Three-Dimensional Echocardiographic Anatomical Intelligence for Mitral Valve Quantification

Brief title: Anatomical Intelligence in Mitral Valve Quantification

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ABSTRACT

Background: Quantitative analysis of mitral valve with three-dimensional (3D) transesophageal echocardiography (TEE) provides anatomic information that can assist clinical decisions. However, routine use of mitral valve quantification has been hindered by tedious workflow and high operator-dependence. The purpose of this paper was to evaluate the feasibility, accuracy and efficiency of a novel computer-learning algorithm using anatomically intelligent ultrasound (AIUS) to automatically detect and quantify mitral valve anatomy.

Methods and Results: A novice operator used AIUS to quantitatively assess mitral valve anatomy on the 3D TEE images of 55 patients (33 with mitral valve prolapse, 11 with functional mitral regurgitation, and 11 normal valves). The results were compared to that of manual mitral valve quantification by an experienced 3D echocardiographer and, in the 24 patients who underwent mitral valve repair, the surgical findings. Time consumption and reproducibility of AIUS were compared to novice manual measurements. AIUS mitral valve quantification was feasible in 52 patients (95%). There were excellent agreements between AIUS and expert manual quantification for all mitral valve parameters ($r=0.85\sim0.99$, $p<0.05$). AIUS accurately classified surgically defined location of prolapse in 139 of 144 segments analyzed (97%). AIUS improved the intra- [intraclass-correlation coefficient (ICC)=0.91~0.99] and inter-observer (ICC=0.86~0.98) variability of novice users, surpassing the manual approach (intra-observer ICC=0.32~0.95; inter-observer ICC=0.45~0.93), yet requiring significantly less time (144±24s vs. 770±89s, $p<0.0001$).

Conclusion: Anatomical intelligence in 3D TEE image can provide accurate, reproducible, and rapid quantification of the mitral valve anatomy.

Key words: mitral valve, computer imaging, anatomical intelligence, three-dimensional echocardiography, transesophageal echocardiography

INTRODUCTION

Mitral regurgitation is the most common form of valve dysfunction in industrialized countries.[1] Accurate assessment of the mitral valve anatomy is crucial for understanding of the pathogenic mechanism of mitral valve dysfunction and planning for surgical and/or transcatheter interventions. Echocardiography has been the standard imaging technique to assess the mitral valve. Recently, three-dimensional (3D) transesophageal echocardiography (TEE) has been increasingly used to assess the mitral valve anatomy with high accuracy with reference to surgery, surpassing its 2D counterpart.[2]

Currently, 3D TEE of the mitral valve involves mainly visualization and qualitative interpretation of volume-rendered images. This “qualitative” approach typically involves few quantitative measurements of the mitral valve anatomy and is prone to subjectivity. Meanwhile, the increasing complexity and variety of techniques used in mitral valve surgery and interventions demand more quantitative, reproducible, and sophisticated assessment of the mitral valve. There is now emerging data suggesting that quantitative parameters such as annular diameters, leaflet billowing volume, height, and length, etc, provide important, incremental information on the complexity of mitral valve repair.[3] Moreover, quantification of the 3D leaflet geometry and annular non-planarity provides important insights to the mechanisms of mitral regurgitation,[4-6] potentially assisting diagnosis[7, 8] and guiding treatment[9].

Quantification of the mitral valve is performed via a data modeling process called segmentation. During the segmentation process, the operators reconstruct a mitral valve model by manually placing anatomical markers (e.g. annulus, leaflets) at precise locations of the valve. This process requires the operators to have prior knowledge of the many variations of normal and pathological anatomy. Because of the need for manual inputs, substantial measurement errors can be introduced, especially by less experienced operators.[10] The segmentation process is also cumbersome and time-consuming.[11] As a result, although being able to provide incremental, important information, mitral valve quantification has not been embraced clinically.

“Anatomically intelligent ultrasound” (AIUS) is a term used to describe ultrasound imaging systems that employ adaptive intelligence and rich databases of anatomic models to “interpret” images based on individual patients’ anatomical variation.[12] The new technology enables automatic image data processing and presentation with minimal human input, with the potential to enhance reproducibility and efficiency for such complex tasks as mitral valve quantification. Accordingly, the aims of the present study were (1) to evaluate the accuracy of AIUS in mitral valve quantification with reference to expert manual measurements, and (2) to assess the usefulness of AIUS in mitral valve quantification by less experienced users.

