Three-dimensional evaluation of the mitral valve area and commissural opening before and after percutaneous mitral commissurotomy in patients with mitral stenosis

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Aims Management of patients with mitral stenosis (MS) relies on accurate evaluation of the mitral valve area (MVA). Planimetry (MVA2D) is considered as the reference method but must be performed at the tips of the leaflets with the correct plane orientation and therefore requires experienced operators. Real-time three-dimensional echocardiography (RT3DE) may overcome this limitation but its usefulness for experienced when compared with less experienced operators has not been evaluated. In addition, superiority of RT3DE for the evaluation of commissural splitting after percutaneous mitral commissurotomy (PMC) is unknown.

Methods and results 60 patients were prospectively evaluated by 2D and RT3DE before and after PMC by experienced operators. Before PMC, MVA3D was slightly higher than MVA2D (1.15 ± 0.25 vs. 1.06 ± 0.22 cm², P = 0.0001) but correlation between methods was excellent (r = 0.73, P < 0.0001), mean difference was small (0.09 ± 0.18 cm²) and clinically meaningless (three patients misclassified, two of whom had borderline MS severity). After PMC, MVA3D did not differ from and correlated well with MVA2D (1.87 ± 0.37 vs. 1.85 ± 0.32 cm², P = 0.36; r = 0.76, P < 0.0001; mean difference 0.03 ± 0.24 cm²). Twenty-five additional patients were also evaluated both by an experienced and a less experienced operators. Bland–Altman analysis showed the better agreement between MVA3D measured by the less experienced operator and MVA2D measured by the experienced operator than between MVA2D measured by the less experienced and the experienced operators (mean difference 0.03 ± 0.34 vs. −0.13 ± 0.46 cm², P = 0.03). When compared with RT3DE, 2DE underestimated the degree of commissural opening in 33% of patients and agreement between methods was weak (κ = 0.41).

Conclusion RT3DE provides accurate MVA measurements similar to 2D planimetry performed by experienced operators. Thus, it does not provide a real advantage for experienced operators, whereas it seems particularly helpful for less experienced operators. In addition, RT3DE improves the description of valvular anatomy.

Introduction

Rheumatic mitral stenosis (MS) is a frequent cause of valve disease in developing countries. In Western countries, it remains a significant problem, despite the striking decrease in the prevalence of rheumatic fever and still accounts for 12% of native valvular heart disease. Management of MS relies on accurate echocardiographic assessment of the mitral valve orifice area (MVA). Planimetry (MVA2D) is considered as the reference method, but must be precisely performed at the tips of the leaflets in a well-oriented plane and therefore requires experienced operators. Difficulty in acquiring this plane is one major limitation of the method.

Three-dimensional (3D) echocardiography is a relatively recent imaging technique allowing 3D visualization of heart structures. With improvement of transducer technology (matrix array transducer), on-line 3D acquisition, visualization, and analysis have become possible [real-time three-dimensional transthoracic echocardiography (RT3DE)]. It has been recently suggested that this new echocardiographic modality, allowing a precise cross-section of the mitral orifice at the tips of the leaflets with correct plane orientation, may provide more accurate assessment of MS severity than two-dimensional echocardiography (2DE). However, two important limitations of these previous studies need to be underlined. First, superiority of RT3DE against 2DE was demonstrated using haemodynamic measurements and the Gorlins’ equation, which cannot be...
considered as a gold standard. Secondly, only 3D-guided 2D measurements were considered and because RT3DE ‘only’ offers the opportunity to perform a well-oriented planimetry, its superiority for experienced operators can be questioned. In contrast, RT3DE may be particularly helpful for less experienced operators but this has not been clearly evaluated. 3DE could visualize commissural splitting more accurately than 2DE. In these series, a transoesophageal probe interfaced with a workstation was used. Clinical use of RT3DE for the assessment of the degree of commissural splitting has never been evaluated.

