

Radiocardiographic Formula for the Calculation of the Area of the Stenotic Mitral Valve

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The procedure of injecting a radioisotope intravenously and graphically recording its appearance and concentration over the precordium was first reported by Prinzmetal *et al* (1). They used the term radiocardiography to describe this technique. With the development of more sensitive equipment and availability of nondiffusible tracers, subsequent workers introduced several important refinements to the original technique (2-6). The present work aimed at applying radiocardiography to patients with mitral stenosis, who were being prepared for commissurotomy. If some of the data offered by the radiocardiogram would correlate with the size of the mitral orifice, as estimated by the surgeon during operation, that might provide a useful and simple approach to the preoperative assessment and calculation of the area of the stenotic mitral valve.

METHODS AND MATERIALS

Twenty-three patients with pure mitral stenosis, and in whom commissurotomy was indicated, constitute the subject of the present study. There were 13 males and 10 females ranging in age from 19 to 45 years. Twelve normal control subjects, 7 males and 5 females, with ages ranging between 19 and 39 years were also studied. Each subject was weighed, had his height measured and his body surface area calculated from special charts prepared from the formula of Du Bois and Du Bois.

For each of these subjects a thorough clinical examination, a full electrocardiographic and radiographic study of the heart, as well as radiocardiography were done. The latter test was performed with the subject lying comfortably on a couch in the morning, while fasting. An injection of 10-20 mC of radioiodinated human serum albumin—¹³¹I. H.S.A., contained in 0.2-0.4 ml of saline, was rapidly made into a suitable antecubital vein, through a wide bore needle. The radioactivity travelling through the heart was detected by a collimated scintillation probe placed along the left sternal border opposite the

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fifth rib, and recorded by an attached rate-meter and strip chart recorder, on which the radiocardiogram was inscribed (Figs. 1, 2). At the same time the pulse was counted for one minute, which covered the period during which the whole radiocardiogram was recorded on the chart. The recorder was stopped after the inscription of the primary curve and some recirculations, to be reoperated 10 minutes later to obtain an equilibrium level reading (Eq.).

The handling of the radiocardiogram is as shown in both figure one, showing the radiocardiogram of a normal subject, and figure two, showing the tracing obtained in a patient with mitral stenosis. The pulmonary circulation time (P.C.T.) used in the present study is the peak to peak pulmonary circulation time, i.e., the interval in seconds between the two peaks of the common radiocardiographic curve obtained. The descending limb of the radiocardiogram was extrapolated to zero according to an exponential decrease as demonstrated by Hamilton *et al* (7,8). The readings of radioactivity every second on the descending limb (D.L.) of the radiocardiogram were replotted on semilogarithmic paper and the straight line that best fits the replotted points was drawn. From this line two parameters were measured:

A. The $T_{1/2}$ of the descending limb, which is the time in seconds necessary for the radioactivity to reach a halved value.

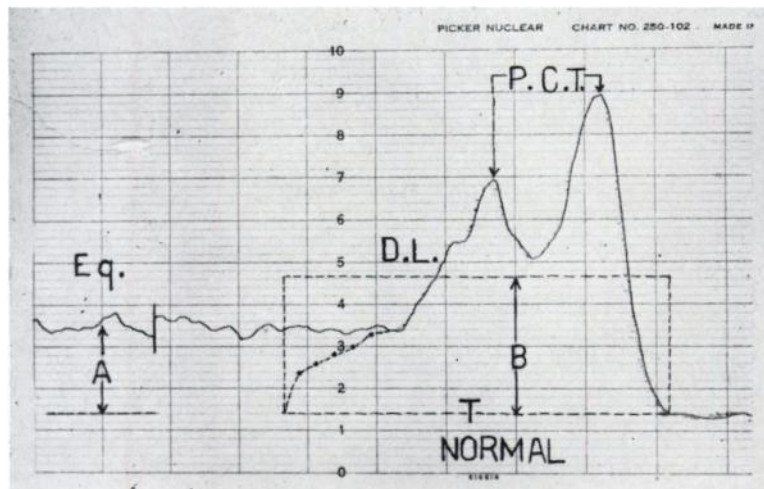


Fig. 1. Radiocardiogram of a normal subject.

D. L. : Descending limb of the radiocardiogram.

P.C.T.: Peak to peak pulmonary circulation time.

