A multidimensional dynamic quantification tool for the mitral valve

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Abstract

OBJECTIVES: The mitral valve (MV) is a complex three-dimensional (3D) intracardiac structure. 3D transthoracic and transoesophageal echocardiography are used to evaluate and describe the changes in the mitral valve apparatus due to degenerative or functional mitral regurgitation. These techniques are, however, not accurate enough to capture the dynamic changes during the cardiac cycle. We describe a novel multistage modelling (MSM) technique, using three-dimensional transoesophageal echocardiography (3D TOE), to visualize and quantify the MV during all the phases of the cardiac cycle.

METHODS: Using 3D TOE, sets of images were obtained from 32 individuals who were undergoing surgery for other reasons and who did not have MV disease. These images were divided into six steps whereby every step represented one cardiac cycle. The image sets were then cropped and sliced at the level of MV, then imported and segmented by the open source software (3D Slicer) to create 3D mathematical models. The models were synchronized with patient’s ECGs and then reunited and exported as multiphase dynamic models. The models were analysed in two steps: (i) direct step-by-step visual inspections of the MV from various angles and (ii) direct measurements of anteroposterior, intercommissural, anterolateral–posteromedial diameters, anterolateral angles and anteroposterior angles in systole and diastole at different levels.

RESULTS: The segmentation results in 32 × 6 high-quality cropped MV. The division of models into six steps allows quantification and tracking of MV movement. Reunion of the models leads to creation of a full real-time simulation of the MV during the cardiac cycle. Synchronization of the models with ECG enables accurate simulation. Measurements of the diameters showed: median intercommissural diameters were increased with 10% from mid-systole to mid-diastole [31.9 mm (28.9–34.9), 34.8 mm (31.2–38.2), respectively, P-value <0.001]. This was also observed for anteroposterior diameters [33.8 mm (29.8–35.2), 37.1 mm (31.8–38.5), respectively, P-value <0.001]. Anterolateral–posteromedial diameter did not change significantly in both phases [43.7 mm (36.3–48.9), 43.5 mm (35.5–47.5), respectively]. Intercommissural and anteroposterior diameters were approximately the same in systole [31.9 mm (28.9–34.9) and 32.5 mm (29.8–35.2)] and diastole [34.8 mm (31.2–38.2) and 35.2 mm (31.8–38.5)]. Measurements of anteroposterior angle at the anterolateral junction showed that this angle was accentuated acutely in diastole rather in systole [115° (104–129), 126° (113–137), respectively, P-value <0.001]. It was the same when measuring the anterolateral angle [105° (97–113), 119° (106–130), respectively, P-value <0.001].

CONCLUSIONS: The novel MSM technique allows precise quantification of shape changes in MV, which may help in better understanding the normal MV physiology, facilitate the diagnosis of MV pathologies and lead to numerical simulation of MV flow and displacement. It can also help cardiac surgeons and cardiologists gain a better understanding of the MV and assist them in obtaining a reliable orientation in order to choose optimal treatment strategies and plan surgical interventions. The measurement of the new anterolateral angle allowed better quantification of mitral annulus angulation and could be considered as new parameter that may help in future development of a new generation of mitral rings.

Keywords: Mitral valve • Multidimensional modelling • Quantification

† Peyman Sardari Nia and Saeed Ashraf contributed equally to this study.
**INTRODUCTION**

The mitral valve (MV) is a complex intracardiac structure that changes dynamically and repetitively, in three dimensions, during the cardiac cycle. While general pathologies of the MV are well described, each patient with MV disease has their own specific valve and annular characteristics, which could affect optimal surgical intervention. This ‘tailored to the patient’ therapy will be aided by a complete understanding of the precise nature of their MV, its anatomy and physiology and its relationships to neighbouring structures [1].

Multiple-imaging modalities are necessary to study the valve [2] and to assess its pathologies according to Carpentier’s classification [3]. Echocardiography, either transthoracic (TTE) or transoesophageal (TOE), remains the most commonly used imaging technique [4], but has limitations. Other imaging techniques are evolving.

