Journal of the American College of Cardiology
© 1999 by the American College of Cardiology
Published by Elsevier Science Inc.
Vol. 33, No. 6, 1999
ISSN 0735-1097/99/$20.00
PII S0735-1097(99)00041-8

Three-Dimensional Color Doppler: A Clinical Study in Patients With Mitral Regurgitation

Raffaele De Simone, MD,* Gerald Glombitza, PHD,† Christian Friedrich Vahl, MD,* Jörg Albers, MD,* Hans Peter Meinzer, PHD,† Siegfried Hagl, MD*

Heidelberg, Germany

OBJECTIVES The purpose of this study was to assess the clinical feasibility of three-dimensional (3D) reconstruction of color Doppler signals in patients with mitral regurgitation.

BACKGROUND Two-dimensional (2D) color Doppler has limited value in visualizing and quantifying asymmetric mitral regurgitation. Clinical studies on 3D reconstruction of Doppler signals in original color coding have not yet been performed in patients. We have developed a new procedure for 3D reconstruction of color Doppler.

METHODS We studied 58 patients by transesophageal 3D echocardiography. The jet area was assessed by planimetry and the jet volumes by 3D Doppler. The regurgitant fractions, the volumes, and the angiographic degree of mitral regurgitation were assessed in 28 patients with central jets and compared with those of 30 patients with eccentric jets.

RESULTS In all patients, jet areas and jet volumes significantly correlated with the angiographic grading ($r = 0.73$ and $r = 0.90$), the regurgitant fraction ($r = 0.68$ and $r = 0.80$) and the regurgitant volume ($r = 0.66$ and $r = 0.90$). In patients with central jets, significant correlations were found between jet area and angiography ($r = 0.86$), regurgitant fraction ($r = 0.64$) and regurgitant volume ($r = 0.78$). No significant correlations were found between jet area and angiography ($r = 0.53$), regurgitant fraction ($r = 0.52$) and regurgitant volume ($r = 0.53$) in the group of patients with eccentric jets. In contrast, jet volumes significantly correlated with angiography ($r = 0.90$), regurgitant fraction ($r = 0.75$) and regurgitant volume ($r = 0.88$) in the group of patients with eccentric jets.

CONCLUSIONS Three-dimensional Doppler revealed new images of the complex jet geometry. In addition, jet volumes, assessed by an automated voxel count, independent of manual planimetry or subjective estimation, showed that 3D Doppler is also capable of quantifying asymmetric jets. (J Am Coll Cardiol 1999;33:1646–54) © 1999 by the American College of Cardiology

Three-dimensional (3D) reconstruction of echocardiographic images has been made possible by the recent advances in ultrasound and computer technology (1–3). Up to now this technique has been mainly applied for assessing intracardiac anatomy (4–6) and for quantifying heart chamber volumes (7–9). The 3D reconstruction of color Doppler flow signals and visualization in original color coding is still the object of investigations. With commercially available systems 3D reconstructions of both Doppler flow information and cardiac structures can be made, but up to now the Doppler signal could only be visualized in a gray scale format (10); cumbersome segmentation of cardiac structures and flows is still needed for visualizing and for obtaining quantitative information from Doppler data.

We have developed a new technique for reconstructing color flow signals in 3D by using Doppler data sets in digital format which have been directly derived from the echocardiographic system. The aims of this study were: 1) to assess the clinical impact of 3D Doppler images of regurgitant jets in the original colors, 2) to develop an automated procedure for segmentation and measurement of jet volumes, and 3) to compare the parameter jet volume to other clinical parameters for quantitative assessment of mitral regurgitation.

METHODS

Echocardiographic studies. We studied 58 patients (27 men, 31 women; age 51.3 ± 13.6 years) with isolated mitral regurgitation who underwent echocardiographic examinations before cardiac surgery. The etiology of mitral regurgitation was: mitral valve prolapse (24 patients), coronary artery disease (20), rheumatic valve disease (10) and dilated cardiomyopathy (4). Ten patients had grade I mitral regurgitation, 13 patients grade II, 10 patients grade III and 12 patients grade IV according to preoperative left ventricular

From the *University of Heidelberg and †Deutsches Krebsforschungszentrum, Heidelberg, Germany. This work was supported by the German National Foundation for Scientific Research (SFB 414).

Manuscript received August 20, 1998; revised manuscript received December 15, 1998, accepted January 14, 1999.

Abbreviations and Acronyms

2D = two-dimensional
3D = three-dimensional

angiography. The examinations were performed using commercially available equipment (Sonos 2500, Hewlett-Packard, Andover, Massachusetts) with a multiplane transesophageal probe (5 MHz) and a conventional transthoracic probe (2.5 MHz). The echocardiographic system was equipped with dedicated software for dynamic 3D acquisition which steers the rotation of the transducer at any angle between 0° and 180°. The acquisitions of a complete heart cycle were performed with 2° increments for obtaining 90 views during 90 heart beats. The rotation angle for acquisition was increased to 5° after statistical analysis of the volume data had shown no significant changes in the accuracy of measurements (11). The digital data from two-dimensional (2D) echocardiography, coded as a gray scale, and the data from 2D Doppler flow signals, coded as a color palette, were separately stored on magneto-optical disks. The diameter of left ventricular outflow tract was measured at the aortic annulus in the parasternal long-axis view; the mitral valve annulus diameter and pulsed Doppler velocities were measured in the apical four-chamber view (12). The aortic stroke volume and the forward mitral stroke volume were calculated from the product of the time–velocity integrals and the aortic and the mitral valve areas (13). The mitral regurgitant stroke volume was calculated by subtracting the aortic flow from the mitral forward flow; the mitral regurgitant fraction (%) was calculated by dividing the mitral regurgitant volume by the total diastolic mitral flow (14). Color Doppler flow images were performed with a pulse repetition frequency ranging from 5.0 to 6.2 kHz. The typical Nyquist limit was 86 cm/s at 10 cm. A constant color flow gain was set just below the level that produces random noise in the signal. Scanning rates ranged from 12 to 25 frames/s, according to the maximal repetition rate of the echo system. In our system, the color Doppler settings did not influence the acquired data, since they only affect the display of the data on the echo screen, but not the actual Doppler velocity values and the variance data. Regurgitant jet areas were traced on the systolic frame from the 2D images taken at the views where the greatest area could be measured. The maximal jet area included the turbulent portion of the color flow signals. An average of five consecutive beats was used for measurements. Jet morphology was classified according to the spatial distribution within the left atrium (15, 16). Eccentric (or asymmetric) jets were directed toward lateral or septal left atrial walls or along the mitral valve leaflets. Central jets originated from the middle of the mitral valve and did not strike atrial walls or mitral valve leaflets. The severity of mitral regurgitation was graded by left ventricular angiography on a scale from I to IV according to Seller's method (17).