T : Transit time, i.e., the time during which the radioactive bolus was able to traverse all cardiac chambers.

Eq. : Equilibrium.

A. : This height represents the concentration of the injected radioactive dose at equilibrium time, 10 minutes after injection.

B. : This height represents the average concentration of the injected radioactive bolus during its passage through the heart.

(For Calculation, Read Text).

B. The actual slope or lambda (λ) of the descending limb which was calculated by the formula:

$$\text{Lambda } \lambda = \frac{0.693}{T^{\frac{1}{2}}}$$

The transit time (T) in seconds, is the time necessary for the radioactive bolus to traverse all cardiac chambers. This was measured after semilogarithmic extrapolation of the descending limb of the radiocardiogram to meet the base line as shown by the dotted line of figures one and two. This is important to get an idealized curve, excluding recirculation effects. The mathematical methods used for the calculation of the cardiac output were similar to those outlined by Shipley *et al* (5). The area under the idealized curve was measured

TABLE I

<i>Correlation of M.V.A. with:</i>	<i>R-Correlation Coefficient</i>	<i>Computed t-statistic</i>	<i>P-Level of Significance of Correlation Coefficient</i>
1. FCO/P/m ²	+0.50	2.63	<0.01
2. P.C.T. (Seconds)	-0.537	2.92	<0.005
3. FCO/P	+0.23	1.08	0.14 Insignificant
4. FCO/min.	+0.10	0.46	0.32 Insignificant
5. FCO/min/m ²	+0.10	0.46	0.32 Insignificant
6. T-Transit time (Secs.)	-0.20	0.93	0.17 Insignificant
7. T ¹ / ₂ of descending limb of RCG (Secs.)	+0.208	0.98	0.16 Insignificant
8. Slope (λ) of descending limb of RCG.	-0.10	0.46	0.32 Insignificant

Table I: Showing the correlation coefficient observed between the mitral valve area (M.V.A.) in cm² and each of the parameters indicated. P- the level of significance of the calculated correlation coefficient was computed by application of the student's t-test.

FCO/P/m²: Fractional stroke volume per square metre body surface area.

P.C.T.: Peak to peak pulmonary circulation time.

FCO/P: Fractional stroke volume.

FCO/min.: Fractional cardiac output per minute.

FCO/min/m²: Fractional cardiac output per minute per square metre body surface area.

by planimetry. Knowing this area, and the transit time— T —the average concentration of the injected radioactive dose during its transit time through the heart could be calculated and is represented by the height (B). The average concentration of radioactivity at equilibrium time is represented by the height (A). The cardiac output (C.O.) can now be measured as:

$$C.O. = \frac{A}{B \cdot T} \times B.V.$$

where B.V. is the patient's total blood volume in which the radioactivity was finally diluted. If both sides of this equation are divided by B.V., the value of the fractional cardiac output per minute (FCO/min) is obtained, which is the fraction of the blood volume, expelled from the heart per minute. If the fractional cardiac output per minute is divided by the pulse rate (P), the quantity obtained is the fractional stroke volume (FCO/ P). When the FCO/min is divided by the body surface area, the fractional cardiac output per minute per square metre of body surface area (FCO/min/m²) is obtained. When the FCO/ P is divided by the body surface area, the fractional stroke volume per square metre of body surface area (FCO/ P /m²) is obtained.

The patients were subjected to mitral commissurotomy. At cardiotomy, the clinical diagnosis was confirmed in all cases and the cross sectional area of the mitral valve opening estimated, using a special measure. This measure consisted of a rectangular metal plate having a series of holes of appropriate shape and increasing known and accurately measured size. The plate is autoclaveable. The size of these holes were measured several times after autoclaving, and it was checked that no change occurred in the size of the different holes after sterilization. The surgeon with the index finger of the right hand feeling the mitral orifice, found out with the index of the left hand the orifice of corresponding size on the measuring plate. The indicated area of this orifice would then be a measure of the mitral valve area in question. All measurements of the mitral valve area were carried out by the same surgeon, Dr. G. A. Senna, in whom no differences in size of the index fingers were noted. Repeated measurements of the mitral valve area on the same occasion were always identical, thus denoting that distensibility of the mitral valve compared with the rigid metal plate had no effect on the estimations.

