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# Real-Time Three-Dimensional Echocardiography for Rheumatic Mitral Valve Stenosis Evaluation

## An Accurate and Novel Approach

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**OBJECTIVES** Our aim was to assess which echo-Doppler method has the best agreement with the mitral valve area (MVA) invasively evaluated by the Gorlin's formula. We also evaluated the feasibility and reproducibility of real-time three-dimensional echocardiography (RT3D) for the estimation of MVA and the Wilkins score in patients with rheumatic mitral stenosis (RMVS).

**BACKGROUND** Real-time three-dimensional echocardiography is a novel technique that allows us to visualize the mitral valvular anatomy in any desired plane orientation. The usefulness and accuracy of this technique for evaluating RMVS has not been established.

**METHODS** We studied a series of consecutive patients with RMVS from two tertiary care hospitals. Mitral valvular area was determined by conventional echo-Doppler methods and by RT3D, and their results were compared with those obtained invasively. Real-time three-dimensional echocardiography planimetry and mitral score were measured by two independent observers and then repeated by one of them.

**RESULTS** Eighty patients with RMVS comprised our study group (76 women; 50.6 ± 13.9 years). Compared with all other echo-Doppler methods, RT3D had the best agreement with the invasively determined MVA (average difference between both methods and limits of agreement: 0.08 cm$^2$ [−0.48 to 0.6]). Interobserver variability was as good for RT3D (intraclass correlation coefficient [ICC] = 0.90) as for pressure half-time (PHT) (ICC = 0.95). For PHT and RT3D, the intraobserver variability was similar (ICC 0.92 and 0.96, respectively). Real-time three-dimensional echocardiography valvular score evaluation showed a better interobserver agreement with RT3D than with 2D echocardiography.

**CONCLUSIONS** Real-time three-dimensional echocardiography is a feasible, accurate, and highly reproducible technique for assessing MVA in patients with RMVS. Real-time three-dimensional echocardiography has the best agreement with invasive methods. (J Am Coll Cardiol 2004;43: 2091–6) © 2004 by the American College of Cardiology Foundation

Rheumatic mitral valve stenosis (RMVS) still remains an important public health concern in developed countries due to the immigration of patients from underdeveloped countries. To define the best therapeutic strategy, clinical data and accurate measurements of the mitral valve orifice area (MVA) are necessary. Nevertheless, currently employed noninvasive methods have various limitations (1,2).

Three-dimensional echocardiography provides a unique "en-face" view of the complete mitral valve apparatus and could, therefore, improve the accuracy of MVA planimetry (3,4). However, it has not been routinely performed due to the cumbersome nature of current platforms, prolonged data acquisition, and offline processing time. With the advent of a new transthoracic three-dimensional matrix array probe (Philips, Andover, Massachusetts) that allows real-time three-dimensional rendering, many of the above limitations could be circumvented.

Our aim was to compare the accuracy of current echo-Doppler methods and real-time three-dimensional echocardiography (RT3D) for the assessment of MVA in patients with RMVS. The gold standard method was the MVA invasively determined by means of the Gorlin method (5). We also evaluated the interobserver variability of Wilkins score by using two-dimensional echocardiography (2D) and RT3D.

## METHODS

**Patient population.** Eighty consecutive patients with an established diagnosis of RMVS (6) recruited from two tertiary care Hospitals (Hospital Clínico San Carlos, Madrid, Spain, and University of Chicago Hospitals, Chicago, Illinois) comprised our study group.

**Noninvasive evaluation.** A complete echo-Doppler study was performed in all patients using a Sonos 7500 ultrasound machine and a S3 probe (Philips). Two-dimensional echocardiography views of the mitral valve were obtained from the parasternal window, and planimetry was performed. Continuous-wave Doppler recordings through the mitral valve were obtained from the apical four-chamber window, and MVA was estimated by using the formula 220/PHT (1). Data required to measure the MVA using the proximal

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**Abbreviations and Acronyms**

| | | |
|---|---|---|
| ICC | = | intraclass correlation coefficient |
| MVA | = | mitral valvular area |
| PHT | = | pressure half-time |
| PISA | = | proximal isovelocity surface area |
| RMVS | = | rheumatic mitral valve stenosis |
| RT3D | = | real-time three-dimensional echocardiography |
| 2D | = | two-dimensional echocardiography |
| 3D | = | three-dimensional echocardiography |

isovelocity surface area (PISA) method were recorded from the apical window (2). Three cardiac cycles for patients in sinus rhythm and five for patients in atrial fibrillation were recorded, and their results averaged for every patient. The values for comparison were an average of two observers' measurements.

