Detection, Localization, and Quantification of Bioprosthetic Mitral Valve Regurgitation

An In Vitro Two-Dimensional Color-Doppler Flow-Mapping Study

Byron F. Vandenberg, MD, Kevin C. Dellsperger, MD, PhD,
Krishnan B. Chandran, DSc, and Richard E. Kerber, MD

The usefulness of two-dimensional color-Doppler flow-imaging (2D Doppler) in the detection, localization, and quantitation of bioprosthetic mitral valve regurgitation is uncertain. Mitral bioprostheses, before and after the creation of transvalvular (n = 33), paravalvular (n = 17), or combined (n = 23) defects, were mounted in a pulsed duplication system (flow rates, 2.5–6.5 l/min; pulse rate, 70 beats/min). An Aloka 880 2D Doppler system (Japan) was used to image the regurgitant jets in the simulated left atrial chamber, analogous to images obtained with transesophageal echocardiography. Jet area was corrected to an estimate of stroke volume: 2D Doppler measurements were divided by [(valve effective orifice area) × (continuous-wave Doppler–determined mean diastolic filling velocity)]/pulse rate. Regurgitant fraction and regurgitant volume were measured by an electromagnetic flow probe. 2D Doppler correctly identified the presence and location of paravalvular regurgitation. In transvalvular and combined transvalvular-paravalvular defects, there were six incorrect interpretations, all having transvalvular regurgitant volumes less than 4 ml/beat. In the presence of transvalvular regurgitation, jet area, length, and width correlated linearly with regurgitant volume (r = 0.82, 0.80, and 0.68, respectively; p < 0.0001) and regurgitant fraction (r = 0.62, 0.61, and 0.45, respectively; p < 0.001). Correlations with regurgitant fraction were improved when 2D Doppler measurements were corrected for stroke volume (r = 0.78, 0.79, and 0.67, respectively; p < 0.0001). Mitral bioprostheses with transvalvular defects were also studied at varying flow rates (3.2–7.5 l/min) and pulse rates (70, 90, and 110 beats/min). The correlation between jet area and regurgitant volume was improved with a second-order polynomial regression (r = 0.93, p < 0.0001). Our conclusions are that 1) in this in vitro model analogous to transesophageal imaging, 2D Doppler accurately detects and localizes bioprosthetic mitral valve regurgitation; 2) in transvalvular bioprosthetic mitral valve regurgitation, 2D Doppler measurement of jet area has a curvilinear relation with regurgitant volume, and correlation with regurgitant fraction is improved with correction for stroke volume; and 3) in paravalvular bioprosthetic mitral valve regurgitation, correlations between 2D Doppler measurements and regurgitant volumes are weaker, possibly because of jet eccentricity. (Circulation 1988;78:529–538)

Pulsed-wave (PW) and continuous-wave (CW) Doppler ultrasound techniques are useful in the detection of native and prosthetic mitral valve regurgitation.1–15 Two-dimensional color-Doppler flow-imaging (2D Doppler) provides a spatial display of mitral regurgitation, but there are few data on the quantitation of the regurgitation.16–18 In addition, preliminary data suggest that 2D Doppler may be useful in distinguishing transvalvular from paravalvular prosthetic mitral valve regurgitation.14,19–21

Our purpose was to evaluate 2D Doppler in the detection, localization, and quantitation of bioprosthetic mitral valve regurgitation over a wide range of pulse rates and flow rates in an in vitro model that optimizes visualization of regurgitant jets, simulating imaging from a transesophageal approach to the left atrium.

From the Cardiovascular Center, Department of Internal Medicine, and Department of Biomedical Engineering, College of Engineering, University of Iowa, Iowa City, Iowa.
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Address for reprints: Byron F. Vandenberg, MD, Department of Internal Medicine, University of Iowa, Iowa City, IA 52242.
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Materials and Methods