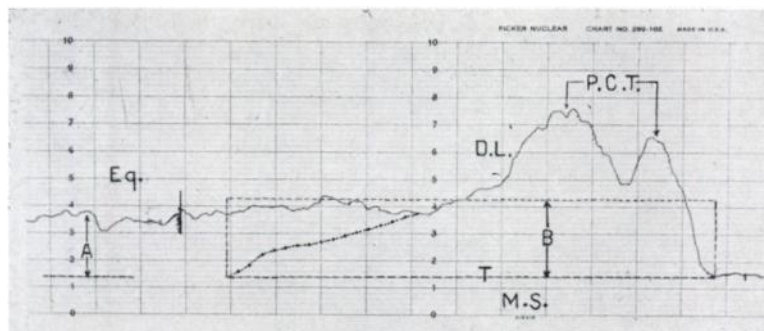


Fig. 2. Radiocardiogram of a patient with mitral stenosis (M.S.)
Abbreviations have the same meaning as in Figure 1.

The assessment of the mitral valve area after commissurotomy could not be done by this method, since in all our patients the extent of splitting of the mitral valve increased its area to more than could be measured by the widest hole in our plate. Nevertheless, the radiocardiographic study was repeated on each of our 23 patients, after a minimal interval of one month following the operation.

RESULTS

The correlation between the mitral valve area as estimated by the surgeon during operation and each of the radiocardiographic parameters studied in the 23 patients of pure mitral stenosis was assessed by the calculation of the correlation coefficient, R. The significance of the obtained correlation coefficient was

TABLE II

Ser. No.	M.V.A. Mitral Valve Area Cm^2	$\frac{\text{FCO/P/m}^2}{\text{P.C.T.}} \times 100$ (Q)	FCO/P/m ²	P.C.T. Secs.
1	0.9	11.4	1.25	11
2	1.2	11.5	0.86	7.5
3	0.7	14.3	1.14	8
4	1.7	28.5	1.08	3.8
5	0.9	15	1.25	8.3
6	1.6	24.7	1.73	7
7	2.2	33	1.65	5
8	0.8	6.1	0.73	12
9	0.2	6.4	0.54	8.4
10	1.4	11.6	1.16	10
11	0.5	8.3	0.83	10
12	0.9	13.6	1.23	9
13	0.8	17.1	1.96	11.5
14	0.4	19.2	1.15	6
15	1.5	24	1.68	7
16	1.2	19.2	1.44	7.5
17	1.3	15.4	1.12	7
18	1.4	22	1.1	5
19	1.3	10.5	0.84	8
20	2	31	1.86	6.6
21	0.3	12	1.2	10
22	0.5	3.75	0.52	14
23	0.4	18.7	1.31	7

Table II: Showing the Mitral Valve Area (M.V.A.) as estimated by the surgeon during operation, the fractional stroke volume per square metre body surface (FCO/P/m²) expressed as per cent of the patients blood volume (B.V.), the pulmonary circulation time (P.C.T.), and the quotient (Q) in the 23 patients of mitral stenosis studied.

tested using tables of the distribution of student's t-test, which was calculated by the formula:

$$t = \frac{R \sqrt{N-2}}{\sqrt{1-R^2}}$$

and entering the tables with $N-2$, i.e., 21 degrees of freedom. N is the number of cases studied.

The results are shown in Table I. A study of this table would show that of all 8 radiocardiographic parameters thus tested, the mitral valve area showed a significant correlation with only two: namely, the fractional stroke volume per square metre of body surface area ($FCO/P/m^2$) and the pulmonary circulation time (P.C.T.). The correlation coefficient with the $FCO/P/m^2$ was +0.50 (P less than 0.01) and with the P.C.T. was -0.537 (P less than 0.005).

Since it is obvious that these two parameters vary in opposite directions, the quotient (Q) was also obtained by the formula:

$$Q = \frac{FCO/P/m^2}{P.C.T.} \times 100$$

Table II shows the values of each of the mitral valve area, $FCO/P/m^2$, P.C.T., and the quotient (Q) in the 23 cases studied. It was then seen that the correlation of the mitral valve area with the suggested quotient (Q) was higher ($R + 0.93$) and much highly significant (P much less than 0.0005), as seen in the scatter diagram Figure III. The regression equation for the mitral valve area (M.V.A.) was calculated to be:

$$M.V.A. (cm^2) = 0.0645 Q - 0.01$$

where Q is the quotient $\frac{FCO/P/m^2}{P.C.T.} \times 100$.

