near-normal thickness (4–5 mm) or only thick segment	1
Even fibrosis/calcification (no thin segments)	2
Uneven fibrosis/calcification (thinner segments >5 mm thick)	3
Uneven fibrosis/calcification (thinner segments ≤5 mm thick)	4
III. Commissural calcification	
Unicommissural mild fibrosis/calcification	1
Bicommissural mild fibrosis/calcification	2
Bicommissural calcification, one mildly diseased	3
Bicommissural calcification, both markedly diseased	4
IV. Subvalvular disease	
Chordal thickening, just below the valve	1
Chordal thickening, affecting one-third of chordal length	2
Chordal thickening, affecting two-thirds of chordal length	3
Chordal thickening, affecting the entire chordal length	4
Total	Maximum, 16[a]

AML, anterior mitral leaflet; PML, posterior mitral leaflet.
[a]A cut-off value of ≥10 provided the highest predictive value for severe MR.

predictors of post-procedural increase in MR, while the Wilkins score was not. In another study enrolling 344 patients (Wilkins score ≤10, Inoue technique),[7] significant MR developed in 19% (severe 6.7%, moderate 11.9%). The revisited echo score was a predictor of significant MR, albeit with poor discrimination (C-statistic 0.60; 95% CI 0.51–0.68), while the Wilkins score was not.

Real-time 3D echocardiography (Anwar) score

In 2010, Anwar *et al.*[25] generated a real-time 3D echocardiography (RT3DE) score in 17 patients and validated the score in 74 consecutive young patients (Wilkins score ≤9) undergoing PMC at Al-Hussein University Hospital, Al-Azhar University (Cairo, Egypt). Leaflet scallops were scored for thickness, mobility, and calcification, with higher weight given to commissural/juxta-commissural calcification, while the three levels of the SVA were scored for thickening and separation (*Table 6*). The RT3DE score correlated with 2D assessment (Wilkins score) of leaflet thickening and calcification, but not leaflet mobility or subvalvular disease. Interobserver agreement of the Wilkins score was fair for leaflet thickness and mobility, but poor for calcification and subvalvular disease. As for the RT3DE score, reproducibility was excellent for chordal splitting ($k = 0.95$), good for leaflet thickness and mobility ($k = 0.66$ and 0.63, respectively), fair for calcification ($k = 0.42$), and weak for chordal thickening ($k = 0.21$). Among score parameters, calcification and subvalvular thickness were independent predictors of PMC success, and calcification predicted the development of >grade 2 MR. Finally, the power of the RT3DE score (cut-off >13) to predict PMC success was marginally higher than that of the Wilkins score (cut-off >8; C-statistic 0.87 vs. 0.80).

An acquisition protocol was suggested to optimize the score's yield,[47] entailing multibeat acquisition for better images, zoom 3D images from parasternal or apical views to enable adequate leaflet scoring, and full-volume 3D apical images (especially in a three-chamber view) to evaluate the chordae throughout their length.

Dedicated MR prediction (Padial) scores

Padial *et al.*[37] published a predictive model of MR (the MR echo score) in 1996 based on surgical data from patients with severe MR post-PMC at the Massachusetts General Hospital (*Table 7*). The score addresses the degree and (even or uneven) distribution of thickening and calcification of each of the leaflets, commissural fibrosis/calcification, and subvalvular disease. A valve with severe subvalvular thickening, severe bicommissural calcification, and heterogeneous thickening of both leaflets was being assigned the maximum score of 16. PMC was performed using the double-balloon technique in all but 2 patients and 37 (6.5%) developed severe MR. Compared with matched patients, those who developed severe MR had a similar Wilkins score but significantly higher MR score [independent of age, MVA, MR before PMC, and effective balloon dilating area (corrected for body surface area)]. A cut-off value ≥10 provided the highest predictive power (sensitivity 87 ± 5%, specificity 74 ± 7%, PPV 77 ± 7%, and NPV 85 ± 5%). The same group published a validation of this score in 1999 in a cohort undergoing Inoue technique, where 14/117 patients (11.9%) developed severe MR.[48] Total score (and individual components) was higher in those who developed severe MR, and the score independently predicted the development of severe MR at a cut-off value ≥10 (sensitivity 82%, specificity 91%, and NPV 97%).