Experiment 1—Detection, Localization, and Quantitation of Regurgitation

Bioprosthetic valves. Hancock Model 342 (Johnson and Johnson, Anaheim, California) and Carpentier-Edwards Model 6625 (American Edwards, Irvine, California) bioprosthetic mitral valves of either 27 or 29 mm were studied in a pulse duplication system and imaged by 2D Doppler before and after creation of a regurgitant defect. The individual valves were donated by the manufacturers and were of nonclinical quality (i.e., considered by the manufacturer to be not acceptable for human implantation). The bioprosthetic valves were sutured into a Lucite ring, and the cloth-covered surfaces were sealed with silicone rubber cement to prevent leakage. As a model of paravalvular regurgitation, defects of 2, 4, and 6 mm were drilled into the Lucite ring. Transvalvular regurgitation was created by punching the valve leaflet with 20- and 15-gauge hypodermic needles and then cutting 1 x 2-mm and 2 x 3-mm defects. Combined defects were produced by either drilling increasingly larger holes in the valve ring after producing a 20-gauge transvalvular defect or by cutting progressively larger leaflet defects after initially drilling a 2-mm hole in the Lucite valve ring.

Pulse duplication system. The pulse duplication system modeled the left heart as previously described by Wieting,22 with the exception of a modified left atrial chamber (Figure 1). The inflow to the mitral valve chamber was oriented 30° to the axis of flow through the valve to minimize turbulence (Figure 2). The bioprosthetic valves were mounted in the mitral valve chamber with commissure posts oriented at 2, 6, and 10 o’clock when viewed from the simulated left atrial chamber. All defects were located at a 12 o’clock position when the valve was mounted in the pulse duplication system to reduce variability in comparing imaging data.

The pulse duplication system was filled with normal saline mixed with cornstarch (1 tbsp/l) to provide scattering of ultrasound waves. The system was adjusted until the left atrial, left ventricular, and aortic pressures resembled physiological wave forms. Mean left atrial pressure was maintained at less than 20 mm Hg. Left ventricular end-diastolic pressure was maintained at 5–10 mm Hg. Simultaneous left atrial and left ventricular pressures were not measured. The pulse duplication system was
adjusted to maintain aortic pressure at 100 ± 5 mm Hg. The pressures were measured with transducer-tipped catheters (Millar Instruments, Houston, Texas). Mitral valve flow signals were measured with an In Vivo Metric System (Healdsburg, California) electromagnetic flow probe (Model K) connected to a Carolina (King, North Carolina) square-wave flowmeter (Model 501D) incorporated upstream to the simulated mitral valve chamber. The flow and pressure signals were recorded on FM tape for off-line playback into a PDP 11/34 minicomputer (Digital Equipment, Maynard, Massachusetts). The flow and pressure signals were digitized and ensemble-averaged over 25 cardiac cycles and used to compute the time-averaged flow rate (i.e., cardiac output), the regurgitant fraction [(backflow/forward flow) × 100%] and the regurgitant volume measured in milliliters per beat [(regurgitant fraction × flow rate)/pulse rate].23,24

All experiments were performed at time-averaged flow rates of 2.5, 4.5, and 6.5 l/min and a pulse rate of 70 beats/min. The systolic duration was 350 msec, which corresponded to the QT interval of a heart rate of 70 beats/min.

Thus, for a given pulse rate, the antegrade flow rate was altered by changing systemic impedance or increasing the fluid volume in the system. Mechanical resistance (Figure 1) was adjusted with a clamp, monitoring flow rate with a rotameter-type flowmeter. Retrograde flow (i.e., regurgitant volume) was adjusted by creating progressively increasing defects in the valve leaflets or in the mounting ring.

Two-dimensional color-Doppler flow-mapping. 2D Doppler was performed with an Irex-Aloka 880 system that produces color images at 10 frames/sec. Regurgitant jets were imaged with a 2.5-MHz transducer secured to the left atrial chamber 13 cm from the plane of the mounting ring. A 15-cm sample depth was used, and the images were recorded on 1/2-in. videotape. The transducer was oriented parallel to flow in a vertical position to optimally visualize the defects placed in the same plane. While imaging from the left ventricular side of the mitral valve would approximate the transthoracic clinical situation, the distance of the mitral valve from the transducer at the left ventricular position exceeded the range of the 2D Doppler system. Thus, our in vitro studies were limited to evaluating regurgitation from a transducer positioned behind the left atrium, analogous to transesophageal echocardiography. Systolic and diastolic timing were provided on the 2D Doppler images with a simultaneous signal from an electronic timer of the pulsed duplication system. In an effort to reduce background color artifact, color gain was adjusted so that color background just appeared.18 The area, length, and maximal width of the regurgitant jets with maximal area were measured with an off-line computer (Irex-Cardio 80, Ramsey, New Jersey). CW Doppler was performed through the mitral bioprosthetic valve and recorded at a paper speed of 50 mm/sec. Mean diastolic filling velocity was measured as the velocity-time integral. The 2D and CW Doppler measurements were averaged from three beats and performed by an observer unaware of defect size and flow rate.

