A New Method for Quantification of Regurgitant Flow Rate Using Color Doppler Flow Imaging of the Flow Convergence Region Proximal to a Discrete Orifice

An In Vitro Study

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While color Doppler flow mapping has yielded a quick and relatively sensitive method for visualizing the turbulent jets generated in valvular insufficiency, quantification of the degree of valvular insufficiency has been limited by the dependence of visualization of turbulent jets on hemodynamic as well as instrument-related factors. Color Doppler flow imaging, however, does have the capability of reliably showing the spatial relations of laminar flows. An area where flow accelerates proximal to a regurgitant orifice is commonly visualized on the left ventricular side of a mitral regurgitant orifice, especially when imaging is performed with high gain and a low pulse repetition frequency. This area of flow convergence, where the flow stream narrows symmetrically, can be quantified because velocity and the flow cross-sectional area change in inverse proportion along streamlines centered at the orifice. In this study, a gravity-driven constant-flow system with five sharp-edged diaphragm orifices (ranging from 2.9 to 12 mm in diameter) was imaged both parallel and perpendicular to the direction of flow through the orifice. Color Doppler flow images were produced by zero shifting so that the abrupt change in display color occurred at different velocities. This “aliasing boundary” with a known velocity and a measurable radial distance from the center of the orifice was used to determine an isovelocity hemisphere such that flow rate through the orifice was calculated as \( 2\pi r^2 \times V_r \), where \( r \) is the radial distance from the center of the orifice to the color change and \( V_r \) is the velocity at which the color change was noted. Using \( V_r \) values from 54 to 14 cm/sec obtained with a 3.75-MHz transducer and from 75 to 18 cm/sec obtained with a 2.5-MHz transducer, we calculated flow rates and found them to correlate with measured flow rates (\( r = 0.94 - 0.99 \)). The slope of the regression line was closest to unity when the lowest \( V_r \) and the correspondingly largest \( r \) were used in the calculation. The flow rates estimated from color Doppler flow imaging could also be used in conjunction with continuous-wave Doppler measurements of the maximal velocity of flow through the orifice to calculate orifice areas (\( r = 0.75 - 0.96 \) correlation with measured areas). In a clinical series of 20 patients studied prospectively, radius of the flow convergence area separated patients with angiographically mild from those with moderate (\( p \leq 0.001 \)) and patients with angiographically moderate from those with severe (\( p \leq 0.005 \)) mitral regurgitation and showed good correlation with the angiographic severity of regurgitation (\( r = 0.87 \)). Color Doppler visualization of the flow convergence region is a method that appears promising for providing a calculated value of flow rate for a regurgitant orifice in the cardiovascular system. When used in conjunction with continuous-wave Doppler, color Doppler flow imaging can be used to predict the orifice area. (Circulation 1991;83:594–604)
Color Doppler flow mapping has provided new insights into the dynamics of regurgitant jet flow and has greatly enhanced our appreciation of the complexities of regurgitant jets and other intracardiac flows. The concept initially employed for the quantification of regurgitation, that the spatial distribution of mitral regurgitant jets within the left atrium is closely related to the severity of regurgitation, has not proved to be accurate and, at best, provides a rough estimate of the severity of mitral insufficiency. These initially disappointing results, however, have led to directed research and a better understanding of the dynamics of regurgitant jet flow. Specifically, it has become increasingly recognized that a number of instrumentation factors as well as physical factors can affect the spatial distribution of jets. In vitro and in vivo studies have demonstrated that the spatial distribution of mitral regurgitant jets is highly dependent on the flow rate and the velocity of regurgitation as well as on the regurgitant pressure drop. The spatial distribution is also dependent on factors related to the left atrium such as interaction with the atrial wall or mitral valve and compliance of the atrial chamber. In addition, the wide range of velocity values and the varying directional flow components of a turbulent jet within the left atrium make accurate velocity determinations by both spectral Doppler and color Doppler flow mapping difficult. The combined effects of these physiological and technical variables make it unlikely that the spatial distribution of mitral regurgitant jets within the left atrium can serve as a rational basis for quantifying the severity of mitral regurgitation.

