Level of agreement between three-dimensional transthoracic and transesophageal echocardiography for mitral annulus evaluation: a feasibility and comparison study

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June 14, 2022

Abstract

Introduction: Mitral annulus (MA) assessment is of utmost importance for the management of patients with mitral valve (MV) abnormalities and Three-dimensional transesophageal echocardiography (3D-TOE) has been the only reliable echocardiographic method for the evaluation of the mitral annulus by now. However, newer transthoracic echocardiography (TTE) probes have enabled to provide accurate measurements when TOE is contraindicated. The aim of this study is to assess the feasibility of 3D-TTE analysis of MA and the level of agreement with 3D-TOE measurements. Methods: A total of 121 consecutive patients were assessed with 3D-TTE and TOE. All MA parameters were retrospectively analyzed with the dedicated 4D-autoMVQ application. Bland-Altman analysis and intraclass correlation coefficient were used for the comparison and agreement between the two methods. Half of our patients had normal mitral valves and served as control group, while the other half had various mitral valve pathologies. Results: AutoMVQ analysis was not feasible in 11 out of 121 TTE examinations (91% feasibility) and in 4 out of 121 TOE examinations (96% feasibility). MA area and perimeter were slightly larger in TTE than those measured by TOE (12.7±3.6 vs 12.4±3.2cm2 for area and 12.7±1.7 vs 12.5±1.6cm for perimeter), however still showing strong correlation (r=0.942 and r=0.922 respectively). The majority of MV measurements were similar between the two methods with strong correlation (r>0.80). Conclusions: Assessment of the MV with 3D TTE with dedicated MVQ software is feasible and accurate, showing strong correlation and agreement with TOE measurements.

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Data Availability statement

All data are available in the workstation of our Echocardiography department

Funding Statement

No funding was received for the purpose of this publication

Conflict of Interest disclosure

There are no conflicts of interest from all authors of the manuscript

Ethics Approval Statement

The current study was approved by the ethics committee of our hospital

Patient Consent Statement

All patients have given written consent for this publication

Permission to reproduce material from other sources

No material was used from other sources

Clinical Trial registration

Not applicable

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Methods: A total of 121 consecutive patients were assessed with 3D-TTE and TOE. All MA parameters were retrospectively analyzed with the dedicated 4D-autoMVQ application. Bland-Altman analysis and intraclass correlation coefficient were used for the comparison and agreement between the two methods. Half of our patients had normal mitral valves and served as control group, while the other half had various mitral valve pathologies.

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Brief title : Mitral annulus assessment with 3D TTE and TOE

Key words : 3D echocardiography, mitral annulus, transesophageal echocardiography

Introduction

Mitral valve (MV) pathologies are very common and represent approximately one-third (35%) of all valvulopathies in the Euro Heart Survey (1). Echocardiography is the gold standard imaging method for MV assessment, and all patients in need for a precise mitral valve analysis, undergo a transesophageal examination (TOE) for detailed assessment of the leaflets and the mitral annulus. Precise quantification of mitral regurgitation (MR), localization of the prolapsing scallops and accurate MV area assessment are of paramount importance for the management of this subgroup of patients (2). However, considering the semi-invasive nature of the method; repeated, routine TOE examinations cannot be the common practical approach during the follow up visits of these patients. In daily practice, echocardiographers use TTE, with standard two-dimensional (2D) protocols that rarely include information about mitral annular dimensions. Three-dimensional (3D) TTE protocols are also seldomly used and depend on the performer's training and level of expertise. Technical advancements in echocardiography, offered the option for MV and annulus reconstruction and assessment through new, dedicated, post-processing softwares that provide measurements of all mitral annular and leaflet dimensions. Until recently, TOE was the only method for correct measurements. However, TTE probes have evolved and they can achieve higher spatial and temporal resolution and allow echocardiographers to assess the mitral annulus accurately without the need of the TOE probe. This remains as the main advantage of TTE, as we do not have to sedate the patient and perform this semi-invasive transesophageal method.