Detection criteria for regurgitant jets. The following 2D Doppler criteria were used to distinguish between control, transvalvular leak, paravalvular leak, and combined transvalvular and paravalvular leaks: 1) a control valve was defined as a valve with a regurgitant jet equal to or less than 1 cm in length, 2) a transvalvular leak was defined as a regurgitant jet more than 1 cm in length and appearing to arise within the valve commissure posts, and 3) a paravalvular leak was defined as a regurgitant jet more than 1 cm in length and appearing to arise outside of the valve commissure posts (Figure 3). The valves used in our in vitro model were not for clinical use and may have contained defects resulting in incompetent valve closure. The demonstration of regurgitation in normal valves was therefore not unexpected. While the selection of 1 cm as the criterion for normal versus abnormal jet length was arbitrary, jet length has been shown to correlate with mitral regurgitation severity.16–18 In addition, the clinical interpretation of "physiological" mitral regurgitation with PW Doppler has been defined as regurgitation within 1 cm of the valve plane.25

Experiment 2—Effect of Varying Pulse Rate

Bioprosthetic valves. Two Hancock Model 342 27-mm mitral bioprosthetic valves were studied in the pulsed duplication system before and after the creation of transvalvular defects.

Pulsed duplication system. The system used in experiment 2 was identical to that in experiment 1. However, studies were performed at pulse rates of 70, 90, and 110 beats/min with systolic durations of 350, 320, and 290 msec, respectively. At each pulse rate, flow rates of 3.2, 5.3, and 7.5 were studied. The mean arterial pressure was 103 ± 6 mm Hg during these studies.

Two-dimensional color-Doppler flow-mapping. The transducer position, gain setting, and range depth were the same as in experiment 1. The jet area and length of the regurgitant jets were measured with the off-line computer by an observer unaware of the pulse and flow rates. In addition, he was unaware of whether the valve was control or defective.

Data Analysis

Results are presented as the mean ± SD. Correlations were performed with a linear (simple) or second-order polynomial regression. Analysis of variance (ANOVA) was used to compare regurgitant fractions and regurgitant volumes at different flow rates. If a significant difference was present, Tukey's multiple range test was used to identify the specific differences. The difference in means was significant if p<0.05.
TABLE 1. Electromagnetic Flowmeter-Pulsed Duplication System Data

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Flow rates (l/min)</th>
<th>Regurgitant fraction (%)</th>
<th>Regurgitant volume (ml/beat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment 1</td>
<td>2.5</td>
<td>21 ± 12</td>
<td>6 ± 3</td>
</tr>
<tr>
<td></td>
<td>4.5</td>
<td>11 ± 9*</td>
<td>6 ± 4</td>
</tr>
<tr>
<td></td>
<td>6.5</td>
<td>7 ± 6*</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>Experiment 2</td>
<td>3.2</td>
<td>11 ± 10</td>
<td>4 ± 4</td>
</tr>
<tr>
<td></td>
<td>5.3</td>
<td>6 ± 6†</td>
<td>4 ± 4</td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>4 ± 3‡</td>
<td>4 ± 3</td>
</tr>
</tbody>
</table>

*p<0.05 vs. 2.5 l/min; †p<0.05 vs. 3.2 l/min; ‡p<0.05 vs. 5.3 l/min.

Results

Experiment 1

Detection and localization of regurgitation. At control, a mean regurgitant volume of 3 ± 2 ml/beat (range, 0.2–7 ml/beat) and regurgitant fraction of 6 ± 6% (range, 0.2–21%) were present.

When a valve with a defect was placed in the pulsed duplication system and flow rate was increased, regurgitant volume per beat did not change, but regurgitant fraction decreased (because stroke volume increased) (Table 1).

Paravalvular regurgitant fraction ranged from 6% to 48% (mean, 22 ± 14%) and regurgitant volume ranged from 4 to 19 ml/beat (mean, 11 ± 6 ml/beat). 2D Doppler correctly identified the presence and location of paravalvular regurgitation in the 11 valves studied and the absence of regurgitation in the six control valves.