The proximal flow convergence region, a zone of progressive laminar velocity acceleration with concordant narrowing of the flow cross-sectional area, may not be subject to many of the limitations associated with quantifying jet flow in the left atrium. It is known that flow acceleration occurs proximal to restrictive orifices in obstructive lesions, but it is not well recognized that there is also a small region of flow convergence proximal to regurgitant lesions. For valve regurgitation this zone of proximal flow acceleration is characterized by a region of unbounded laminar flow that passes through the regurgitant orifice. Because flow in this region is laminar and not contaminated by entrained flow, it is attractive to use this region for quantifying mitral regurgitation. The high spatial resolution of color Doppler flow mapping and its potential for quantifying flow velocity and velocity gradients make it a promising technique for the investigation of this proximal flow convergence region.

The present in vitro study was designed to investigate the ability of color Doppler flow mapping to characterize the flow convergence region proximal to a regurgitant orifice and to assess whether color Doppler flow imaging can be used to accurately estimate the regurgitant flow rate. Since the flow rate varies with inlet velocity and orifice size and since continuous-wave (CW) Doppler provides a measure of velocity in the contracted section of the jet, we also calculated regurgitant orifice area from the color Doppler flow mapping and CW Doppler data. In addition, we studied a series of patients with mitral insufficiency to test the ability of color Doppler flow mapping to image the flow convergence region and to predict the angiographic grade of mitral insufficiency.

Methods

Theory of Flow Rate Estimation From Flow Convergence Region

Theoretically, the flow convergence region proximal to a discrete regurgitant orifice in a flat planar surface is a hemispheric volume in which flow accelerates toward the regurgitant orifice along radial streamlines. This zone of proximal flow acceleration is made up of concentric hemispheric shells of equal and accelerating velocities (velocity isopleths) (Figure 1); the smallest hemispheres near the orifice have the highest velocities. If we assume that all of the blood within the flow convergence zone passes through the regurgitant orifice and that this flow...
convergence zone conforms to the laws of the continuity principle, then at any hemisphere the product of the hemispheric surface area and its velocity will be constant. Flow rate for any given isovelocity hemisphere will then be given by the equation 

\[ Q = 2\pi r^2 \times V_r \times 60 \div 1,000, \]

where \( Q \) is the flow rate expressed in liters per minute, \( 2\pi r^2 \) is the area of the hemisphere at a radial distance \( r \) from the orifice, and \( V_r \) is the velocity in centimeters per second at the radial distance \( r \). If the continuity principle is observed, then this \( Q \) will be identical to the regurgitant flow rate. The predicted proximal zone of flow acceleration has been demonstrated by color Doppler flow mapping both in vivo\(^{12,13} \) and in vitro.\(^{14} \)

The velocity of a regurgitant jet at the orifice (i.e., the maximum jet velocity) can be measured by CW Doppler.\(^{18} \) Theoretically, it is possible to estimate the regurgitant orifice area by applying the continuity principle; similar methods have been described for estimating the area of stenotic aortic valves.\(^{19-21} \) In the present study this involved using the flow rate \( (Q) \) estimated by color Doppler flow images of the zone of flow convergence and the maximum velocity at the orifice \( (V_o) \) measured by CW Doppler to estimate the orifice area as \( Q/V_o \times C_c \), where \( C_c \) is the coefficient of contraction. It is necessary to include \( C_c \) in this calculation because the true area of the orifice will be larger than the flow area.\(^{20} \)

**In Vitro Flow Model**

To test these concepts a closed-circuit constant-flow model was designed to simulate the proximal flow acceleration region associated with mitral regurgitation. As shown in Figure 2, this model consisted of a centrifugal electric pump, a rotometer, a reservoir, a chamber, and connecting tubing. Sharp-edged, discrete circular diaphragms with diameters of 2.9, 3.9, 6.6, 10.0, and 12.0 mm were inserted at the outlet of the chamber to simulate mitral regurgitant orifices of differing sizes. The chamber was constructed to permit imaging of the flow convergence region from several directions. The model was filled with an aqueous glycerin solution (25% by volume) to simulate the physiological viscosity of blood (3.5 cp at 22°C). After adjustment for viscosity, the solution was prepared as a 2% (by weight) cornstarch particle suspension to provide physiological ultrasound reflection characteristics for color Doppler flow imaging.

