Myxomatous mitral valve disease: comparison of different echocardiography methods and protocols. A transesophageal echocardiography study

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Abstract: Echocardiography is the main method for mitral valve (MV) anatomy assessment. To establish the relative importance of different imaging modalities, we compared four echocardiographic methods for MV prolapse diagnosis: standard 2D transesophageal echocardiography (TEE), complete 2D-TEE (including additional views to properly visualise all scallops), 3D-TEE, and 3D colour coded TEE modelling. Methods and results – We analysed MV morphology in 137 patients (57,11 +/- 11 year, 57% male) by these four methods: 38 normal subjects and 99 patients with mitral regurgitation. The complete 2D-TEE reclassified as prolapsing 34 scallops considered normal by standard 2D-TEE (mainly A1 and A3 scallops). By 3D-TEE 15 segments classified as normal by complete 2D-TEE were reclassified as prolapsing, allowing a better diagnosis of A1, P3, and commissural prolapse. Based on 3D-model data 8 segments have been reclassified compared to 3D-TEE. The accuracy of the other methods compared with the gold-standard 3D-TEE was 98% for complete 2D-TEE, 93% for standard 2D-TEE, and 98% for the 3D modelling. Conclusion – The MV cannot be properly analysed by 2D examination without a full, careful, and experienced evaluation (A1, A3, P3, the commissures are more challenging). Therefore, 3D-echocardiography becomes an essential tool for the precise diagnosis of MV prolapse in everyday clinical practice. Keywords: mitral valve, prolapse, myxomatous mitral valve disease, transesophageal echocardiography, three-dimensional echocardiography

INTRODUCTION

Mitral valve repair is the surgical method of choice for patients with severe mitral regurgitation due to myxomatous mitral valve disease whenever the valve is deemed reparable by detailed imaging assessment and the required surgical expertise is available.

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Rezumat: Ecografia reprezintă principala metodă imagistică de apreciere a morfologiei valvei mitrale. Pentru a stabili importanţa diferitelor modalităţi în diagnosticul prolapsului de valvă mitrală, am comparat patru metode: ecografia transesofagiană (ETE) 2D standard, ETE 2D protocol complet (incluzând secţiuni suplimentare pentru vizualizarea tuturor segmentelor), ETE-3D şi modelul matematic 3D. Metode şi rezultate – Am analizat morfologia valvei mitrale în cazul a 137 de pacienţi (57,11 +/- 11 ani, 57% bărbaţi) prin cele patru metode, 38 de normali şi 99 pacienţi cu regurgitare mitrală. ETE-2D protocol complet a reclasificat drept prolaps 34 de segmente considerate normale de ETE-2D standard (mai ales din categoria segmentelor A1 şi A3). ETE-3D a reclasificat drept prolaps 15 segmente considerate normale prin ETE-2D protocol complet. Modelul 3D matematic a reclasificat 8 segmente comparativ cu ETE-3D. Accurateţea metodelor comparativ cu standardul de aur ETE-3D a fost 99% pentru ETE-2D protocol complet, 93% pentru ETE-2D standard şi 98% pentru modelul 3D. Concluzii – Morfologia valvei mitrale nu poate fi evaluată în întregime corespunzător prin ecografie 2D, aprecierea caracteristicilor segmentelor A1, A3, P3 şi comisurilor fiind dificilă. Astfel ecografia 3D a devenit un instrument esenţial în diagnosticul prolapsului de valvă mitrală în practica clinică de zi cu zi.
riized by fibromyxomatous changes, mucopolysaccha-
ride accumulation and collagen alternation. However, the
echocardiographic definition of this pathology is still
debatable and has changed in parallel with diffe-
rent technical developments (from M-mode echocar-
diography to bi-dimensional echocardiography and 3D
echocardiography). In general, it is characterized by
systolic displacement of abnormally thickened mitral
leaflet\textsuperscript{2} into the left atrium. However, looking at
the same patient by different echocardiographic modalities
may sometimes lead to different conclusions regarding
the mitral valve: prolapsing vs non-prolapsing. There-
fore, the purpose of this study was to compare four
echocardiographic methods for the diagnosis of mitral
valve prolapse: standard 2D transesophageal echocar-
diography (TEE) (including just the four chamber, two
chamber, long axis, and bi-commisural views), com-
plete 2D TEE (including additional and modified views for
the proper visualisation of all scallops and the commis-
sures), 3D TEE, and 3D colour coded TEE modelling.