Categorical schemes

Nobuyoshi *et al.*[38] graded leaflet restriction and calcification and subvalvular disease as mild, moderate, or severe and used these parameters to categorize patients into three groups (*Table 8*). Group 3 (rigid or generalized valve calcification with fused SVA) derived the least symptomatic benefit and MVA gain with a higher rate of post-procedural severe MR (20% vs. 3% in Group 1).[38]

Vahanian *et al.*[39] classified patients according to suitability for surgical commissurotomy based upon valve calcification, AML pliability, and degree of chordal shortening (length <1 cm = significant subvalvular disease) into three grades with increasing valvular/subvalvular deformity (Grade 1 = ideal for commissurotomy, Grade 3 = unsuitable for commissurotomy; *Table 8*). Multivariable analysis identified the echocardiographic grade as the factor most predictive of immediate PMC result.

Similarly, Hung *et al.*[40] classified patients into two groups according to valve calcification and severity of subvalvular disease (*Table 8*). Group 2 (calcified valves and/or severe subvalvular disease) showed a smaller MVA gain while multivariable analysis identified a Wilkins score ≥9, valve calcification, and severe subvalvular disease as independent predictors of MVA gain <50%. The frequency of increased MR (by >1 grade) was 9% in Group 1 vs. 14% in Group 2 ($P < 0.001$).

In a large series ($n = 1514$), Iung *et al.*[28] classified valvular/subvalvular disease (assessed using echocardiography and fluoroscopy) to predict suboptimal PMC results (*Table 8*). Groups 2 (severe subvalvular disease) and 3 (calcified valves) had a higher risk of suboptimal

Table 8 Multiparameter categorical schemes for the prediction of PMC immediate result

Study	Number (technique)	Age (years)	Class	Definition	Success rate (%)	Final MVA (cm^2)
Nobuyoshi *et al.*[38a]	106 (Inoue)	53 ± 11	Group 1 ($n = 37$)	Pliable, non-calcified valve, free of subvalvular lesion	97	2.14 ± 0.52
			Group 2 ($n = 59$)	Semi-pliable, locally calcified valve, with subvalvular shortening/thickening	93	1.95 ± 0.44
			Group 3 ($n = 10$)	Rigidity or generalized calcification of the valve with subvalvular fusion	60	1.56 ± 0.66
Vahanian *et al.*[39b]	200 (SB/DB)	43 ± 16	Grade 1 ($n = 58$)	Flexible leaflets and mild subvalvular disease	98	
			Grade 2 ($n = 75$)	Flexible leaflets but extensive subvalvular disease	91	
			Grade 3 ($n = 67$)	Valvular calcifications detected by echocardiography and confirmed by fluoroscopy	67	
Hung *et al.*[40]	219 (Inoue)	43	Group 1 ($n = 139$)	Pliable, non-calcified leaflets with mild subvalvular disease		2.1 ± 0.8
			Group ($n = 80$)	Calcified leaflets, severe subvalvular disease, or both		1.8 ± 0.5
Iung *et al.*[28c]	1514 (SB/DB/ Inoue)	45 ± 15	Group 1	Pliable non-calcified anterior mitral leaflet and mild subvalvular disease (thin chordae ≥10 mm long)	97.8	
			Group 2	Pliable non-calcified anterior mitral leaflet and severe subvalvular disease (thickened chordae <10 mm long)	92.6	
			Group 3	Calcification of mitral valve of any extent, as assessed by fluoroscopy, whatever the state of the subvalvular apparatus	77.7	

DB, double balloon; MVA, mitral valve area; SB, single balloon.
[a]Clinical success defined as significant symptomatic improvement based on NYHA classification.
[b]Good immediate result defined as final MVA >1.5 cm^2 without MR >2+.
[c]Good immediate result defined as an MVA ≥1.5 cm^2 with MR Sellers' grade ≤2.