The development of numerical models, both static and dynamic, has improved understanding of MV complexity [5], which use computational fluid dynamics and fluid–structure interactions—to describe the flow of blood through the MV and its interactions with MV structures [6, 7].

The utility of such models is influenced by many factors, particularly quality and limitations of imaging and the ‘virtual’ character of biomedical dynamic models, which do not reflect authentic movements of MV, being influenced by virtual haemodynamic parameters and material properties.

The aims of this study were to create a multistage modelling (MSM) technique. This technology is a comprehensive visualization tool, based on three-dimensional TOE (3D TOE), to analyse the dynamicity of the MV throughout the entire cardiac cycle, and to generate a real-time dynamic mathematical model for better quantification. In this study, the cardiac cycle was divided into six phases or steps (early, mid- and late systole and early, mid- and late diastole) in order to gain multiple-imaging sets for accurate consecutive detection of MV mobility (Fig. 1).

**MATERIALS AND METHODS**

**Study subjects**

The images were obtained from digitally stored 3D TOE examination previously performed by a variety of clinicians on 32 individuals, who were undergoing non-valvular cardiac surgery and who were judged to have normal MV anatomy and function, and to have preserved ventricular function, based on their clinical histories and TTE findings. All patients were in sinus rhythm. The patient data were anonymized.

**Image acquisition and processing**

We obtained images, using a Philips iE33 with a 3D TOE probe (Philips Medical Systems, Andover, MA, USA), throughout the entire cardiac cycle. Image datasets were stored digitally and were taken using Live 3D-zoomed images. The images were cropped at the border of the left side of the heart using QLab 9.1 (Philips Medical Systems, Andover, MA, USA; Fig. 1). The cropped geometries were sliced in 0.5 mm thickness to have accurate reconstruction. These were then divided into six groups, where every group represented one phase of the cardiac cycle (Fig. 1).

**Segmentation, cleaning, meshing and generation of dynamic model**

The slices were imported using the open source segmentation software (3D Slicer) [8]. These were reconstructed and then thresholded automatically to create robust solid models [9]. Further cropping of the models at the level of MV annulus was necessary to dissect the MV from encircling structures.

**Figure 1:** Three-dimensional (3D) modelling process of the mitral valve (MV). (A) Full-volume 3D transoesophageal data acquisition of the MV. (B) Cropping and slicing 3D transoesophageal echocardiography (TOE) image of the heart at the (level of left-sided heart) and focusing on the MV. (C) After importing the real-time 3D echocardiography (RT3DE) dataset into the modelling software, automated representation in full-volume view, left atrial view and long-axis view. (D) 3D reconstruction and segmentation of 3D TOE volume for MV and surrounding structures. (E) Tetrahedral meshing of the model from anteroposterior and profile views.
Cleaning of the models, without degrading accurate representation, is an important process. By wrapping and smoothing the edge of every structure, one can create a full mesh geometry. The models were cleaned, in which the originality of the model structures was preserved (Figs 1D and 2). The cleaned models were meshed in tetrahedral shapes and in normal fine mesh for quick processing using the open source meshing software (MeshLab, V1.3.3) [10] (Fig. 1E).

The meshed models were synchronized with the ECG recorded by the echocardiographic machine to calculate the time interval for each of the six cardiac cycle steps. These were then reunited in a single 3D dynamic model.

Measuring of three-dimensional geometric variables

The models were analysed by the same observer in two steps:

(i) Step-by-step visual inspections of the models were carried out from different angles.
(ii) Direct measurements were taken of different distances and angles (Figs 3–5).