Transvalvular regurgitant fraction ranged from 2% to 30% (mean, 11 ± 8%) and regurgitant volume ranged from 1 to 10 ml/beat (mean, 5 ± 2 ml/beat). 2D Doppler detected and localized transvalvular regurgitation in 21 (88%) of 24 valves. Three valves were interpreted as normal (control) but actually had small defects produced by the 20-gauge hypodermic needle. Their regurgitant fractions ranged from 3% to 13%, and regurgitant volumes were 3–4 ml/beat. 2D Doppler was 100% specific for the nine control valves.

In combined transvalvular and paravalvular regurgitation, regurgitant fraction ranged from 6% to 38% (mean, 16 ± 11%) and regurgitant volume ranged from 5 to 9 ml/beat (mean, 7 ± 1 ml/beat). 2D Doppler correctly detected regurgitation in all valves but predicted a combined defect in 14 (82%) of 17

![Figure 3](http://circ.ahajournals.org/attach/4297/2000002/Figure3.png)

**Figure 3.** Examples of two-dimensional Doppler imaging of the left atrial chamber at control (Panel A) and after the creation of transvalvular (Panel B), paravalvular (Panel C), and combined transvalvular (left jet) plus paravalvular regurgitation (right jet) (Panel D).
**Figure 4.** Plots of regurgitant volume versus two-dimensional Doppler measurement of jet area in the presence of paravalvular (left panel) and transvalvular (right panel) regurgitation.

Valves. Three valve studies were interpreted as paravalvular regurgitation only but had superimposed transvalvular regurgitation of only 0–2 ml/beat (total regurgitant volumes, 5–7 ml/beat). The six control valves were correctly identified.

Quantitation of regurgitation. In the presence of transvalvular regurgitation, jet area (Figure 4), length, and width (Table 2) correlated significantly with regurgitant volume ($r=0.82$, 0.80, and 0.68, respectively; $p<0.0001$). When compared with regurgitant fraction (Table 2), the correlation of the jet area, length, and width decreased ($r=0.62$, 0.61, and 0.45, respectively; $p<0.001$). Because the regurgitant volume correlated well with jet area and the regurgitant fraction is equal to [(regurgitant volume)/(stroke volume)], regurgitant fraction was compared with [(jet area)/(Doppler-derived estimate of stroke volume)]. The Doppler-derived stroke volume = [(CW Doppler–determined mean diastolic velocity) × (valve effective orifice area)]/(pulse rate). The effective orifice areas were obtained from the manufacturer: Carpentier-Edwards Model 6625 27-mm mitral bioprosthetic valve = 2.0 cm$^2$ (Edwards Laboratories, personal communication); Hancock Model 342 27-mm mitral bioprosthetic valve = 1.50 cm$^2$ (at cardiac output of 3.0 l/min), 1.70 cm$^2$ (at cardiac output of 4.5 l/min), 1.84 cm$^2$ (at cardiac output of 6.0 l/min), or 1.92 cm$^2$ (at cardiac output of 7.5 l/min); and Hancock Model 342 29-mm mitral bioprosthetic valve = 1.50 cm$^2$ (at cardiac output of 3.0 l/min), 1.81 cm$^2$ (at cardiac output of 4.5 l/min), 2.02 cm$^2$ (at cardiac output of 6.0 l/min), or 2.14 cm$^2$ (at cardiac output of 7.5 l/min) (Hancock Laboratories, personal communication). The correction of regurgitant jet area (Figure 5), length, and width (Table 2) for stroke volume resulted in improved correlations with regurgitant fraction ($r=0.78$, 0.79, and 0.67, respectively; $p<0.0001$).

In the presence of paravalvular regurgitation, jet area (Figure 4), length, and width (Table 2) demonstrated weaker correlations with regurgitant volume ($r=0.73$, 0.71, and 0.65, respectively; $p<0.001$) and regurgitant fraction ($r=0.60$, 0.59, and 0.55, respectively; $p<0.05$). When jet area (Figure 5), length, and width (Table 2) were corrected for stroke volume, there was no change in the correlation with regurgitant fraction ($r=0.62$, 0.60, and 0.59 respectively; $p<0.01$).