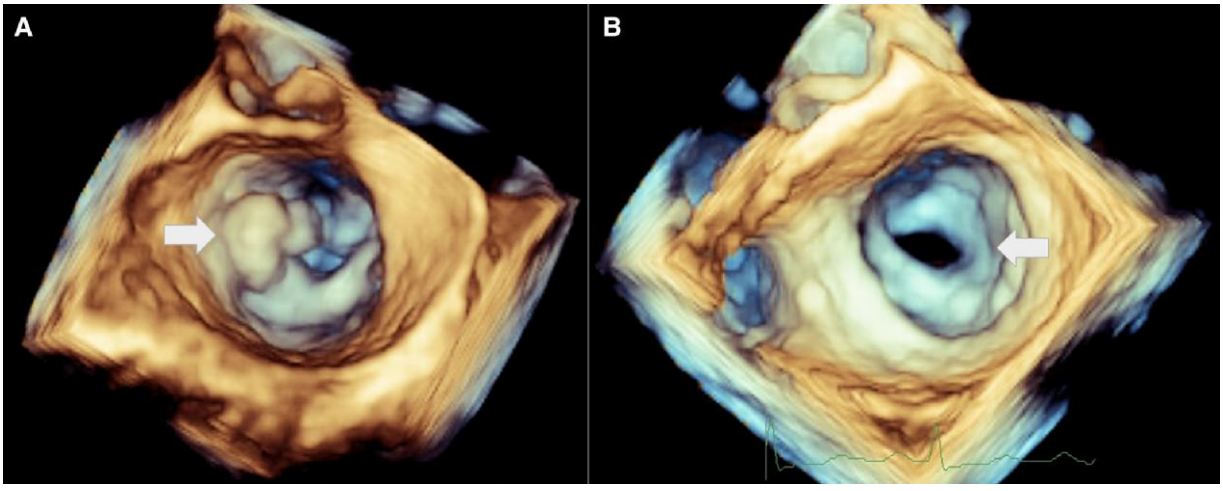

Figure 7 Commissural thickening and calcification in rheumatic MS demonstrated using 3D-TEE with zoomed view of the MV. (*A*) High-resolution image with clear visualization of anterolateral commissural calcification. (*B*) Posteromedial commissural thickening (arrow) with asymmetric commissural involvement.

result (OR [95% CI]: 2.3 [2.5–3.5] and 5.3 [2.3–12.4], respectively), while the three-group model showed 92% sensitivity, 25% specificity, and 87% predictive accuracy (C-statistic 0.72). Despite low specificity, several studies have confirmed its predictive value, and this model (often called the 'Cormier score') is widely used in clinical practice.[49]