Flow rates were measured using the rotometer; color Doppler flow mapping was performed at 11
Color Doppler Flow Mapping

Color Doppler flow mapping was performed with a Toshiba SSH 65A system (Tokyo, Japan) using both 2.5- and 3.75-MHz transducers, a 45° color flow sector, a constant color flow gain (just below the level that produces random noise in the signal), a 4-KHz pulse repetition frequency, and a sector depth setting of 10 cm. Two-dimensional color Doppler flow images and color-overlayed M-mode (Q/M-mode) images were obtained in both the axial (parallel to the flow through the orifice and perpendicular to the surface of the diaphragm containing the orifice) and the lateral (parallel to the diaphragm surface) directions (Figures 1 and 2) with the transducer positioned 5 cm from the regurgitant orifice. Images were recorded on ½-in. videotape for subsequent analysis.

Because the “first color alias” was to be used for velocity isopleth localization and because several different velocity isopleths were desired, color Doppler flow mapping was performed with different zero-shifted velocity limits to alter the position (or distance) at which the first abrupt color change (alias) occurred. All other instrumentation factors (including color flow gain, pulse repetition frequency, and frame rate) were kept constant. For the 3.75-MHz transducer imaging was performed with aliasing velocities of 54 cm/sec and zero-shifted velocities of 41, 27, and 14 cm/sec, and for the 2.5-MHz transducer imaging was performed at aliasing velocities of 75 cm/sec and zero-shifted velocities of 56, 37, and 18 cm/sec.

CW spectral Doppler was performed using the 2.5-MHz stand-alone transducer of the Toshiba system in a direction parallel to the flow through the orifice. The maximum velocity of the regurgitant jet through the orifice was used to estimate the regurgitant orifice area by the continuity principle.

Flow Rate Estimation

Since it is a reproducible and easily identifiable boundary on color flow images and since it represents the position of a known velocity, the first alias proximal to the regurgitant orifice was chosen as the position of the isovelocity hemisphere to be used for calculating the regurgitant flow rate. Because in this study the flow was imaged going away from the transducer, the first alias was determined as the wrap-around from blue of increasing intensity to red (Figure 3). The radial distance of this isovelocity hemisphere from the center of the orifice (along a vector parallel to the direction of interrogation) was easily measured. The center of the orifice in the axial direction was determined as the midpoint between the two imaged orifice edges on the chamber surface. For imaging in the lateral direction, the center of the orifice was judged to be where two different colors came together (Figure 3, arrow in lower left panel). The radius was always measured along a vector parallel to the direction of interrogation and in the center of the sector and was then used to calculate the hemispheric surface area.

Regurgitant flow rate and regurgitant orifice area were estimated using the formula described above for each flow rate and regurgitant orifice size using both the 3.75- and the 2.5-MHz transducers at each conventional and zero-shifted velocity limit. For estimation of the regurgitant orifice area, a Cc of 0.611 was used. The estimated flow rates expressed in liters per minute and the estimated orifice areas expressed in square millimeters were compared with the actual values. All primary measurements were made by two independent observers who estimated flow rate and orifice area without knowledge of the actual values.

Clinical Study

To explore the use of this method in a clinical series, data were collected from a prospective study of 20 patients (15 men and five women, mean age 36 years) who underwent left ventriculography and two-dimensional echocardiography with color Doppler flow imaging at Pavia University Hospital. The interval between angiography and ultrasound examination did not exceed 48 hours; no patient had a change in clinical status during the intervening period. The etiology of mitral regurgitation was rheumatic heart disease in five patients, ischemic heart disease in three, cardiomyopathy in seven, and mitral valve prolapse in five.

For the clinical echocardiographic studies, a Toshiba SSH 65A system with a 2.5-MHz transducer was used at a 4-KHz pulse repetition frequency and with the optimal color gain setting, defined as the maximum gain possible without producing artifactual color Doppler noise extending over the image. Imaging was obtained from an apical four-chamber view adjusted to best visualize the flow convergence region on the left ventricular side of the mitral valve. The area of flow convergence was initially identified using

