Use of Indicator Dilution Techniques in Measuring Combined Aortic and Mitral Insufficiency

By Dennis A. Bloomfield, M.B., Edward J. Battersby, M.D., and Bruce C. Sinclair-Smith, M.B., F.R.C.P. (E), M.R.A.C.P.

When aortic and mitral valvular insufficiency are present in the same patient, indicator injected into the aortic root regurgitates into the left ventricle and thence into the left atrium. The purpose of this paper is to describe the indicator distribution in such patients and to compare the relationships found with those predicted from a theoretical model of bivalvular insufficiency.

Indicator distribution across a single incompetent valve may be extrapolated to the case of two incompetent valves in series. Using the fundamental relationship: flow \times concentration \times time = units of indicator moved, the ratios of the areas of indicator dilution curves that will be inscribed in the several chambers after injection into the aortic root can be derived. It has been shown for two chambers when indicator is introduced into the chamber immediately distal to the regurgitant valve:

$$\frac{A_{PC}}{A_{DG}} = \frac{V_I}{V_I + V_E}$$

where $A_{PC}$ = curve area in the proximal chamber

$A_{DG}$ = curve area in the distal chamber

$V_I$ = regurgitant stroke volume

and $V_E$ = forward stroke volume.

The ratio $\frac{V_I}{V_I + V_E}$ is defined as the regurgitant fraction ($f$).

In the case of combined valvular insufficiency we may define

For the mitral valve: For the aortic valve:

$$A_{PC} = A_{ATRIUM} \quad A_{PC} = A_{VENTRICLE}$$

$$A_{DG} = A_{VENTRICLE} \quad A_{DG} = A_{AORTA}$$

$$V_I = V_{MI} \quad V_I = V_{AI}$$

$$\frac{V_{MI}}{V_{MI} + V_E} = f_m; \quad \frac{V_{AI}}{V_{AI} + V_E} = f_a$$

From the two relationships

$$\frac{A_{ATRIUM}}{A_{VENTRICLE}} = \frac{V_{MI}}{V_{MI} + V_E}$$

and

$$\frac{A_{VENTRICLE}}{A_{AORTA}} = \frac{V_{AI}}{V_{AI} + V_E}$$

it follows that:

$$\frac{A_{ATRIUM}}{A_{AORTA}} = \frac{V_{MI}}{V_{MI} + V_E} \times \frac{V_{AI}}{V_{AI} + V_E} = f_m \times f_a$$

As $\frac{A_{ATRIUM}}{A_{AORTA}}$ also represents the curve area ratio of indicator regurgitating serially into the atrium from an aortic injection, and is defined as the combined regurgitant fraction ($f_c$), it follows further than $f_c = f_m \times f_a$ that is, the combined regurgitant fraction across both valves is equal to the product of the regurgitant fractions across each valve (the regurgitant product).

The assumptions that must be fulfilled for the validity of this proposition are that (i) at the beginning of each ventricular systole, the indicator has been mixed in the ventricle in such manner that the ratio of mass of indicator moved from the ventricle to the atrium in volume $V_{MI}$ to the mass moved forward by volume $(V_E + V_{AI})$ is proportional to the ratio of those volumes, (ii) such relations obtain both for the mass of indicator moved into the ventricle from the aortic root in volume $V_{AI}$.

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and for the mass leaving the aortic root in volume \( V_g \). If the latter assumption holds, then the area of a curve drawn from a peripheral artery will be identical with the area of the aortic root curve and may be used in place of that area in the above relationships, as well as to calculate forward cardiac output in the usual manner. These assumptions imply that measurement of valvular insufficiency by this indicator dilution technic is independent of the presence or severity of regurgitation at another valve, and that the same information is present in the estimation of \( f_c \) and either \( f_m \) or \( f_a \), as is present in the estimation of both \( f_m \) and \( f_a \). In order to validate in the real system the relationship, \( f_a = f_m \times f_a \), three values were measured in patients with combined aortic and mitral insufficiency, and the combined regurgitant fractions were compared with the regurgitant products.

