Radionuclide Angiography in the Quantitation of Mitral Regurgitation

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First pass radionuclide angiography (RA) was used to assess its ability to detect and quantitate the presence of left-sided regurgitation due to isolated mitral regurgitation (MR). In this study the nuclear regurgitant fraction (NRF) obtained from first pass RA was correlated with the results of contrast ventriculography (CV) in 50 patients, 18 with and 32 without MR. The correlation between CV and RA in the confirmation and quantification of isolated MR revealed a sensitivity of 100 percent and a specificity of 97 percent in patients with LVEF ≥ 35 percent.

In the very recent past, attention has been directed toward detecting the presence of left-sided regurgitation using radionuclide angiography. While reports of the detection and quantification of left-sided regurgitation have appeared in the literature, the accuracy of the techniques has been variable. Some authors have confirmed the accuracy of left-sided regurgitant fraction calculations, but have failed to differentiate aortic regurgitation from mitral regurgitation. This study was designed to quantitate isolated mitral regurgitation by first pass nuclear angiography and to correlate the results with contrast ventriculography.

Material and Methods

All patients from 1979-1982 with unequivocal isolated mitral regurgitation by contrast ventriculography who had radionuclide angiography were included in this study. They were chosen consecutively according to the following criteria from the contrast studies: 18 patients with mitral regurgitation due to either valvular or coronary artery disease, 16 patients who had coronary artery disease without mitral regurgitation but with a left ventricular ejection fraction of ≤ 35 percent, and 16 patients with poor left ventricular function (left ventricular ejection fraction ≤ 34 percent) without mitral regurgitation. The last group was included to determine the effects of poor left ventricular function on the accuracy of the study. The selection of a left ventricular ejection fraction of ≤34 percent as a reflection of poor left ventricular function was arbitrary. Patients with any degree of aortic regurgitation seen on contrast aortography, patients judged to have tricuspid regurgitation by radionuclide angiography,2 and patients with ventricular arrhythmias during either study were eliminated. Fifty patients (32 men and 18 women, mean age 60 ± 6 years [range 43 to 71 years]), who were evaluated with both techniques, remained in the study.

The contrast ventriculograms was performed in the right anterior oblique projection following injection of 35 to 45 ml of contrast medium (Renografin) through a pigtail catheter at a rate of 10 to 15 ml/sec using an automatic injector. Data were recorded on a 35mm camera at 45 frames/sec for later review.

The severity of mitral regurgitation was graded as follows:

1+ regurgitation—the contrast material essentially clears the left atrium with each beat, but never opacifies the entire atrium.
2+ regurgitation—the contrast material does not clear the atrium with one beat and generally does opacify the entire atrial chamber. Opacification of the atrium does not equal that of the left ventricle.
3+ regurgitation—the contrast material completely opacifies the left atrium which is as opacified as the left ventricle.
4+ regurgitation—the contrast material completely opacifies the entire left atrium in one beat, and becomes progressively more dense with each succeeding beat. The contrast material can be seen regurgitating into the pulmonary veins during left ventricular systole.3

All contrast ventriculograms were reviewed independently on two different days by each of three experienced angiographers, to determine interobserver and intraobserver variation. For comparison with the radionuclide angiographic results, quantification of mitral regurgitation from contrast studies was as follows: 1+ mitral regurgitation was reported as mild, 2+ and 3+ as moderate, and 4+ mitral regurgitation as severe. The intraobserver variability in determining the degree of mitral regurgitation was analyzed using the Pearson product moment correlation coefficient. The coefficient for observers 1 and 2 was 0.96, for 1 and 3 was 0.82, and for 2 and 3 was 0.84.

Radionuclide angiography was performed using the first pass technique, in which a bolus of 15 mCi of technetium-99m pertechnetate was injected into an antecubital vein and rapidly flushed with 20 ml of normal saline solution. The study was obtained with the patient in a 20° right anterior oblique position in front of the detector head of a multi-crystal camera equipped with a one-inch parallel hole collimator. Each study was accumulated at 20 frames per second for 50 seconds and then corrected and stored for processing by physicians. After defining the left ventricle as the region of interest, the left ventricular ejection fraction was obtained. The entire study was temporally smoothed, and left ventricular total stroke volume counts were obtained using the manufacturer’s specific software which sums the stroke volume count for all contractions between the lung phase background frame and the end of the study, before recirculation begins. After computer processing, the systoles and diastoles identified by the software are compared with those displayed in the histogram. Any contraction missing from the computer analysis are added to the data manually and the results are recalculated.