METHODS

Patient Population

The 3D TEE images of mitral valve acquired from 55 consecutive patients, including 33 patients with mitral valve prolapse, 11 patients with functional mitral regurgitation, and 11 normal subjects, were analyzed. Clinical indication for TEE included evaluation of mitral regurgitation, preoperative assessment of mitral valve reparability, exclusion of suspected endocarditis, and evaluation of cardiac source of embolism. Mitral valve prolapse was defined as systolic displacement (>2 mm) of 1 or both mitral leaflets into the left atrium, below the plane of mitral annulus, as indicated in the long-axis view. Functional mitral regurgitation was diagnosed when mitral regurgitation was associated with left ventricular global or regional dysfunction without intrinsic mitral valve structural abnormalities. The severity of mitral regurgitation was quantified by calculating the effective regurgitant orifice area using the proximal flow convergence method.[13] The institutional review board approved this study.

Image Acquisition

3D TEE of the mitral valve was performed with an EPIQ7 or iE33 ultrasound system (Philips Healthcare, Andover, MA) equipped with a fully sampled matrix transducer (X7-2t). Zoomed 3D TEE images of the mitral valve apparatus were acquired. The region of interest was adjusted to the smallest pyramidal volume that encompassed the mitral valve, with multi-beat (if the patient was in sinus rhythm) or high volume rate (if in atrial fibrillation) acquisition, to maximize temporal resolution (>15Hz). Acquisition of 3D data sets was repeated several times to ensure optimal image quality.

Mitral Valve Segmentation and Quantification

All 3D TEE images were analyzed offline on QLAB workstations (Philips Healthcare). Automated mitral valve quantitative segmentation was performed for all images using AIUS (Mitral Valve Navigator, QLAB 10, Philips Healthcare) operated by a novice user with no experience of manual segmentation apart from a brief tutorial on how to operate the software. The novice operator was also asked to perform mitral valve segmentation for all images using the manual approach (MVQ, QLAB 9, Philips Healthcare) a week later. An experienced echocardiographer (American Society of Echocardiography level 3) with extensive (>500 cases) manual segmentation experience[4] performed quantitative analysis of the mitral valve anatomy for all stored images. Both operators were blinded to the measurements performed by each other and to the clinical data. The time spent on each method for each case by the novice operator was recorded.

Initially, volumetric data sets of the mitral valve were oriented on the workstations such that the two long-axis planes bisected the mitral valve on the sagittal and dorsal planes, and that the short-axis plane was parallel to the plane of the valve. Four mitral annular points (anterior, posterior, anterolateral, and posteromedial) were tagged, followed by placement of the markers for the aorta and coaptation nadir. For the AIUS analysis, placement of these anatomical markers initiated a fully automated annulus and leaflet segmentation with no manual tracing of the annulus or leaflet contour required (Phase 1: annulus-leaflet model). Optionally, the leaflet coaptation line can be further delineated by manually marking the coaptation points, which are usually readily identified as the nadir of each parallel planes (Phase 2: annulus-leaflet-coaptation model). In contrast, the manual segmentation approach required the operator to place markers on all intermediate annular reference points (up to 36 points) rotated around the long axis and then manually trace the leaflet contour and the coaptation points on multiple parallel long-axis planes spanning the valve from commissure to commissure.[4] A color-coded parametric model of the mitral valve would then be generated for both approaches (Figure 1). Based on the reconstructed model, important anatomic parameters of the mitral valve including annular diameters, height, and areas, leaflet billowing height and volume, tenting height and volume, leaflet surface area, and leaflet closing angles were automatically calculated (Figure 2).

Reproducibility Analysis

To determine the reproducibility of mitral valve quantification by each approach, AIUS and manual analyses were repeated by another novice operator as well as by the same reader at least 10 days later, blinded to the results of all prior measurements.

Statistical Analysis

Data was expressed as mean ± SD or number (percentage) as appropriate. The agreement of AIUS with manual mitral valve quantification by expert for each anatomic parameter was evaluated using Bland–Altman analysis by calculating the bias (mean difference) and the limits of agreement (1.96 SD around the mean difference). The significance of the biases was tested using paired t-tests with a two-tailed distribution. The relation between AIUS and expert manual mitral valve quantification were evaluated by linear regression. Inter- and intra-observer variability of both AIUS and manual techniques performed by the novice operators were tested by intra-class correlation coefficient (ICC). Average time used for AIUS and manual mitral valve quantification was compared using Student's t-test. Anatomic parameters were compared among normal subjects, patients with mitral valve prolapse and functional mitral regurgitation using ANOVA. Analyses were performed with SPSS 20.0 (IBM Inc, Armonk, NY) and JMP 9.0 (SAS Institute Inc, Cary, NC). P values <0.05 were considered significant.