\section*{METHODS}

\subsection*{Study population}

All patients with an established diagnosis of significant
mitral regurgitation (MR) due to myxomatous disease
referred to our department for transesophageal echo-
cardiography (TEE) were included. A control group
composed of patients who were sent to our echocar-
diography laboratory for clinically indicated TEE, but
in whom no significant cardiovascular pathology was
identified - were also analysed.

The exclusion criteria were: ischemic heart disease,
history of rheumatic fever or rheumatic valve disease,
significant calcification of the mitral annulus, significant
concomitant aortic or tricuspid valve disease (\textgreater;mild),
left ventricular systolic dysfunction (left ventricular
ejection fraction <60\%), non-sinus rhythm.

The following clinical data were collected for all pa-

tients: age, gender, history of hypertension, symptoms
(e.g. dyspnoea, chest pain, palpitations, syncope). The
clinical status was defined according to the New York
Heart Association (NYHA) classification. Physical ex-
amination and 12-lead electrocardiography were per-
formed in all patients.

\subsection*{Transesophageal 2D and 3D echocardiography}

All patients had complete echocardiographic examina-
tions (EAE protocol) followed by 3D acquisitions for
the mitral valve (3D and colour 3D). Electrocardiogra-
phically gated full-volume loops were acquired over 4
heart cycles at a frame rate of 15 to 45 frames/s. The
volume for mitral valve was a multi-beat acquisition
with at least 15 frames per second.

The mitral valve morphology was analysed off-line
in standard 2D TEE views following a complete TEE
protocol\textsuperscript{4}. The standard TEE exam included the four
basic views for mitral valve analysis: four chamber, bi-
commisural, two chamber and long axis views. The
complete 2D TEE exam included all views described
in at least two separate views. We used the Carpen-
tier classification to describe the components of each
leaflet. The posterior mitral leaflet is formed by three
scallops: P1 (anterolateral), P2 (middle), and P3 (post-
eromedial), while the corresponding segments of the
anterior mitral leaflet are labelled A1, A2, and A3\textsuperscript{5}. Every
scallopin the mitral valve was characterized as being
normal, prolapsing, or flail. The prolapse was defined
as supra-annular displacement of the leaflet body, with
leaflet tips pointing towards the left ventricle, while
flail was defined the orientation of free margin of the
mitral leaflet towards the left atrium, with the leaflet
tip pointing towards the left atrium during systole. The
visualisation of ruptured chordae was noted. Using 2D
images we measured the following parameters of mi-
tral annulus (MA): antero-posterior diameter in mid-
esophageal long axis view, anterolateral-posteromedial
diameter in mid-esophageal commissural view, and of
mitral valve leaflets: the length of the anterior and pos-
terior leaflets in the mid-esophageal long axis view.

The morphology of every scallop was also appreci-
ted by 3D echocardiography: from the ‘surgical view’
and from specific cut planes used in this volumetric
data set (Figure 2). Based on the number of scallops
affected we subdivided the group of patients with MR
in limited mitral valve disease (1-2 scallops affected by
prolapse/flail) and extensive (3-6 scallops affected by
prolapse/flail).