This formula was calculated from the regression equation (9,10)

$$(X - \bar{X}) = R \left(\frac{S_x}{S_y} \right) (Y - \bar{Y})$$

where:

X = Mitral valve area. M.V.A.

\bar{X} = Mean M.V.A. of the 23 cases studied.

Y = The quotient Q i.e., $\frac{FCO/P/m^2}{P.C.T.} \times 100$

\bar{Y} = Mean value of Q in the 23 cases studied.

S_x = Standard deviation of the observed values of X.

S_y = Standard deviation of the observed values of Y.

R = The calculated correlation coefficient between X and Y.

To assess the degree of uncertainty of such an estimation, we calculated its standard error (10) by the formula:

Standard error of estimated M.V.A. = $S_x \sqrt{1 - R^2}$, where S_x is the standard deviation of the observed values of the mitral valve area and R is the calculated correlation coefficient. The standard error proved to be 0.2 cm², that is to say, that in about 69% of calculation of the mitral valve area by this regression equation, the actual values will lie within plus or minus one standard error, i.e., 0.2 cm² of the estimate values given by the regression equation. In about 95% of the cases, the actual values of the mitral valve area will lie within plus or minus two standard errors, i.e., 0.4 cm² of the estimated value.

We proceeded to calculate the mitral valve area (M.V.A.) for each of our patients using this suggested radiocardiographic formula. Table III shows the actual as well as the calculated M.V.A., and the difference observed between both values in each of the cases studied. It can be seen that 10 estimations, i.e., 43.4% fell within ± 0.2 cm² of the actual mitral valve area, 17 estimations, i.e., 73.9%, within 0.4 cm², and 19 estimations, i.e., 82.6%, within ± 0.5 cm². In the remaining four cases, the differences between the calculated and the actual mitral valve area were 0.62, 0.65, 0.8 and 0.85 cm² respectively.

Duplicate radiocardiograms were performed for five patients preoperatively, on two separate occasions, one or more weeks apart, and the mitral valve area was calculated from the data of each radiocardiogram as shown in Table IV. It is obvious that the results of these duplicate estimations checked within 0.1 cm² in three cases, within 0.2 cm² in the fourth, and within 0.3 cm² in the fifth case, a reasonably good reproducibility.

It is evident that regression applies within the range of the observed data and we extrapolate always at our peril. The range of the mitral valve area observed in our cases and upon which our regression equation is based varied from 0.2 to 2.2 cm², a reasonably good range covering almost all grades from the mildest, to the extreme cases of mitral stenosis (11).

Nevertheless, we applied our suggested radiocardiographic formula for calculating the mitral valve area in the 12 normal subjects studied. The results are shown in Table V. The range of the calculated mitral valve area in these normal subjects varied from 2.62 to 5.99 cm² with an average value of 3.72 cm². These values seem to lie within a reasonable range between the cross-sectional area of the central pathway of the mitral valve (3 cm²) through which most of the blood normally enters the left ventricle (11), and the normal area of the fixed orifice of the mitral valve (12) of 5 cm². However, these estimations of the mitral valve area in the normal subjects lack confirmation, since their variability from the true values cannot be assessed.

Similarly, we applied the formula for the calculation of the mitral valve area in our 23 patients, from their post-operative radiocardiograms. The calculated post-operative mitral valve area for these patients was found to vary from 2.8-4.6 cm², with an average value of 3.2 cm². Although these values seem reasonable, the validity of these estimations could not be assessed, since we were unable to determine with sufficient accuracy the post-operative mitral valve area. Thus, deviation of the calculated from the true values of the mi-

tral valve area in these patients after commissurotomy could not be ascertained. We still are fully aware that regression applies within the range of the observed data and extrapolation is always at our peril. The post-operative mitral valve area is well above the range of the data upon which our regression equation was based. Yet, the increase in the calculated mitral valve area after the operation in the patients studied is obvious.

