Quantitation of Left-to-right Cardiac Shunts with Radionuclide Angiography

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SUMMARY
A quantitative radionuclide angiogram technique using an intravenous injection of technetium-99m (Tc-99m) pertechnetate is described for quantitation of left-to-right shunts in the central circulation. Data analysis assumes exponential indicator clearance from normal cardiac chambers by dilution. A late prolongation of tracer disappearance compared to the initial clearance rate indicates an abnormally early return of indicator to the cardiac chamber. Patients with left-to-right shunts demonstrate prolonged clearance of radioactivity from all cardiac chambers distal to the site of shunt. The magnitude of curve distortion is quantitatively related to the size of shunt, and counts recorded from the right lung are used for shunt quantitation. Quadratic regression analysis of data from 21 patients with left-to-right shunts and eight normal subjects demonstrated a correlation coefficient of 0.951 between measurements of left-to-right shunts by the radionuclide and by the Fick method. Observations on 14 patients with aortic or mitral valve disease revealed this method of shunt evaluation to be of limited value in the presence of severe cardic valvular disease. However, the method permits detection of left-to-right shunts that are too small to be diagnosed by the Fick method and accurately quantitates shunts which are not at either extreme in size and flow. This technique appears to be potentially useful for the initial diagnosis and serial evaluation of patients with these disorders.

Additional Indexing Words:
- Atrial septal defect
- Partial anomalous pulmonary venous return
- Ventricular septal defect
- Technetium-99m
- Aortic valve disease
- Mitral valve disease
- Cardiac catheterization

A TECHNIQUE for detection and quantitation of left-to-right cardiac shunts that does not require cardiac catheterization would greatly facilitate the management of patients with these disorders. A variety of approaches utilizing radionuclides has proven successful in documenting the presence of left-to-right cardiac shunts.1-7 However, shunt quantitation using radionuclides has proven more difficult. Previous reports have outlined the qualitative changes associated with left-to-right shunts in radionuclide angiograms obtained using a multiple crystal gamma-camera.8 The present report describes a radionuclide method that enables accurate quantitation of left-to-right shunts and which separates the normal patient from the patient with a left-to-right shunt that is too small for detection by the Fick method.

Methods
Control radionuclide angiograms were obtained in eight normal subjects during injection for brain scan. History and physical examination identified no cardiac disease in these patients who ranged in age from two to 22 years with a mean of 9.4 years. Twenty-two patients with left-to-right shunts were studied who had the following defects: ten, ventricular septal defect; eleven, atrial septal defect; one, partial anomalous pulmonary venous drainage into the superior vena cava. The mean age of patients with left-to-right shunts was 21 years with a range from four to 64 years. The mean age for patients with a ventricular septal defect was 12 years, and the mean age for patients with an atrial septal defect was 30 years. To further evaluate the method of analysis, studies were obtained in a third group of patients with mitral or aortic valvular heart disease. These 14 patients ranged in age from 17 to 62 years with a mean age of 36 years. Complete cardiac catheterization confirmed the diagnosis of cardiac...
disease in all patients. Cardiac output and shunt flow were determined by the Fick method, and valvular areas were determined using the Gorlin formula. Grading of valvular insufficiency was by cineangiographic criteria.\textsuperscript{9, 10}

The System 70 Gamma Camera* was used to obtain quantitative radionuclide angiocardiograms immediately after cardiac catheterization.\textsuperscript{11} Performance characteristics of this instrument pertinent to cardiovascular studies have been previously described. The detector of this instrument is a matrix of 294 sodium iodide crystals, each with a 1 cm square front surface, arranged in a 14 by 21 array. A 1.5 inch thick multihole collimator was used. Counts from each crystal were recorded onto computer tape at 1.0 sec intervals during the study. The detector was positioned directly anterior to the precordium of quietly breathing, supine patients, in contact with the chest. A 20 mCi bolus of technetium-99m (Te-99m) pertechnetate (0.3 mCi/kg in children) in a volume less than 2 cc was rapidly injected into a large arm vein through a 19 gauge needle. Studies were completed in less than five minutes and were well tolerated by all patients. An IBM 370/165 computer provided necessary data manipulation. Data distortion caused by lack of uniform detector response and by instrument dead-time count loss was corrected by previously described techniques.\textsuperscript{12}

Initial data analysis performed after these corrections delineated detector units corresponding to discrete cardiac regions by computer identification of the time response of each detector.\textsuperscript{13} Time-activity curves were obtained from the right atrium, right ventricle, pulmonary artery, lung, left atrium, left ventricle, and aortic arch.

Data analysis was based on the assumption that indicator clearance from cardiac chambers follows a single exponential decline. In the presence of a left-to-right cardiac shunt, central recirculation of indicator carried by shunted blood interrupts the exponential decline in counts observed in cardiac regions distal to the shunt. The magnitude of interruption in decline of counts relates to the magnitude of shunt flow and provides a method for quantitating left-to-right shunting. Analysis of counts recorded over the lung by a single scintillation counter after radionuclide injection into the right pulmonary artery have demonstrated the validity of this approach to the data.\textsuperscript{6} Although indicator dilution curves were obtained from each cardiac chamber in the present study, calculations of the magnitude of left-to-right shunting were made from data recorded over the right lung. Data from adjacent cardiac chambers were useful in documenting the presence of the shunt and excluding other cardiac pathology. However, the anatomic configuration of the heart makes difficult the total separation of counts arising from individual cardiac chambers. Therefore, quantitation of the magnitude of shunt proved most accurate when data were obtained from the lung which could be recognized as an anatomically pure region.