**RT3D.** Real-time three-dimensional echocardiography was performed immediately after the 2D study. Data were recorded using the aforementioned probe. The system scans a 60° × 30° three-dimensional pyramid of data. From different acoustic windows, multiple cardiac cycles of the mitral valve were recorded using the "zoom" mode. Cardiac cycles were also acquired using the "full-volume" mode that consists of the acquisition of a larger single pyramid of data (120° × 60°) recorded during four consecutive cardiac cycles. All images were stored in a magneto optical disk or compact disk and transferred for offline analysis using Tomtec software (4D Cardio-View RT 1.0 Build 983, Tomtec Imaging Systems, GmbH, Unterschleissheim, Germany).

Real-time three-dimensional echocardiography planimetry was performed "en-face" at the ideal cross-section of the mitral valve during its greatest diastolic opening. The ideal cross-section was defined as the most perpendicular view on the plane with the smallest mitral valve orifice (Fig. 1).

**Invasive evaluation.** Invasive hemodynamic evaluation was performed within 24 h of the echocardiographic recordings. Using the catheter-based data and the Gorlin's equation, the MVA was obtained (5). Cardiac output was determined by means of the thermodilution method by using a Swan-Ganz catheter. Left ventricle and left atrium pressure tracings were recorded simultaneously by using a 6F pig-tail catheter and a conveniently placed percutaneous transeptal catheter. Planimetry of the area between left atrium and left ventricle pressure tracings was averaged for five beats.