Color Doppler signals were processed off-line by a UNIX workstation (SGI Challenge, Mountain View, California). The Doppler data stored on magneto-optical disks contain information on velocity and turbulence (coded as variance). The "variance" has been used as a way to identify turbulent flow. The two values are stored together in 1 byte: the resolution for these values was 5 bit for the velocity and 3 bit for the turbulence. The transformed data set was postprocessed by a 3D median filtering (i.e., the median value was extracted from the contiguous voxels in three dimensions). Regurgitant jets were defined as the fast, turbulent flow component located above the atrioventricular valves. The segmentation algorithm includes a combination of turbulence (expressed as variance) and high velocity according to the formula $J = M(V^2 + 4T^2)$, where V = velocity, T = turbulence (or variance) and M = median filter. We used the "entropy of the histogram" method for automatic thresholding (18), since this procedure was able to provide a segmentation of regurgitant jet similar to that achieved by experienced examiners. The 3D reconstructions of Doppler data were obtained by means of the "Heidelberg Raytracing Model" (19,20), an algorithm initially developed for computer tomography and magnetic resonance images.

Analysis of reproducibility. All echocardiographic studies were performed by the same investigator to avoid interobserver variability. The measurements of regurgitant fraction and regurgitant stroke volume were performed in 10 patients and 10 healthy subjects. In addition, two or more 3D acquisitions were performed in 12 patients with mitral valve regurgitation by two independent examiners. Intraobserver and interobserver variability was obtained by calculating the SD of the differences between two consecutive measurements; the coefficients of variability were calculated as the SD of the differences divided by the mean value. The severity of mitral regurgitation was angiographically estimated by two independent observers.

Statistics. All data are reported as mean ± SD. Linear regression analysis was used to describe the correlations of jet volumes and jet areas to regurgitation fraction and regurgitant stroke volume. The correlation of jet volumes and jet areas to the angiographic grade was calculated by Spearman rank-order test. The differences between groups with different angiographic grade of mitral regurgitation were assessed by analysis of variance with the Bonferroni method. The differences between groups of patients with symmetric and asymmetric jets were assessed by Student *t* test for unpaired data. The method of Bland and Altman (21) was used for the agreement of different methods for assessing mitral valve regurgitation. Differences were considered statistically significant at a value of $p < 0.01$.

JACC Vol. 33, No. 6, 1999
May 1999:1646–54

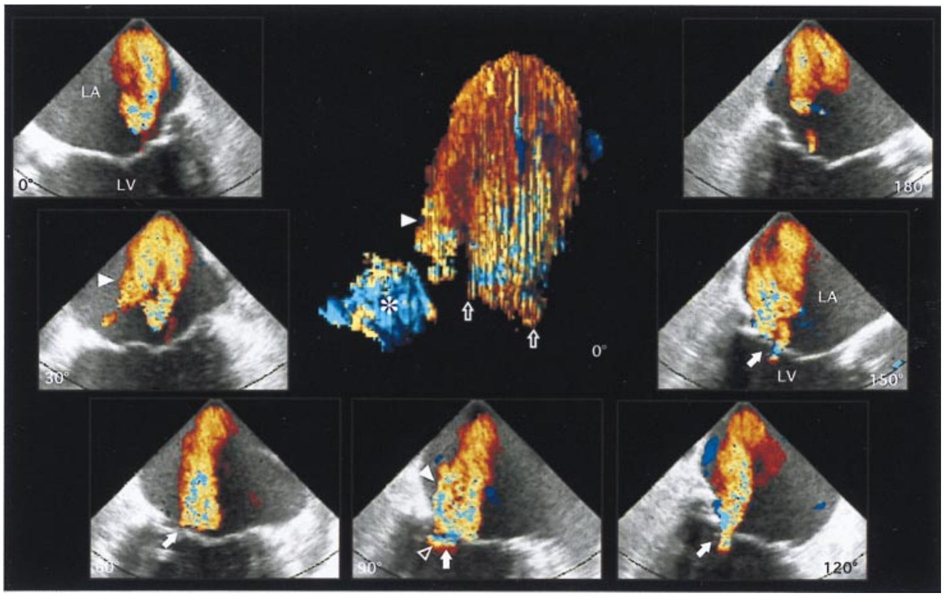

Figure 1. Central jet in a patient with a moderate-to-severe mitral regurgitation. The origin of the regurgitant jet can be visualized in different views from 60° to 150° **(arrows)**. The empty arrows in the three-dimensional reconstruction show the extension of the regurgitant orifice, which consists of a large linear coaptation defect of the commissures. The **arrowheads** show a small, additional jet, the origin of which **(empty arrowheads)** can be observed in the multiplanar examination at 90°. The volume of the regurgitant jet is consistent with a large mitral regurgitation. LA = left atrium; LV = left ventricle. * = left ventricular outflow tract.