The descending portion of the right lung angigram was replotted on semilogarithmic coordinates, and the initial washout slope of tracer was extrapolated to a value 1% of the maximum count (fig. 1). The extrapolated line formed the division between two adjacent areas, x and y. The other borders of area y were the angiographic curve, the baseline and a line extending from the curve peak perpendicular to the baseline. If area y included the entire area underneath the lung curve rather than being limited by the line extending from the curve peak perpendicular to the base line, the resulting area would demonstrate some relationship to the pulmonary flow rate. However, the variation among patients in the initial portion of the right lung angigram resulting from different configurations of tracer bolus arriving in the right heart provided ratios of x to y that did not have as good a correlation with the size of the left-to-right shunt as when the area of y began at the curve peak. The borders of area x were selected to include tracer that had recirculated at a time earlier than normal, thereby representing the amount of left-to-right shunt. The borders of area x


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\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Analysis of right lung angiograms: A) normal; B) ventricular septal defect, 26% left-to-right shunt; C) partial anomalous pulmonary venous drainage, 46% left-to-right shunt; D) ventricular septal defect, 70% left-to-right shunt. The ratio of areas x to y were used for comparison with the calculated percent left-to-right shunt by the Fick method. Note the prominent break in the exponential decline in patients B, C, and D with the early central recirculation due to the shunt. P = peak value of the curve, 0.01P = 1% of the peak value.}
\end{figure}
included the angiographic curve, the extrapolated exponential decline and a line perpendicular to the baseline at the point where the extrapolation reached 1% of the peak value. Use of a ratio of areas to quantify left-to-right shunts obviated the need for actual scale factors for curve calibration. Areas were measured by planimetry, and the ratio of x to y was compared graphically and statistically to the magnitude of the shunt determined by the Fick data using multiple regression analysis, and statistical evaluation was performed utilizing a digital computer program.

Results

In figure 2 the data for the patients with left-to-right shunts and those with no cardiovascular abnormality are presented together with the solution of the quadratic equation which provided the best correlation. The correlation coefficient was 0.951, (standard deviation 6.8% and standard error 7.1%). When the size of the shunt exceeded 70% of pulmonary blood flow, the solution of the equation showed a paradoxical decrease in the size of the shunt as the ratio of the areas became larger. This saturation of the method of analysis at this point is of no clinical significance because the management of the patient with a 70% left-to-right shunt is the same as that for the one with a larger left-to-right shunt due to a similar anatomic abnormality.

All normal patients had a ratio of x/y less than 0.8 while all patient with shunts in excess of 70% had a ratio in excess of 1.9. Between these values there was a monotonic increase in the ratio which correlated with the increase in the shunt flow from 30 to 70% of the pulmonary blood flow. Additionally, the method detected shunts that were so small they were detectable by cineangiography but not by the Fick method. Yet no false positive values appeared in the normal group.

The application of this method of analysis to radionuclide angiograms obtained from patients with mitral stenosis, mitral insufficiency, aortic stenosis, and aortic insufficiency, or a combination of these lesions confirmed the findings of other quantitative techniques.6 Severe mitral or aortic valvular insufficiency distorts the indicator dilution curve so that the fall in the radioactivity of the lung curve no longer approximates a single exponential (fig. 3). The area ratios obtained in these patients confirm that significant distortion occurred when the lesions were hemodynamically severe (table 1). Patients with severe mitral insufficiency demonstrated ratios greater than unity. Patients with moderate mitral stenosis (valve area 1.3–1.7 cm²) had ratios which were at the upper limits of normal, i.e., 0.9. Patients with moderate aortic insufficiency had ratios within the normal range, but all those with severe aortic insufficiency demonstrated ratios greater than the normal.

![Figure 2](image1)

**Figure 2**

Regression analysis of normals and patients with left-to-right shunts relating percent left-to-right shunt to the ratio x/y. N = number of patients in regression analysis; r = correlation coefficient; SD = standard deviation, see = standard estimated error; ASD = atrial septal defect; VSD = ventricular septal defect.