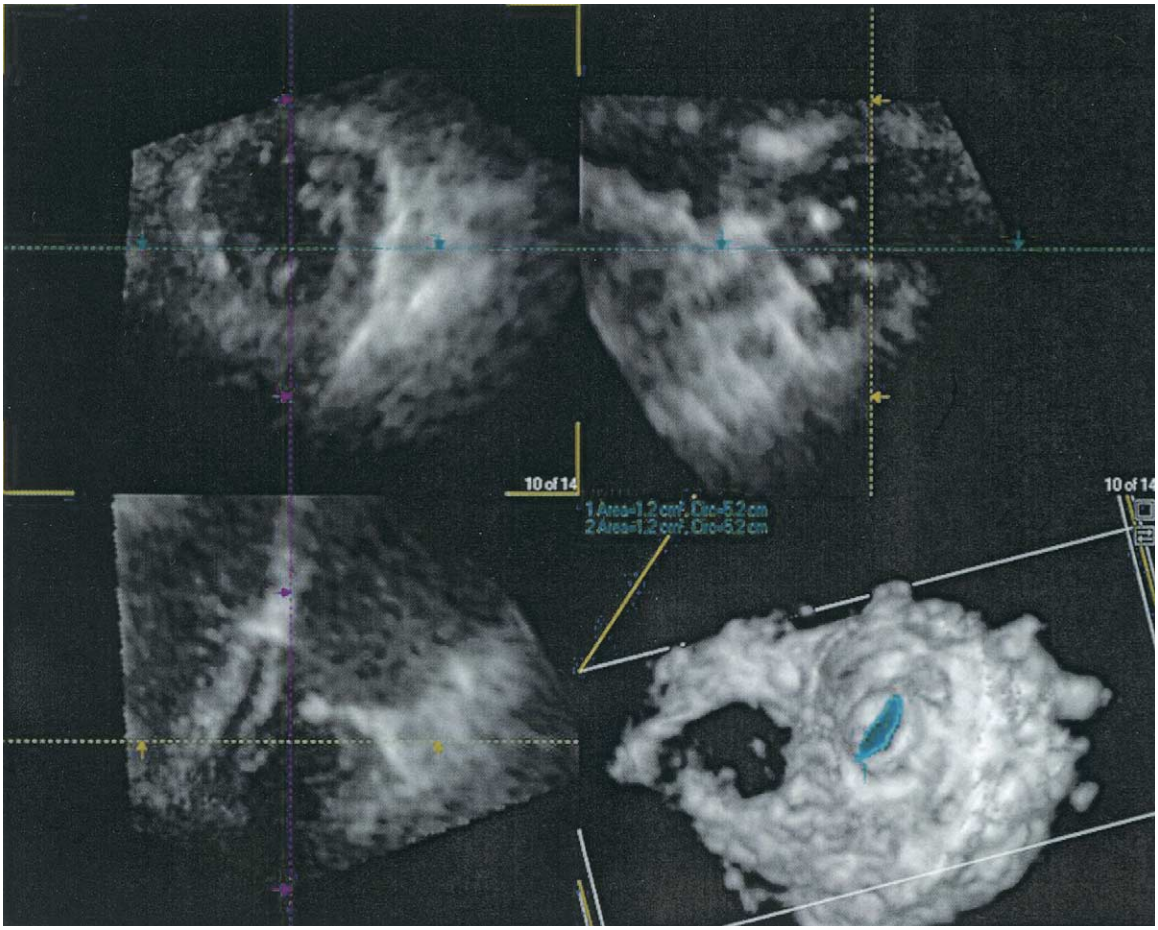


**Figure 1.** Mitral valve orifice. Figure shows the accurate way that real-time three-dimensional echocardiography provides orientation of the mitral valvular orifice in the three planes of space and a measurement of mitral valve orifice.