RESULTS

The acquisition time of the echocardiographic data ranged from 50 s to 4 mins, 15 s (mean 1 min, 58 s). Adequate reconstructions of Doppler signals were achieved in all patients. The 3D reconstructions and jet volume measurements were obtained in 3 to 5 min according to the different angle resolutions.

Morphology of regurgitant jets. The regurgitant jets were visualized in 3D by showing the systolic frame with the largest jet volume. Central regurgitant jets were found in 28 patients. The 3D images of these central jets provided little additional information on the direction and geometry of regurgitation (Fig. 1). Thirty patients showed eccentric jets. The 3D reconstructions of the asymmetric jets allowed us to describe completely new patterns of mitral regurgitation. Some 3D reconstructions can be mentally accomplished by viewing conventional 2D images at different angles (Fig. 2). In contrast, 3D reconstructions of jets with more complex geometry renders 3D images that cannot be mentally conceived even by experienced examiners (Fig. 3). Figures 4 and 5 show different patterns of regurgitant flow jets, some of which can only be recognized by 3D Doppler. Since the Doppler data were matched with the same color table, the 3D reconstructions truly reproduced the original colors of the echo system. However, due to the virtual illumination by the ray tracer, these images might seem to lose the "fine texture" of colors. These 3D images also include shadows for rendering the perception of the third dimension. Although they have been obtained during a time delay, they are still able to provide unique geometric information and entirely fulfill the task of revealing origin, direction, shape, extension and size of regurgitant jets.

Quantitative assessment of regurgitant jets. Table 1 shows the data from patients with central jets and from patients with eccentric jets. The angiographic degree of mitral regurgitation, maximal jet area and jet volume were significantly greater in patients with eccentric jets. In all patients ($n = 58$) the jet area showed significant correlations with the angiographic grade of regurgitation ($r = 0.73$), the regurgitant fraction ($r = 0.68$) and the regurgitant volume ($r = 0.66$). Regression analysis of jet volumes also showed significant correlations with the angiographic grade of regurgitation ($r = 0.90$), the regurgitant fraction ($r = 0.80$) and the regurgitant volume ($r = 0.90$) in all patients. In the group of patients with central jets ($n = 28$) the jet area significantly correlated with the angiographic grade of regurgitation ($r = 0.85$), the regurgitant fraction ($r = 0.64$) and the regurgitant volume ($r = 0.78$). In the patients with eccentric jets ($n = 30$) no significant relations between the jet area and the angiographic grade of regurgitation ($r = 0.53$), the regurgitant fraction ($r = 0.52$) or the regurgitant volume ($r = 0.53$) were found (Fig. 6). In both groups of patients the volume of regurgitant jets showed significant correlations with the angiographic grade of regurgitation (central, $r = 0.93$; eccentric, $r = 0.90$), the regurgitant fraction (central, $r = 0.77$; eccentric, $r = 0.75$) and the regurgitant volume (central, $r = 0.84$; eccentric, $r = 0.88$). The differences in jet areas and jet volumes between the groups of patients with different angiographic grades of mitral regurgitation were statistically significant ($p < 0.01$).

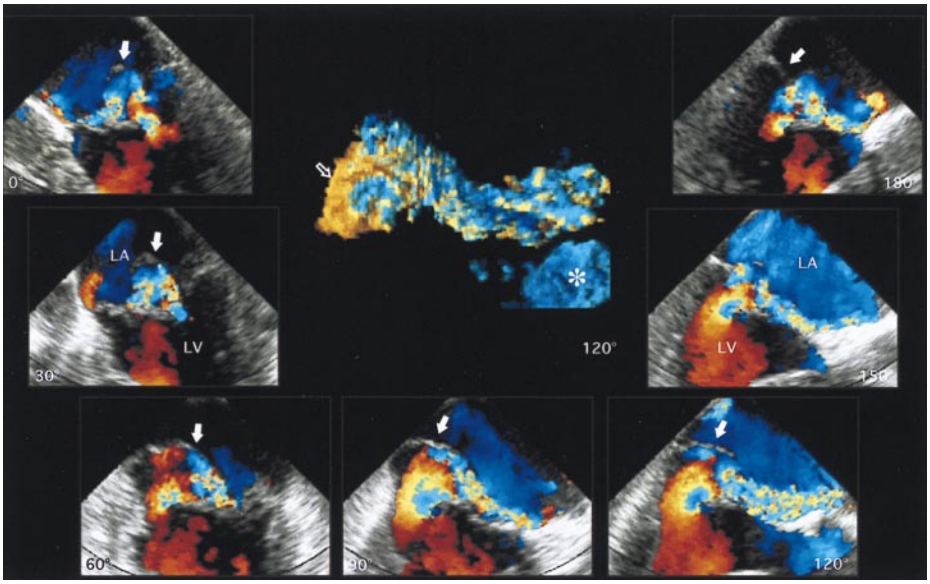

Figure 2. Mitral valve regurgitation in a patient with posterior mitral valve prolapse. The prolapse of the posterior leaflet can be observed at the multiplanar examinations from 0° to 180° **(arrows)**. The regurgitant jet is directed along the atrial surface of the anterior leaflet and has a "tongue" pattern. The main direction of the regurgitant flow can be visualized at about 120°. The proximal isovelocity region of the jet **(empty arrow)** appears very irregular. LA = left atrium; LV = left ventricle. * = left ventricular outflow tract.