RESULTS

Mitral valve quantification by AIUS was feasible in 52 out of 55 (95%) patients (age=61±13years, 22 women). Three patients with mitral valve prolapse were excluded due to suboptimal image quality. Table 1 showed the patient characteristics.

The agreement between AIUS and expert manual mitral valve quantification was shown in Table 2. The 2 methods demonstrated excellent agreement in all mitral valve parameters (r=0.85 to 0.99; p>0.05 for all bias) (Figure 3). Twenty-four of the 33 patients with mitral valve prolapse underwent mitral valve repair with surgical localization of segmental prolapse. AIUS accurately classified the surgically defined location of leaflet pathology in 139 of 144 leaflet segments analyzed (97%) (Table 3). Of the 5 misclassified segments, 2 segments (A3, P1) were classified as prolapse by AIUS but not detected during surgery and 3 segments (1 P2, 2 P3s) were not classified as prolapse by AIUS but detected during surgery. Involvement of multiple adjacent segments was evident in all misclassified cases. Moreover, AIUS correctly differentiated patients with surgically confirmed mitral valve prolapse from normal subjects in 32 out of 35 subjects (91%), using the 1mm cut-off for leaflet billowing height as proposed by Chandra et al.[7]

The overall intra- and inter-observer reproducibility of the novice operators improved when using the AIUS (intra-observer ICC=0.91 to 0.99; inter-observer ICC=0.86 to 0.98) as compared to using the manual method (intra-observer ICC=0.32 to 0.95; inter-observer ICC=0.45 to 0.93) (Table 4). Although novice manual quantification of annular anteroposterior diameter and leaflet billowing volume demonstrated relatively good reproducibility (ICC>0.9), reproducibility of other parameters were only moderate (ICC~0.7). Novice manual quantification is associated with particularly low reproducibility in the measurement of annular height (intra- and inter-observer ICC=0.32 and 0.45, respectively) and annular height-to-commissural width ratio (intra- and inter-observer ICC=0.62 and 0.58, respectively), which were significantly improved by AIUS (ICC>0.85).

AIUS was able to demonstrate differences in the mitral valve parameters among patients with mitral valve prolapse, functional mitral regurgitation, and normal valves (Table 5). As expected, the annular diameters, circumference, and area in patients with mitral valve prolapse and functional mitral regurgitation were significant increased compared to normal subjects (all ANOVA p<0.0001; Bonferroni-corrected p<0.05 for both mitral valve prolapse and functional mitral regurgitation vs. normal). The annular height-to-commissural width ratio, an indicator of annular nonplanarity, was significantly reduced in both disease groups (ANOVA p=0.004; Bonferonni-corrected p<0.05 for both mitral valve prolapse and functional mitral regurgitation vs. normal). Anterior leaflet length was significantly longer in patients with both mitral valve prolapse and functional mitral regurgitation than in normal subjects (ANOVA p=0.007; Bonferroni-corrected p<0.05 for both mitral valve prolapse and functional mitral regurgitation vs. normal). Patients with mitral valve prolapse had significantly longer posterior leaflet length (Bonferroni-corrected p<0.05 vs. normal). Patients with functional mitral regurgitation had significantly increased leaflet tenting volume (ANOVA p<0.0001) and height (ANOVA p=0.002) than patients with mitral valve prolapse and normal subjects (Bonferroni-corrected p<0.05 vs. both mitral valve prolapse and normal). Patients with mitral valve prolapse showed significantly increased leaflet billowing volume (ANOVA p=0.022) and height (ANOVA p<0.0001; both Bonferroni-corrected p<0.05 vs. both functional mitral regurgitation and normal), which were similar between the other two groups. The leaflet surface area was significantly larger in patients with mitral valve prolapse and functional mitral regurgitation compared to normal subjects (Bonferroni-corrected p<0.0001). As expected, the anterior and posterior leaflet angles were significantly larger (Bonferroni-corrected p<0.05) in patients with functional mitral regurgitation, indicative of subvalvular leaflet tethering.

The average time needed to obtain the annulus-leaflet model (Phase 1) and of the annulus-leaflet-coaptation model (Phase 2) by the AIUS technique were about 2 and 5 minutes, respectively, which were significantly shorter than that needed for the manual technique (12 minutes, p<0.0001 vs both Phase 1 and Phase 2 of AIUS reconstruction) (Figure 4).