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**TABLE 1. Hydraulic Variables for Each Experiment**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Orifice diameter (mm)</th>
<th>Flow rate (l/min)</th>
<th>Maximum jet velocity (cm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.9</td>
<td>1.1</td>
<td>452</td>
</tr>
<tr>
<td>2</td>
<td>3.9</td>
<td>2.2</td>
<td>340</td>
</tr>
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<td>372</td>
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<tr>
<td>4</td>
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<td>2.5</td>
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<td>5</td>
<td>6.6</td>
<td>5.0</td>
<td>378</td>
</tr>
<tr>
<td>6</td>
<td>10.0</td>
<td>11.5</td>
<td>450</td>
</tr>
<tr>
<td>7</td>
<td>12.0</td>
<td>2.5</td>
<td>60</td>
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<td>9</td>
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<td>14.0</td>
<td>330</td>
</tr>
<tr>
<td>10</td>
<td>12.0</td>
<td>16.0</td>
<td>436</td>
</tr>
<tr>
<td>11</td>
<td>12.0</td>
<td>19.0</td>
<td>455</td>
</tr>
</tbody>
</table>

Jet velocity measured with continuous-wave Doppler.
the origin of the jet visualized in the left atrium as a guide. For the clinical study, we used an aliasing velocity of 37 cm/sec for flow away from the transducer. The distance from the first alias to a point at the trailing edge of the mitral leaflets nearest the regurgitant orifice was determined along a vector parallel to the direction of interrogation and at a point in midsystole when the distance was maximal. No attempt was made to quantify the maximal flow rate by CW echocardiography. Clinical studies were assessed by one blinded observer who was not involved in the angiographic grading.

Cardiac catheterization. Left ventriculography was accomplished by injecting 40–50 ml of Urografin-76 at 15 ml/sec using a 30° right anterior oblique projection. The angiographic severity of mitral regurgitation was graded by an observer blinded to the echocardiographic results into three grades.23

Statistical Analysis
Regurgitant flow rates estimated by color Doppler flow mapping and calculated orifice areas were regressed against actual flow rates and orifice areas using simple regression analysis, with 5% chosen as the level of statistical significance. Intraobserver and interobserver variabilities were analyzed by performing one-way analysis of variance. For the data of the clinical study, Pearson correlation coefficients were calculated. Differences between angiographic grades were assessed with the use of Student’s t test for unpaired data; *p*≤0.05 was considered significant. The mean and standard deviation were also calculated for each angiographic grade.

Results
High-quality color Doppler flow images of the flow convergence region with at least one alias were obtained for all regurgitant flow rates.

Calculation of Flow Rate
The results of linear regression analysis of data obtained with the 3.75-MHz transducer in the axial direction are shown in Figure 4. In Figure 5, a similar comparison is shown for data obtained with the 3.75-MHz...
MHz transducer in the lateral direction. Similar correlations were found using the 2.5-MHz transducer in the axial and lateral directions ($r=0.90-0.98$). For flow convergence areas imaged in the axial direction, estimated flow rates tended to be less than the actual flow rates. This underestimation was less when lower aliasing velocities were used (Figure 4, lower right panel). The slopes were closer to unity for images obtained in the lateral direction than for images obtained in the axial direction. Considering all the aliasing velocities used in this study, while the actual flow rate ranged from 1.1 to 19.0 l/min, the estimated flow rate ranged from 1.1 to 18.0 l/min, with a mean of 6.23 l/min, in the axial direction and from 1.2 to 24.8 l/min, with a mean of 9.38 l/min, in the lateral direction. In the axial direction, the mean percentage error between the actual flow rate and the flow rate estimated by color Doppler flow mapping was $-22\%$, with a maximal underestimation of $140\%$. In the lateral direction, the mean percentage error was $-25.2\%$, with a maximum underestimation of $77.5\%$.

**Calculation of Orifice Area**

The maximum jet velocities through the orifice measured by CW Doppler for the individual orifices and flow rates varied from 60 to 455 cm/sec (Table 1). Linear regression analyses of the actual orifice areas and the orifice areas estimated using calculated flow rates and CW Doppler velocities are shown in Figures 6 and 7 for flow convergences imaged in the axial and lateral directions, respectively, using the 3.75-MHz transducer. Results with the 2.5-MHz transducer were similar, with good correlations between actual and calculated data ($r=0.75-0.96$). For measurements obtained in the axial direction, the estimated orifice areas ranged from 3.9 to 129 mm$^2$, with a mean of 46 mm$^2$, the correlation coefficients ranged from 0.75 to 0.96, and the slopes ranged from 0.47 to 0.95 with the two transducer frequencies at the various aliasing velocities used. For imaging in the lateral direction, the estimates of orifice areas ranged from 4.5 to 180 mm$^2$, with a mean of 77.0 mm$^2$, the correlation coefficients ranged from 0.92 to 0.95, and the slopes ranged from 0.81 to 1.25 for the same transducers and aliasing velocities.