![Figure 3](image2)

**Figure 3**

Analysis of the right lung angiogram of a patient with severe mitral insufficiency. Note the absence of a single exponential curve with a definite break point compared to curves in figure 1 for patients with shunts. An attempt to analyze the curve provides an area ratio much greater than the mean ratio for the normals.
Table 1

Comparison of the Hemodynamic Severity of Valvular Lesions to the x/y Ratios Obtained from Right Lung Angiograms

<table>
<thead>
<tr>
<th>Valve disease</th>
<th>Severity/valve area</th>
<th>Ratio x/y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MI</td>
<td>4+</td>
<td>1.91</td>
</tr>
<tr>
<td>2. MI</td>
<td>4+</td>
<td>1.38</td>
</tr>
<tr>
<td>3. MS</td>
<td>1.7 cm²</td>
<td>0.90</td>
</tr>
<tr>
<td>4. MS</td>
<td>1.7 cm²</td>
<td>0.87</td>
</tr>
<tr>
<td>5. MS</td>
<td>1.3 cm²</td>
<td>0.80</td>
</tr>
<tr>
<td>6. AI</td>
<td>4+</td>
<td>1.17</td>
</tr>
<tr>
<td>7. AI</td>
<td>4+</td>
<td>1.02</td>
</tr>
<tr>
<td>8. AI</td>
<td>4+</td>
<td>1.02</td>
</tr>
<tr>
<td>9. AI</td>
<td>2+</td>
<td>0.59</td>
</tr>
<tr>
<td>10. AI</td>
<td>3+</td>
<td>0.55</td>
</tr>
<tr>
<td>11. AS</td>
<td>0.8 cm²</td>
<td>0.90</td>
</tr>
<tr>
<td>12. AS</td>
<td>1.4 cm²</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Abbreviations: AS = aortic stenosis; AI = aortic insufficiency; MS = mitral stenosis; MI = mitral insufficiency.

Discussion

Quantitative radionuclide angiograms obtained by utilizing a detector with a multiple crystal matrix demonstrate characteristic abnormalities in patients with left-to-right cardiac shunts and those with valvular abnormalities. Studies in patients with left-to-right cardiac shunts typically show: 1) early left heart appearance of tracer, 2) early reappearance of isotope in the right heart chambers at the level of the shunt, if the shunt flow exceeds 30% of the pulmonary flow, and 3) persistence of radioactivity in the central circulation at a relatively high level for a prolonged period. The present study shows that this third finding in the radionuclide angiogram lends itself to a method for estimating shunt flow in lesions with predominant left-to-right flow. The distortion of the curve away from the exponential decline increases progressively as a function of the size of the shunt. This change was demonstrated regardless of whether the anomaly was an atrial septal defect, partial anomalous pulmonary venous drainage, or ventricular septal defect. Although no patient with a patent ductus arteriosus or aortico-pulmonary communication was evaluated, this technique would appear to be of value in approximating the size of the shunt in these disorders.

On the other hand, this method of quantitating the size of a left-to-right shunt fails when significant bidirectional shunting is present such as in tetralogy of Fallot or truncus arteriosus. The presence of a right-to-left shunt allows a portion of the tracer to enter the systemic circulation and return to the right heart inappropriately early, as the radionuclide has bypassed the pulmonary circuit. This early reappearance of indicator in the right lung will distort the initial exponential fall of radioactivity and result in overestimating the size of the left-to-right shunt. In addition, the patient with a coarctation of the aorta may have a lung angiogram which is falsely positive for a left-to-right shunt due to collateral flow through the intercostal and internal mammary arteries carrying labeled blood through the area identified as the right lung.

Departure from a single exponential decline of lung radioactivity in patients with severe aortic or mitral valve abnormalities may result from congestive heart failure with the resultant low cardiac output producing a slow disappearance of tracer which is difficult to accurately describe by a single exponential curve. On the other hand, the departure from a single exponential decline may result from reflux of labelled blood back into the pulmonary veins or from nonuniform mixing of tracer within the pulmonary blood volume. Regardless of the cause of the distortion, analysis of these angiograms using the area ratio technique would provide values compatible with a left-to-right shunt which might decrease the value of the technique in a patient with hemodynamically severe aortic or mitral valve disease and a suspected left-to-right shunt. However, patients with valvular abnormalities can be distinguished from those with left-to-right shunts by radionuclide angiogram data from all cardiac chambers. Patients with valve disorders characteristically demonstrate prolonged pulmonary transit time compared to normal subjects or patients with left-to-right shunts and lack early reappearance of radioactivity in the right heart.

The primary determinant of the accuracy of this approach is the quality of the observed data. Factors necessary to obtain reproducible data include proper positioning of the patient, a discrete bolus injection, and an accurate selection of anatomic areas for count analysis. A slow injection produces curves with an excessively shallow slope which are difficult to accurately extrapolate. Improper area selection results in even greater inaccuracy. For example, inclusion of left atrium counts with data from the lungs might distort the exponential count decline in the curve used for shunt calculation. Patient motion, particularly likely to occur in young children, represents another potential source of error. However, reasonable care in performing the studies will avoid these errors, and the technique has proven simple to apply to large groups of patients.
This study demonstrates quantitative radionuclide angiograms can be used to quantitate left-to-right shunts with high accuracy when the ratio of areas method of analysis is used. The method permits detection of small left-to-right shunt in patients with equivocal physical findings. In addition, patients with a large shunt can be followed with serial assessment of shunt magnitude thereby aiding the decision to perform catheterization when a decrease in shunt flow is associated with clinical findings suggesting the onset of Eisenmenger's syndrome. Moreover, the technique would appear promising in evaluating patients after surgical closure of septal defects. The technique imposes little risk or discomfort to the patient, and radiation exposure to the patient is low compared to cineangiography.3,4,14

References