Color Doppler Regurgitant Jet Area for Evaluating Eccentric Mitral Regurgitation: An Animal Study With Quantified Mitral Regurgitation

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Objectives. The purpose of the present study was to rigorously evaluate the accuracy of the color Doppler jet area planimetry method for quantifying chronic mitral regurgitation.

Background. Although the color Doppler jet area has been widely used clinically for evaluating the severity of mitral regurgitation, there have been no studies comparing the color jet area with a strictly quantifiable reference standard for determining regurgitant volume.

Methods. In six sheep with surgically produced chronic mitral regurgitation, 24 hemodynamically different states were obtained. Maximal color Doppler jet area for each state was obtained with a Vingmed 750. Image data were directly transferred in digital format to a microcomputer. Mitral regurgitation was quantified by the peak and mean regurgitant flow rates, regurgitant stroke volumes and regurgitant fractions determined using mitral and aortic electromagnetic flow probes.

Results. Mean regurgitant volumes varied from 0.19 to 2.4 liters/min (mean [±SD] 1.2 ± 0.59), regurgitant stroke volumes from 1.8 to 29 ml/beat (mean 11 ± 6.2), peak regurgitant volumes from 1.0 to 8.1 liters/min (mean 3.5 ± 2.1) and regurgitant fractions from 8.0% to 54% (mean 29 ± 12%). Twenty-two of 24 jets were eccentric. Simple linear regression analysis between maximal color jet areas and peak and mean regurgitant flow rates, regurgitant stroke volumes and regurgitant fractions showed correlation, with r = 0.68 (SEE 0.64 cm²), r = 0.63 (SEE 0.67 cm²), r = 0.63 (SEE 0.67 cm²) and r = 0.58 (SEE 0.71 cm²), respectively. Univariate regression comparing regurgitant jet area with cardiac output, stroke volume, systolic left ventricular pressure, pressure gradient, left ventricular/ left atrial pressure gradient, left atrial mean pressure, left atrial n wave pressure, systemic vascular resistance and maximal jet velocity showed poor correlation (0.08 < r < 0.53, SEE >0.76 cm²).

Conclusions. This study demonstrates that color Doppler jet area has limited use for evaluating the severity of mitral regurgitation with eccentric jets.

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The color Doppler jet area method has been widely used for assessing the severity of mitral regurgitation (1-2). This method has limitations because of instrumentation variability and hemodynamic and hydrodynamic factors (3-17). Although other methods, including transesophageal echocardiography with analysis of pulmonary vein flow pattern or the proximal flow convergence methods, or both, have been proposed as being useful for evaluating the severity of mitral regurgitation (18-22), color jet planimetry still continues to be used as a first approach for evaluating the severity of mitral regurgitation probably because of its visual simplicity and ease of use. Because only a limited number of studies detailing the capability of this method for determining regurgitation used an adequate quantifiable reference standard to determine mitral regurgitant volume in a model that closely mimics clinical disease, the present study using regurgitant volumes quantified by electromagnetic flow probes was performed to assess the applicability of color Doppler jet area method for evaluating the severity of mitral regurgitation.

Methods

Experimental preparation. Six sheep weighing 31 to 36 kg were studied. Four to 5 months before hemodynamic and ultrasound studies, two or three secondary chordae to the anterior leaflet (three sheep) or posterior leaflet (three sheep) of the mitral valve were severed under direct vision using cardiopulmonary bypass. All operative and animal management procedures were approved by the Animal Care and Use Committee of the National Heart, Lung, and Blood Institute. Preoperative, intraoperative and postoperative animal management and husbandry methods are described in detail elsewhere (23). After surgery the sheep were maintained on digoxin and furosemide.

Four to 5 months later the sheep were returned to the animal surgery facility for the physiologic studies that are the subject of this report. Anesthesia was induced with intravenous sodium pentobarbital (25 mg/kg body weight) and maintained with 1% to 2% isoflurane with oxygen, and the animals were...
ventilated by means of an endotracheal tube using a volume-cycled ventilator.