The mitral valve was reconstructed from the acquis-
ited 3D volume using a specific software (4D MV
Assessment 2.0 TomTec imaging Systems). The mathe-
ematical model illustrates graphically the leaflet topo-
logy by colouring each point of the leaflet surface of
the model according to its distance to the best fitting
plane of the mitral annulus. This plane is defined as the
plane that fits the majority of points of the mitral an-
nulus and minimizes the distance to points that are
not on the plane. Generally, this plane is located lower
than the highest points of the mitral annulus and hi-
gher than the lowest points of the mitral annulus. The

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\textsuperscript{2} Myxomatous mitral valve disease

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points of mitral valve leaflets located above this plane, in the left atrium, are coded in red, the points located below this plane, towards the left ventricle, are coded in blue, while the points located in this plane are coded in white (Figure 3). Therefore, the part of mitral valve leaflets displayed in red is considered prolapsing. The antero-posterior and anterolateral-posteromedial mitral annulus diameters, as well as the anterior and posterior leaflet areas, were automatically calculated by the software.
 due to poor image quality and inadequate temporal re-
solution. Therefore, 137 patients were included in the
final study group: 38 normal subjects and 99 patients
with mitral regurgitation (MR).

The mean age (54.9±10.6 vs 58.3±11.7, p=0.12)
and gender distribution (57% men vs 57% men, p=0.9)
were similar in the group of patients with mitral regur-
gitation and in the normal group. The normal subjects
had no symptoms, while in the MR group there were
52 patients in NYHA I class, 37 patients NYHA II class
and 10 patients NYHA III class.

Using the 3D TEE protocol in the MR group 28 pa-
tients (28%) had just one scallop affected by prolapse,
22 patients (22%) had two scallops, 12 patients (12%)
had three scallops, 9 patients (9%) had four scallops, 5
patients (5%) had five scallops and 21 patients (21%)
had all scallops affected. Two patients with severe mi-
tral regurgitation had an isolated lesion of the poste-
rior commissure, with no evidence for prolapse. In 6
patients (6%) the pathology was seen only at the level
of the anterior mitral lea-
fl
et, in 49 patients (49%) the
pathology was seen only at the level of the posterior
mitral lea-
fl
et, while in 44 patients (44%) both mitral
lea-
fl
ets were affected. The patients' classi-
fi
cation based

The data obtained by 3D TEE analysis were consi-
dered the gold standard method\textsuperscript{6}. The MV assessment
by standard 2D TEE, complete 2D TEE, 3D TEE, and 3D
mathematical model was performed remotely, blinded,
by an experienced echocardiographer, holding EACVI
certification in TEE (MMG).

Statistical Analysis
Continuous data are presented as mean +/- SD and
nonparametric data as median and ranges.

For testing the differences between two groups we
used Student's t-test and between three groups we used
one-way ANOVA. The relationships between different
parameters were assessed by correlation analysis:
Pearson's method or Spearman's r method, as appro-
priate. Reproducibility of the 3D parameters measu-
rements was assessed in a randomly chosen group
of 15 patients. Intraobserver variability was assessed
using repeated measurements performed by the same
observer one month apart, while interobserver vari-
ability was evaluated by repeating the analysis by a se-
cond independent observer, blinded to the results of
all prior measurements. The intraobserver variability
was 96% for standard 2D TEE, 94% for complete 2D
TEE, 98% for 3D TEE and 98% for 3D model TEE, while
interobserver variability was 84% for standard 2D TEE,
84% for complete 2D TEE, 84% for 3D TEE and 96%
for 3D model TEE. Statistical analyses were performed
using SPSS version 21.0 (SPSS, Inc., Chicago, IL). P valu-
es <0.05 were considered significant.

RESULTS
One hundred and fifty patients were included: 110 pati-
ents with organic mitral regurgitation due to myxoma-
tous mitral valve disease, and 40 normal subjects. Thir-
ten patients were excluded after the echo analysis

| Table 1 |
|---|---|---|---|---|
| Number of | 2D TEE | 2D TEE | 3D TEE | 3D model |
| segments with prolapse | standard | complete | TEE | TEE |
| No prolapsing scallops | 41 | 39 | 40 | 40 |
| 1 | 38 | 32 | 28 | 29 |
| 2 | 22 | 25 | 22 | 19 |
| 3 | 9 | 9 | 12 | 15 |
| 4 | 10 | 6 | 9 | 7 |
| 5 | 3 | 6 | 5 | 7 |
| 6 | 14 | 20 | 21 | 20 |

Figure 3. The graphic representation of the best fitted plane for a saddle shape structure (A). The mathematical 3D model reconstructs the mitral valve annulus (yellow line), the mitral valve leaflets (green), and the coaptation line (red line) (B). The colour coded model allows the possibility to appreciate mitral valve prolapse: the points of MV leaflets located above the best fitted plane are coloured in blue, the points of MV leaflets located below the best fitted plane are coloured in red, while the points located at the best fitted plane level are coloured in white (C). The colour intensity (i.e. blue and red) is proportional with the distance from the best fitted plane.
on the extension of mitral valve prolapse by the four methods is presented in Table 1.