Therefore, the aim of the present study was to compare, in a large series of patients with MS, 2DE and RT3DE evaluation of (i) MVA measurements by planimetry before and after PMC by experienced and less experienced operators and (ii) degree of commissural splitting after PMC.

Methods
Population
We prospectively evaluated 72 consecutive patients with severe MS (MVA2D < 1.5 cm²) referred to our institution for PMC. Exclusion criteria were a non-feasible 2D or 3D planimetry or a contraindication to PMC [left atrial (LA) thrombus, mitral regurgitation (MR) grade ≥ 2/4, extensive calcification]. Patients in atrial fibrillation (AF) were not excluded. The procedure was not performed in four patients (extensive calcification in two, MR grade 2/4, extensive calcification [chordae 10 mm long] in one, and LA thrombus in one). Eight additional patients were also excluded because of poor image quality. Thus, 60 patients were enrolled in the present study and evaluated using 2DE and RT3DE the day before and 24–48 h after the procedure (first subset). This sample size was specified beforehand and allowed to detect difference as small as 0.15 cm² and correlation as small as 0.35 (α = 0.05, β = 0.80).

A second subset of 25 additional patients was also considered to compare RT3DE vs. 2DE accuracy for less experienced operators as defined below. Informed consent was obtained in all patients.

Echocardiographic examination
Two-dimensional echocardiography
Comprehensive 2D transthoracic echocardiography was performed the day before and 24–48 h after PMC using a commercial ultrasound system (S3 probe and Sonos 7500, Philips, Andover, MA, USA). Planimetry was performed in parasternal short-axis view, adjusting the probe for an optimal mitral valve orifice. Mean transmitral gradient and systolic pulmonary artery pressure (S-PAP) were also assessed using continuous wave Doppler. Three to five beats were analysed and averaged. Mitral valve anatomy was classified in three groups:11 flexible valves and mild subvalvular disease (chordae >10 mm long) (Group I), flexible valves and extensive subvalvular disease (chordae <10 mm long) (Group II), and calcified valves (Group III). MR was semi-quantitatively graded from zero to four.12 Left ventricular (LV) dimension and function and LA diameter were measured as recommended by the American Society of Echocardiography. After the procedure, MVA2D, mean transmitral gradient, S-PAP, and degree of MR were also assessed as well as the degree of commissural opening semi-quantitatively scored for each commissure as none, partial (splitting of a commissure of only several millimetres from the valve orifice), and complete (splitting of a commissure up to the level of the mitral annulus).

Real-time 3D echocardiography
RT3DE was also performed the day before and 24–48 h after PMC during the same examination as 2DE, using the same system and a matrix array transducer (X4, Philips). RT3DE images were obtained in parasternal view and stored on optical disks. The recorded images were analysed offline on a workstation using dedicated software (QLab 3 and 4, Philips) in a random order, blinded of 2D results. MVA was measured at the best cross-section of the mitral valve defined as the most perpendicular and smallest orifice (Figure 1). Acquisition were performed with average gain and luminosity, which were adjusted offline (from +30 to +60 in QLab) to provide the better border detection. As for 2D echocardiography, the degree of commissural opening, for both the medial and lateral commissure, was semi-quantitatively scored after PMC as none, partial, or complete.

Measurements by experienced and less experienced operators
First, in 60 patients, 2D and 3D assessments of the MVA and of the degree of commissural opening by experienced operators (level III operators who perform transthoracic echocardiography for MS at least 10 times every month) were compared. Two-dimensional acquisition and measurements of the 60 patients were performed by the same experienced operator (one the two first authors). Three-dimensional acquisition and measurements were all performed by the first author. In 15 randomly selected patients, 3D measurements were repeated by the two first authors for intra- and inter-observer variability.

Secondly, in the additional subset of 25 patients, 3D measurements of the MVA were also performed in a blinded manner, before and/or after PMC (32 measurements) by a less experienced operator (third author, level I training in echocardiography) and compared with MVA2D. Those 2D measurements were all performed (acquisition and measurements) both by the same less experienced operator and by an experienced operator (first author). In 15 randomly selected patients, both 3D acquisition and measurements were also performed by the less experienced operator.