**Experiment 2**

At control, the mean regurgitant volume per beat was $1.6±0.9$ ml/beat (range, 0.3–3.5 ml/beat), and the mean regurgitant fraction was $3.1±2.1%$. The mean transvalvular regurgitant volume per beat was $4.4±2.9$ ml/beat (range, 0.8–15.8 ml/beat), and the mean regurgitant fraction was $8.5±8.1%$ (range, 1.2–40.5%).

Jet area and length again correlated with transvalvular regurgitant volumes. As pulse rate increased from 70 to 90 and 110 beats/min, the linear correlations improved between regurgitant volumes and both jet area ($r=0.76$, 0.78, and 0.86, respectively; $p<0.0001$) and length ($r=0.61$, 0.61, and 0.73, respectively; $p<0.001$) (Table 2). As pulse rate increased from 70 to 90 and 110 beats/min, there was no change in the weak linear correlation between regurgitant fraction and jet area, but the correlation with jet length improved slightly (Table 2). When jet area and length were “corrected” for stroke volume, the correlation with regurgitant fraction improved (Table 2).

The use of a second-order polynomial regression model improved the correlations between regurgitant volume and jet area ($r=0.93$, 0.95, and 0.94 for pulse rates 70, 90, and 110 beats/min, respectively; $p<0.0001$) and jet length ($r=0.72$, 0.73, and 0.83 for pulse rates 70, 90, and 110 beats/min, respectively; $p<0.0001$). The polynomial regression model also improved the correlations between regurgitant fraction and jet area ($r=0.84$, 0.78, and 0.78 for pulse rates 70, 90, and 110 beats/min, respectively; $p<0.0001$) and jet length ($r=0.60$, 0.60, and 0.70 for pulse rates 70, 90, and 110 beats/min, respectively; $p<0.01$). "Correction" of jet area and length for stroke volume improved the correlations with regurgitant fraction. When all pulse rates were evaluated with the second-order polynomial regression model, there was excellent correlation between regurgitant volume and both jet area ($r=0.93$, $p<0.0001$; Figure 6) and jet length ($r=0.74$, $p<0.0001$). Correlation of
TABLE 2. Linear Correlations of Two-Dimensional Doppler Measurements With Regurgitant Volume and Regurgitant Fraction

<table>
<thead>
<tr>
<th>Experiment 1</th>
<th>r</th>
<th>Regression</th>
<th>SEE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transvalvular regurgitation (n = 33)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JA vs. RF</td>
<td>0.62</td>
<td>y = 0.5x + 3.8</td>
<td>6.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>JL vs. ml/beat</td>
<td>0.80</td>
<td>y = 0.6x + 1.5</td>
<td>1.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>JL vs. RF</td>
<td>0.61</td>
<td>y = 1.2x + 2.9</td>
<td>6.1</td>
<td>0.0002</td>
</tr>
<tr>
<td>JL (corrected) vs. RF</td>
<td>0.79</td>
<td>y = 2.4x + 2.1</td>
<td>4.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>JW vs. ml/beat</td>
<td>0.68</td>
<td>y = 1.6x + 1.5</td>
<td>2.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>JW vs. RF</td>
<td>0.45</td>
<td>y = 3.0x + 3.5</td>
<td>6.9</td>
<td>0.0008</td>
</tr>
<tr>
<td>JW (corrected) vs. RF</td>
<td>0.67</td>
<td>y = 6.8x + 1.9</td>
<td>5.7</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

| Paravalvular regurgitation (n = 17) |      |                  |      |        |
| JA vs. RF    | 0.60 | y = 0.8x + 9.0   | 10.7 | 0.01   |
| JL vs. ml/beat | 0.71 | y = 0.9x + 3.4   | 3.9  | 0.001  |
| JL vs. RF    | 0.59 | y = 1.8x + 7.7   | 10.8 | 0.01   |
| JL (corrected) vs. RF | 0.60 | y = 3.5x + 8.2   | 10.7 | 0.01   |
| JW vs. ml/beat | 0.65 | y = 3.8x + 1.1   | 4.2  | 0.004  |
| JW vs. RF    | 0.55 | y = 7.8x + 2.8   | 11.2 | 0.02   |
| JW (corrected) vs. RF | 0.59 | y = 15.5x + 3.1  | 10.8 | 0.01   |