The ventricle was next zoned to include all crystals bounded by the pulmonic valve, the tricuspid valve and the right ventricular border and included all crystals from 100 percent to a 30 percent level at the periphery. Processing for the right ventricular total stroke volume counts were obtained as for the left ventricle.

The regurgitant fraction was then calculated by the following formula:

\[ RF = \frac{LV\ total\ stroke\ volume\ count}{RV\ total\ stroke\ volume\ count} \]
Table 1—Regurgitant Fractions

<table>
<thead>
<tr>
<th>Group</th>
<th>Mitral Regurgitation by Contrast Studies</th>
<th>Regurgitant Fraction by Nuclear Studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>39</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>54</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>64</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>68</td>
</tr>
</tbody>
</table>

volume count × 100 ÷ LV total stroke volume count.

In the normal patient without valvular disease the right ventricular total stroke volume count exceeds that of the left. In each case, therefore, the ratio is a negative number. When the total left ventricular stroke volume count is greater than that of the right, giving a positive ratio, left sided regurgitation is suggested.

The results of both radionuclide and contrast angiography were obtained independently and later correlated. The mean ± 1 standard deviation are given throughout the text. The standard Student t test for unpaired data were used to determine the significance of the differences between the means.

RESULTS

Our patient population consisted of six patients with rheumatic heart disease, two of whom had only mitral regurgitation and four of whom had mitral regurgitation and mitral stenosis. One patient had mitral valve prolapse and nine had coronary artery disease with mitral regurgitation due to papillary muscle dysfunction. Two patients had combined coronary artery disease and rheumatic heart disease with mitral stenosis and regurgitation. Thirty-two patients with coronary artery disease and no coexisting valvular lesions provided our control population.

In this study, the patients were grouped according to the degree of mitral regurgitation seen on contrast ventriculography (Table 1).

Group 1 consisted of 16 patients with no mitral regurgitation demonstrated by contrast ventriculography. Of these, radionuclide angiography demonstrated no regurgitation in 15 and a regurgitant fraction of 3 percent in one patient.

Group 2 included five patients with mild (1+) mitral regurgitation determined by contrast studies; all patients had mitral regurgitation on radionuclide angiography with regurgitant fractions ranging from 10 to 15 percent (mean 13 ± 2 percent).

Group 3 consisted of seven patients who had moderate (2+ and 3+) mitral regurgitation demonstrated by contrast left ventriculography. All seven patients had mitral regurgitation determined by radionuclide angiography, with a mean regurgitant fraction of 32 ± 11 percent (range 21-54 percent).

Group 4 included six patients with severe (4+) mitral regurgitation by contrast studies; all of these had mitral regurgitation demonstrated by radionuclide angiography with a mean regurgitant fraction of 69 ± 6 percent (range 59-78 percent). All patients in groups 1-4 had a left ventricular ejection fraction ≥35 percent (mean 56 ± 21 percent, range 36-94 percent).

Group 5 consisted of 16 patients without mitral regurgitation, but with a left ventricular ejection fraction of ≤34 percent. Fourteen were found to have “mitral regurgitation” of varying degree (mean 35 ± 20 percent, range 3-74 percent) demonstrated by radionuclide studies, and in two, no regurgitation was found.

Table 1 demonstrates the correlation between the quantification of mitral regurgitation by contrast ventriculography and by contrast studies. All of the patients with mild mitral regurgitation detected by contrast ventriculography were found to have a regurgitant fraction of 15 percent or less. The patients with moderate mitral regurgitation demonstrated by contrast ventriculography had a regurgitant fraction between 21 and 54 percent; six of these were between 21 and 39 percent. The six patients with severe mitral regurgitation had a regurgitant fraction of ≥59 percent. The differences between the regurgitant fraction of groups 1-4 is statistically significant (p <0.01).

Using contrast ventriculography as the standard to detect the presence of left-sided regurgitation due to isolated mitral regurgitation, radionuclide angiography was found to have a sensitivity of 100 percent and a specificity of 97 percent if the left ventricular ejection fraction was ≥35 percent.

DISCUSSION

The quantification of left-sided regurgitation can be accomplished during contrast ventriculography by using the Fick cardiac output and stroke volume derived from two end-diastolic and two end-systolic volumes. Although reliable, this technique requires precise analysis, is time-consuming, and is not practical for routine use. To date, no noninvasive technique has been shown to have comparable accuracy.