Percutaneous mitral commissurotomy
PMC was performed by anterograde transvenous approach using the Inoue balloon with stepwise inflation under echocardiographic guidance. In brief, balloon size was chosen according to the patient’s height and the balloon was inflated in steps of 1–2 mm. Valve area (planimetry), mean transmitral gradient, commissural splitting, and the degree of MR were assessed by transthoracic echocardiography after each inflation. Our criteria for stopping the procedure were complete opening of at least one commissure with an MVA2D > 1.5 cm² or the occurrence or increase of regurgitation >1/4. A good immediate result was defined as a good valve opening (final MVA2D ≥ 1.5 cm²) with no regurgitation >2/4.

Statistics
Quantitative variables were expressed as mean ± SD. Comparisons of MVA obtained by 2D and 3D echocardiography before and after PMC were analysed using paired t-tests, Pearson’s correlation, and Bland-Altman analysis. Analysis was performed overall on 60 patients and according to patients rhythm and the presence or absence of calcification, which may potentially affect MVA measurements. Intra- and inter-observer variability was calculated as mean difference ± SD. Agreement between the two methods of assessment of the degree of commissural opening was assessed by the κ-value. Comparison was performed overall and for each commissure. All tests were two-sided. Statistical significance was defined with P < 0.05.
Results

Population

Mean age of the 60 patients of the first subset was $47 \pm 13$ years, 72% were female and 37% were in AF. All had an LV ejection fraction $\geq 50\%$. A grade 2/4 MR was present in one patient (2%). Mean $MVA_{2D}$ was $1.06 \pm 0.22$ cm$^2$ (range 0.50–1.45) before PMC and significantly increased to $1.85 \pm 0.32$ cm$^2$ (range 1.10–2.55; $P < 0.0001$) after PMC. A good valve opening ($MVA_{2D} \geq 1.5$ cm$^2$) was observed in 55 patients (92%), an MR grade $\leq 2/4$ in four (7%), and a good immediate result (good valve opening with no MR grade $\leq 2/4$) in 52 patients (87%). Clinical and echocardiographic characteristics of the population are summarized in Table 1.

3D assessment of MVA by experienced operators

The time required to acquire RT3DE images and to perform MVA measurements was $7 \pm 2$ min.

Overall measurements before and after PMC

Before PMC, $MVA_{3D}$ was slightly higher than $MVA_{2D}$ ($1.15 \pm 0.25$ vs. $1.06 \pm 0.22$ cm$^2$, $P = 0.0001$) but mean difference between methods was small ($+0.09 \pm 0.18$ cm$^2$) and correlation excellent ($r = 0.73$, $P < 0.0001$) (Figure 2A). Bland–Altman analysis is presented in Figure 2B and shows the good agreement between methods [lower limit $-0.26$, 95% CI ($-0.33$; $-0.17$); upper limit $0.44$, 95% CI ($0.36$; $0.52$)].

After PMC, $MVA_{3D}$ did not differ from and correlated well with $MVA_{2D}$ ($1.87 \pm 0.37$ vs. $1.85 \pm 0.32$ cm$^2$, $P = 0.36$; $r = 0.76$, $P < 0.0001$) (Figure 2C). Bland–Altman analysis (Figure 2D) shows the agreement between methods with no trend for under- or overestimation with RT3DE [mean difference $0.03 \pm 0.24$ cm$^2$, lower limit $-0.45$, 95% CI ($-0.56$; $-0.34$); upper limit $0.51$, 95% CI ($0.40$; $0.61$)].