DISCUSSION

AIUS represent a type of computer-learning technology that uses a library of previous patient information to read and assess images and is an approach of automating image analysis. As a form of knowledge-based identification, AIUS uses the base models to examine global aspects of an image and assess whether a specific anatomic structure is normal, abnormal, or grossly abnormal. Using AIUS the ultrasound system has knowledge of how a structure (e.g. the mitral valve) should look in the image and it puts the boundary definition of the structure automatically.[12] As shown by the present study, the AIUS approach is much more efficient than the traditional manual method because users do not have to do the tedious tracing. Another major advantage of using AIUS is to improve reproducibility across operators. Manual placement of anatomic landmarks tends to introduce measurement bias, errors and variability. Of note, although it appears that good reproducibility in manual mitral valve quantification can be achieved by experienced operators in research settings,[3, 4, 7, 11, 14, 15] the reproducibility of less experienced users is rather low in this study. Manual quantification of the annular height appears to be particularly prone to errors. The AIUS improves reproducibility of mitral valve quantification, especially for the annular non-planarity measurements, which may be useful in annular ring selection.[16]

As the numbers and complexity of mitral valve procedures are increasing and more operators with various levels of experiences are being involved in mitral valve imaging, observer variability becomes more importantly an issue. AIUS may be able to help organizing and converting digital data into useful clinical information. The current American Heart Association/American College of Cardiology guidelines recommend mitral valve repair in preference to replacement when surgical treatment is indicated for patients with severe primary mitral regurgitation.[17] The guidelines also recommend assigning complex repairs to surgeons with established record of successful and durable repair. However, the challenge lies in accurately predicting repair complexity preoperatively. Standard 2D echocardiography provides useful information on morphology allowing highly experienced clinicians to determine valve complexity, but this level of interpretation is subjective. In this regard, quantitative assessment of mitral valve anatomy may aid in the triage process by providing objective and reliable anatomic data. Chandra et al provided the first evidence that quantifiable parameters in terms of leaflet billowing height and volume allows objective classification of lesion complexity in degenerative mitral valve disease.[7] Chikwe et al demonstrated that 3D parameters of leaflet areas, annular circumference, leaflet angles, billowing and tenting heights and volumes were predictive of repair complexity.[18] In another series reported by Drake et al., commissural width and number of prolapsing segments were independently correlated with complexity of repair,[9] similar to findings reported by Biaggi.[3] In patients undergoing undersized annuloplasty for ischemic mitral regurgitation, a posterior leaflet angle ≥45° predicts poor outcome.[19] For nonischemic functional mitral regurgitation, a distal anterior leaflet angle >25° is highly predictive of post-annuloplasty FMR recurrence.[6] Therefore, a quantitative, protocol-driven, 3D echo-guided approach has the potential to become the new standard of repair strategy for mitral valve repair and catheter-based mitral valve intervention.

Conclusions

We demonstrated that AIUS had excellent agreement with tedious manual measurements by experienced operators, and improved the reproducibility and efficiency of mitral valve quantification. Incorporation of adaptive intelligent system in 3D TEE can provide rapid, accurate, and reproducible quantification of mitral valve anatomy, with potential for routine clinical use especially when quantitative data are required for complex decisions.