DISCUSSION

Before proceeding with the discussion, two technical objections are thought to be worthy of comment. First, in the estimation of the pulmonary circulation time as the interval between peaks, it might be objected that the injected dose arrives in the right ventricle more nearly as a bolus than it does in the left ventricle, since there is a descending limb to the right heart output which

TABLE III

<i>Ser.</i> <i>No.</i>	<i>M.V.A.</i>		<i>Difference</i> <i>calculated-Actual</i>
	<i>Actual</i>	<i>Calculated</i>	
1	0.9	0.74	-0.16
2	1.2	0.75	-0.45
3	0.7	0.93	+0.23
4	1.7	1.85	+0.15
5	0.9	0.97	+0.07
6	1.6	1.60	0
7	2.2	2.14	-0.06
8	0.8	0.40	-0.40
9	0.2	0.42	+0.22
10	1.4	0.75	-0.65
11	0.5	0.54	+0.04
12	0.9	0.88	-0.02
13	0.8	1.11	+0.31
14	0.4	1.25	+0.85
15	1.5	1.56	+0.06
16	1.2	1.25	+0.05
17	1.3	1	-0.30
18	1.40	1.43	+0.03
19	1.30	0.68	-0.62
20	2	2.01	+0.01
21	0.3	0.78	+0.48
22	0.5	0.24	-0.26
23	0.4	1.20	+0.80

Table III: Comparison between the actual mitral value area (M.V.A.) as estimated by the surgeon during operation and the calculated (Calc.) mitral value area using the suggested radiocardiographic formula in the 23 patients of mitral stenosis studied.

affects the rate at which it is seen to arrive at the left ventricle and that this would affect such an estimation of the P.C.T. Yet prolongation of the descending limb of the R wave was reported to occur in mitral stenosis (13) because of delayed right ventricular emptying as a result of the complicating pulmonary hypertension. This in fact was blamed as a cause of prolongation of the pulmonary circulation time in these cases (13). Since pulmonary hypertension correlates with the degree of mitral stenosis, prolongation of the descending limb of the right heart curve would therefore also show the same correlation. Correlation of the mitral valve area with the peak to peak P.C.T. would thus not be invalidated by such a change in the descending limb of the R wave.

In fact, we estimated the mean pulmonary circulation time (14), M.P.C.T. in our cases by the formula:

$$M.P.C.T. = \frac{S_{ct}}{S_c}$$

where S_{ct} is the sum of the product of concentration for the times in the interval between minimum and maximum times in the radiocardiographic curve, and S_c is the sum of concentrations. The M.P.C.T. showed the same correlation with the mitral valve area as the peak to peak P.C.T., and so we chose the latter for our calculations, since it is simpler and applying the more elaborate calculation of the M.P.C.T. would not serve our purpose to any greater extent.

The second technical objection may be in the projection of the D.L. to the base line. The curve would approach the base exponentially and technically never reach the base line. Yet, for practical purposes, it is seen to reach the base line at a reasonably defined point, allowing a reproducible measurement of the area inscribed by the primary dilution. In fact, such a technique was applied for cardiac output measurement by many workers in this field (15-22). Various workers have found that this method of cardiac output determination is capable of a high degree of reproducibility (23). This is also confirmed by the reasonable reproducibility of the calculation of the mitral valve area that we obtained from our data.

Various workers have reported various radiocardiographic findings in patients with mitral stenosis (24-28). Prolongation of the P.C.T. in mitral stenosis was observed by different investigators (24-27). Pietila and Hakkila (26) reported a significant correlation between the P.C.T. on one hand and both the relative radiologic heart size and the degree of impairment of physical performance on the other. Whitley *et al* (29), have shown that the fractional cardiac output per minute (FCO/min.) and the fractional stroke volume (FCO/P) were diminished in patients with mitral stenosis.