The following analysis was performed in a sequential manner as previously published [11]:

(b) Anteroposterior (AP) diameter: the distance between the mid-anterior and mid-posterior annulus (Fig. 3B).
(c) Anterolateral-posteromedial (AL–PM) diameter: the largest distance between the anterolateral and posteromedial annulus (Fig. 3C).
(d) Anterior annulus length: the curve length of the anterior annulus between the bilateral commissures.
(e) Posterior annulus length: the curve length of the posterior annulus between the commissures.
(f) Annular circumference: the complete length of the entire annulus.
(g) AP angle I: the angle between the anterior and the posterior annulus at the commissural level (Fig. 3D).
(h) Anterolateral angle: the angle at the junction between the midpoint of anterior and lateral annulus (Fig. 4). This angle is measured as a new parameter for better quantification of the annulus and potential tool for future design of a more accurate generation of mitral rings.
(i) AP angle II: the angle between the anterior and the posterior annulus at the coaptation level in systole (Fig. 5A).

A comparison was made between all diameters and angles.

Statistical analysis was performed using IBM SPSS Statistics Version 20 (IBM Deutschland GmbH, Ehningen, Germany). A probability value of <0.05 was considered statistically significant. Distances and angles are presented as median values and ranges.

RESULTS AND STATISTICAL ANALYSIS

Complete datasets from 32 patients (median age of 66 years (29–77); 21 male; Table 1) were included in the study to analyse MV geometry: 11 (34%) had previous myocardial infarction (MI), 10 (31%) had a previous history of hypertension, 26 (81%) had good left ventricular function, 6 (18.7%) had mild LV dysfunction.
and 3 (9.4%) had patent foramen ovale. None of these patients had been known to have any MV disorder.

Next, 32 high-quality image sets were obtained during six steps of the cardiac cycle, in which the cropping of the image volumes allowed virtual dissection of the MV from its neighbouring structures. This segmentation resulted in multiple high-quality reconstructed MV models (Fig. 2), which after cleaning facilitated better meshing. Dividing the models into multi-phases allows for better quantification and better evaluation of MV movements (Fig. 3).

Later synchronization of the models with the ECG allows recognition of each phase of the cardiac cycle so that amalgamation of the models leads to the creation of a complete ‘real-time’ simulation of the MV over one complete cardiac cycle that was exported as multiframe movie (Video 1).

Measurements of the diameters showed: median IC diameter increased by 10% between mid-systole and mid-diastole [31.9 mm (28.9–34.9) and 34.8 mm (31.2–38.2), respectively, P < 0.001]. Similar changes were witnessed for the median AP diameter [33.8 mm (29.8–35.2), 37.1 mm (31.8–38.5), respectively, P-value <0.001]. Anterolateral-posteromedial diameter did not change significantly over the cardiac cycle [43.7 mm (36.3–48.9), 43.5 mm (35.5–47.5), respectively, P-value <0.001]. IC and AP diameter were approximately the same in mid-systole [31.9 mm (28.9–34.9), 32.5 mm (29.8–35.2), respectively, P-value <0.001] and in mid-diastole [34.8 mm (31.2–38.2), 35.2 mm (31.8–38.5), respectively, P-value <0.001; Tables 2 and 3; and Fig. 3].

Both the AP angle at the commissural level and the anterolateral angle increased acutely in diastole compared with the measurement during systole; for the AP angle, this increase was from 115° (104–129) to 126° (113–137), P-value <0.001, and for the anterolateral angle it was from 105° (97–113) to 119° (106–130), P-value <0.001 (Tables 2 and 3; and Fig. 4).

Analysis of the models showed that the MV annulus is angulated at the level of the anterolateral junction, making an inverted flat cap shape rather than a saddle shape (Figs 4 and 5).

**DISCUSSION**

Echocardiography in all forms provides clinicians good image quality and resolution [12]. The 3D imaging and modelling methods...
of MV are emerging as potentially superior methodologies compared with conventional 2DE [13]. The main limitation of current 3D imaging is that it cannot visualize fast moving structures such as vegetations, or assess the dynamic behaviour of mitral annulus [14]. But some annular variables (diameters and angels) can be obtained by 2DE, their accuracy may be compromised by incorrect viewing plane selection or regional valvular asymmetry.

We are unaware of any attempt at validation of full multidimensional modelling and measurements of the entire MV variables including its annulus and leaflets. To our best knowledge, this MSM technique is the first to report the use of MSM to generate a multidimensional, comprehensive and patient-specific, dynamic model of the MV derived from that patient's 3D TOE. Using information from the entire cardiac cycle, the MSM accurately captures different and changing geometric configurations of the MV, expressed both in terms of measured distances and angles between valve structures. Moreover, the MSM is the first to report measuring the parameters in multidimensional space.