3D TOE and CT are essential for planning transcatheter (TCT) interventions of the MV (3,4) and 3D TOE is the standard method used to evaluate the MV anatomy. The mitral annulus size is one of the key parameters necessary to predict outcomes in transcatheter edge-to-edge repair (TEER), and to decide about the sizing of the valve during transcatheter mitral valve replacement (TMVR) (3,4). Cardiac CT with ECG gating is the gold standard method for anatomy assessment and annulus measurements prior to TCT. However, when contrast CT is contraindicated, 2D/3D TOE may be an alternative, accurate option for MV quantitation. Insertion of TOE probe is feasible in more than 99% of the patients that undergo this examination. However, TOE with the common adult probe may not be possible in patients with esophageal disorders (5-10) and as pediatric TOE probes do not provide a sufficient image quality, we should not rely on them for accurate results. In such conditions, 3D TTE may offer the option for annulus assessment with a non-invasive way.

A direct comparison of 3D TTE and 3D TOE for mitral annulus assessment has never been previously described. The aim of this study is to demonstrate the feasibility of MVQ analysis using both methods and to evaluate the level of agreement for assessing the mitral annular geometry.

Methods

Study population

We retrospectively analyzed the data obtained from 121 consecutive patients, who visited our echocardiography department between October 2019 and August 2020 for TOE examination. 67 patients were males (55.7%), while 54 were females (44.3%), aged 64±13 years. All patients underwent TTE and TOE evaluation during the same visit and all data were stored and analyzed by two cardiologists experienced on echocardiography (KP and II). The only exclusion criterion for this study was previous history of surgical or transcatheter MV repair or replacement. A written informed consent form was obtained from all participants and the protocol was approved by the local ethics committee.

3D transthoracic and transesophageal echocardiographic data

All examinations were performed with the GE Vivid E95 echo machine (GE Vingmed Ultrasound, Horten, Norway), using the 4Vc TTE and the 6VT-D TOE probes. All data were stored and retrospectively analyzed with the EchoPAC v.203 workstation.

For 3D TTE measurements, MV was demonstrated in four-chamber view and 4D "en face" views were acquired by using "4D zoom prepare" method, with a frame rate of more than 12 volumes per second (vps). For TOE measurements, the MV was visualized in the commissural view (approx. 60-70°) and 4D "en face" MV views were captured by using "4D zoom prepare" method, also with a frame rate of more than 12vps. In patients with sinus rhythm, multi-beat acquisitions were used in order to achieve high temporal and spatial resolution, whereas single-beat acquisition was used in patients with atrial fibrillation (AF) or other rhythm abnormalities, and in patients that were unable to perform a satisfying breath hold.

All data were stored in an EchoPAC workstation and 3D datasets were analyzed using the 4D AutoMVQ software. This is a semi-automated software dedicated for mitral annulus and leaflets analysis. The operator performs the following three steps for MV assessment: 1) alignment of the commissural and long axis views so that the vertical axis crosses through the center of the MV and the horizontal axis is parallel to the MV, 2) setting the six landmark points of MV annulus, aortic valve and leaflet coaptation point and 3) review of the MV model that is generated automatically by the software. In the final screen, different layouts of the mitral valve can be demonstrated (2D views, volume rendering en face view and MV model) along with all the measurements for the annulus and the leaflets. (Figure 1)

The variables that were analyzed and compared in our protocol are: 1) 2D & 3D annulus area, 2) annulus perimeter, 3) anterior-posterior diameter, 4) medial-lateral diameter, 5) commissural diameter, 6) inter-trigonal diameter, 7) aorto-mitral angle, 8) anterior leaflet area, 9) posterior leaflet area, 10) anterior leaflet length, 11) posterior leaflet length, 12) tenting height, 13) tenting area and 14) tenting volume.

Statistical analysis

Continuous variables are presented as mean ± SD when normally distributed and as median and interquartile range otherwise. Categorical variables are expressed as percentages of the population. Continuous variables were tested by the Kolmogorov-Smirnov test to assess the normality of distribution. An independent t-test or Wilcoxon signed-rank test was used for various comparisons among groups [MV pathologies, atrial fibrillation (AF), left atrial (LA) dilatation, left ventricular (LV) dilatation and coronary artery disease (CAD)] and Bland-Altman methodology and intraclass correlation coefficient (ICC) were used for comparison of the two methods (TTE and TOE). All tests were 2-sided, and a significance level of 5% was used ($p<0.05$). Statistical analysis was performed using the SPSS 23.0 statistical software package (SPSS Inc, Illinois, USA).