Cardiac catheterization and electromagnetic flow meters.

A Swan-Ganz catheter was positioned in the main pulmonary artery through the femoral vein, and another catheter was positioned in the right common femoral artery for monitoring systemic arterial pressure and arterial blood gases. These catheters were interfaced with a physiologic recorder (ES 1000, Gould Inc.) using fluid-filled pressure transducers (model PD23 ID, Gould Statham). Arterial blood gases and pH were maintained within physiologic ranges. A bilateral transverse thoracotomy was performed. After institution of cardiopulmonary bypass, an electromagnetic flow probe (model EP455c, Carolina Medical Electronics, Inc.) was sutured into the left atrium above the mitral annulus. The left atrium was closed, and the sheep was weaned from cardiopulmonary bypass. Another electromagnetic flow probe (Model EP455, Carolina Medical Electronics) was placed snugly around the skeletonized ascending aorta distal to the coronary ostia and proximal to the brachiocephalic trunk. Both flow probes were connected to flow meters (Model FM501, Carolina Medical Electronics), and these were connected to the same physiologic recorders (ES 1000, Gould Inc.) used for hemodynamic pressure recordings. Left atrial and left ventricular pressures were obtained from intracavitary catheter-tipped transducers (model SPC-350, Millar Instruments, Inc.) positioned transmurally. All hemodynamic data were recorded at paper speeds of 250 mm/s (Fig. 1). Four consecutive cardiac cycles were analyzed for each hemodynamic determination.

Occlusive zeros for the aortic and mitral flow probes were confirmed on cardiopulmonary bypass. Calibration factors for the flow probes were corrected for the sheep's hematocrits according to the manufacturer's specification. The integrals of instantaneous flows over time were determined by planimetry of the flow signal recordings. The problem of zero baseline drift was managed by the techniques described by Dent et al. (24). The aortic flow zero-level baseline was adjusted according to the contour of its electromagnetic flow probe signal; this baseline was confirmed by the occlusive zeros. No sheep had physiologically important aortic regurgitation. For the purpose of this study, coronary artery blood flow during ventricular systole was considered to be negligible. The baseline for the mitral flow was adjusted until the forward minus the backward mitral flow volumes equaled the aortic flow volumes. The correlation coefficient for the regression of aortic forward flow versus mitral forward minus mitral regurgitant flow was 0.97 (SEE 0.116 liter/min). Regurgitant fraction was calculated as backward mitral flow volume per minute divided by forward mitral flow volume per minute. A hydrostatic standard was used for calibration of all pressure recordings. Left ventricular and left atrial pressures were recorded simultaneously. All hemodynamic recordings were performed simultaneously in tandem with the echocardiographic studies. After baseline measurements, varying degrees of severity of mitral regurgitation were produced by altering preload or afterload, or both, using blood transfusion or angiotensin infusion, or both. A total of 24 stable hemodynamic states (3 to 5 sheep) were obtained. Systolic stroke volume was obtained from the aortic flow meter and was multiplied by the heart rate to obtain cardiac output. Left ventricular systolic and left atrial mean and peak v wave pressures were obtained from the pressure tracings. The data were averaged over at least four measurements for each determination.

Color Doppler echocardiography. Color Doppler flow mapping was performed with a Vingmed 750 system (Vingmed Sound, A/S, Oslo, Norway) using a 5-MHz transducer placed epicardially. Pulse repetition frequency was 4.0 kHz for color Doppler scanning. Color gain was adjusted to eliminate random color in areas without flow. The typical aliasing velocity for imaging the color jet area was 72 cm/s. Color sector size was limited to 45° to allow frame rates up to 45 frames/s and to maximize angular line density for color Doppler interrogation. The color Doppler filter was held constant and set with a rolloff to minimize velocities <8 cm/s. From various approaches, including the apical and basal positions on the heart, the maximal color jet areas of mitral regurgitation were sought by slight modifications of the transducer positions (Fig. 2). All color Doppler flow images were transferred as digital cine loops to a Macintosh computer (Iici) for later analysis. In views that showed the regurgitant jets going away from the transducer and parallel to the direction of interrogation, continuous wave Doppler velocities were obtained under imaging guidance.