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Disclosure

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FIGURES

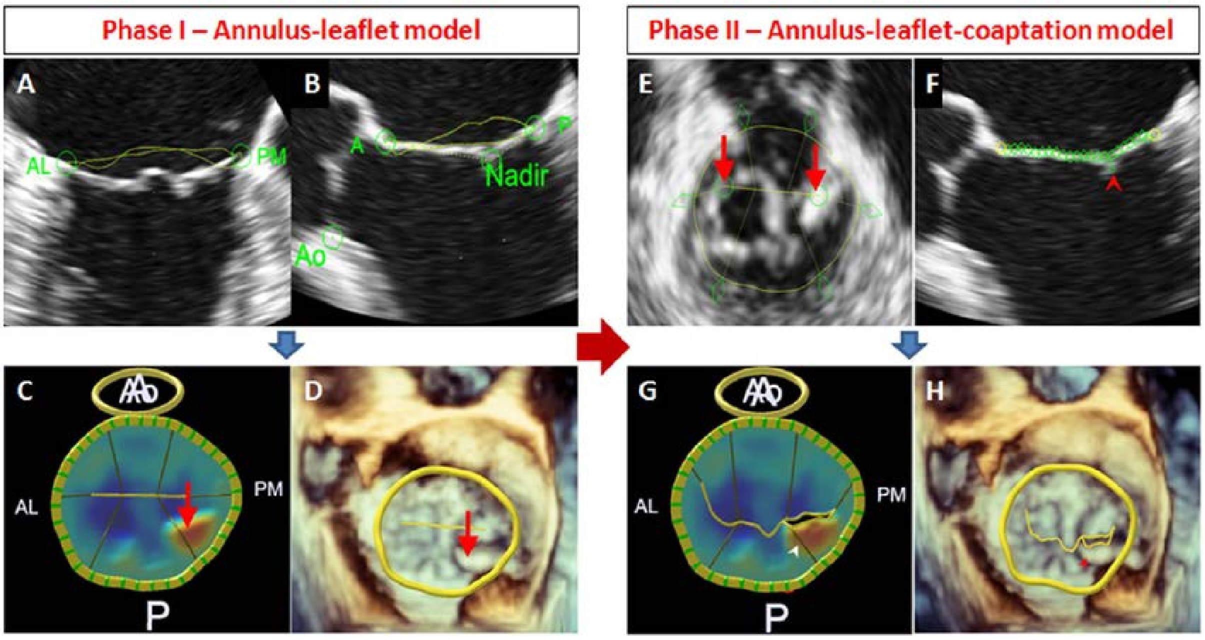

Figure 1. Mitral valve quantification using anatomical intelligence in three-dimensional transesophageal echocardiography. A-D: Anterolateral (AL), posteromedial (PM), anterior (A), and posterior (P) mitral annulus points; aortic annulus (Ao); and coaptation (Nadir) points were tagged in the 2 orthogonal long-axis planes (A and B). Then, a color-coded 3-dimentional topographical surface is displayed with leaflet billowing above the annular plane (minimal surface) depicted red (arrow) and leaflet below the annular plane blue (C). The surgeon's view of mitral valve with automatically tracked annular contour (yellow line) superimposed on the volume-rendered image showing P3 scallop billowing (arrow) (D). E-H: the two commissures were marked in the short-axis plane (arrows) (E). Points of leaflet coaptation (arrow) were marked plane by plane from commissure to commissure to delineate the line of coaptation (F). The final mapping is displayed as a color-coded topographical map (G) and annular contour (yellow line) with the line of coaptation superimposed on the volume-rendered image showing P3 scallop prolapse with involvement of the leaflet edge (arrow) (H).