Using a cut-off value of $<1.5$ cm$^2$ for severe MS, four patients over 120 (3%) were misclassified by RT3DE, three before PMC (including two patients with MS of borderline severity), and one after PMC.
Subgroup analysis
Similar results were observed when analyses were repeated according to patients' rhythm or the presence or absence of calcifications. A good agreement was observed in all subgroups, despite a slight 3D overestimation before PMC. As an example, Bland–Altman analysis of 3D and 2D measurements before and after PMC in patients with and without calcifications are presented in Figure 3.

Intra- and inter-observer variability
Intra- and inter-observer variability of 3D measurements for experienced operators were +0.09 ± 0.21 cm² and +0.02 ± 0.18 cm², respectively.

Measurements by the less experienced operator
In the second subset of 25 patients (32 measurements), MVA²D measured by the less experienced operator did not differ from and correlated well with MVA³D assessed by the experienced operator (1.66 ± 0.58 vs. 1.63 ± 0.54 cm², \(P = 0.68; r = 0.82, P < 0.0001\)), whereas there was a borderline statistical significance between MVA²D assessed by the less experienced and the experienced operator (1.50 ± 0.56 vs. 1.63 ± 0.54 cm², \(P = 0.12; r = 0.64, P < 0.0001\)). Bland–Altman analysis showed the better agreement between MVA³D measured by the less experienced operator and MVA²D measured by the experienced operator than between MVA²D measured by the less experienced and the experienced operators (mean difference 0.03 ± 0.34 vs. -0.13 ± 0.46 cm², \(P = 0.03\)) (Figure 4). Also, 3D measurements performed using experienced and less experienced 3D acquisition in 15 randomly selected patients (among patients of the second subset) were not different (1.63 ± 0.57 vs. 1.58 ± 0.55 cm², \(P = 0.60\)).

Evaluation of commissural opening after PMC
Comparison of 2D and 3D assessment of the degree of commissural opening (assessed by experienced operators) was performed on the first subset, first overall on 120 commissures. Using 2DE, fused commissures were observed in 30%, partially open in 24%, and completely open in 46%, whereas using RT3DE, 14% were fused, 24% partially open, and 62% completely open (Table 2). Agreement between methods was weak (\(\kappa = 0.41, 63\%\) of agreement) and an underestimation of the degree of commissural opening using 2DE was observed in 33%. Underestimation of the degree of commissural opening was similarly observed for the medial and lateral commissures with a poor agreement (both \(\kappa \leq 0.41\)). A similar weak or moderate degree of agreement was observed in the subgroup of patients with non-calcified and calcified valve (\(\kappa = 0.33\) and \(\kappa = 0.58\), respectively).

Discussion
In the present study, we compared MVA measurements using RT3DE with those obtained using 2DE before and after PMC. For experienced operators, agreement between methods was good, despite a slight but clinically meaningless difference before PMC. Measurements could be performed in a few minutes and intra- and inter-observer variabilities were low. Importantly, RT3DE provided a better accuracy than 2DE for less experienced operators. Furthermore, an underestimation of the degree of commissural opening was observed using 2DE when compared with RT3DE.

Mitrval valve area
Management of patients with MS relies on accurate echocardiographic assessment of the MVA.² Planimetry (2D), which provides an anatomic measurement of the mitral valve orifice, is considered as the reference method, but must be performed at the tips of the leaflets with a correct plane orientation. Minor changes in the depth or angle of the ultrasound beam may indeed lead to important MVA overestimation.¹⁶ This requirement is the major limitation of the planimetry method.

RT3DE allows a 3D acquisition of the entire mitral valve, which can be sliced along any plane as desired and overcomes this limitation. Previous studies have shown promising results³–⁴ and suggested that RT3DE may provide more accurate MVA measurements than 2DE. In addition to the fact that in these studies, the authors used the Gorlin's method, which cannot be considered as a gold standard,⁵–⁷ such conclusions can be questioned for experienced observers because only 3D-guided 2D measurements were considered. Thus, with experience, accurate MVA measurements at the tips of the leaflet in a well-oriented plane are expected with 2DE and indeed, in the present study, similar results were observed using 2DE and RT3DE. However, the main interest of RT3DE may be for less experienced operators. We found a better accuracy of 3D than 2D measurements performed by less experienced operators (level I training in echocardiography). These findings reflect the greater accuracy of RT3DE to provide the image plane with the true orifice of the mitral valve for less experienced operators. Therefore, RT3DE, with only 3D-guided 2D measurements, is not intrinsically more