Inter-observer and intra-observer variability

Thirty patients were selected and analyzed by two cardiologists, experienced in TOE and 3D echocardiography, blinded to each other's results. Intra-observer variability was assessed by repeating measurements of the same patients at different times, whereas inter-observer variability was assessed by analyzing the same patients by two cardiologists. Both variabilities were calculated by intraclass correlation coefficient (ICC) and the standard error of measurement. Among all variables provided by the software, 3D area and annulus perimeter were chosen for variability evaluation. Both TTE and TOE AutoMVQ measurements of the 3D area and perimeter demonstrated satisfying intra-observer and inter-observer variability with ICC values of more than 0.78 (table 1).

Results

Demographics and Clinical characteristics

A total of 121 consecutive patients, who underwent a TOE examination were considered as candidates for this study. AutoMVQ analysis was feasible in 110 out of 121 TTE examinations (91% feasibility) and in 117 out of 121 TOE examinations (96% feasibility). Eventually, 106 patients met the eligibility criteria for inclusion in the study, while the rest 15 patients didn't have adequate images for 3D modeling of the MV and were not included in the study. The most common reasons for poor TTE acquisition were lung disease, obesity, irregular rhythm and severe mitral annular calcification. On the other hand, the most common reasons for poor imaging in TOE were arrhythmias, stitching artifacts, low frame rate and non-cooperative sedated patients. The baseline patient characteristics and the clinical indications for TOE are depicted in Table 2. The most common indication for TOE was MV pathology (47.1%), followed by the need for left atrial appendage (LAA) evaluation before AF cardioversion.

The majority of patients (92 patients, 86.8%), had normal LV function (mean LV ejection fraction 56.8±9.7%). Some degree of LA dilatation was present in 79 patients (74.5%), whereas 72 patients (67.9%) had normal LV volumes. With respect to MV anatomy, 56 patients (52.8%) suffered from MR or stenosis and 50 patients (47.2%) had normal MV anatomy and served as control group. More specifically, 24 patients (22.6%) suffered from primary MR, 16 patients (15.1%) suffered from functional MR and 16 patients (15.1%) suffered from mitral stenosis.

3D echocardiography data

A 3D modeling of MV with AutoMVQ analysis was performed in TTE and TOE examinations of all patients enrolled in the study (figure 2). The software automatically provided results for all mitral annulus and leaflets variables. All TTE and TOE measurements and the agreement between the two methods are shown in Table 3. 3D TTE proved to be accurate in the assessment of mitral annulus and showed strong correlation with TOE. Among the TTE variables that were analyzed, tenting height, tenting area, posterior leaflet length and inter-trigonal diameter, showed the weakest correlation with TOE (Table 3), while 3D annulus area and perimeter that are most important measurements for MV, demonstrated the highest correlation (Table 3). (figure 3). Most MV components (annulus and leaflets) were found to be significantly larger in the subgroup of patients with MV pathologies either measured by TTE or TOE (Table 4).

The 3D MV area and mitral annulus perimeter were analyzed and compared in different subgroup of patients. Clinical and echocardiographic factors that affected the size of the annulus significantly were AF ($p<0.001$), LA dilatation ($p<0.001$ for TTE comparisons and $p=0.001$ for TOE comparisons) and LV dilatation ($p<0.01$ for all comparisons) (Table 5). Patients with CAD showed a trend but not statistically significant differences in the 3D annulus area ($p=0.121$) and perimeter (p=0.105) compared to controls.