Measurements of the AP (also called septal–lateral distance SLD [15]) and IC diameters reveal significant variations during the cardiac cycle—increases of ~10% in mid-diastole compared with mid-systole—while there is virtually no variation in anterolateral and posteromedial annular diameters. This confirms and extends previous knowledge on normal mitral annulus dimensions [16].

While Warraich et al. have previously measured the MV and annulus angle and described the AP angle at the commissural level as a non-planarity angle [17], we describe the new 3D angle, that between the anterior and lateral annulus—the anterolateral angle. Measurement of this new angle (anterolateral angle) showed that the annulus is angulated acutely during the diastole rather during the systole. This was also confirmed by measuring the AP angle at the commissural level in both systole and diastole.

Appreciation of changes in this angle allows for a more precise quantification of the nature and varying degree of concavity of the MV compared with just recording the AP angle at the level of coaptation of the leaflets and at the commissural level. This is because

(i) The change in angulation of the MV annulus can be appreciated at the level of the anterolateral junction and not at the level of coaptation of the leaflets.

| Table 1: Demographic data
<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 (29–77) years</td>
</tr>
<tr>
<td>Male</td>
<td>21 (65.63%)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (34.38%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (31.25%)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>11 (34.38%)</td>
</tr>
<tr>
<td>Good LV function</td>
<td>26 (81.25%)</td>
</tr>
<tr>
<td>Mild LV dysfunction</td>
<td>6 (18.75%)</td>
</tr>
<tr>
<td>PFO</td>
<td>3 (9.38%)</td>
</tr>
</tbody>
</table>

MI: myocardial infarction; LV: left ventricular; PFO: patent foramen ovale.

Figure 5: (A and B) Correlation between anteroposterior angle at the commissural level (red angle) with anteroposterior angle at the coaptation level (blue angle) in which the mitral leaflets are angulated at the coaptation level and form a saddle shape. (C) The shape of the mitral valve annulus, in which the mitral annulus is angulated at the anterolateral junction and forms an inverted flat cap shape.

Video 1: The video showing patient specific dynamic displacement during all step of one cardiac cycle and from different views.
(ii) Localization of the AP angle at the commissural level is not accurate due to inherent approximations used in creating a reference point in the IC diameter.

(iii) The measurement of an AP angle at the coaptation level is disturbed in pathological situations, for example, in ischaemic and degenerative MV diseases [18, 19]. This angle may, in such cases, accentuate obtusely in degenerative MV due to the plugging of MV leaflets into the left atrium. It may also accentuate acutely in MV disorders caused by myocardial ischaemia due to tenting of the MV leaflets [18, 19].

(iv) Measurement of the new anterolateral angle can be performed at any phase of the cardiac cycle, whereas the AP angle at the leaflet coaptation level can only be measured during the systolic phase. Measurements of the three angles showed that the AP angle was at the commissural level; and the anterolateral angle describes the concavity of the MV annulus, which has the appearance of an inverted flat cap, whereas the AP angle at the coaptation level describes the concavity of the MV leaflets which, at the coaptation level, is saddle shaped.

We believe that measurements of the anterolateral angle, within the 3D model derived from TOE, reflect both an accurate description of MV annulus angulation and may also help in the diagnosis of MV disease. Detection of MV movement throughout the cardiac cycle may accurately help in describing the normal physiology of MV and enable reliable comparisons between normal and pathological situations of MV displacement and deformities. This may guide the surgeons to pre-plan MV repair of different surgical repair procedures through direct analysis of the lesions. These models are based on mathematical models which one can create a mesh and can be applicable for further numerical simulation [20]. Precise knowledge of these measurements for each patient may assist surgeons preoperatively to choose the correct size of the mitral ring especially in minimally invasive techniques where exposure can be challenging. In addition, visualization of the mitral annulus may help design new mitral rings that can take account of dynamic descriptions of MV annular movement and comprehensive measurements. Furthermore, MSM may help identification of the impact of various tapes of MV annuloplasty on MV components.