| Experiment 2 |      |                  |      |        |
| Pulse rate, 70 beats/min (n = 29) |      |                  |      |        |
| JA vs. ml/beat | 0.76 | y = 0.3x + 0.5   | 2.7  | 0.0001 |
| JA vs. RF    | 0.65 | y = 0.5x + 0.2   | 6.5  | 0.0001 |
| JA (corrected) vs. RF | 0.76 | y = 1.2x - 0.4   | 5.5  | 0.0001 |
| JL vs. ml/beat | 0.61 | y = 0.6x + 0.9   | 3.3  | 0.0005 |
| JL vs. RF    | 0.50 | y = 1.0x + 1.1   | 7.4  | 0.005  |
| JL (corrected) vs. RF | 0.60 | y = 2.1x + 0.7   | 6.8  | 0.0005 |

| Pulse rate, 90 beats/min (n = 29) |      |                  |      |        |
| JA vs. ml/beat | 0.78 | y = 0.3x + 0.7   | 2.0  | 0.0001 |
| JA vs. RF    | 0.64 | y = 0.5x + 1.3   | 6.2  | 0.0002 |
| JA (corrected) vs. RF | 0.76 | y = 1.1x + 0.6   | 5.2  | 0.0001 |
| JL vs. ml/beat | 0.61 | y = 0.5x + 1.1   | 2.6  | 0.0005 |
| JL vs. RF    | 0.50 | y = 0.9x + 1.9   | 6.9  | 0.0006 |
| JL (corrected) vs. RF | 0.61 | y = 1.8x + 1.5   | 6.3  | 0.0005 |

| Pulse rate, 110 beats/min (n = 30) |      |                  |      |        |
| JA vs. ml/beat | 0.86 | y = 0.2x + 0.8   | 1.3  | 0.0001 |
| JA vs. RF    | 0.70 | y = 0.5x + 2.1   | 5.0  | 0.0001 |
| JA (corrected) vs. RF | 0.82 | y = 1.0x + 1.5   | 4.0  | 0.0001 |
| JL vs. ml/beat | 0.73 | y = 0.5x + 0.9   | 1.8  | 0.0001 |
| JL vs. RF    | 0.60 | y = 1.0x + 2.2   | 5.6  | 0.0004 |
| JL (corrected) vs. RF | 0.71 | y = 1.8x + 1.9   | 5.0  | 0.0001 |

| All pulse rates (n = 88) |      |                  |      |        |
| JA vs. ml/beat | 0.79 | y = 0.3x + 0.6   | 2.1  | 0.0001 |
| JA vs. RF    | 0.65 | y = 0.5x + 1.3   | 5.8  | 0.0001 |
| JA (corrected) vs. RF | 0.77 | y = 1.1x + 0.6   | 4.9  | 0.0001 |
| JL vs. ml/beat | 0.63 | y = 0.5x + 0.9   | 2.6  | 0.0001 |
| JL vs. RF    | 0.53 | y = 1.0x + 1.8   | 6.5  | 0.0001 |
| JL (corrected) vs. RF | 0.64 | y = 1.9x + 1.4   | 6.0  | 0.0001 |

JA, jet area; JL, jet length; JW, jet width; RF, regurgitant fraction.

**Detection and Localization of Regurgitation**

Although the initial clinical studies of Okumachi et al. demonstrated the usefulness of 2D Doppler in differentiating transvalvular from paravalvular origin of regurgitant jets, subsequent studies suggested potential limitations of the technique. Goyal et al. correctly differentiated transvalvular from paravalvular regurgitation in six of 12 patients with prosthetic mitral regurgitation, but they were unable to make the distinction in patients with prosthetic aortic regurgitation. In 24 patients with bioprosthetic mitral regurgitation, Nakamura et al. correctly diagnosed a transvalvular location in 18 of 20 (90%) but demonstrated paravalvular regurgitation in only one of four patients.
In our in vitro model, 2D Doppler correctly identified the presence of paravalvular regurgitation. Six incorrect interpretations occurred in the presence of transvalvular and combined paravalvular and transvalvular defects. The transvalvular regurgitant volumes of these studies were all less than 4 ml/beat. The accuracy of detection and localization of regurgitation may have improved by considering any leak detected by 2D Doppler as pathological regurgitation. However, the arbitrary requirement that jet length exceed 1 cm permitted the exclusion of the control valves that had regurgitant volumes of 3 ± 2 ml/beat. The demonstration of minimal regurgitation in normally functioning mitral bioprostheses is consistent with the findings of clinical PW Doppler studies.13,15 While normal valves studied in our model had regurgitant volumes up to 7 ml/beat and regurgitant fractions up to 21%, the valves were nonclinical, so that there may have been imperfections in valve leaflet closure, resulting in slightly excessive regurgitation.