We overall analysed 137 segments of each type (A1, A2, A3, P1, P2, P3) by the four methods: standard 2D TEE, complete 2D TEE, 3D TEE, and 3D model TEE. The results are presented in Figure 4 and Table 2.

The advantages of complete 2D TEE compared to standard 2D TEE are demonstrated by the high number of segments classified as normal by standard 2D TEE and reclassified as prolapsing by complete 2D TEE (34 segments: 4.1% of all the scallops analysed). In fact, 29% of prolapsing A1 scallops, 37% of prolapsing A3 scallops and 17% of prolapsing P3 scallops were not detected by sole analysis of standard 2D TEE views.

3D TEE provides new incremental information and 15 segments classified as normal by complete 2D TEE were reclassified as prolapsing by 3D TEE, while one scallop considered prolapsing by complete 2D TEE was considered normal by 3D TEE. Of note, 8 P3 scallops considered normal by complete 2D TEE were considered prolapsing after 3D TEE analysis (i.e. 5% of all P3 scallops analysed). Compared to complete 2D TEE, 3D modelling reclassified as prolapsing 4 A2 scallops, 3 A3 scallops and 5 P3 scallops. Comparing 3D TEE data with 3D model TEE data 8 segments from 822 have been reclassified based on 3D model (4 A2 scallops were considered prolapsing and 3 P3 scallops were considered non-prolapsing by 3D model TEE) (Figure 5).

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Number of pts in which this scallop was prolapsing by 3D TEE</th>
<th>Number of prolapsing segments reclassified by 3D TEE comparing to standard 2D TEE</th>
<th>Number of prolapsing segments reclassified by 3D TEE comparing to complete 2D TEE</th>
<th>Number of prolapsing segments reclassified by 3D TEE comparing to 3D model TEE</th>
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<tbody>
<tr>
<td>A1</td>
<td>25</td>
<td>11</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>A2</td>
<td>47</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>A3</td>
<td>35</td>
<td>15</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>P1</td>
<td>36</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>P2</td>
<td>82</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>P3</td>
<td>70</td>
<td>19</td>
<td>8</td>
<td>3</td>
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<tr>
<td>overall</td>
<td>49</td>
<td>15</td>
<td>8</td>
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classified patients vs 40.3% of non-reclassified patients have severe mitral regurgitation, p<0.001) and extensive mitral valve disease (61.5% of reclassified patients vs 51.4% of non-reclassified patients have more than 3 scallops affected, p<0.001). Patients with scallops reclassified from non-prolapsing to prolapsing by 3D vs complete 2D TEE have more frequent severe mitral regurgitation (53.2% from reclassified patients vs 45.1% from non-reclassified patients have severe mitral regurgitation, p<0.001) and limited mitral valve disease (92.3% from reclassified patients vs 43.4% from non-reclassified patients have less than 2 scallops affected).

Based on complete 2D TEE exam, 20 patients have the anterior commissure affected, and 38 patients have the posterior commissure affected. The anterior commissure was generally affected in patients with extensive mitral valve disease (just in one case less than two scallops were affected) and the posterior commissure was affected in 11 cases with limited mitral valve disease and 27 cases with extensive mitral valve disease. Using 3D echocardiography one case with anterior commissure involvement and three more cases with posterior commissure involvement were detected (Figure 6). 3D TEE was useful for the detection of one case with P1-P2 and P2-P3 pseudo-commissures, and one case with posterior mitral valve cleft (Figure 7).