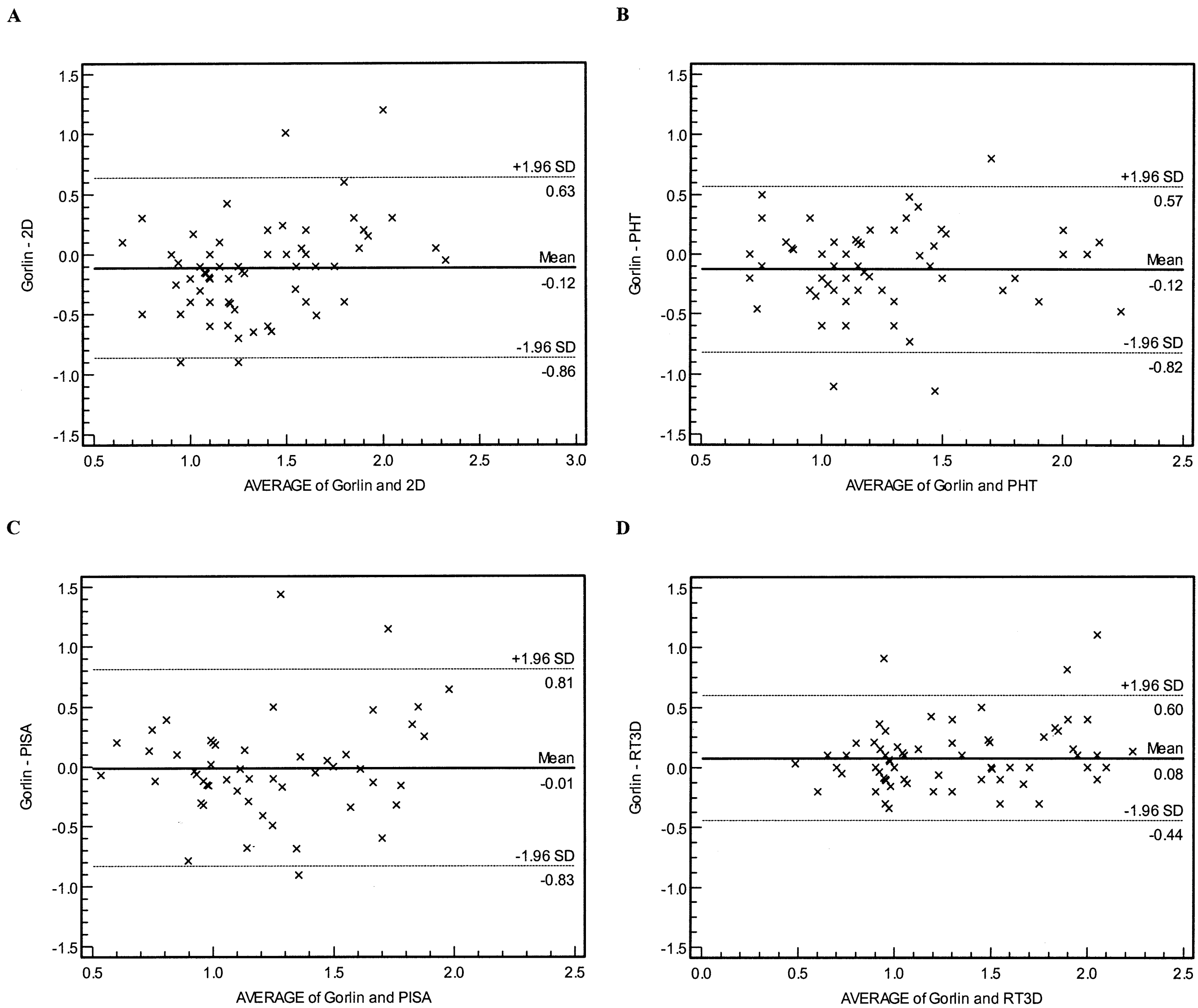


**Figure 2.** Bland-Altman graphs displaying differences against average values between traditional noninvasive and real-time three-dimensional (RT3D)-determined mitral valvular area. The **thick line** represents mean difference, and the **thin lines** represent the limits of agreement (all measurements in $cm^2$). PHT = pressure half-time; PISA = proximal isovelocity surface area; 2D = two-dimensional echocardiography.

**Interobserver and intraobserver variability.** All the recorded images were analyzed offline at different times by two independent observers. The same images were also analyzed on a different day by one of these same observers.

**Wilkins score analysis.** The Wilkins score (7) was determined using 2D and RT3D echocardiography by two independent observers at different times. Flexibility, calcification, and subvalvular involvement were assessed. Valvular "thickening" was not evaluated as it is an objectively measurable parameter.

**Statistical analysis.** The statistical package used was SPSS version 11.0 (SPSS Inc., Chicago, Illinois). Quantitative data were expressed as mean ± SD. Qualitative data were expressed as absolute number (percentage). Inter- and intraobserver reproducibility were evaluated by means of the intraclass correlation coefficient (ICC) or Kappa index. Intermethods agreement was evaluated by means of Bland-Altman's method (8). Comparisons were considered significant in presence of a p value $<0.05$.

## RESULTS

Eighty consecutive patients with RMVS comprised our study group. Four patients were not enrolled due to the presence of an inadequate acoustic window. There were 76 (95%) women, and mean age was 50.6 ± 13.9 years. Mitral stenosis was the predominant valvular lesion in all of them, but concomitant mitral regurgitation ≥grade III/IV was present in nine patients and aortic regurgitation ≥grade II/IV was present in two patients. Forty-six patients were in