Agreement between 3D TTE and TOE measurements

The Bland-Altman analysis showed a good agreement between 3D TTE and TOE measurements of mitral annular area and perimeter for the whole study cohort (Figures 3a and 3b) as well as in the subgroups with MV pathology (Figures 3c and 3d) and those with normal MV (Figures 3e and 3f). More specifically, for mitral annular area measurements, the Bland–Altman analysis indicated a mean difference between 3D TOE and TTE of a) -0.34 cm^2 (CI: 0.56–0.11cm^2) with limits of agreement -2.6–1.8cm^2, for all subjects, b) of -0.57 cm^2(CI: 0.89–0.25cm^2) with limits of agreement -2.8–1.6cm^2, for those with MV pathology c) of -0.08 cm^2(CI: 0.40–0.22cm^2) with limits of agreement -2.2–2.0cm^2, for those with normal MV. For mitral annular perimeter measurements similarly, the Bland–Altman method indicated a mean difference between 3D TOE and TTE of a) -0.19 cm (CI: 0.33–0.06cm) with limits of agreement -1.5-1.1cm, for all subjects b) of 0.34 cm (CI: 0.17–0.51cm) with limits of agreement -0.9–1.5cm, for those with MV pathology c) of 0.04 cm (CI: 0.16–0.24cm) with limits of agreement -1.3–1.4cm, for those with normal MV. Therefore, the Bland–Altman analysis demonstrated acceptable limits of agreement between 3D TTE and TOE MV measurements.

We also calculated the intraclass correlation coefficient (ICC) for every parameter among the 3D TTE and TOE (with the same operator in every measurement for all patients). The ICC for MV annular area was 0.94 (CI: 0.91–0.95) whereas it was 0.92 for MV annular perimeter (CI: 0.88–0.95) between 3D TTE and TOE, in all subjects. For tenting area and posterior leaflet length, the ICC was 0.68 (CI: 0.56-0.77) and 0.69 (CI: 0.57-0.78) respectively.

Similar values of ICC were obtained for 3D MV parameters both in those with MV pathology and those with normal MV.

Discussion

The main findings of our study were as follows: 1) MV anatomy can be quantified by TTE using dedicated algorithms such as 4D AutoMVQ in the vast majority of patients undergoing TOE for the same purpose, 2) there is high level of agreement of all mitral annulus and leaflets measurements between 3D TTE and TOE, 3) the mitral annulus dimensions quantified by 3D TTE are abnormal in patients with MV pathologies, atrial fibrillation, LV and LA dilatation, as compared to healthy subjects.

Routine methods of analyzing mitral annulus

The European Society of Cardiology (ESC) recommendations suggest A-P diameter of the mitral annulus to be the gold standard measurement for guiding surgical interventions and do not take into account the annulus area and circumference (11). However, one of the first indications for 3D echocardiography was MV assessment (12,13) and the development of probes and software helped in understanding the exact complex anatomy of the annulus and the leaflets, label the scallops and commissures, localize the pathology and provide corresponding "surgical" 3D en face views of the MV (13,14). This advanced quantitative assessment of the annular geometry helped the surgeons to improve the reparative surgery results (15). Still, all these measurements were provided from TOE examinations and, through several previous clinical studies, it has been confirmed that these data correlate well with the ones measured with cardiac computed tomography (3, 4, 16), cardiac magnetic resonance (17,18) and even the direct valve measurements during the operations (19). Nevertheless, it is practically difficult to follow up every patient with TOE, as this is a semi-invasive method that mostly requires sedation which may alter the hemodynamics of the patient resulting in inaccurate assessment during mitral regurgitation evaluation. TTE is the gold standard method for routine evaluation of patients, as TTE probes achieve high quality 2D and color Doppler images that make the assessment relatively easy (11). Recent developments in TTE probes increased the spatial and temporal resolution and provided more detailed evaluation of the MV. Thus, 3D TTE became more reproducible and accurate. Our study demonstrated a strong correlation between TTE and TOE in mitral annular assessment, however further investigation needs to be done to establish TTE for routine MV assessment.

Feasibility of AutoMVQ and comparison between TTE and TOE

There are a few studies in the literature which have included patients that were examined with TTE for MV analysis with promising results (20-22). In our study, we analyzed consecutive patients who were referred to our echo lab for TOE. All annulus and leaflet parameters were calculated in both TTE and TOE and statistical analysis demonstrated strong agreement between the two methods. 4D AutoMVQ analysis was more feasible and simpler with TOE rather than with TTE (96% vs 91%) due to clinical parameters that led to suboptimal TTE imaging, such as obesity, lung disease and inability for breath-hold for multi-beat acquisitions, or echocardiographic parameters that reduced the reproducibility of the method, such as irregular rhythm, extremely enlarged ventricles or atria and severe mitral annulus calcification.