The interobserver and intraobserver variabilities for measurements of the radial distance were 2% and 10%, respectively. For axial measurements with aliasing velocities of $\geq 41$ cm/sec, the interobserver variability was $\leq 5\%$ and the intraobserver variability was 2%. Measurements for aliasing velocities of $<41$ cm/sec showed an interobserver variability of 2% and an intraobserver variability of $<2\%$. The interobserver and intraobserver variabilities for measurements of the radial distance obtained in a lateral direction with aliasing velocities of $\geq 41$ cm/sec were...
both 10%. The latter were the only measurements found to differ significantly between observers. With aliasing velocities of <41 cm/sec, the interobserver and intraobserver variabilities were both 5%. All CW Doppler velocity measurements showed interobserver and intraobserver variabilities of <5%.

Clinical Study

Color flow Doppler imaging versus angiography. Flow convergence zones with an identifiable alias were imaged and measured in 18 of the 20 patients; two patients had acceleration in blue visualized in the left ventricle but no alias was detected. These two patients had only mild mitral regurgitation on angiography. A clear relation existed between measurements of the radial distance from the mitral valve leaflets to the 37 cm/sec Doppler aliasing cutoff and the angiographic grade of mitral incompetence (Figure 8). Individual values of the radius for the seven patients with mild mitral regurgitation were ≤4 (mean±SD=1.7±1.46) mm. The five patients with moderate mitral regurgitation had radii of 4–8.7 (mean±SD=5.9±1.4) mm; the eight patients with severe mitral regurgitation had radii of 8.6–16.4 (mean±SD=11.4±4.6) mm. Although the group means were significantly separable, between the mild and moderate (p≤0.001) and between the moderate and severe (p≤0.005) groups there was overlap (Figure 8).

Discussion

The results of this study suggest that color Doppler flow mapping of the flow convergence region proximal to a regurgitant orifice provides a basis for the estimation of regurgitant flow rate and regurgitant orifice area. This serves as an alternative to studying the spatial distribution of downstream velocities within the distal receiving chamber. The proximal flow convergence region also has the theoretical advantage of being a region of laminar flow.

The validity of using the method described to estimate regurgitant flow rate is subject to several assumptions. First, we must assume that flow converges toward the orifice in a uniform manner with symmetric zones in three-dimensional space where it reaches a given velocity. Since the velocity of flow increases as it approaches the orifice due to convective acceleration, this should produce multiple isovelocity hemispheres that have proportionally higher velocities as their surface areas decrease nearer the orifice. However, this is an oversimplification of the true situation. It is likely that viscous forces are important, particularly in the region along the left ventricular side of the mitral valve leaflets, which are perpendicular to the regurgitant orifice. Viscous drag may produce a boundary layer of low-velocity flow in this region and reduce the effective surface area of
the assumed isovelocity hemisphere. Velocities could also be underestimated (and aliasing radii reduced) because flow progresses at an angle to the direction of interrogation on axial images. In our model, however, we did not observe a surface effect on the lateral images, which were as accurate as or more accurate than the axial images for predicting flow rate at high aliasing velocities (small radii). In addition, the flow profile in the region close to the regurgitant orifice is likely to undergo a gradual transition to the more parallel flow stream traversing the orifice, with velocity vectors changing direction like a stream going over a waterfall. This may account for the underestimation of flow rate when the first alias was very close to the orifice. A short distance from the orifice to the first alias also accentuates any errors in the measurement of radial distance, and the display of flow velocities close to the orifice can be obscured by ultrasound reflections from the structural images around the orifice itself. The results of our study suggest that the assumption of an isovelocity hemisphere is valid in the flow convergence zone at greater distances from the orifice, where accurate estimates of flow rate were obtained. Large errors (as much as 140% underestimation) occasionally occurred and could be due to measurement error or unstable flow even in this highly controlled model.