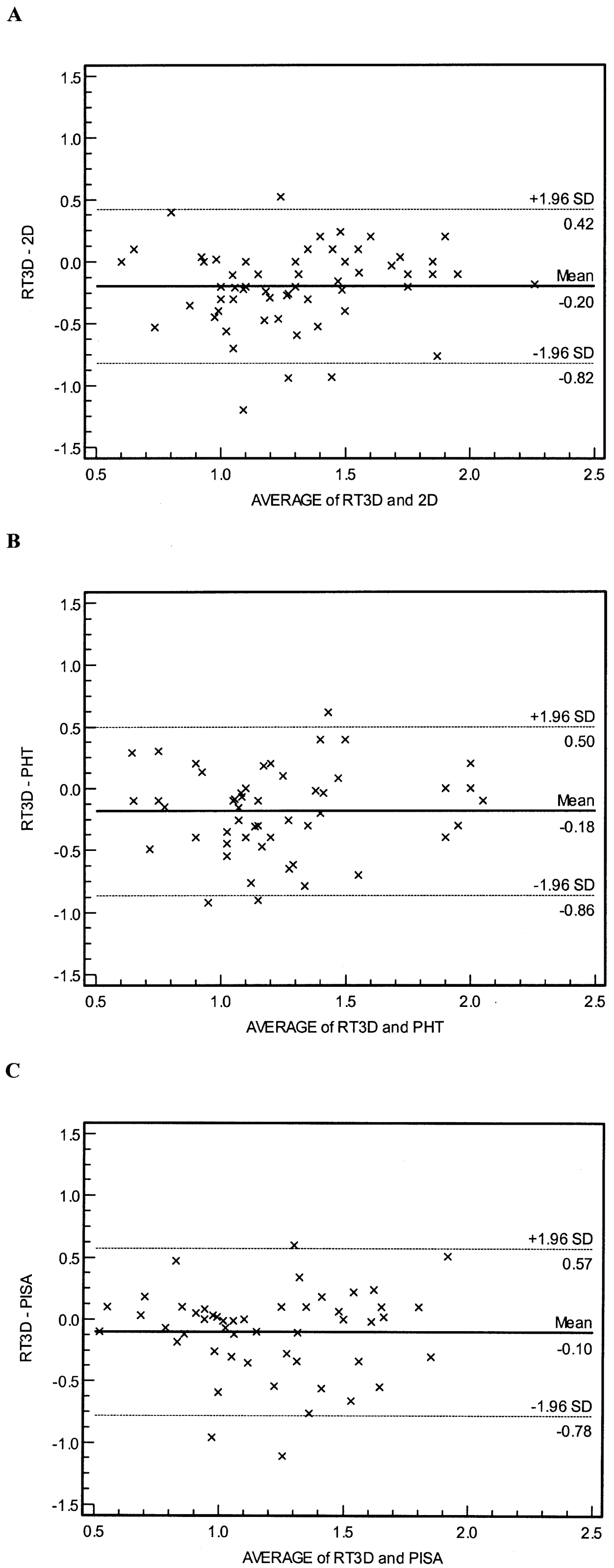


**Figure 3.** Bland-Altman graphs displaying differences against average values between noninvasive and Gorlin-determined mitral valvular area. The **thick line** represents mean difference, and the **thin lines** represent the limits of agreement (all measurements in $cm^2$). PHT = pressure half-time; PISA = proximal isovelocity surface area; RT3D = real-time three-dimensional echocardiography; 2D = two-dimensional echocardiography.

normal sinus rhythm, 31 in atrial fibrillation, and three patients were paced.

**Comparison of noninvasive with invasive methods.** Mitral valvular area determined by the different methods was: pressure half-time (PHT): 1.28 ± 0.39 $cm^2$; 2D: 1.39 ± 0.37 $cm^2$; PISA: 1.24 ± 0.39 $cm^2$; RT3D: 1.26 ± 0.43 $cm^2$; and Gorlin's method: 1.30 ± 0.48 $cm^2$.

Bland-Altman's analysis showed a better agreement when comparing the invasively determined MVA with RT3D-determined MVA than when comparing the former with the 2D-, PHT-, and PISA-determined MVA (Fig. 2). Agreement between RT3D and 2D, PHT, and PISA was also evaluated, showing acceptable results (Fig. 3).

The time required to obtain and analyze the RT3D images, evaluated in 20 consecutive patients, was 23 ± 7 min. The best three-dimensional echocardiography method to obtain adequate images for planimetry was the RT3D by using zoom method in all but in two patients (2.5%). The most frequently used view for RT3D planimetry was the apical window (63 patients; 79%) followed by the parasternal window (12 patients; 15%).

**Comparison of centers.** In both centers, RT3D planimetry had a better agreement with the Gorlin-derived MVA, while the PISA method had the weakest correlation (Table 1).

**Inter- and intraobserver variability.** Interobserver agreement was excellent: ICC was 0.95 and 0.90 for PHT and RT3D, respectively. Similar results were noted for intraobserver agreement: ICC was 0.92 and 0.96 for PHT and RT3D, respectively.

**Valvular score.** Evaluation of valvular score was different for 2D compared with RT3D. The RT3D assessment showed the best interobserver agreement (Table 2). The best interobserver agreement when using 2D echocardiography was noted in the evaluation of mitral valve calcification and for RT3D in valvular flexibility.

## DISCUSSION

To define the best therapeutic strategy in patients with RMVS, clinical data and accurate measurements of MVA are necessary. Doppler-based methods are heavily influenced by hemodynamic variables, left ventricular hypertrophy, and associated valvular disease (9–13). Accordingly, methods based on direct measurement of valvular orifice should be more accurate. To date, direct measurements of the MVA area can only be performed using planimetry traced on 2D echocardiography images. However, this method has multiple limitations, the major one being the correct image plane orientation.