Quantitation of Regurgitation

Previous authors have measured the jet length, width,16–18 area,17,18 and jet area: left atrial area ratio18 in studies of native mitral valve regurgitation. Jet length, width, and area have demonstrated poor-to-fair correlation with qualitative angiographic assessment of mitral regurgitation severity.16–18 The single measurement of jet width or length ignores other jet dimensions and may explain the relatively poor correlations with regurgitation.18 In addition, jet area, length, and width are increased with increasing afterload.27 Thus, changes in systolic blood pressure between catheterization and echocardiography may affect regurgitant jet size and, therefore, interfere with the assessment of regurgitation. In our study, mean aortic pressure was maintained at 100 ± 5 (experiment 1) and 103 ± 6 (experiment 2) mm Hg for all valves studied at all hemodynamic settings.

Helmcke et al18 have demonstrated improved correlation between the angiographic (both qualitative and quantitative) assessment of mitral regurgitation and jet area (maximum or an average from three planes) normalized for left atrial area.18 The same authors applied this method to patients with prosthetic mitral valve regurgitation, and preliminary data demonstrated a good correlation with qualitative angiography.19

The limitations of previous studies have included the reliance on qualitative angiography as a gold standard, a method often at variance with the regurgitant volume index,28 and the inability of

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**FIGURE 5.** Plots of regurgitant fraction versus "corrected" jet area in the presence of paravalvular (left panel) and transvalvular (right panel) regurgitation.

**FIGURE 6.** Plots of regurgitant volume versus jet area at pulse rates of 70, 90, and 110 beats/min (left panel). Regurgitant fraction versus "corrected" jet area at pulse rates of 70, 90, and 110 beats/min (right panel).
clinical studies to control heart rate and cardiac output, variables that may alter regurgitant volumes.\textsuperscript{29} We attempted to avoid these difficulties by using a pulse duplication system with an electromagnetic flowmeter to quantitate regurgitation during three flow rates and pulse rates.

In transvalvular mitral regurgitation, the correlation of jet area, length, and width was better with regurgitant volume than with regurgitant fraction. In the presence of a regurgitant defect, regurgitant volume did not change during increases in stroke volume; however, regurgitant fraction \([\text{regurgitant volume}/(\text{stroke volume})]\) decreased because of increases in stroke volume. Thus, there was more spread of data points when comparing jet area with regurgitant fraction. The regurgitant fraction varied inversely with flow, consistent with the findings of Dellasperger et al.\textsuperscript{29} To correct the 2D Doppler measurements for changes in flow rates, the jet area, length, and width were divided by a CW Doppler estimate of the stroke volume, resulting in improved correlations with regurgitant fraction. Because regurgitant fraction is equal to regurgitant volume (which correlated with jet area) divided by total stroke volume, it was expected that a comparison of jet area divided by an estimate of total stroke volume with regurgitant fraction would improve the correlation. While the calculation of forward stroke volume depends on the manufacturer-provided valve area (which was affected by flow rates), an estimate of mitral bioprosthetic valve area may be obtained in vivo with the Doppler half-time method.\textsuperscript{12,13,15}

The linear correlations of jet area and length with regurgitant volume were not affected by changes in pulse rate except that correlations improved somewhat at a pulse rate of 110 beats/min. The improved correlation between transvalvular regurgitant volume and jet area with a second-order polynomial regression (experiment 2) suggested that the relation may be nonlinear.\textsuperscript{30} Second-order polynomial regression did not improve correlations in experiment 1, possibly because most of the studies were performed at regurgitant volumes of less than 10 ml/beat. The curvilinear relation became apparent at regurgitant volumes more than 10 ml/beat (Figure 6).