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**Table 1** Clinical and echocardiographic characteristics of the 60 patients at baseline and after PMC

| Age (years) | 47 ± 13 |
| Female gender | 43 (72) |
| AF | 22 (37) |
| LVEF (%) | 66 ± 7 |
| LA diameter (mm) | 51 ± 7 |
| Anatomic group | |
| I | 6 (10) |
| II | 36 (60) |
| III | 18 (30) |
| Before PMC | |
| MVA²D (cm²) | 1.06 ± 0.22 |
| MVA³D (cm²) | 1.15 ± 0.23 |
| Gradient (mmHg) | 9 ± 5 |
| S-PAP (mmHg) | 43 ± 13 |
| After PMC | |
| MVA²D (cm²) | 1.85 ± 0.32 |
| MVA³D (cm²) | 1.88 ± 0.37 |
| Gradient (mmHg) | 5 ± 2 |
| S-PAP (mmHg) | 38 ± 11 |
| MR grade >2/4 | 4 (7) |

Data presented are number of patients (%) or mean ± SD. Gradient, mean transmitral gradient, MVA²D, planimetry of the MVA measured by 2D echocardiography, MVA³D, planimetry of the MVA measured by 3D echocardiography.
accurate than 2DE but allows, for less experienced operators, to achieve more accurate MVA measurements, closer to those obtained in 2D by experienced operators. This should be considered as a major indication for RT3DE. This is of particular importance because MS is a relatively rare disease, in which few physicians have high expertise. Of note, although RT3DE improves accuracy of MVA measurements by less experienced operators, difference between less experienced MVA3D and experienced MVA2D (+0.03 ± 0.34 cm²) was slightly larger than the difference between MVA3D and MVA2D measured by experienced operators (+0.09 ± 0.21 cm² before PMC and +0.02 ± 0.18 cm² after PMC). This difference between methods underlines the need of using multiple methods for the assessment of MS severity, especially for less experienced operators.

It should also be emphasized that unlike all previously reported study, we used newly developed dedicated software built into the machine systems. With this system, measurements can be performed online in a few minutes (compared to more than 20 min with previous systems). It is also worth noting that a slight but significant overestimation was observed before PMC by RT3DE. This is surprising because theoretically RT3DE should provide the smallest results. This discrepancy is unlikely to be related to the lower 3D definition, no difference was observed after PMC, and we do not have any clear explanation. Nevertheless, this discrepancy was clinically meaningless. Mean difference between 2D and 3D was small (+0.09 ± 0.18 cm²), three patients (5%) were misclassified before PMC but two had MS of borderline severity.

**Assessment of commissural opening**

PMC is a safe and effective procedure for patients with MS and improvement of MVA is mainly related to commissural splitting. Preliminary data have shown that degree of commissural opening was underestimated in almost 50% of patients by 2DE compared with transoesophageal 3DE. In the present study, in a larger series of patients examined after PMC, we confirm and extend these finding to RT3D transthoracic echocardiography. Underestimation of the degree of commissural opening was observed in one-third of our patients. RT3DE providing multiple views, en face of both atrial or ventricular perspective and lateral rotations, allows an easy visualization of the degree of commissural opening (Figure 5). It is worth noting that 2DE underestimated the degree of commissural opening compared with
RT3DE, whereas there was no difference between MVA2D and MVA3D. This apparent paradox is probably due to the fact that the mitral valve orifice is not flat and that parts of the commissures, not located in the same plane, are not planimetrated. With improvement of 3D technology, real 3D measurements are expected.