### Table 2: 3D geometric data, measurements of different diameters, lengths and angles

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Results, median (range) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercommissural diameter in mid-systole</td>
<td>31.93 (28.96–34.90)</td>
</tr>
<tr>
<td>Intercommissural diameter in mid-diastole</td>
<td>34.88 (31.20–38.21)</td>
</tr>
<tr>
<td>Anterolateral-posteromedial diameter in mid-systole</td>
<td>43.77 (36.35–48.93)</td>
</tr>
<tr>
<td>Anterolateral-posteromedial diameter in mid-diastole</td>
<td>43.53 (35.54–47.53)</td>
</tr>
<tr>
<td>Anteroposterior diameter mid-systole</td>
<td>32.59 (29.88–35.27)</td>
</tr>
<tr>
<td>Anteroposterior diameter mid-diastole</td>
<td>35.25 (31.83–38.56)</td>
</tr>
<tr>
<td>Anterior annulus length</td>
<td>41.83 (39.98–45.35)</td>
</tr>
<tr>
<td>Posterior annulus length</td>
<td>80.28 (65.33–84.36)</td>
</tr>
<tr>
<td>Annular circumference</td>
<td>122.11 (106.31–129.71)</td>
</tr>
</tbody>
</table>

### Table 3: Statistical analysis for every mitral valve parameter

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Median (range) (mm)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercommissural diameter in mid-systole/intercommissural diameter in mid-diastole</td>
<td>31.9 (28.9–34.9)/34.8 (31.2–38.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterolateral-posteromedial diameter in mid-systole/anterolateral-posteromedial diameter in mid-diastole</td>
<td>43.7 (36.3–48.9)/43.5 (35.5–47.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anteroposterior diameter mid-systole/anteroposterior diameter mid-diastole</td>
<td>33.8 (29.8–35.2)/37.1 (31.8–38.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intercommissural diameter in mid-systole/anteroposterior diameter mid-systole</td>
<td>31.9 (28.9–34.9)/32.5 (29.8–35.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intercommissural diameter in mid-diastole/anteroposterior diameter mid-diastole</td>
<td>34.8 (31.2–38.2)/35.2 (31.8–38.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Median (range) (degree)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anteroposterior angle at the coaptation level in systole</td>
<td>140 (127–149)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anteroposterior angle at the commissural level in systole</td>
<td>126 (113–137)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anteroposterior angle at the commissural level in diastole</td>
<td>115 (104–129)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterolateral angle in systole</td>
<td>119 (106–130)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterolateral angle in diastole</td>
<td>105 (97–113)</td>
<td>&lt;0.001</td>
</tr>
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</table>
These segmented geometries can also be converted into 3D printable anatomical models. The printed models can be used in medical education, in explaining diseases, treatments and risks of interventions with patients and in analysing and understanding particular lesions aiding surgical planning (even simulating) repair procedures to the MV in advance of operations [21].

In summary, the MSM technology offers significant opportunities in understanding the MV, the development of preoperative planning models and new imaging methods, which in turn could lead to better clinical outcomes for patients.

Limitations

Although this protocol was designed to study subjects with normal valves, patients were recruited from those referred for clinically indicated TOE. Therefore, these patients are not a true sample of a normal population. However, we feel that we were working with information from patients with clinically normal MV.

This technique segments MV geometry in a semi-automatic way. There remains a requirement for user interaction during automatic separation of the MV from its surrounding structures. The current segmentation of MV, however, is fully automated with direct thresholding of MV components, depending on image quality. Manual separation of the MV from encircling tissues requires time and expertise on MV anatomy, physiology and pathophysiology.

ACKNOWLEDGEMENTS

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Conflict of interest: All authors had full control of the study design, methods used, outcome parameters, analysis of the data and production of the written report. The models were designed and developed by Abdullrazak Hossien.

REFERENCES