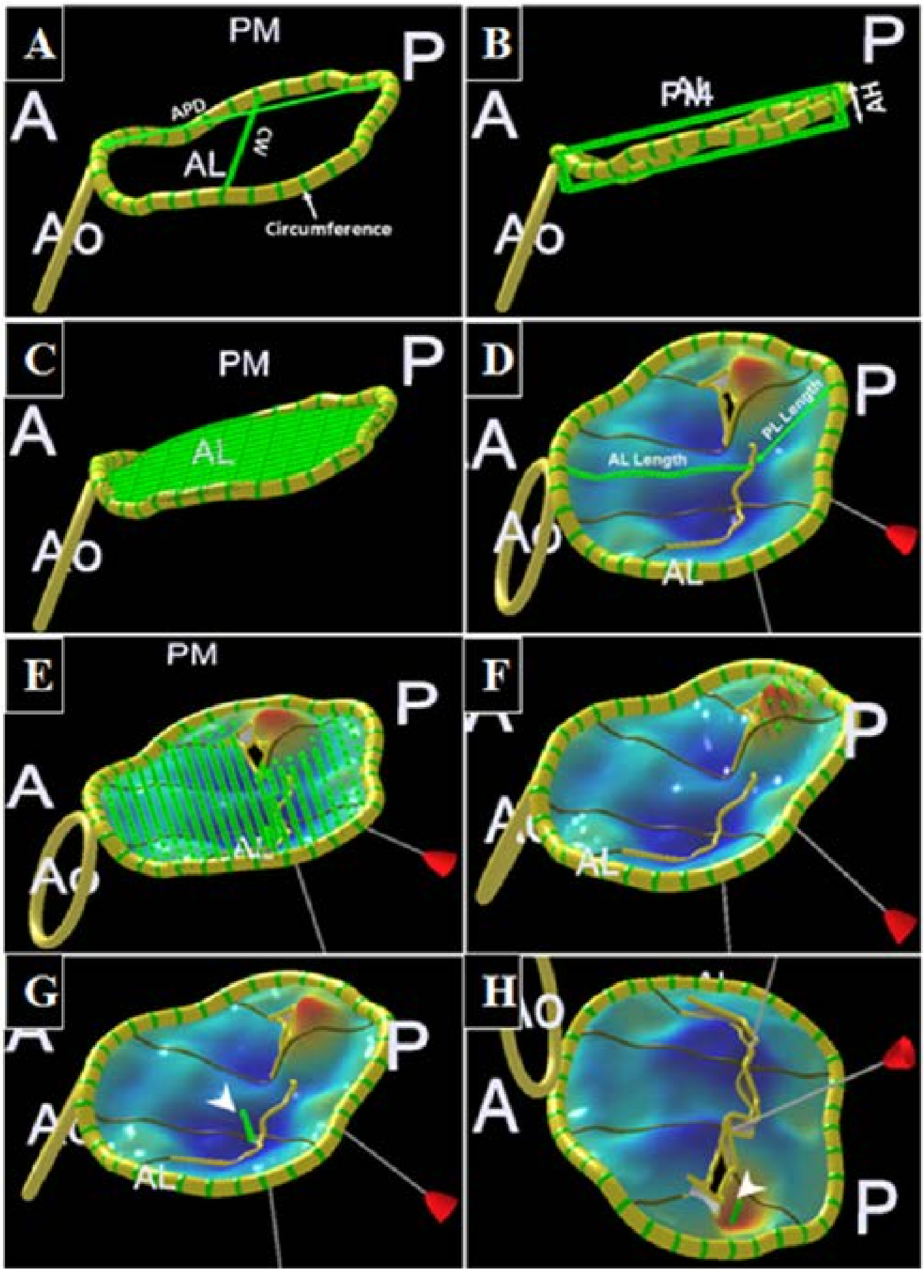

Figure 2. Three-dimensional mitral valve parameters. A, Commissural width (CW), anteroposterior diameter (APD), annular circumference. B, Annular height (AH). C, Annular area on the projected plane. D, Lengths of anterior and posterior leaflets. E, Tenting volume. F, Billowing volume. G, Tenting height (Arrow head). H, Billowing height (Arrow head). Ao indicates aortic annulus.

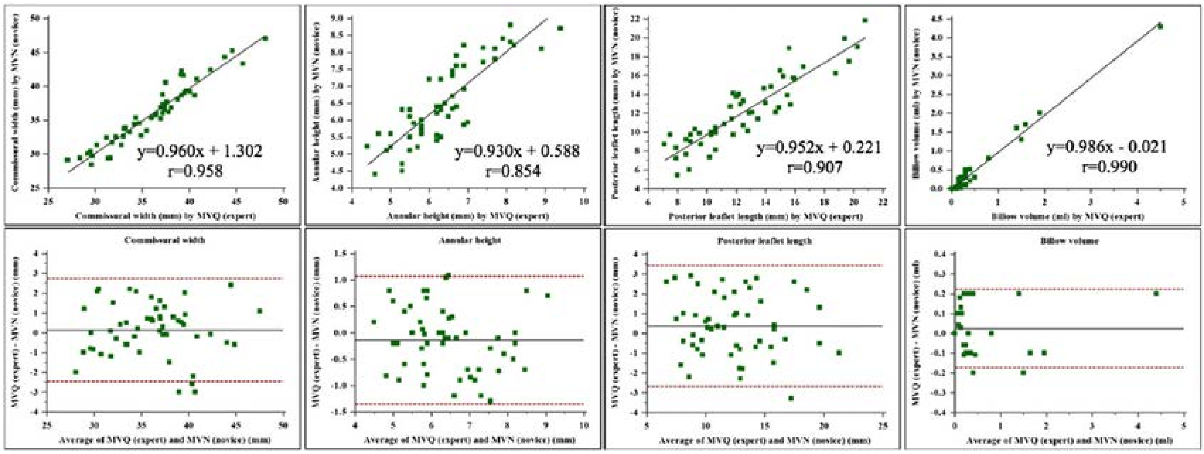

Figure 3. Bland-Altman plots comparing AIUS and expert manual mitral valve quantification. Measurements of commissural width, annular height, posterior leaflet length, and billowing volume made by novice using AIUS showed good agreement with manual measurement performed by expert. Solid lines indicate bias and dashed lines indicate 95% limits of agreement.