Mitral valve flail was detected by complete 2D TEE for 55 scallops (four A2 scallops, one A3 scallop, one P1 scallop, 46 P2 scallops and 3 P3 scallops). Using standard 2D TEE we detected flail in 44 cases (2 A2 scallops and 42 P2 scallops) while using 3D TEE flail was observed in 40 segments (4A2 scallops, 4P3 scallops, and 32 P2 scallops).

The length of the anterior and the posterior mitral leaflets measured by 2D echocardiography in the long axis view had a weak correlation with the area of the anterior and respectively posterior mitral leaflet, mea-

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### Table 3

<table>
<thead>
<tr>
<th>Accuracy comparing to gold standard 3D TEE</th>
<th>Standard 2D TEE</th>
<th>Complete 2D TEE</th>
<th>3D model TEE</th>
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<tbody>
<tr>
<td>A1</td>
<td>68%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>A2</td>
<td>100%</td>
<td>100%</td>
<td>91%</td>
</tr>
<tr>
<td>A3</td>
<td>54%</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>P1</td>
<td>89%</td>
<td>92%</td>
<td>97%</td>
</tr>
<tr>
<td>P2</td>
<td>100%</td>
<td>99%</td>
<td>99%</td>
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<tr>
<td>P3</td>
<td>70%</td>
<td>88%</td>
<td>96%</td>
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</tbody>
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**Figure 5.** Mitral valve analysis in a patient with myxomatous mitral valve disease. The 2D standard TEE showed P2 prolapse visualised in long axis view (A1) and P3 prolapse visualised in bicommissural view (A2); The 2D TEE complete examination proved also A3 prolapse visualised in modified bicommissural view (B1) and P1 prolapse visualised in five chamber view (B2). The 3D TEE surgical view of the mitral valve suggests prolapsing of P2, P3 and A3 scallops (C), while the 3D mathematical model shows that the body of A2 is above the mitral annulus as well (D).

**Figure 6.** Severe mitral regurgitation visualised in the bi-commisural view, the origin of mitral regurgitation jet being adjacent to the P3 scallop (A). The 3D surgical view (B) and the 3D model (C) proved that the P3 scallop is prolapsing and the posterior commissure is also affected.
The antero-posterior MA diameter measured by 2D TEE in the long axis view, and the anterolateral-posteromedial MA diameter measured by 2D TEE in bi-commissural view had moderate correlations with the values of these diameters obtained by 3D geometrical reconstruction (\( r=0.39, p<0.001 \) and \( r=0.53, p<0.001 \)). However, the values obtained by 2D versus 3D echocardiography are significantly different for the antero-posterior diameter of the mitral annulus: 3.4+/-.054 cm vs 3.5+/-.061 cm, \( p=0.002 \).

**DISCUSSION**

Mitrval valve prolapse was described by John Brereton Barlow\(^7\) already 50 years ago, based on clinical auscultation and cine-angiographic exam. However, even after five decades, it remains a difficult to define entity\(^8\).

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<th>Table 4</th>
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<tr>
<td>Study</td>
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<tr>
<td>Pepi et al(^6)</td>
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<tr>
<td>Grewal et al(^21)</td>
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<tr>
<td>Tamborini et al(^22)</td>
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<tr>
<td>La-Canna et al(^23)</td>
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<td>Gracia-Orta et al(^24)</td>
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**Figure 7.** 2D color Doppler TEE in a patient with mixomatous mitral valve disease: in the standard bi-commissural view (A) there is no mitral regurgitation jet, while in the modified bi-commissural view at P1-P2-P3 level there are three jets of mitral regurgitation (B). The 3D atrial view of the mitral valve is very helpful for establishing the diagnosis: one jet is central at the level of A2-P2 that are prolapsing, and the other two jets are located at the level of pseudo-commisures between P1-P2 and P3-P2 (C). In another case of mitral regurgitation, the modified bi-commissural view at P1-P2-P3 level suggests mitral valve prolapse and mitral regurgitation jet at the level of P2 scallop (D, E); the 3D surgical view of the mitral valve is very helpful for establishing the diagnosis: P1-P2 cleft (F).
It was initially recognized as a clinical entity, the most important auscultatory element being the late systolic click, with or without a late systolic murmur\textsuperscript{9}. The first echocardiographic features described by M mode echo (late systolic negative flow)\textsuperscript{10} had low sensitivity and specificity compared to clinical and angiographic data\textsuperscript{11}. Bi-dimensional echocardiography defined mitral valve prolapse as the superior systolic movement of mitral valve leaflet in relation to the mitral annulus\textsuperscript{12}. Therefore, the early studies reported a high incidence of mitral valve prolapse\textsuperscript{13,14}, considering abnormal the superior displacement of mitral valve leaflets even in the four-chamber view. The description of the 3D saddle shape of the mitral annulus\textsuperscript{15} changed the understanding and assessment of mitral valve prolapse. This new information suggested that mitral valve prolapse should be diagnosed only in the long-axis view, but in this view only the A2 and P2 scallops can be analysed. The current agreement is that diagnosis of mitral valve prolapse can be made in any view as long as billowing of the anterior mitral leaflet of less than 5 mm is not considered\textsuperscript{16}. The 3D reconstruction of the mitral valve offers the possibility to overcome these problems and to diagnose and localise accurately the mitral valve prolapse\textsuperscript{17}.