Mitral annulus was larger in patients that were on AF, had MV pathologies (regurgitation or stenosis) or left ventricular and left atrial dilatation. Coronary artery disease did not affect the mitral annulus dimensions, except in case of ischemic cardiomyopathy and dilated LV. Patients with MR or mitral stenosis had increased dimensions of annulus but similar aorto-mitral angle, tenting height and tenting area. Tenting values were unaffected only in primary MR cases since in FMR tenting height is increased due to the tethering of the leaflets. The anterior mitral leaflet length was another variable that did not change along with the annulus enlargement. The presence of the trigonal fibrous tissue and the aorto-mitral continuity work as stabilizers for the anterior part of the valve. The posterior leaflet on the other hand is surrounded by the free wall of the atrium and ventricle which may explain the enlargement of the annulus towards this direction.

Clinical Implications

Cardiac surgeons rely on different annular dimensions measured in the operating room to choose the correct size of annular ring for mitral valvuloplasty (21, 23-28). Sizing is of great importance in FMR and DMR cases in order to avoid residual MR and complications such as iatrogenic MS and systolic anterior motion of the anterior leaflet (SAM). The vast majority of surgeons use the Carpentier sizers to choose the correct annulus ring. These sizers measure the inter-trigonal distance, the commissural diameter, the anterior leaflet length and the annulus circumference. Using the dedicated AutoMVQ software with TTE and TOE, these variables can be measured accurately and help the surgeons to decide about the ring size in advance. In FMR patients, further information about the tenting height and area may guide the decision towards valve repair or replacement, as a very tethered valve appears to be less successfully reparable, with high rates of MR relapse (25, 29).

A more detailed analysis of the mitral annulus can also guide transcatheter therapies for valve repair or replacement (21,23). Transcatheter MV annuloplasty methods require meticulous measurements of the annulus circumference and currently cardiac computed tomography (CCT) is the gold standard technique for this measurement (30). However, previous studies have shown that 3D TOE correlates well with CCT measurements (16). The MV annulus area and circumference can also guide the transcatheter MV replacement either with valve-in-MAC (Mitral Annular Calcification) technique or transcatheter valves dedicated for the mitral position (intrepid, Tendyne, etc.). (31) All these therapies use CCT for pre-procedural planning and sizing of the device. 3D echocardiography though becomes inevitable in patients with renal failure who cannot undergo a CT scan with iodine contrast due to acute kidney injury risk. As 3D TOE and CCT correlate well for mitral annular measurements, 3D TTE can be the first-line diagnostic method for this subgroup of patients. Moreover, as 3D echocardiography, has the advantage of avoiding contrast agent and radiation exposure, the need for further investigation of MVQ analysis and establishment of the method is warranted.

Finally, another noteworthy feature of this software is the aorto-mitral angle assessment (27,28). As already known, patients referred for MV replacement (surgical or transcatheter) are not suitable for that surgery if abovementioned angle is too narrow due to high probability of creating a small neo-LVOT with high gradients. The aorto-mitral angle may also increase the risk of creating SAM in MV repair cases where an annular ring is placed.

Till recently, all these data were depicted from analysis of TOE images. However, there is a subgroup of patients that have relative or absolute contraindications for TOE (5-10) or cannot tolerate the adult TOE probe even under sedation. As shown in our study, all necessary information for mitral annulus and leaflets can be provided with analysis of 3D TTE images with the AutoMVQ software with high accuracy and good correlation with TOE and CCT measurements.

Conclusions

The AutoMVQ analysis is feasible in TTE and TOE examinations of the MV, applicable in patients who need to be treated surgically or with transcatheter therapies. The level of agreement of all mitral annulus measurements between TTE and TOE is strong enough to allow for the less invasive TTE diagnostic method for our patients and give the option for annulus assessment in patients with contraindications for cardiac CT or TOE. However, when a more extensive anatomical and functional MV interrogation is deemed necessary for proper decision making, and the patient's characteristics allows it, TOE should be preferred over TTE. Further clinical studies with large series of cases are needed in order to establish 3D TTE as an accurate and reproducible method for annulus assessment compared to TOE.