Three-dimensional echocardiography improves the operator's ability to perform a well-oriented and accurate MVA planimetry (3,4). To date, routine transthoracic use of three-dimensional echocardiography has not been performed due to the cumbersome nature of old methods (14,15). With the recent advent of RT3D, many of these limitations have been overcome. Real-time three-

**Table 1.** Linear Regression Coefficient and Intraclass Correlation Coefficient Between Noninvasive Methods (Averaged Value of Two Observers' Measurements) and Gorlin Estimated MVA in Both Centers

| | Hospital Clinico San Carlos | | University of Chicago Hospitals | |
|---|---|---|---|---|
| | r | ICC | r | ICC |
| PHT vs. Gorlin | 0.84 | 0.78 (0.5–0.78) | 0.55 | 0.53 (0.17–0.66) |
| | $p < 0.001$ | $p < 0.001$ | $p = 0.002$ | $p < 0.001$ |
| 2D vs. Gorlin | 0.86 | 0.64 (0.21–0.82) | 0.78 | 0.62 (0.35–0.76) |
| | $p = 0.003$ | $p = 0.0024$ | $p < 0.001$ | $p < 0.001$ |
| PISA vs. Gorlin | 0.66 | 0.66 (0.046–0.84) | 0.54 | 0.46 (0.11–0.67) |
| | $p = 0.05$ | $p = 0.019$ | $p = 0.012$ | $p = 0.0056$ |
| RT 3D vs. Gorlin | 0.98 | 0.84 (0.63–0.9) | 0.97 | 0.83 (0.69–0.9) |
| | $p < 0.001$ | $p < 0.001$ | $p < 0.001$ | $p < 0.001$ |

Gorlin = Gorlin's methods of invasive mitral valvular area (MVA) assessment; ICC = intraclass correlation coefficient; PHT = half pressure time MVA assessment; PISA = proximal isovelocity surface area method MVA assessment; r = linear regression coefficient; RT3D = real-time three-dimensional echocardiography MVA assessment; 2D = two-dimensional echocardiography MVA assessment.

**Table 2.** Mitral Score as Assessed by Two Independent Observers by 2D and RT3D

| | 2D 1 | 2D 2 | Kappa 2D | 3D 1 | 3D 2 | Kappa 3D |
|---|---|---|---|---|---|---|
| Mobility | 1.8 ± 0.8 | 2 ± 0.7 | 0.59 | 1.7 ± 0.7 | 1.7 ± 0.7 | 0.96 |
| Sub. app. | 1.6 ± 0.7 | 1.7 ± 0.8 | 0.35 | 1.7 ± 0.7 | 1.5 ± 0.6 | 0.66 |
| Calcification | 1.7 ± 0.8 | 1.4 ± 0.6 | 0.76 | 1.6 ± 0.6 | 1.6 ± 0.6 | 0.91 |

Sub. App. = subvalvular apparatus; 2D = two-dimensional echocardiography mitral valvular area assessment; 2D 1 = 2D echocardiography evaluation, observer 1; 2D 2 = 2D echocardiography evaluation, observer 2; RT3D = real time three-dimensional echocardiography mitral valvular area assessment; 3D 1 = RT3D echocardiography evaluation, observer 1; 3D 2 = RT3D echocardiography evaluation, observer 2.

dimensional echocardiography allows evaluation of the MVA "en-face." Additionally, flexibility, rotation, and orientation of the mitral valve to the desired plane are easy and independent of the orientation of the acoustic window where image acquisition is done.

This study shows that RT3D is the most accurate echocardiography parameter for measuring MVA using invasively determined data as the gold standard. Independent analysis of the results from both centers showed that RT3D planimetry is the most accurate method to measure MVA. Furthermore, RT3D measurements have excellent inter- and intraobserver variability and provide the best interobserver agreement for morphologic evaluation.

**Study limitations.** Gorlin's method has multiple recognized limitations (16,17). Ideally, the desired gold standard should have been the measurement performed in the surgical specimen inspection. Another limitation is that the echocardiography delineation of the MVA is always dependent on the quality of the image.