Reproducibility of measurements. Intraobserver variability of regurgitant fraction and regurgitant volume were 5.8 ± 5.1% and 6.6 ± 5.3%, respectively. Interobserver variability of regurgitant fraction and regurgitant volume were 6.0 ± 5.2% and 6.6 ± 4.0%. Intraobserver variability of jet area and jet volume were 8.5 ± 6.3% and 4.7 ± 4.1%. Interobserver variability of jet area and jet volume were 4.3 ± 3.0% and 4.0 ± 3.3%.

DISCUSSION

The present study describes the first clinical application of 3D color Doppler in patients with mitral valve regur-

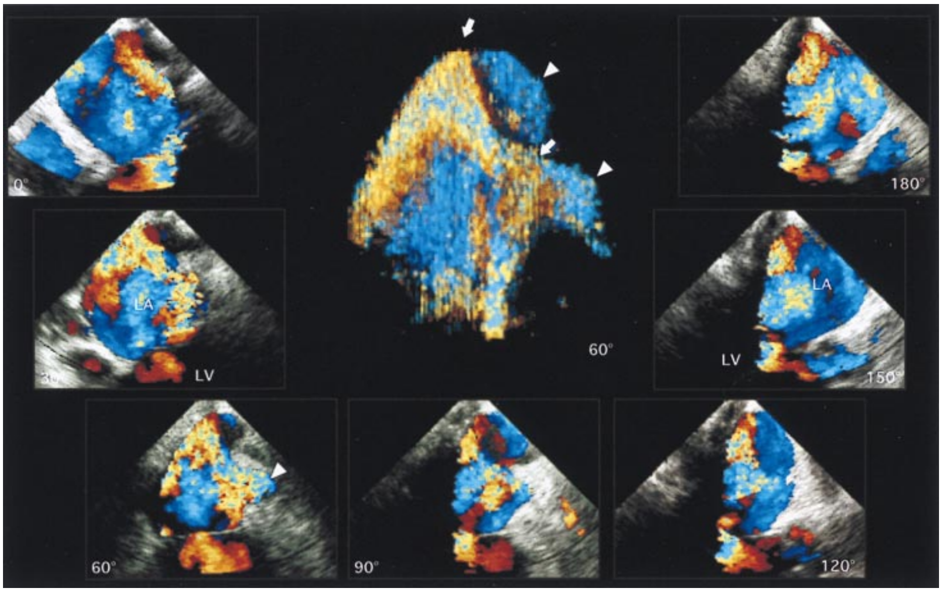

Figure 3. Mitral regurgitant jet with a "spiral" pattern in a patient with anterior prolapse. This jet is directed perpendicular to the mitral annulus, then it turns twice in direction **(arrows)**, according to the curvature of the left atrial wall. The transverse section of the jet proximal to its origin has a circular shape. The **arrowheads** in the three-dimensional image at 60° show the reverse systolic flow in the left upper and lower pulmonary veins. Due to the particular direction of the regurgitant jet, the detection of reverse systolic pulmonary flow by pulsed Doppler does not indicate a severe degree of mitral regurgitation. LA = left atrium; LV = left ventricle.

JACC Vol. 33, No. 6, 1999
May 1999:1646–54

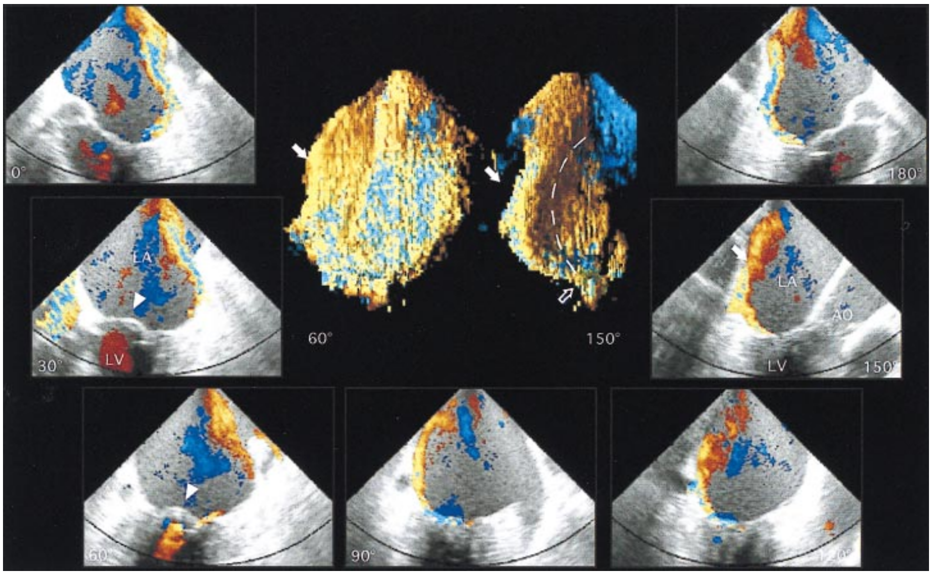

Figure 4. Anterior mitral valve prolapse. The shape of the regurgitant jet has a "spoon" pattern. The origin of this jet has a wide and short initial portion, first directed along the atrial surface of the posterior mitral leaflet and then against the atrial wall **(arrows)**. The extent of its lateral spreading cannot be visualized by conventional color Doppler. The two-dimensional view at 60° can only visualize the initial portion of the jet at its origin **(empty arrow)**. The convex face of this jet can be observed at three-dimensional Doppler from 0° to 120°, the concave face **(dashed line)** at 180°. The prolapse of the anterior mitral leaflet can be observed in the multiplanar view at 30° and 60°. AO = aortic valve; LA = left atrium; LV = left ventricle.