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Table 1: Intra-observer and inter-observer variability

	Intraclass correlation coefficient (ICC, 95% CI)	**Intraclass correlation coefficient (IC**
Variables	**Intra-observer variability**	**Inter-observer variability**
TTE 3D annulus area	0.89, 95% CI:0.83-0.93	0.87, 95% CI:0.8-0.92
TTE annulus perimeter	0.93, 95% CI:0.86-0.96	0.78, 95% CI:0.6-0.89
TOE 3D annulus area	0.97, 95% CI:0.94-0.99	0.96, 95% CI:0.89-0.98
TOE annulus perimeter	0.95, 95% CI:0.89-0.98	0.85, 95% CI:0.78-0.9

Table 2: Clinical and echocardiographic characteristics of study population

Clinical characteristics	
Age (years)	64.5±13.3
Males, n (%)	67(55.7%)
NYHA (class)	2±1
AFib, n (%)	34(32.1%)
CAD, n (%)	26(24.5%)
EF (%)	57±10
MV pathologies, n (%) *1.MR 2.MS*	56(52.8%) 40(37.7%) 16(15.1%)

Clinical characteristics	
LV dilatation, n (%)	34(32.1%)
LA dilatation, n (%)	79(74.5%)
Indication for TOE	
1.MV pathologies (MR+MS)	50(47.2%)
2.LAA evaluation	18(17%)
3.PFO assessment	11(10.4%)
4.Aortic stenosis	8(7.5%)
5. Other indications	19(17.9%)

Table 3: Comparison of 3D MV measurements with TTE and TOE

Echocardiography data	**3D TTE**	**3D TOE**	**correlation**	p value
Number of patients	106	106		
Annulus area 3D (cm^2)	12.7±3.6	12.4±3.2	0.942	*<0.001*
Annulus area 2D (cm2)	12±3.4	11.6±3	0.938	*<0.001*
Annulus perimeter (cm)	12.7±1.7	12.5±1.6	0.922	*<0.001*
A-P diameter (cm)	3.6±0.5	3.6±0.5	0.831	*<0.001*
M-L diameter (cm)	3.9±0.6	3.9±0.5	0.900	*<0.001*
Commissural diameter (cm)	3.9±0.5	3.8±0.5	0.799	*<0.001*
Inter-trigonal diameter (cm)	2.7±0.4	2.7±0.4	0.687	*<0.001*
Mitral-aortic Angle (degrees)	124±11	124±10	0.844	*<0.001*
Anterior leaflet area (cm2)	6.4±1.7	6.1±1.5	0.845	*<0.001*
Posterior leaflet area (cm2)	7.8±2.7	7.5±2.4	0.912	*<0.001*
Anterior leaflet length (cm)	2.4±0.4	2.3±0.4	0.806	*<0.001*
Posterior leaflet length (cm)	1.7±0.4	1.7±0.4	0.687	*<0.001*
Tenting height (cm)	0.6±0.3	0.6±0.3	0.634	*<0.001*
Tenting area (cm2)	1.7±0.8	1.6±0.7	0.683	*<0.001*
Tenting volume (ml)	2.7±1.8	2.7±1.8	0.831	*<0.001*