The maximal jet area was obtained using frame-by-frame analysis of the cine loops with a computer software program
Figure 2. Apical color Doppler image of an eccentric mitral regurgitant jet at peak systole (heart rate 119 beats/min, area 1.91 cm², circumference 9.21 cm). LA = left atrium; LV = left ventricle.

(Echo Disp). The jet area was measured by planimetry of the outer border of clearly definable maximal color-encoded jet area using the variance-encoded central jet with and without the contiguous less turbulent velocities moving in the same direction as the central jet (3,5). Left atrial size was also measured by the computer-assisted planimetry system in the same frame in which the maximal color jet area was observed. Continuous wave Doppler velocities were available in digital files matched to the hemodynamic states and the color jet images. Maximal color jet areas, the ratio of the maximal jet area to the size of left atrium and the maximal jet velocity were measured and averaged (for at least 3 beats) on the computer.

To evaluate interobserver variability, all of the color jet areas were measured by two independent observers who had no knowledge of electromagnetic flow data or the other observer's data.

Statistical analysis. Simple linear regression analysis was used for obtaining correlation coefficients for the reference electromagnetic flow data and other hemodynamic data with color regurgitant jet area and the ratio of the jet size to the left atrial size. In addition, because multiple points were obtained in the same animals, a multivariate regression analysis was used to examine the relation of data between sheep. To do this, we created the design matrix in a spreadsheet of a statistical computer program (Stat View 1988, Abacus Concepts, Inc.) using dummy variables as columns to encode the different sheep (25) and used the multiple regression function of Stat View. A probability value < 0.05 was considered statistically significant.

Results

Measurable color Doppler jets were recorded for all 24 hemodynamic conditions and ranged from 0.23 to 3.66 cm² in area (mean ±SD 1.99 ± 0.85). Heart rates ranged from 84 to 142 beats/min (mean 110 ± 13). Twenty-two of 24 regurgitant jets were eccentric, veering toward a left atrial wall. The remaining two regurgitant jets were free or central in the left atrial cavity (5,6).

Severity of mitral regurgitation. Quantitation of the regurgitation with the electromagnetic flow probes indicated clinically relevant severities of regurgitation: Peak regurgitant flow rates ranged from 1.0 to 8.1 liters/min (mean 3.5 ± 2.1), mean regurgitant flow rates from 0.19 to 2.4 liters/min (mean 1.2 ± 0.59), regurgitant stroke volumes from 1.8 to 29 ml/beat (mean 11 ± 6.2) and regurgitant fraction from 8.0% to 54% (mean 29 ± 12%).

Relation between color jet areas and severity of mitral regurgitation. Simple linear regression analysis between the maximal color jet areas, including the contiguous, less turbulent velocities moving in the same direction as the central jet, and the peak and mean regurgitant flow rates, regurgitant stroke volumes and regurgitant fractions showed only moderately good correlation (r = 0.68 (SEE 0.64 cm), r = 0.63 (SEE 0.67 cm²), r = 0.63 (SEE 0.67 cm²) and r = 0.58 (SEE 0.71 cm²), respectively, Fig. 3). When the ratio of color jet size to left atrial size was used, the correlations improved somewhat (r = 0.70, 0.65, 0.68 and 0.65, respectively), but significant scatter in the data still existed, resulting in a limited ability of the color Doppler jet planimetry method to predict the severity of mitral regurgitation. The relation between the maximal color jet areas excluding the contiguous, less turbulent velocities moving in the same direction as the central jet and the peak regurgitant flow rates was similar to that between the jet area with the less turbulent flow and the peak regurgitant flow rate (r = 0.64, SEE 0.63 cm², p < 0.01). When a multiple-regression model was used to eliminate associations based on data from within one sheep, a decreased relation between the maximal color jet areas and the peak regurgitant flow rates was obtained. (The slope of the regression was 0.19, which was <0.26, the slope of the simple regression analysis, and the standard error of estimate was 0.07, which was larger than 0.05, the standard error of estimate by the simple regression analysis, p < 0.05.) In addition, there was no significant relation between the color jet area and the mean regurgitant flow rate, the regurgitant stroke volume or the regurgitant fraction, all p > 0.05, when accounting for variability between sheep in the linear regression.