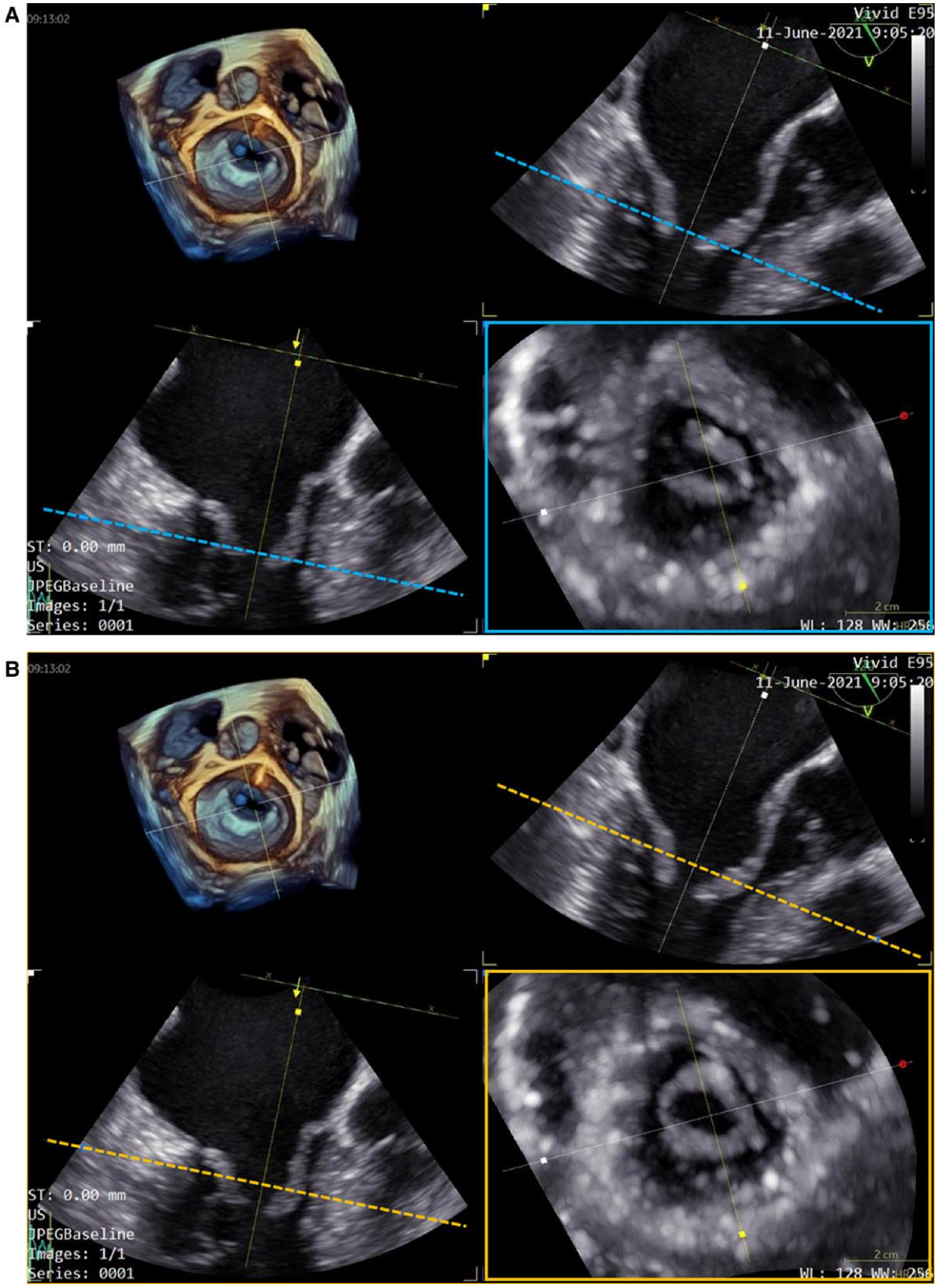

Figure 8 Mitral restenosis 8 years after prior commissurotomy. (*A*) Multiplanar reconstruction of 3D data set enables cutting at both leaflet tips and accurate measurement of orifice area to reveal fused posteromedial and split anterolateral commissures. (*B*) Cropping at a higher (atrial) level reveals that the anterolateral commissure is partially fused, suggesting that re-do commissurotomy is feasible.

Critical appraisal and reconciliation

There is unequivocal evidence that PMC success is multifactorial and dependent upon anatomical and clinical determinants.[30] Assessment of anatomical suitability is challenging given the complexity of rheumatic MV pathology involving different components of the valvular/subvalvular complex.

Leaflet thickening, restriction, and calcification; commissural remodelling/fusion pattern and calcification; subvalvular thickening, fusion, and contracture; and baseline MVA are the major factors previously investigated. In several predictive models and subsequent validations,[14–16,26–28,35,36,38,39] valvular calcification (defined by echocardiography and/or fluoroscopy) and subvalvular disease have been consistent predictors of PMC outcomes (*Table 2*). However, 2D echocardiography has significant interobserver variability and may underestimate the severity of both, while 3D imaging may be superior.[25,50] Compared with leaflet body calcification, commissural calcification may directly interfere with adequate commissural split and outperforms leaflet body calcification in predicting immediate PMC result.[13] Again, 3D evaluation of commissural calcification improves its predictive yield, especially regarding the development of MR.[25] Further advantages of modern 3D echocardiography include the improved visualization of valvular orifice and commissural morphology, a more reliable evaluation of the valve area,[51] and the degree of commissural opening[21] (*Figures 7* and *8*; Supplementary data online, *Videos S1* and *S2*).