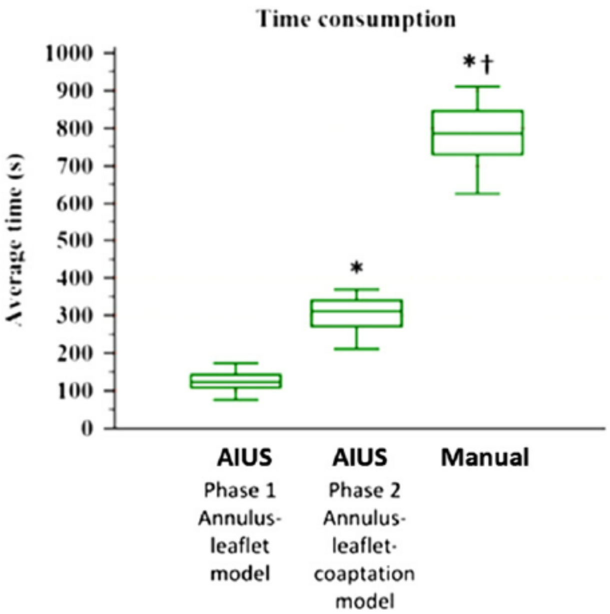

Figure 4. **Comparison of time consumption for AIUS vs manual mitral valve quantification.** *p<0.0001 vs AIUS annulus-leaflet model; †p<0.0001 vs AIUS annulus-leaflet-coaptation model.

TABLES

Table 1. Clinical and demographic characteristics of the study population

Parameters	
Age, y	61±13
Female, n (%)	22 (42)
Body surface area, m^2	1.66±0.16
Heart rate, bpm	76±14
Systole blood pressure, mm Hg	132±19
Diastole blood pressure, mm Hg	76±12
Left ventricular ejection fraction, %	55±12
Effective regurgitant orifice area, cm^2	
Patients with mitral valve prolapse patients (n=33)	0.49±0.20
Patients with functional mitral regurgitation (n=11)	0.19±0.14

Data expressed as mean ± SD or number (percentage).

Table 2. Comparisons between AIUS and expert manual quantification of mitral valve anatomy

Parameters	Expert manual method	AIUS method	p	Bias	LOA	r
Commissural width, mm	36.2±4.6	36.0±4.8	0.432	0.2	(-2.5, 2.8)	0.96
Anteroposterior diameter, mm	32.8±5.1	32.5±5.1	0.159	0.3	(-0.1, 0.6)	0.96
Annulus height, mm	6.4±1.1	6.5±1.2	0.111	-0.1	(-1.4, 1.1)	0.85
AHCWR, %	17.8±3.4	18.3±3.6	0.070	-0.5	(-4.1, 3.1)	0.86
Circumference, mm	115.1±16	114.0±15	0.119	1.1	(-8.5, 10.7)	0.95
Annulus area, mm^2	966±258	949±261	0.080	17	(-117, 151)	0.97
Anterior leaflet length, mm	24.1±4.1	24.0±4.4	0.704	0.1	(-3.1, 3.2)	0.93
Posterior leaflet length, mm	12.5±3.5	12.2±3.7	0.086	0.4	(-2.8, 3.5)	0.91
Tenting volume, ml	1.4±1.2	1.5±1.2	0.124	-0.1	(-0.8, 0.6)	0.96
Tenting height, mm	5.1±2.1	4.9±2.1	0.196	0.2	(-2.1, 2.5)	0.85
Billowing volume, ml	0.3±1.0	0.3±0.7	0.071	0.0	(-0.2, 0.2)	0.99
Billowing height, mm	3.0±2.9	2.8±3.1	0.081	0.2	(-1.6, 2.1)	0.95
Leaflet surface area, mm^2	1143±342	1129±356	0.222	14	(-156, 170)	0.98
Anterior leaflet angle, °	16.4±6.3	16.5±6.0	0.892	-0.1	(-5.8, 5.6)	0.89
Posterior leaflet angle, °	34.5±13.7	35.3±14.0	0.074	-0.7	(-5.5, 5.0)	0.98

*Paired t-test comparing AIUS performed by novice and expert manual measurements. AIUS, anatomical intelligence in ultrasound; AHCWR, annular height to commissural width ratio; LOA, limits of agreement.