**Clinical implications.** Real-time three-dimensional echocardiography can improve the assessment of RMVS severity in patients with discordant results between different methods and in clinical scenarios where these methods are known as nonuseful (i.e., the early postvalvuloplasty period). Thus, it is able to replace other noninvasive methods and make invasive evaluation unnecessary.

**Conclusions.** Real-time three-dimensional echocardiography is feasible, accurate, and highly reproducible for estimating MVA in patients with RMVS. Compared with other currently used modalities, RT3D echocardiography has the best agreement with the invasively determined Gorlin formula. This methodology could be of great value in certain scenarios such as immediately after balloon valvuloplasty.

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## REFERENCES

1. Hatle L, Angelsen B, Tromsdal A. Noninvasive assessment of atrioventricular pressure half-time by Doppler ultrasound. Circulation 1979;60:1096–104.
2. Rodriguez L, Thomas JD, Monterroso V, et al. Validation of the proximal flow convergence method: calculation of orifice area in patients with mitral stenosis. Circulation 1993;88:1157–65.
3. Kupferwasser I, Mohr-Kahaly S, Menzel T, et al. Quantification of mitral valve stenosis by three-dimensional transesophageal echocardiography. Int J Cardiac Imaging 1996;12:241–7.
4. Chen Q, Nosir YF, Vletter WB, Kint PP, Salustri A, Roelandt JR. Accurate assessment of mitral valve area in patients with mitral stenosis by three-dimensional echocardiography. J Am Soc Echocardiogr 1997;10:133–40.
5. Gorlin R, Gorlin SG. Hydraulic formula for calculation of the stenotic mitral valve, other cardiac valves, and central circulatory shunts. Am Heart J 1951;41:1–12.
6. Oh J, Seward J, Tajik A. Valvular heart disease. In: Oh JK, editor. The Echo Manual. 2nd ed. Philadelphia and New York: Lippincott, 1999:113.
7. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J 1988;60:299–308.

8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
9. Smith MD, Wisenbaugh T, Grayburn PA, Gurley JC, Spain MG, DeMaria AN. Value and limitations of Doppler pressure half-time in quantifying mitral stenosis: a comparison with micromanometer catheter recordings. Am Heart J 1991;121:480–8.
10. Nakatani S, Masuyama T, Kodama K, Kitabatake A, Fujii K, Kamada T. Value and limitations of Doppler echocardiography in the quantification of stenotic mitral valve area: comparison of the pressure half-time and the continuity equation methods. Circulation 1988;77:78–85.
11. Karp K, Teien D, Bjerle P, Eriksson P. Reassessment of valve area determinations in mitral stenosis by the pressure half-time method: impact of left ventricular stiffness and peak diastolic pressure difference. J Am Coll Cardiol 1989;1:594–9.
12. Fredman CS, Pearson AC, Labovitz AJ, Kern MJ. Comparison of hemodynamic pressure half-time method and Gorlin formula with Doppler and echocardiographic determinations of mitral valve area in patients with combined stenosis and regurgitation. Am Heart J 1990;119:121–9.
13. Flachskampf FA, Weyman AE, Gillam L, Liu CM, Abascal VM, Thomas JD. Aortic regurgitation shortens Doppler pressure half-time in mitral stenosis: clinical evidence, in vitro simulation and theoretic analysis. J Am Coll Cardiol 1990;16:396–404.
14. Binder TM, Rosenhek R, Porenta G, Maurer G, Baumgartner H. Improved assessment of mitral valve stenosis by volumetric real-time three-dimensional echocardiography. J Am Coll Cardiol 2000;36: 1355–61 4.
15. Binder T, Globits S, Zangeneh M, et al. Three-dimensional echocardiography using a transesophageal imaging probe: potentials and technical considerations. Eur Heart J 1996;17:619–28.
16. Hammermeister KE, Murray JA, Blackmon JR. Revision of Gorlin constant for calculation of mitral valve area from left heart pressures. Br Heart J 1973;35:392–6.
17. Klarich KW, Rihal CS, Nishimura RA. Variability between methods of calculating mitral valve area: simultaneous Doppler echocardiographic and cardiac catheterisation studies conducted before and after percutaneous mitral valvuloplasty. J Am Soc Echocardiogr 1996;9: 684–90.