Relations to other variables. Univariate regression for the jet areas compared with cardiac output, systolic volume, left ventricular systolic pressure, left ventricular and left atrial pressure gradients, systemic vascular resistance and maximal jet velocity showed poorer correlation (r = 0.22, 0.16, 0.08,
0.14, 0.11, 0.30, respectively, none of which was statistically significant). For all hemodynamic indexes, statistical significance was obtained only between jet area and left atrial mean and maximal v wave pressures ($r = 0.46$, SEE $0.77 \text{ cm}^2$; $r = 0.53$, SEE $0.74 \text{ cm}^2$, respectively, $p < 0.02$) (Fig. 4). When the multivariate analysis was used to focus on predictability between sheep and to eliminate data tracking induced by serial measurements within the same animal, no significant relation was found between the color jet area and left atrial mean or maximal v wave pressures ($p > 0.05$).

**Interobserver variability.** There was good agreement between measurements of the color jet areas by two independent observers ($r = 0.89$, SEE $0.02 \text{ cm}^2$, $p < 0.0001$) (Fig. 5).

**Discussion**

This study, in an animal model using quantified mitral regurgitant volume, demonstrates that the color Doppler jet planimetry method has limited utility for estimating severity of regurgitation.

**Previous studies.** Early reports on the color Doppler jet area method for evaluating the severity of mitral regurgitation used angiographic data as a reference for grading the severity of mitral regurgitation and proposed a clinical applicability of this method (1,2). Other experimental and clinical studies, however, have raised questions with regard to the accuracy of the color Doppler jet area method for grading the severity of mitral regurgitation (3-17). Our laboratory and others have reported that jet-wall interactions (the Coanda effect) alter color Doppler flow mapping of regurgitant jets (11,13,15). Chen et al. (5) and Sarano et al. (6) confirmed these in vitro findings, reporting that eccentric regurgitant jets were significantly smaller than free regurgitant jets and that the correlation with Doppler-derived regurgitant volume was poorer with
surface jets than with free or central jets. The Doppler-derived regurgitant fraction or regurgitant volume that was used in these studies as a reference standard may be hampered by the potential inaccuracy of Doppler itself for flow volume calculation (8).

Advantage of our study. Compared with the previously reported clinical or in vivo studies, our present study offers a significant advantage: The mitral regurgitant volume was quantified using electromagnetic flow probes. Grading mitral regurgitation by invasive left ventriculography is the conventional and most widely accepted standard for evaluating the severity of mitral regurgitation (1,2). However, this method is subjective and semiquantitative at best. It is affected by many variables, such as arrhythmia, catheter position, amount of dye injected, left atrial size and X-ray film setting. Actual calculation of regurgitant volume from left ventriculography, derived by subtracting effective forward stroke volume (from thermodilution) from total left ventricular stroke volume, has been widely used for determining the severity of mitral regurgitation, but this method is limited by the problems of deriving quantitated left ventricular volume measurements from planar angiograms and the error in thermodilution determinations (2,3,8).