Errors in accurately measuring the radial distance from the first alias to the orifice can be reduced by altering instrumentation factors to allow the first alias to occur as far from the orifice as possible. This has the advantage of allowing measurements to be made from a flow convergence region that can more properly be assumed to conform to the isovelocity hemisphere described above. The use of a higher-frequency transducer and zero shifting have theoretical advantages because both maximize spatial resolution compared with the distances being measured and both reduce the apparent aliasing velocity.

It is not strictly necessary to use the first alias to calculate flow rate since any isovelocity hemisphere should theoretically provide the same result. However, the first alias is the most apparent and most reproducible region of the flow stream and is therefore most suitable for velocity estimation and measurement of radial distance. Digital computer analysis may allow other regions within the flow convergence zone to be used for estimation of flow rate since any hue within an unaliased flow field can be accurately identified and assigned a velocity relative to the color calibration bar.\footnote{14}

The validity of using the continuity principle to calculate the regurgitant orifice area from color Doppler–estimated flow rate and CW Doppler–measured jet velocity at the orifice may be particularly...
important. Estimation of regurgitant orifice area should not be affected by changes in flow rate since an alteration in flow rate is compensated for by a change in maximum jet velocity if the valve is heavily scarred and noncompliant.\(^9\) Regurgitant orifice area could serve as an index of the severity of regurgitation when normalized for driving pressure.

The results of our study demonstrate that regurgitant flow rate can be estimated from the proximal flow convergence region under constant flow conditions by using discrete symmetric circular orifices. Several steps are required to extrapolate this method into the setting of clinical valve disease, specifically valvular insufficiency. Although color Doppler flow mapping can display spatial velocity information, the requirement for multiple samples along each line to achieve an accurate autocorrelation solution to Doppler shifts results in a temporal sampling limitation. With pulsatile flow, it may be necessary to combine the spatial velocity information of color Doppler flow mapping with the high temporal resolution of the color velocity-encoded M-mode or spectral Doppler to calculate the mean velocity or radial distance to aliasing over the cardiac cycle. Both color M-mode and two-dimensional color Doppler may be limited to some extent in the presence of high heart rates or irregular rhythms. An in vitro series in a pulsatile flow model of mitral regurgitation has been reported, and the results of that preliminary study substantiate this concept.\(^{24}\)

In the clinical setting it may be unusual to encounter a discrete circular regurgitant orifice, and the
presence of multiple or irregular orifices may make application of this methodology difficult. We have preliminary evidence that the observations required for this method still behave consistently with multiple and irregular orifices, especially if the instrument setup is tailored to allow the measurements to be obtained at greater distances (≥2–3 orifice diameters) from the orifice.25,26

The results of our limited clinical study support the theory of velocity distribution within the flow convergence region presented in our in vitro study. The results indicate our ability to discriminate the angiographic severity of mitral insufficiency by measuring the radial distance of the flow convergence region in midsystole. As expected in an area of organized flow converging toward an orifice, a greater flow rate and a higher angiographic grade correspond to a larger radius of the isovelocity hemisphere. Our experience in 100 consecutive adults indicates that the flow convergence region and a measurable alias can be imaged in 82% of subjects when proper instrument setup is employed.

While interrogation of a flow convergence region may have to be performed at a significant Doppler angle in the clinical setting, the need for angle correction has not yet been encountered in our clinical or animal studies.25,27,28

In summary, we have demonstrated that quantitative estimation of valve regurgitation is possible using color Doppler flow mapping of the zone of flow convergence proximal to a regurgitant orifice. Using the flow convergence region may be theoretically more attractive than using the display characteristics of the turbulent downstream jet. Use of the proximal flow convergence region for quantitative analysis should not necessarily be limited to valve regurgitation but should also be applicable to any restrictive orifice lesion.

References


KEY WORDS • color flow mapping Doppler • continuity principle • valvular regurgitation
F Recusani, G S Bargiggia, A P Yoganathan, A Raisaro, L M Valdes-Cruz, H W Sung, C Bertucci, M Gallati, V A Moises and I A Simpson

*Circulation*. 1991;83:594-604
doi: 10.1161/01.CIR.83.2.594

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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