The prognostic value of this new modality of commissural assessment deserves additional studies but RT3DE may help.

Figure 3  Quality control plots using Altman and Bland analysis for 2D echocardiography (MVA2D) and RT3DE (MVA3D) assessed by experienced operators before PMC (A and B) and after PMC (C and D), (A and C) in the absence of calcification and (B and D) in patients with calcifications.

Figure 4  Bland–Altman analysis shows the better agreement between MVA3D measured by the less experienced operator and MVA2D measured by the experienced operator (B) than between MVA2D measured by less experienced and experienced operators (A).
selecting patients for PMC who already have had a previous commissurotomy. It may help distinguish mitral restenosis due to commissural refusion from restenosis due to valvular rigidity with open commissures. Furthermore, it has also been reported that 3D may provide a better visualization of tear that can occur during PMC.\textsuperscript{8} Thus RT3DE may guide and optimize PMC results by visualizing, during the procedure, the extent of commissural splitting so that maximal MVA can be achieved safely.

**Study limitations**

There is no absolute gold standard for MVA measurement in MS. MVA assessed using the hydraulic Gorlin equation in the catheterization laboratory may not be valid under varying haemodynamic conditions and the empirical coefficient of discharge may be inaccurate with different orifice shapes. According to the current ACC–AHA current guidelines,\textsuperscript{2} catheterization is indicated to assess haemodynamics when there is a discrepancy between echocardiographic measurements and the clinical status of a symptomatic patient. All echocardiographic methods have their own limitations. The pressure half-time method\textsuperscript{17} is commonly used but it has been demonstrated that this method should be used cautiously, especially in patients older than 60 years, in AF, or after percutaneous balloon commissurotomy.\textsuperscript{18,19} The continuity equation is invalidated by the commonly associated aortic regurgitation or MR.\textsuperscript{20} The PISA method is accurate and reproducible\textsuperscript{21} but can be technically demanding and time-consuming and is consequently rarely used in practice. Thus, 2D planimetry, which is considered as the reference method, is logically the method to be used for comparison. Nevertheless, in the absence of a gold standard method, the terms of under- or overestimation are only relative but this limitation has a limited impact, as we observed very similar results by 2DE and 3DE.

Also, the gold standard method for the assessment of the degree of commissural opening would be surgery or post-mortem examination, which may lead to selection bias. Therefore, underestimation of the degree of commissural opening by 2DE can only be considered as relative. However, to our knowledge, 2D assessment of the degree of commissural opening has never been validated against such standards and it is very unlikely that the better visualization of commissural opening by 3DE was due to artefact.

<table>
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<td>29 (24%)</td>
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<td>9 (15%)</td>
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<tr>
<td>Partial</td>
<td>17 (28%)</td>
<td>18 (30%)</td>
</tr>
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<td>Complete</td>
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<th>3D echocardiography</th>
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Figure 5 Assessment of commissural opening using RT3DE. Parasternal short-axis view from ventricular perspective, en face, medial, and lateral views of a patient with complete bilateral commissural opening. See online supplementary material for a colour version of this figure.

Finally, the present study was not a feasibility study. Image quality is a major limitation of echocardiography and patients with non-feasible 2D or 3D planimetry were
excluded as well as patients with MR grade > 2/4 or with extensive calcification.

Conclusion
In the present study, we demonstrate that RT3DE is an accurate, fast, and reproducible method for MVA measurements by both experienced and less experienced operators and provides similar results to 2D planimetry performed by experienced operators. Therefore, for MVA assessment, RT3DE should not be recommended for experienced operators in whom it does not seem to provide a real advantage. In contrast, it may be of particular interest for less experienced operators and this should be considered as a major indication of RT3DE. In addition RT3DE improves description of valvular anatomy and provides a unique assessment of the extent of commissural splitting. The prognostic value of this new modality of commissural assessment deserves additional study.

Supplementary material
Supplementary material is available at European Heart Journal online.

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Conflict of interest: none declared.

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