gitation. Although this technique is still under development, this investigation raises many new questions and perspectives which may change the clinical management of patients with valvular regurgitation (22). The quantification of mitral valve regurgitation is still a controversial issue despite the large number of investigations which have dealt with this topic. There is common agreement that no "gold standard" is available for the clinical measurement of regurgitant volumes (23). Up to now, the assessment of mitral regurgitation has been commonly based on the

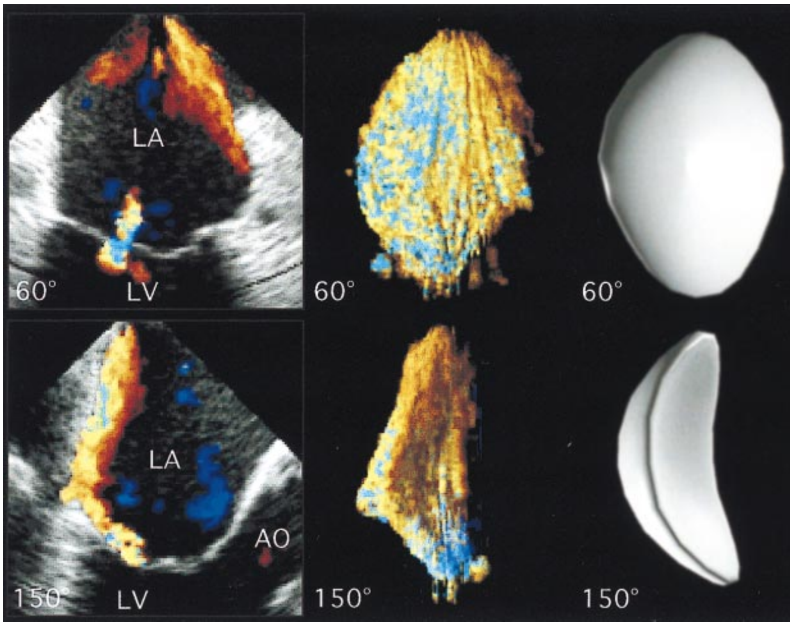

Figure 5. Mitral regurgitant jet with a "spoon" pattern in a patient with anterior prolapse. The pattern of this jet is similar to that in Figure 4. The two-dimensional view at 60° can only visualize the initial portion of the jet at its origin. The two objects to the right show surface three-dimensional reconstructions of the jet viewed from the corresponding view angles (60° and 150°). LA = left atrium; LV = left ventricle.

Table 1. Regurgitation Indexes in Three Groups of Patients

Parameters	All Patients (n = 58)	Central Jets (n = 28)	Eccentric Jets (n = 30)
Angio	2.5 ± 1.0	2.1 ± 1.0	3.2 ± 1.0*
Reg. Fract. (%)	31.5 ± 15.6	24.2 ± 13.8	38.8 ± 17.3*
Reg. Vol.	33.7 ± 17.5	24.3 ± 13.5	43.1 ± 21.5*
JA	5.2 ± 2.05	4.2 ± 1.2	6.2 ± 2.9*
JV	27.15 ± 16.75	18.6 ± 12.7	35.7 ± 20.8*

*$p < 0.01$ vs. central jets; otherwise, p = NS.

Angio = angiographic degree of mitral regurgitation; JA = jet area (cm^2); JV = three-dimensional jet volume (cm^3); Reg. Fract. = regurgitant fraction (%); Reg. Vol. = regurgitant volume (mL).

semiquantitative evaluation of color Doppler flow information by 2D Doppler (24–30).

Morphology of regurgitant jets. Despite the fundamental limitation of displaying velocity instead of flow, 2D Doppler is still the most important method for estimating valve regurgitation, although the most severe mitral regurgitations, for example, those caused by mitral valve prolapse, produce eccentric jet flows that cannot be visualized entirely and measured by 2D imaging. Color Doppler may underestimate the severity of mitral regurgitation, particularly in those patients with a higher degree of regurgitation. The clinical management, indications for surgical intervention and intraoperative decisions after valve repair (31,32) have been based on a subjective estimation of valve regurgitation by 2D Doppler. The 3D reconstruction of color Doppler signals provides unique information about the origin, direction, extension and size of regurgitant jets. In addition, quite new patterns of regurgitant flow can be observed and studied (Figs. 1 to 5). The value of 3D Doppler imaging of regurgitant jets goes beyond the mere visualization of the complex geometry of asymmetric regurgitation flows, and the segmentation procedure is a fundamental advance that provides objective measurements of the jet size, independent of biased, human interpretation of color Doppler.

Quantitative assessment of mitral regurgitation by 3D Doppler. Many methods based on the size of regurgitant jets have been proposed for clinical quantification of mitral regurgitation by color Doppler (24–29). The measurement of jet width at its origin has been suggested for assessing the severity of mitral regurgitation by transesophageal approach (33). However, conventional 2D assessment of asymmetric jets fails to estimate the severity of mitral regurgitation (15,16,33). The results of our study also confirmed the absence of correlation between the jet area and the degree of mitral regurgitation in patients with eccentric jets. The most important finding was the significant correlation between 3D jet volumes and different methods for assessing mitral regurgitation not only in patients with central jets, but also in patients with eccentric jets (Fig. 6).