The usefulness of 3D TEE in the correct identification of prolapsing scallops has been proved previously\textsuperscript{18,19}, with an accuracy of this method compared to intraoperative results of \textgreater\textasciitilde95\%\textsuperscript{6}. The advantages of 3D TEE over 2D TEE in localisation of mitral valve prolapse are even more important for inexperienced echocardiographers, compared to expert echocardiographers\textsuperscript{20}. In our study, the accuracy of 2D vs 3D TEE in the diagnosis of MV prolapse was 98\%, higher than previously reported, probably due to multiple views utilised for MV examination. The advantage of 3D TEE vs complete 2D TEE was important mainly for the diagnosis of A3, P1 and P3 prolapse. The detection of mitral valve flail and chordal rupture was higher for complete 2D TEE comparing to 2D TEE probable due to the higher temporal resolution. Therefore, a complete 2D TEE exam of the MV remains of great value for the diagnosis of prolapse\textsuperscript{25}. Conversely, the standard 2D TEE examination has a low sensitivity for MV prolapse diagnosis, mainly concerning the A3 and P3 scallops.

The new method analysed in our study was the identification of prolapsing scallops based on colour coded mathematical modelling. The differences between 3D TEE and the mathematical model are mainly explained by the model considering the distance from every point of MV leaflets to the best fitting plane, and not to the mitral annulus plane. The accuracy of 3D TEE model vs 3D TEE is 98\%. Of note, this difference is mainly related to the A2 scallop: the basal part of A2 may be superior to the best fitted plane, but still inferior to the highest point of the mitral annulus (the anterior point). The use of this colour coded mathematical model may overcome some of the difficulties in making the diagnosis of MV prolapse\textsuperscript{15,26,27} and may be very useful in everyday clinical practice\textsuperscript{28}, especially for interpreters with limited experience\textsuperscript{29}. The method needs further validation against intraoperative findings.

Three-dimensional TEE is superior in the diagnosis of MV indentations (i.e. grooves separating the posterior mitral leaflets \textless50\% of leaflet length), or clefts indentations (i.e. grooves separating the posterior mitral leaflets less than 50\% of leaflet length)\textsuperscript{30}.

**STUDY LIMITATIONS**

The main limitation of our study was that the mitral valve was evaluated only by echocardiography and no surgical or anatomical information was available for comparison.

**CONCLUSION**

Three-dimensional echocardiography becomes an essential tool for the precise diagnosis of mitral valve prolapse in everyday clinical practice because certain areas of the mitral valve cannot be seen completely without a full, careful and experienced evaluation (A1, A3, P3, commissurres). The 3D colour-coded mathematical model generated semi-automatically may be very useful for less experienced echocardiographers. Two-dimensional TEE remains an important diagnostic tool in experienced hands, able to perform a complete mitral valve examination. The standard 2D TEE exam has a low sensitivity for the diagnosis of mitral valve prolapse and should not be recommended as the only method for mitral valve morphology analysis.

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