Table 4: Comparison of MV quantitation in patients with or without MV pathology

MV measurements	**3D TTE**	**3D TTE**	p value	**3D TOE**	**3D TOE**	p value
MV pathology	Abnormal	Normal		Abnormal	Normal	
Number of patients	56	50		56	50	
Annulus area 3D (cm2)	14.2±3.6	11±2.7	*<0.001*	13.5±3.5	11±2.3	*<0.001*
Annulus area 2D (cm2)	13.5±3.4	10.3±2.5	*<0.001*	13±3.2	10.3±2.1	*<0.001*
Annulus perimeter (cm)	13.4±1.7	11.8±1.4	*<0.001*	13±1.7	11.8±1.3	*<0.001*
A-P diameter (cm)	3.8±0.4	3.3±0.4	*<0.001*	3.8±0.5	3.4±0.4	*<0.001*
M-L diameter (cm)	4.2±0.6	3.6±0.4	*<0.001*	4.1±0.5	3.7±0.4	*<0.001*
Commissural diameter (cm)	4.1±0.5	3.6±0.4	*<0.001*	4±0.5	3.6±0.4	*<0.001*
Inter-trigonal diameter (cm)	2.8±0.5	2.6±0.3	*0.08*	2.8±0.5	2.6±0.3	*0.002*
Mitral-aortic Angle (degrees)	124±9	124±12	*0.994*	124±10	124±10	*0.927*
Anterior leaflet area (cm2)	7.2±1.6	5.6±1.4	*0.001*	6.7±1.5	5.4±1.3	*<0.001*
Posterior leaflet area (cm2)	9±2.6	6.5±2.1	*<0.001*	8.6±2.5	6.3±1.6	*<0.001*
Anterior leaflet length (cm)	2.5±0.4	2.3±0.3	*0.001*	2.4±0.5	2.3±0.4	*0.31*
Posterior leaflet length (cm)	1.8±0.4	1.6±0.4	*0.001*	1.9±0.4	1.5±0.3	*<0.001*
Tenting height (cm)	0.6±0.4	0.7±0.2	*0.251*	0.7±0.3	0.7±0.2	*0.712*

MV measurements	3D TTE	3D TTE	p value	3D TOE	3D TOE	p value
Tenting area (cm2)	1.8±0.9	1.6±0.7	*0.245*	1.8±0.9	1.5±0.6	*0.08*
Tenting volume (ml)	3.1±1.9	2.4±1.7	*0.07*	3.1±2	2.4±1.5	*0.05*

Table 5: Comparison of MV dimensions related to different clinical and echocardiographic characteristics

* Refers to statistical significance with $p<0.05$

Variables	**AFib***	**AFib***	**LV dilatation***	**LV dilatation***
	no	**yes**	**no**	**yes**
TTE 3D annulus area (cm2)	11.8±3	14.8±3.9	12.1±3.6	14±3.1
TTE annulus perimeter (cm)	12.2±1.5	13.7±1.8	12.3±1.8	13.3±1.5
TOE 3D annulus area (cm2)	11.4±2.8	14.4±3	11.7±3.1	13.8±3.1
TOE annulus perimeter (cm)	12±1.5	13.5±1.4	12.1±1.6	13.2±1.5
	LA dilatation*	**LA dilatation***	**CAD**	**CAD**
	no	**yes**	**no**	**yes**
TTE 3D annulus area (cm2)	10.4±2.6	13.6±3.5	12.3±3.4	14.2±3.8
TTE annulus perimeter (cm)	11.5±1.4	13±1.7	12.4±1.7	13.4±1.8
TOE 3D annulus area (cm2)	10.6±2.3	13±3.3	12.1±3.2	13.2±3.3
TOE annulus perimeter (cm)	11.6±1.2	12.8±1.6	12.3±1.6	12.9±1.6