Study limitations. Almost all quantitative methods for assessing mitral regurgitation based on the jet size assume that the spatial distribution of the jet velocities is proportional to the regurgitant volume (26–29). The jet's size on color Doppler also depends on the driving pressure across the regurgitant orifice and on the flow rate (30). In addition, jet size measurements may also be affected by technical factors such as gain settings, pulse repetition frequency and imaging of low velocity flow (34). The temporal variations of jet size during the systole (35) and the characteristics of the receiving chamber (36) also significantly affect jet area. However, the time-related changes of jet areas and volumes should be taken into account to understand the actual correlations between the volumes of Doppler velocity inside the jets and actual regurgitation flow. In our study, conventional measurement of jet areas at maximal systolic expansion was compared with maximal systolic jet volumes for preserving the comparability of our investigation to previously published studies (15,16,33).

Despite a general fluid dynamic theory that predicts an energy loss of a wall-impinging jet, its occurrence and importance has not yet been demonstrated in patients. In contrast, our study demonstrates that even if the jet cannot be visualized in 2D views, it can be displayed and measured in 3D.

The absence of a gold standard for quantitative assessment of mitral regurgitation is a major limitation common to all clinical studies. Regurgitant fractions and volumes obtained by pulsed Doppler (12) and angiographic grade of mitral regurgitation (37) were used in our study for comparing the quantitative assessments of 3D jet volumes. Although these methods have been used in most clinical studies on the subject (15,16,33), they do not provide a gold standard for the assessment of mitral regurgitation. Other methods, based on the jet length at its origin (33) and on proximal isovolumetric surface area (38,39), have not been compared yet with the 3D jet volumes in our series of patients. The significant correlations between jet volumes and conventional methods showed that 3D Doppler provides a good estimation of mitral regurgitation.

The spatial spreading of the regurgitant jets in patients with eccentric, wall-impinging regurgitant jets is another important limitation of 2D methods based on jet size. Chen et al. (15) found that jet area in patients with asymmetric jets was not correlated to regurgitant fraction as assessed by pulsed Doppler, and that the systolic jet area underestimates the severity of mitral regurgitation. Our study confirmed these findings: jet areas of patients with eccentric jets did not correlate either with angiography or with regurgitant fractions and volumes, but the jet volumes showed good correlation with regurgitant fractions, regurgitant volumes and angiographic degree also in patients with eccentric jets.

Three-dimensional Doppler and technical limitations. The 3D reconstruction of color Doppler signals and the visualization in original color coding is still under investi-

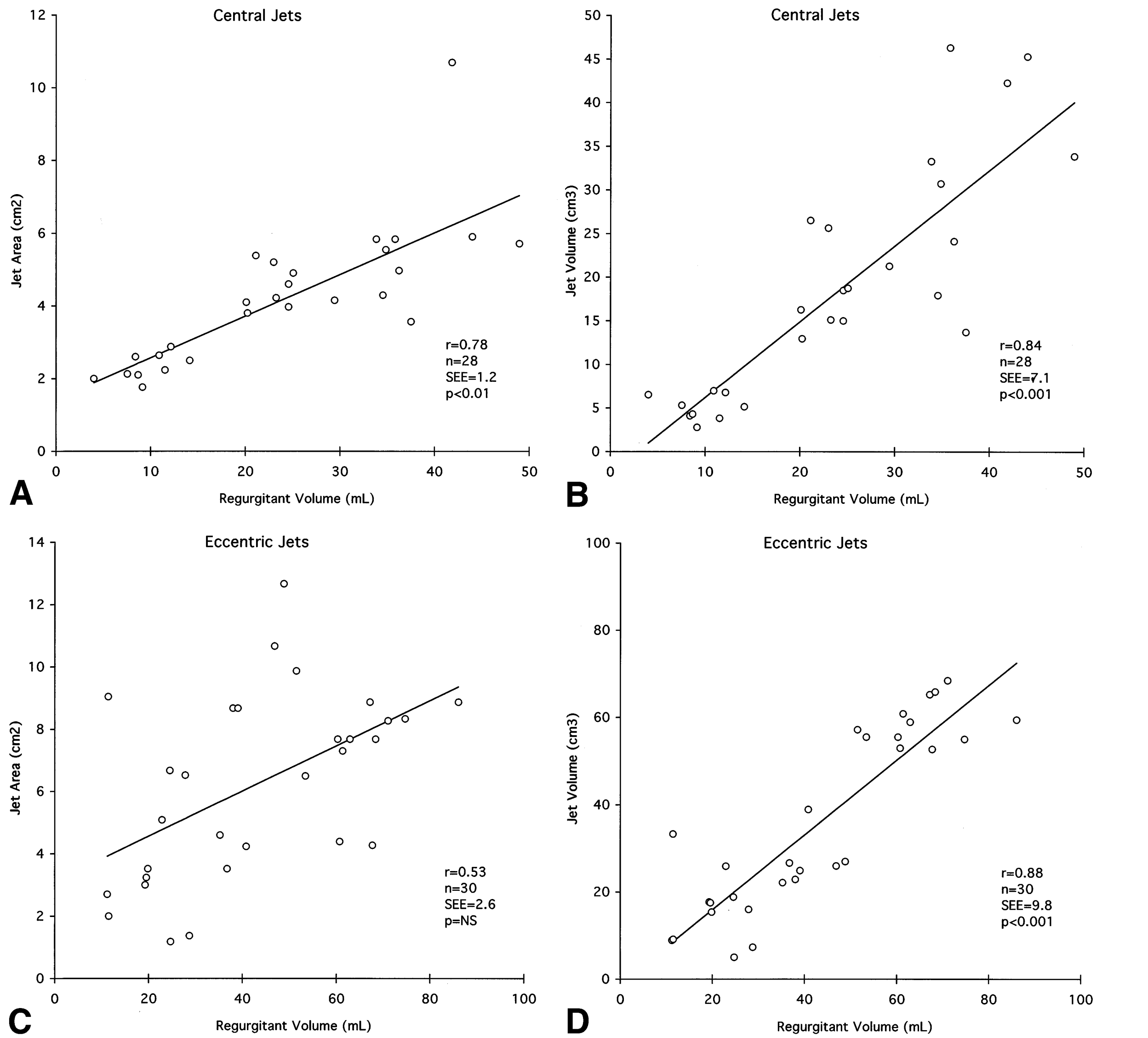

Figure 6. **(A, B)**: Regression analysis of jet areas **(A)** and jet volumes **(B)** versus regurgitation volumes in 28 patients with central jets. **(C, D)**: Regression analysis of jet areas **(C)** and jet volumes **(D)** versus regurgitation volumes in 30 patients with eccentric jets. SEE = standard error of estimate.