**Methods**

Nine patients with combined aortic and mitral insufficiency underwent simultaneous trans-septal left heart and retrograde aortic catheterization. The aortic valve was studied by positioning the trans-septal catheter in the left ventricle and the aortic catheter in the root of the aorta, one to two centimeters distal to the valve. Indocyanine green, in volumes of 2 to 3 cc (0.1 mg/kg body wt), was delivered through the aortic catheter by steady manual injection continued through at least one and one-half cardiac cycles. Simultaneous sampling of the indicator was done from the ventricular catheter and from an indwelling femoral artery needle. Serial determinations were made three times, on average, and the valvular incompetence was calculated by the area ratio method.

The trans-septal catheter was then withdrawn into the left atrium with the tip well clear of the mitral cusps, and without moving the aortic catheter, further aortic injections were made in the manner described above. Simultaneous sampling was obtained from the left atrium and femoral artery. Following this, the aortic catheter was advanced into the left ventricle, and further dye dilution studies were done, with the left ventricular injection site and with left atrial and femoral artery sampling. The same injection catheter and volume of indicator were used throughout the study in each patient.

Paired monochromatic photomultiplier densitometers were used for the indicator curves and the recording equipment was a Sanborn model 350 Polyviso.

**Results**

The regurgitant fractions \( (f_m, f_a) \) for each valve were calculated from the appropriate curve areas, the mean fraction being derived from triplicate or duplicate measurements. The combined regurgitant fraction \( (f_c) \) was calculated as the ratio of the left atrial curve area to the femoral artery curve area following aortic root injection of dye and the regurgitant product \( (f_a \times f_m) \) was calculated from the individual regurgitant fractions. The relationship between this product and the combined regurgitant fraction as determined in nine patients is shown in table 1. The similarity between the measured and derived values can be seen.

The reproducibility of the curve area ratios was measured in these patients and in 43 other patients with aortic valve disease. In the combined series of 52 observations the standard deviation and coefficient of variation are as follows: downstream or arterial curve area \( \pm 11.3 \) and 13.2%; ventricular curve area \( \pm 10.49 \) and 5.06%; curve area ratio (arterial area/ventricular area) \( \pm 0.06 \) and 13.38%. Similar reproducibility is obtained for an analysis of data relating to the mitral valve (79 patients). The correlation between \( f_a \times f_m \) and \( f_c \) is shown in figure 1. The correlation coefficient is 0.99.

In five other patients with combined valvular incompetence the mitral valve could not be crossed. In each patient, \( f_m \) and \( f_a \) were

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Combined Aortic and Mitral Insufficiency—Both Values Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>( f_m )</td>
</tr>
<tr>
<td>WMC</td>
<td>0.61</td>
</tr>
<tr>
<td>WM</td>
<td>0.26</td>
</tr>
<tr>
<td>CD</td>
<td>0.45</td>
</tr>
<tr>
<td>HB</td>
<td>0.09</td>
</tr>
<tr>
<td>BA</td>
<td>0.71</td>
</tr>
<tr>
<td>NS</td>
<td>0.48</td>
</tr>
<tr>
<td>IF</td>
<td>0.89</td>
</tr>
<tr>
<td>CB</td>
<td>0.89</td>
</tr>
<tr>
<td>JD</td>
<td>0.66</td>
</tr>
</tbody>
</table>

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measured in the manner described and $f_a$ was predicted from the formula. Cineangiocardiograms were recorded at the time of catheterization, the radiopaque dye being injected into the aortic root. An estimation of regurgitation was made from the size of the regurgitant jet and the degree and duration of opacification of the left ventricle. In two of these patients, a further visual estimation of aortic insufficiency was made at operation. The agreement between the assessment of insufficiency by these independent methods and the predicted values from the catheter studies is demonstrated in table 2.