Table 3. AIUS-surgery concordance in localization of prolapse in 24 patients who underwent mitral valve repair

	Prolapsing segments classified by AIUS	Prolapsing segments classified by surgery	AIUS-Surgery concordance
Patient 1	A2, A3	A2	-
Patient 2	A2	A2	+
Patient 3	A2, A3	A2, A3	+
Patient 4	A2, A3	A2, A3	+
Patient 5	A3	A3	+
Patient 6	A1-3, P1-3	A1-3, P1-3	+
Patient 7	P1, P2	P1, P2	+
Patient 8	P1, P2	P1, P2	+
Patient 9	P1, P2	P1, P2	+
Patient 10	P1, P2	P1, P2	+
Patient 11	P2	P2	+
Patient 12	P1, P2	P2	-
Patient 13	P2	P2	+
Patient 14	P2	P2	+
Patient 15	P2	P2	+
Patient 16	P2	P2	+
Patient 17	P2, P3	P2, P3	+

Patient 18	P2	P2, P3	-
Patient 19	P2, P3	P2, P3	+
Patient 20	P2, P3	P2, P3	+
Patient 21	P3	P2, P3	-
Patient 22	P2	P2, P3	-
Patient 23	P3	P3	+
Patient 24	P3	P3	+

A1, A2, A3 indicate lateral, middle, medial segments of anterior leaflet correspondingly. P1, P2, P3 indicate lateral, middle, medial segments of posterior leaflet correspondingly.

Table 4. Comparisons of Reproducibility of AIUS and Manual Mitral Valve Quantification by Novice Operators

Parameters	Intra-observer ICC		Inter-observer ICC	
	Manual	AIUS	Manual	AIUS
Commissural width, mm	0.71	0.98	0.75	0.92
Anteroposterior diameter, mm	0.90	0.98	0.93	0.97
Annulus height, mm	0.32	0.91	0.45	0.86
AHCWR, %	0.60	0.92	0.58	0.88
Circumference, mm	0.83	0.99	0.83	0.98
Annulus area, mm^2	0.86	0.99	0.87	0.98
Anterior leaflet length, mm	0.75	0.94	0.81	0.96
Posterior leaflet length, mm	0.73	0.95	0.70	0.89
Tenting volume, ml	0.88	0.94	0.88	0.95
Tenting height, mm	0.78	0.93	0.79	0.88
Billow volume, ml	0.92	0.95	0.92	0.89
Billow height, mm	0.83	0.98	0.87	0.96
Leaflet surface area, mm^2	0.95	0.98	0.93	0.97
Anterior leaflet angle, °	0.83	0.93	0.85	0.88
Posterior leaflet angle, °	0.87	0.95	0.86	0.93

AIUS, anatomical intelligence in ultrasound; AHCWR, annular height to commissural width ratio; ICC, Intra-class correlation coefficient.

Table 5. Comparison of normal and pathological mitral valve anatomy as quantified by AIUS

Parameters	Normal (n=11)	Mitral valve prolapse (n=30)	Functional mitral regurgitation (n=11)	ANOVA p
Commissural width, mm	31.1±2.9	37.2±4.4*	35.7±4.7*	<0.0001
Anteroposterior diameter, mm	26.5±3.0	34.7±4.7*	32.6±5.3*	<0.0001
Annulus height, mm	6.8±1.2	6.5±1.2	6.3±1.3	0.599
AHCWR, %	21.9±3.3	17.6±3.9*	17.3±2.9*	0.004
Annular circumference, mm	97.3±8.9	118.8±14.4*	115.4±12.4*	<0.0001
Annulus area, mm^2	663±120	1031±254*	955±200*	<0.0001
Anterior leaflet length, mm	20.3±2.6	24.2±4.4*	25.8±4.3*	0.007
Posterior leaflet length, mm	9.5±2.5	13.6±4.4*	12.7±2.9	0.013

Tenting Volume, ml	0.9±0.3	1.2±1.0	2.7±1.5*†	<0.0001
Tenting height, mm	3.9±0.8	4.4±2.2	6.8±2.0*†	0.002
Billowing volume, ml	0.0±0.0	0.6±1.0*	0.0±0.0†	0.022
Billowing height, mm	0.6±0.6	4.7±3.2*	0.2±0.2†	<0.0001
Leaflet surface area, mm^2	756±124	1255±345*	1161±273*	<0.0001
Anterior leaflet angle, °	17.3±3.9	14.6±6.1	20.7±5.5†	0.011
Posterior leaflet angle, °	39.7±10.2	29.8±13.1	45.9±12.5†	0.001

AHCWR, annular height to commissural width ratio. *Bonferroni-corrected p<0.05 mitral valve prolapse vs. normal or functional mitral regurgitation vs. normal; Bonferroni-corrected †p<0.05 functional mitral regurgitation vs. mitral valve prolapse.