gation (10,40). The major limitation of these previous approaches is the use of video signals, which only carry poor information and prevent a separate visualization of cardiac structures and flow. In addition, the quantitative analysis of single flow jet components and the differentiation of slow velocities from turbulent flows could not be performed by these procedures. The possibility of processing digital data allowed us to separate Doppler signals from cardiac structures, thus avoiding inaccurate manual segmentation for visualizing the regurgitant jets and for measuring the jet volumes. Although the automated segmentation was able to identify and visualize the regurgitant jet in a way similar to conventional planimetry, this procedure, as well as manual planimetry, may include other small portions of the flow, as laminar accelerations or second alias boundary close to the jet. Our aim was not to exactly identify the "turbulent" portion of the jet, but to develop a parameter independent of subjective judgment and compare it with the traditional planimetry of the jet area. Since these measurements are equally distributed in all examinations, the correlation analyses are not biased.

An important general limitation of most current methods of 3D echocardiography is that the acquisitions are not performed in real time. During the acquisition time it is mandatory that the position of the transesophageal probe is stable (41). In our series of patients it was possible to maintain the transducer in a very stable position, since the examinations were performed under general anesthesia immediately before heart surgery. Beat-to-beat variation of the mitral regurgitation is another important limitation that can affect the accuracy of 3D reconstructions. To avoid significant variations of jet size during our study, the examinations were performed under stable hemodynamic conditions; no significant variations either in arterial blood pressure or in left atrial pressure occurred during data acquisition. A very narrow range of heart rate variations was set for electrocardiographic triggering. The acquisition of Doppler data was first performed at 2° increments; then the rotation's steps were increased to 5° to achieve a higher temporal resolution and a lower effect of beat-to-beat variation in jet size.

Summary. Despite unresolved theoretical questions associated with the assumed correlation between flow and color Doppler size and with the lack of a reference method of comparison, the clinical significance of this study appears clear. These first images of 3D color Doppler show the complex geometry of regurgitant jets and demonstrate how misleading the assessment of regurgitant jets based on 2D color Doppler can be. In addition, the procedure for measuring 3D jet volumes, based on an automated voxel count, and, hence, independent of subjective estimation, holds promise of becoming an essential tool for quantitative assessment of mitral regurgitation. The newly developed 3D color Doppler has a great potential for changing the management of patients with valvular disease.

Reprint requests and correspondence: Raffaele De Simone, MD, University of Heidelberg, Abteilung für Herzchirurgie, Im Neuenheimer Feld, 120, D-69120 Heidelberg, Germany. E-mail: r.de.simone@urz.uni-heidelberg.de.