Cineangiocardiography with aortic injection of contrast medium was performed in three additional patients in whom the degree of mitral regurgitation had been predicted. Although the study confirmed the presence of bivalvular insufficiency, no reliable estimation of degree could be made in regard to the mitral regurgitation.

**Discussion**

The application of indicator dilution techniques for detecting aortic insufficiency in association with mitral insufficiency was first reported by Guidry. Curves were recorded in the left ventricle and left atrium with aortic injection, but no quantitation of the insufficiency was undertaken although its possibility was suggested from these data. In the present study the existence of this relationship has been shown theoretically and its validation demonstrated in nine patients. The high degree of correlation ($r = 0.99$) between measured and predicted values of insufficiency reflects the effective manner in which indicator regurgitating through the aortic valve mixes with the left ventricular blood. Such mixing appears to be as good as, or better than, dispersion following injection of indicator into the ventricle through a catheter. Not only can the degree of insufficiency at one valve be predicted from the combined regurgitant fraction and the measurement of regurgitation at the other valve, but the severity of the insufficiency can be predicted when the only information available is the combined regurgitant fraction.

Figure 2 shows the relationship between the combined regurgitant fraction on the abscissa and the regurgitant fraction at the least regurgitant valve on the ordinate. The upper line defines the maximal value of $f$ for the least insufficient valve at any value of $f_a$. It is derived as $V f_c$ and shows that with $f_a < 0.36$, the least insufficient valve cannot have more than a moderate degree of insufficiency ($f = 0.6$). With $f_a < 0.10$ the least insufficient valve cannot have more than mild insufficiency ($f = 0.3$). The lower line defines the minimal value of $f$ for the least insufficient valve at any value of $f_a$. As the maximal value of $f$ compatible

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**TABLE 2**

*Independent Assessment of Aortic Insufficiency*

<table>
<thead>
<tr>
<th></th>
<th>Measured</th>
<th>Derived</th>
<th>Cineangiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>JB</td>
<td>0.02</td>
<td>0.57</td>
<td>0.04 very slight aortic insufficiency*</td>
</tr>
<tr>
<td>AC</td>
<td>0.08</td>
<td>0.41</td>
<td>0.20 mild aortic insufficiency</td>
</tr>
<tr>
<td>DL</td>
<td>0.17</td>
<td>0.23</td>
<td>0.74 severe aortic insufficiency</td>
</tr>
<tr>
<td>DW</td>
<td>0.34</td>
<td>0.75</td>
<td>0.46 moderate aortic insufficiency*</td>
</tr>
<tr>
<td>RS</td>
<td>0.50</td>
<td>0.70</td>
<td>0.71 severe aortic insufficiency</td>
</tr>
</tbody>
</table>

*Confirmed assessment by surgical inspection.*

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*Circulation Research, Vol. XVIII, January 1966*
with life is considered to be about 0.90, the minimal $f$ for the least insufficient valve is derived as $\frac{f_0}{0.9}$. When $f_0 > 0.54$, the least affected valve must be severely insufficient, and with $f_0 > 0.30$, must be at least moderately insufficient. The hatched area between the lines defines the range of $f$ for any value of $f_c$.

Valve replacement is being performed on an increasing number of patients with combined aortic and mitral insufficiency, in whom prolonged diagnostic catheterization to assess function at both valves is accompanied by considerable risk. The application of the regurgitant relationships for single valve and combined valvular insufficiency, or, in the patients at most risk, of combined insufficiency alone, can produce valuable information with a minimum of time and manipulation.

**Summary**

In patients with combined aortic and mitral valvular insufficiency, the combined regurgitant fraction across both valves has been shown to equal the product of the regurgitant fractions at each valve. This relationship was validated in nine patients, and in eight other patients was used to predict the degree of regurgitation at one valve when the regurgitant fraction at the other valve and the combined regurgitant fraction were known. Confirmation of the predicted degrees of insufficiency were afforded by cineangiography and surgical inspection. Information of considerable usefulness predicting the least possible degrees of valvular insufficiency could be obtained from the measurement of the combined regurgitant fraction alone.

**References**

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