Several point-based scores integrate different combinations of these factors to improve the prediction of procedural outcome beyond the predictive yield of the individual parameters. The most widely used Wilkins score relies on subjective and categorical evaluation of pathology, overlooks commissural disease, does not account for asymmetrical/uneven distribution of pathology, and arbitrarily gives equal weight to its four components, which is not reflective of their actual predictive value.[34] Moreover, correlation between the score (and its components) and final MVA is weak[42–45] with significant overlap between patients with optimal and suboptimal results (*Figure 2*). Nevertheless, the model has been extensively validated in different patient populations treated with various PMC techniques. Although derived and initially validated in single/double-balloon cohorts, the score was shown in the randomized trial by Kang *et al.*[52] ($n = 302$, assigned to double-balloon or Inoue technique) to be a predictor of good immediate result independent of PMC technique, and its predictive value has been subsequently documented in several contemporary PMC cohorts using the Inoue technique.[29,32] Using a rather uncommon PMC technology (ACCURA balloon, Vascular Concepts Limited, Hallstead, UK), Gajjala *et al.*[53] compared the predictive power of the Wilkins, commissural calcification, and revisited echo scores. The three scores demonstrated comparable C-statistic (0.694–0.698), high NPV (85–91%), and low PPV (31–38%), suggesting that these models have complementary strengths. Similarly, the RT3DE score has a marginally higher predictive power than the Wilkins score (C-statistic: 0.87 vs. 0.80) and should be considered as a more objective and reproducible upgrade.[25]

Overall, the complementary use of several scores may improve the predictive yield beyond the individual models, especially in patients with 'intermediate' values. For example, the Wilkins score can serve as an initial screening. Most patients with minimal leaflet and subvalvular disease (Wilkins score ≤6–8) have a favourable result,[42] but can be further risk stratified by the commissural calcification score.[24] On the other hand, surgery is a better option for patients with a very high Wilkins score (>11), not only because success rate is low[32] but also since long-term outcomes remain poor even after an immediately successful PMC.[46] Those with an intermediate Wilkins score (9–11) should be further risk stratified, and the reclassification power of the revisited echo score (with complementary data on commissural morphology and MVA) is most notable in this subgroup.[32]

Post-procedural MR is most frequently commissural or juxtacommissural. Subvalvular damage and tear of the central leaflet scallops (A2/P2) are less common mechanisms and are predictive of cardiovascular death and the need for valve replacement.[7,54] Many attempts to develop models predictive of post-procedural MR have been unsuccessful,[41,45,54–57] not least since this complication seems to be independent of echocardiographic scores. An active inflammatory response in the leaflet tissue may contribute to localized collagen degradation and predispose to leaflet tearing.[58] The dedicated MR echo score developed by Padial *et al.* accounts for heterogenous leaflet pathology, patterns of commissural disease (a resistant commissure may lead to excessive contralateral splitting while bicommissural resistance may lead to leaflet tear), and severity of subvalvular disease (which increases the possibility of inadvertent interchordal balloon passage and dilatation). The model was developed from a double-balloon technique cohort and was then validated by the same group in an Inoue technique cohort.[37,48] Further external validations support the utility of this model.[37,59]

Conclusion

Anatomical suitability for PMC is multifactorial. The long-established Wilkins score can serve as an initial screening to judge anatomical suitability for PMC and provides some prediction of long-term outcomes. However, while patients with extreme scores can be safely advised for or against PMC, those in the intermediate zone require further stratification. Baseline MVA, heterogeneity of leaflet pathology, and the pattern of commissural disease (calcification and symmetry of fusion/remodelling) have incremental predictive value beyond Wilkins score parameters and have been integrated into several models/scores. Moreover, the integration of 3D echocardiography into the evaluation process significantly improves reproducibility and may improve the prediction of PMC outcomes (especially the development—or worsening—of MR).

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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Data availability

Further data enquiries can be directed to the corresponding author, and upon reasonable request, data can be provided.

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