REFERENCES

1. Ghosh A, Nanda N, Maurer G. Three-dimensional reconstruction of echocardiographic images using the rotation method. Ultrasound Med Biol 1982;6:655–61.
2. Sheikh KH, Smith SW, von Ramm OT, Kisslo J. Real time three-dimensional echocardiography: feasibility and initial use. Echocardiography 1991;9:677–87.
3. Pandian NG, Nanda N, Schwartz S, et al. Three-dimensional and four-dimensional transesophageal echocardiographic imaging of the heart and aorta in humans using a computed tomographic imaging probe. Echocardiography 1992;9:677–87.
4. Marx GR, Fulton DR, Pandian NG, et al. Delineation of site, relative size and dynamic geometry of atrial septal defects by real-time three-dimensional echocardiography. J Am Coll Cardiol 1995;25:482–90.
5. Schwartz SL, Cao QL, Azevedo J, Pandian NG. Simulation of intraoperative visualization of cardiac structures and study of dynamic surgical anatomy with real-time three-dimensional echocardiography. Am J Cardiol 1994;73:501–7.
6. Salustri A, Spitaels S, McGhie J, et al. Transthoracic three-dimensional echocardiography in adult patients with congenital heart disease. J Am Coll Cardiol 1995;26:759–67.
7. Gopal AS, Shen Z, Sapin PM, et al. Assessment of cardiac function by three-dimensional echocardiography compared with conventional noninvasive methods. Circulation 1995;92:842–53.
8. Siu SC, Rivera JM, Guerrero JL, et al. Three-dimensional echocardiography. In vivo validation for left ventricular volume and function. Circulation 1993;88:1715–23.
9. Sapin PM, Schroeder KD, Smith MD, et al. Three-dimensional echocardiographic measurement of left ventricular volume in vitro: comparison with two-dimensional echocardiography and cineventriculography. J Am Coll Cardiol 1993;22:1530–7.
10. Delabays A, Sugeng L, Pandian NG, et al. Dynamic three-dimensional echocardiographic assessment of intracardiac blood flow jets. Am J Cardiol 1995;76:1053–8.
11. Aakhus S, Maehle J, Bjoernstad K. A new method for echocardiographic computerized three-dimensional reconstruction of left ventricular endocardial surface: in vitro accuracy and clinical repeatability of volumes. J Am Soc Echocardiogr 1994;7:571–81.
12. Rokey R, Sterling RR, Zoghbi WA, et al. Determination of regurgitant fraction in isolated mitral or aortic regurgitation by pulsed Doppler two-dimensional echocardiography. J Am Coll Cardiol 1986;7:1273–8.
13. Fisher DC, Sahn DJ, Friedman JM, et al. The mitral valve orifice method for noninvasive two-dimensional echo Doppler determination of cardiac output. Circulation 1983;67:872–7.
14. Stewart WJ, Jiang L, Mich R, et al. Variable effects of changes in flow rate through the aortic, pulmonary and mitral valves on valve area and flow velocity: impact on quantitative Doppler flow calculations. J Am Coll Cardiol 1985;6:653–62.
15. Chen C, Thomas JD, Anconina J, et al. Impact of impinging wall jet on color Doppler quantification of mitral regurgitation. Circulation 1991;84:712–20.
16. Pieper EPG, Hamer HPM, Sluijs RAP, et al. Usefulness of multiplane transesophageal echocardiography to improve the assessment of severity of mitral regurgitation. Am J Cardiol 1996;78:1132–9.
17. Sellers RD, Levy MJ, Amplatz L, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease. Am J Cardiol 1964;14:432–42.
18. Pal NR, Pal SK. Entropic thresholding. Signal Processing 1989;16:1053–8.
19. Meinzer HP, Meetz K, Scheppelmann D, et al. The Heidelberg Raytracing Model. IEEE Comput Graphics Appl 1991;6:34–43.
20. Vahl CF, Meinzer HP, Hagl S. Three-dimensional presentation of cardiac morphology. Thorac Cardiovasc Surg 1991;39:198–204.
21. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
22. De Simone R, Glombitza G, Albers J, et al. Three-dimensional reconstruction and quantitative analysis of color Doppler jets in original color coding (abstr). Echocardiography 1997;14:S31.
23. Bolger AF, Eigler NL, Maurer G. Quantifying valvular regurgitation: limitations and inherent assumptions of Doppler techniques. Circulation 1988;78:1316–8.
24. Omoto R, Yokote Y, Takamoto S, et al. The development of real-time two-dimensional Doppler echocardiography and its significance in acquired valvular diseases with specific reference to the evaluation of valvular regurgitation. Jpn Heart J 1984;25:325–40.
25. Sahn DJ. Real-time two dimensional echocardiographic flow mapping. Circulation 1985;71:849–53.
26. Helmcke F, Nanda NC, Hsiung MC, et al. Color Doppler assessment of mitral regurgitation with orthogonal planes. Circulation 1987;75:175–83.
27. Miyatake K, Izumi S, Okamoto M, et al. Semiquantitative grading of severity of mitral regurgitation by real-time two-dimensional Doppler flow imaging technique. J Am Coll Cardiol 1986;7:82–8.
28. Spain MG, Smith MD, Grayburn PA, et al. Quantitative assessment of mitral regurgitation by Doppler color flow imaging: angiographic and hemodynamic correlations. J Am Coll Cardiol 1989;13:585–90.
29. Castello R, Lenzen P, Aguirre F, Labovitz AJ. Quantitation of mitral regurgitation by transesophageal echocardiography with Doppler color flow mapping: correlation with cardiac catheterization. J Am Coll Cardiol 1992;19:1516–24.
30. Maciel BC, Moises VA, Shandas R, et al. Effects of pressure and volume of receiving chamber on the spatial distribution of regurgitant jets as imaged by color Doppler flow mapping. An in vitro study. Circulation 1991;83:605–13.
31. De Simone R, Lange R, Tanzeem A, et al. Adjustable tricuspid valve annuloplasty assisted by intraoperative transesophageal color Doppler echocardiography. Am J Cardiol 1993;71:926–31.
32. De Simone R, Lange R, Hagl S. Atlas of Transesophageal Color Doppler Echocardiography and Intraoperative Imaging. Berlin: Springer-Verlag, 1994.
33. Tribouilloy C, Shen WF, Quere JP, et al. Assessment of severity of mitral regurgitation by measuring regurgitant jet width at its origin

with transesophageal Doppler color flow imaging. Circulation 1992; 85:1248–53.
34. Sahn DJ. Instrumentation and physical factors related to visualization of stenotic and regurgitant jets by Doppler color flow mapping. J Am Coll Cardiol 1988;12:1254–61.
35. Smith MD, Kwan OL, Spain MG, DeMaria AN. Temporal variability of color Doppler jet areas in patients with mitral and aortic regurgitation. Am Heart J 1992;123:953–60.
36. Yoganathan AP, Cape EG, Sung H-W, et al. Review of hydrodynamic principles for the cardiologist: applications to the study of blood flow and jets by imaging techniques. J Am Coll Cardiol 1988;12: 1344–53.
37. Croft CH, Lipscomb K, Mathis K, et al. Limitations of qualitative angiographic grading in aortic or mitral regurgitation. Am J Cardiol 1984;53:1593–8.
38. Recusani F, Bargiggia GS, Yoganathan AP, et al. A new method for quantification of mitral regurgitant flow rate using color Doppler flow imaging of the flow convergence region proximal to a discrete orifice. An in vitro study. Circulation 1991;83:594–604.
39. Bargiggia GS, Tronconi L, Sahn DJ, et al. A new method for quantification of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation 1991;84:1481–9.
40. Bohs LN, Friemel BH, Kisslo J, et al. Three-dimensional flow images by reconstruction from two-dimensional vector velocity maps. J Am Soc Echocardiogr 1995;8:915–23.
41. Legget ME, Martin RW, Sheehan G, et al. How positionally stable is a transesophageal echocardiographic probe? Implications for three-dimensional reconstruction. J Am Soc Echocardiogr 1996;3: 257–65.