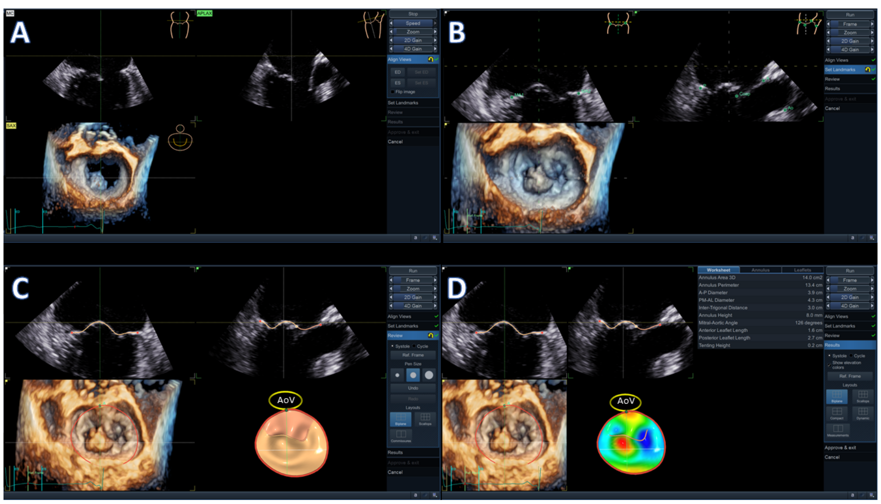

Figure 1: Step-by-step approach for AutoMVQ analysis. AoV=aortic valve. A) alignment of commissural and long axis views according to the suggested figures on the top of the screen, B) setting landmarks at mitral annulus (MA1 & MA2), posterior leaflet (P), anterior leaflet (A), coaptation point (Coapt) and aortic valve hinge point (Ao), C) review and change of the tracing of the leaflets at both views, D) results analysis and demonstration of mitral valve model.

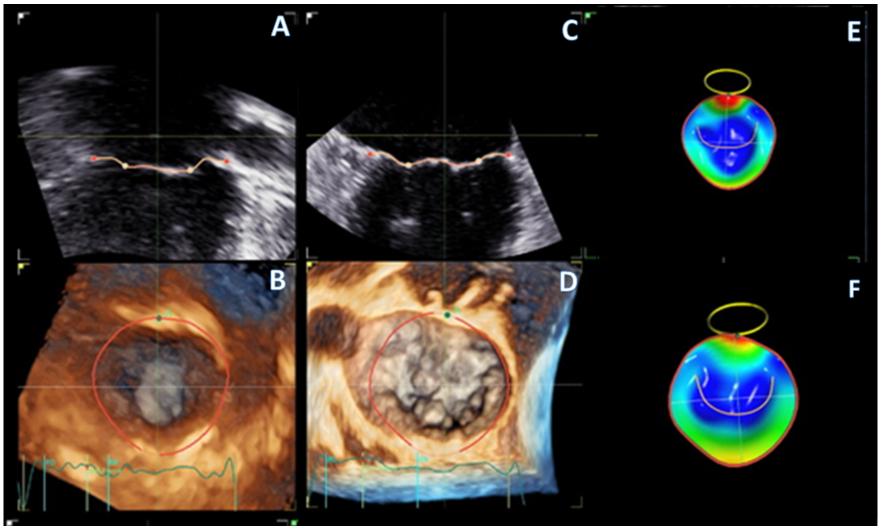

Figure 2: Analysis of mitral annulus with 3D transthoracic and transesophageal echocardiography in a patient with severe functional mitral regurgitation (FMR). A) 2D TTE image of mitral valve, B) Volume rendering 3D TTE image, c) 2D TOE image of MV, D) volume rendering 3D TOE image, E&F) TTE and TOE model of mitral valve

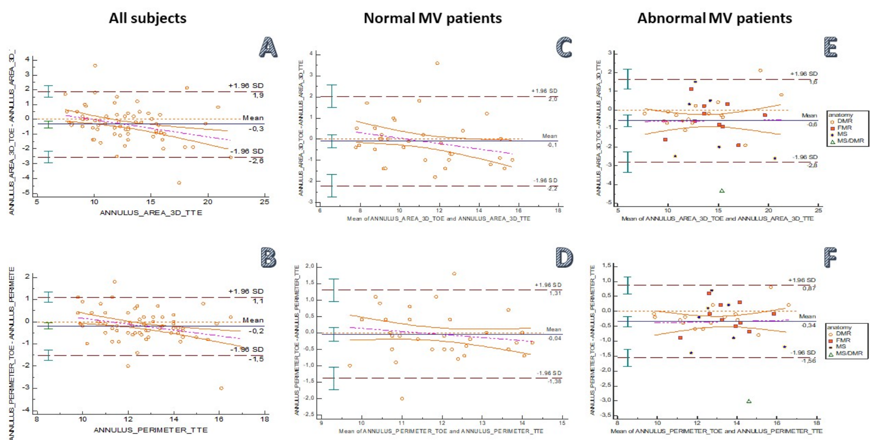

Figure 3: Bland-Altman analysis of MV annulus area and perimeter in i) all subjects (figures A and B), ii) in patients with normal mitral valve (figures C and D) and iii) in patients with mitral valve abnormalities (figures E and F)