Considering the excellent correlation coefficient for the regression of aortic forward flow versus mitral forward minus mitral regurgitant flow \(r = 0.97\), the electromagnetic flow reference for the regurgitant volume appears more accurate and reliable than the left ventricular cineangiographic or the Doppler methods for determining the severity of regurgitation (2,3,8,26,27). Importantly, the synchronous on-line nature of the electromagnetic flow recordings allows peak regurgitant flow rates as well as mean regurgitant flow rates, regurgitant fractions and regurgitant stroke volumes to be available for comparison with maximal color Doppler jet areas. The comparison between the peak regurgitant flow rate and the color Doppler jet area has rarely been investigated. The color Doppler planimetry method is based on a single still frame showing the maximal jet area. Only the peak regurgitant flow rate should be expected to correlate with the maximal color jet area. Therefore, it is not surprising that the peak regurgitant flow rate showed the highest correlation coefficient with the maximal color jet area and with the ratio of maximal jet area to left atrial size. Despite intermediate-range correlation coefficients, the wide ranges of the standard error of the estimate determinations for the linear regression preclude using these for prediction. Because multiple points were obtained in the same sheep, a multiple-regression analysis was used to examine differences between sheep. This showed an even weaker relation between maximal jet area and peak regurgitant flow rate.
(The slope of the regression was 0.19, which was <0.26, the slope of the simple regression analysis.) Other variables, such as mean regurgitant flow rate and regurgitant fraction, showed no significant relation with the color jet area when the multiple analysis was used. In contrast, in a preliminary extension of the present study, instantaneous mitral regurgitant flow rates obtained by the electromagnetic flow probes and meters divided by the corresponding instantaneous Doppler velocity provided instantaneous orifice areas during systole. The average of instantaneous orifice areas during systole was closely related (r = 0.87, p < 0.0001) to mean regurgitant flow rates and therefore to severity of mitral regurgitation (28). Thus, methods providing the regurgitant orifice size (such as dividing flow convergence calculated flows divided by the appropriate continuous wave Doppler velocities) may prove more useful than the jet area method for evaluating mitral regurgitation.

Smith et al. (29) recently reported temporal variability of the maximal development of color Doppler jet area in patients with mitral regurgitation. In the present study, we compared the time period from the Q wave of the electrocardiogram with the maximal color Doppler jet area and with the peak flow rate obtained by the electromagnetic flow meters. A close relation (r = 0.89) was found between the two peak timings, with a significant delay (average 24 ms) of maximal color jet appearance compared with the electromagnetic peak flow rate. This could be important for understanding the temporal relation of color jet area as computed and displayed by “real-time” Doppler flow mapping and the pathophysiology of mitral regurgitation.

Relation between left atrial pressure and color jet area. Hemodynamic indexes, including stroke volume and cardiac output, did not correlate with maximal jet area. Of the indexes studied, only mean atrial pressure and size of the r wave showed any relation to maximal jet area. In addition, the relations were weak, with standard errors precluding clinical usefulness. In vitro studies (12,14) have indicated that high left atrial pressures produce minor differences in color jet areas. A recent clinical study (30) has demonstrated the development of higher left atrial pressures with more severe degrees of mitral regurgitation as graded by color Doppler jet size.

Study limitations. The majority of the jets (22 of 24) in this study were eccentric, impinging on the atrial wall. Only two of the jets were central and could therefore be expected to expand symmetrically; this small number was not considered sufficient for independent analysis. Therefore, our conclusion may be overly pessimistic, applying mainly to eccentric mitral regurgitant jets. Nonetheless, the type of mitral regurgitation that we studied, in terms of leaflet pathology and jet type, mimics common clinical findings.

Finally, the mean body weight of the animals in our study was 33 ± 2.0 kg, and the ranges of volumes of forward flows as well as regurgitant flows reflected these body weights. Thus, for animals of larger size, one might anticipate proportionately larger absolute regurgitant volumes.

Conclusions. Our study of chronic mitral regurgitation quantified in an animal model indicates that the color Doppler jet planimetry method has limited use for determining regurgitant flow rates. Although our observations were limited to eccentric jets associated with flail leaflets as a result of disrupted chordae tendineae, the observation may also have implications for other types of mitral regurgitation encountered in clinical practice.

References