Between jet areas of 25–30 cm\(^2\), further increases in regurgitant volumes resulted in only slight increases in jet area. We observed that despite only slight increases in jet area during progressively worsening mitral regurgitation, regurgitant jets qualitatively contained variations in the relative proportions of red, green, and blue pixels, suggestive of turbulent flow. The apparent increase in turbulence may result from increases in velocity or regurgitant orifice area. Analysis of pixel color intensity was not performed in our study, but others have demonstrated a correlation between pixel color intensity and velocity.\textsuperscript{31} Tamura et al\textsuperscript{32} have demonstrated a correlation between the relative amounts of red, green, and blue pixels in color-Doppler jets and the Reynolds numbers of the jets, which are proportional to the velocity of the fluid.\textsuperscript{32} These studies suggest that indicators of turbulence, as well as measurements of jet area, may be important in the quantitation of regurgitation. Therefore, under the conditions of turbulent flow, a nonlinear relation may be expected between regurgitant volume and jet area.

The weaker correlations of 2D Doppler measurements with paravalvular regurgitation might be related to the eccentricity of the jets\textsuperscript{11} out of the 2D Doppler imaging plane; we did not attempt to compensate for eccentricity. Further improvement in the quantitation of these jets may be achieved by the use of orthogonal imaging planes.\textsuperscript{18}

2D Doppler provides a useful adjunct to other noninvasive methods in the study of bioprosthetic valve dysfunction. M-mode and two-dimensional echocardiography are valuable in the detection of excessive stent movement,\textsuperscript{33,34} thombi,\textsuperscript{33–35} vegetations,\textsuperscript{34–38} stenosis,\textsuperscript{34,36–39} and cusp deterioration\textsuperscript{34,36–39} but are unable to quantitate stenosis and regurgitation. PW and CW Doppler provide accurate estimates of prosthetic mitral valve area and mean diastolic gradient,\textsuperscript{13,14} but the techniques have had variable success in the differentiation of transvalvular from paravalvular origin of regurgitation,\textsuperscript{11,13,14,40} A noninvasive evaluation that combines PW, CW, and 2D Doppler may improve accuracy in the detection, localization, and quantitation of bioprosthetic mitral valve regurgitation.

Limitations

Clinical applicability of these data is uncertain because of the limitations inherent in an in vitro model.

Our in vitro model has the transducer positioned on the left atrial side of the mitral valve, whereas in clinical transthoracic imaging, the transducer is on the left ventricular side of the mitral valve. Imaging from the atrial side of the mitral valve avoids possible artifacts generated from metal and plastic components of prosthetic valves. Thus, our conclusions may have relevance only to imaging performed with transesophageal transducers.\textsuperscript{41} The arrangement of the transvalvular and paravalvular regurgitant orifices parallel to the ultrasound beam should bias the results of the study in favor of 2D Doppler in the detection and localization of regurgitant jets. However, despite orientation of the transducer position in relation to regurgitant defects, incorrect interpretations occurred in the presence of regurgitant volumes of less than 4 ml/beat. Thus, the optimal orientation of the transducer provided information relating to the threshold for accurate regurgitant jet detection.

The gain compensation is usually determined by the echocardiographer in an effort to optimize imaging of regurgitant jets and to minimize background “noise.” The variability in gain settings may affect the accuracy of regurgitant jet measurements. How-
ever, we used a previously described method for establishing the time-gain compensation. That is, the color gain was adjusted so that color background just appeared.

Regurgitant volumes up to 7 ml/beat and regurgitant fractions up to 21% were obtained in normal valves. Because the individual valves were of non-clinical quality, there may have been defective closure of the valve leaflets, although not apparent to visual inspection. Physiological regurgitation was defined as jet length of less than 1 cm, and abnormal regurgitation was defined as jet length of more than 1 cm. While the definitions were arbitrary, they affected only the qualitative interpretation of jet detection and localization. The distinction between physiological and abnormal regurgitation was not made in the quantitative interpretation of regurgitation.

Conclusion

2D Doppler detected and localized the site of regurgitation in an in vitro model of bioprosthetic mitral regurgitation analogous to transesophageal detection of this lesion. The limitation of the technique occurred in the presence of small defects, which were difficult to distinguish from the minimal regurgitation occurring in normal bioprosthetic valves. Transvalvular jet area and length correlated better with regurgitant volume than with regurgitant fraction, but correlation of these 2D Doppler measurements with regurgitant fraction improved when the measurements were corrected to an estimate of the stroke volume. Changes in heart rate did not have a major effect on the correlations between 2D Doppler measurements and regurgitation severity. The relatively weaker correlations between paravalvular regurgitant volumes and 2D Doppler measurements may be because of jet eccentricity.

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B F Vandenberg, K C Dellsperger, K B Chandran and R E Kerber

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