Application of a radionuclide technique to the determination of a left-sided regurgitant index (fraction) has been reported previously utilizing gated systems. Taylor et al, using the left anterior oblique projection, reported difficulty in quantitating left-sided regurgitation with this technique. The problems inherent in using the anterior view were confirmed in the report of Janowitz and Fester who used the first-pass tech-
Nuclear mitral regurgitant fraction vs left ventricular ejection fraction. Scattergram displays patients in whom the presence or absence of mitral regurgitation by radionuclide angiography was affected by the level of the left ventricular ejection fraction.

Since first-pass radionuclide angiography can provide the temporal separation of the right and left sides of the heart, it permits the quantification of isotope flow through these areas. This eliminates the shortcomings of the previously reported gated radionuclide studies. In our study, using first-pass techniques in the right anterior oblique projection, both temporal and spatial separation of the right and left ventricles aided the calculation of the nuclear regurgitant fraction which was shown to correlate well with the qualitative method used to assess the regurgitation detected from contrast cineangiograms.

In patients with left ventricular ejection fractions of ≥35 percent without valvular disease, a larger total stroke volume count was always seen in the right ventricle since the total dose traverses this chamber without dilution. The total stroke volume count in the left ventricle is less than or may be equal to the total right ventricular stroke volume count due possibly to two factors: 1) the sequestration or diffusion of isotope in the pulmonary vascular bed which is reflected by the slowly decreasing count rate in the lungs as the isotope bolus traverses the left ventricle before recirculation begins, and 2) the loss of counts from the left ventricle due to its more posterior position. A larger total stroke volume count in the left ventricle could only result from recirculation within the chamber due to regurgitation.

Although first-pass radionuclide angiography appears valid for isolated mitral regurgitation, the method can be affected by other conditions. One of the significant problems with this procedure was the high number of false-positive results in patients without valvular disease but with a left ventricular ejection fraction of ≤34 percent. This was evident in the widely diverse regurgitant fractions found in the group 5 patients (Fig 1). We assumed the elevated left ventricular total stroke volume count was based on prolonged sequestration of isotope within the left ventricle due to poor forward flow. In these patients, the time required for the isotope to clear the left ventricle is greater than normal. The number of systoles and diastoles included in the calculation of the total stroke volume count increases, thereby falsely elevating the resulting ratio. In each of these patients, right ventricular function remained normal. The effect of abnormal right ventricular function on the regurgitant fraction has not been determined.

The presence of tricuspid regurgitation can increase the right ventricular total stroke volume count secondarily to recirculation resulting in an underestimation of the degree of left-sided regurgitation. Coexisting aortic regurgitation can also complicate the localization of left-sided regurgitation, since the aortic regurgitant flow could not be separated from the mitral flow. Patients with both of these valvular lesions were excluded from this study. The presence of mitral stenosis in patients with adequate ventricular function did not
effect the total isotope count in either ventricle, even with prolonged transit times, because the isotope was cleared by forward flow with no recirculation in the left ventricle. However, this may not apply to patients with mitral stenosis and poor left ventricular function (LVEF ≤34 percent).

Ventricular arrhythmias have been reported by Lam et al to produce false positive results. They found that the regurgitant index (which is equivalent to our regurgitant fraction) of patients with ventricular premature contractions did not correlate with the catheterization data. The effect of arrhythmias was not investigated in this study because these patients were eliminated.

The close correlation of the radionuclide angiograms with contrast studies allows this safe and simple noninvasive procedure to be used to confirm and quantitate the presence of suspected mitral regurgitation. The procedure also becomes helpful in the extended care of patients with rheumatic heart disease, since the severity of mitral regurgitation can be assessed periodically to help determine the appropriate time for more definitive invasive studies and/or valve replacement.

In summary, the presence and degree of isolated mitral regurgitation seen with contrast ventriculography was correlated with the presence of mitral regurgitation and the nuclear regurgitant fraction obtained from radionuclide angiography in 30 patients. Radionuclide angiography identified the 15 patients with and 14 of the 15 patients without regurgitation. Radionuclide angiography was not reliable in patients with low left ventricular ejection fractions or patients with concomitant disease of the aortic or tricuspid valves. The data support the use of radionuclide angiography as a simple and easy noninvasive method of determining the presence and severity of left-sided regurgitation due to isolated mitral regurgitation.

REFERENCES