The present work has shown that the quotient $\frac{FCO/P/m^2}{P.C.T.} \times 100$ correlated well with the size of the mitral valve area. This phenomenon is explainable by the fact that the narrower the mitral orifice, the lesser would be the cardiac output and the longer the P.C.T., the lower the value of the quotient. On the other hand, the wider the mitral orifice, the higher the cardiac output and the shorter the P.C.T., the higher the value of the quotient. The determination of the cardiac output by this radiocardiographic technique is reliable and ca-

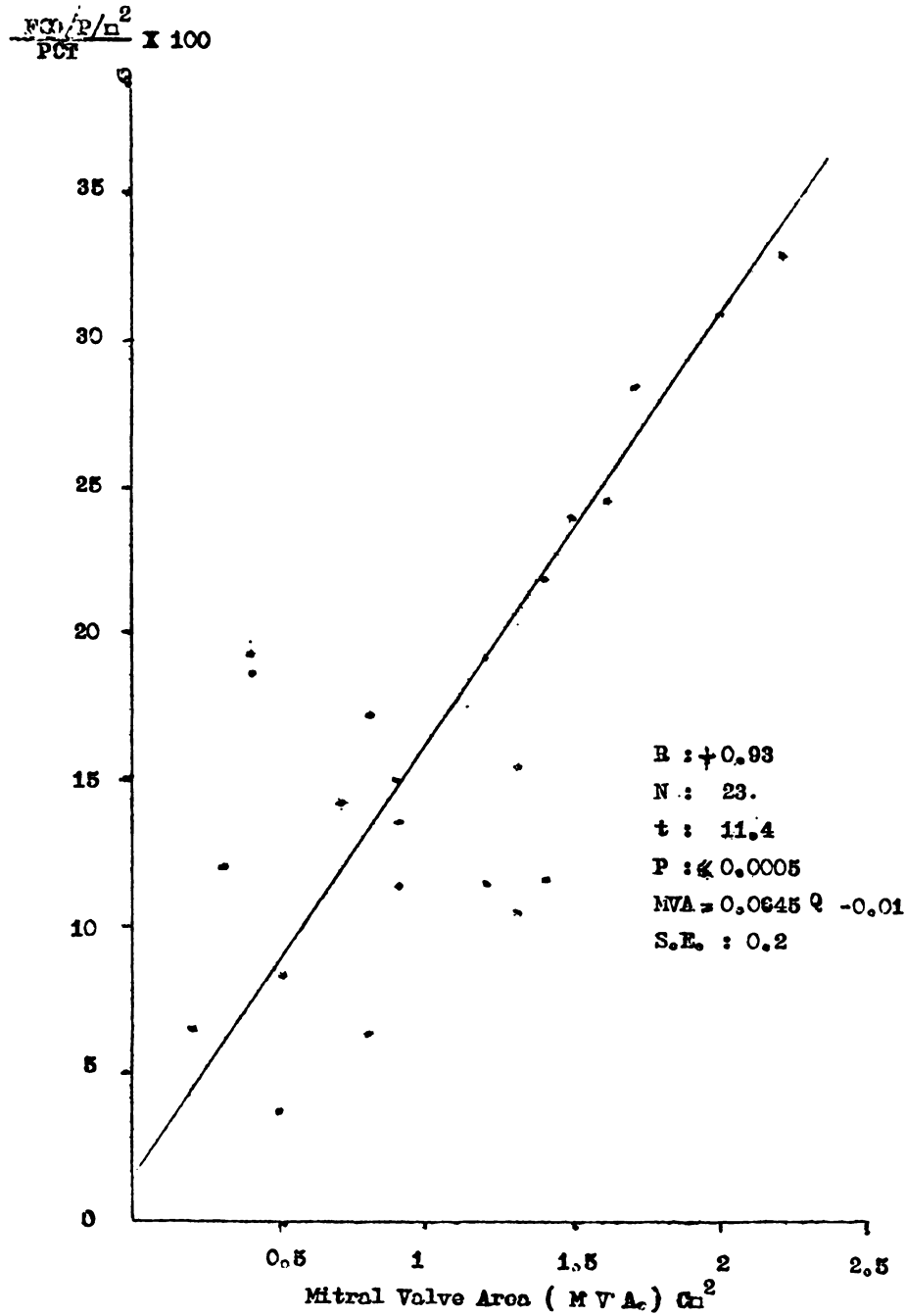


Fig. 3. Scatter Diagram showing the significant positive correlation between the quotient (Q) and the mitral valve area (MVA) in Cm² as estimated by the surgeon during operation in the 23 cases of mitral stenosis studied.

$$Q : \frac{FCO/P/m^2}{PCT} \times 100$$

FCO/P/m² : Fractional stroke volume per square meter body surface area

R : Calculated correlation coefficient. t : Computed t-statistic.

P : Level of significance of R. S.E. : Standard error. N : Number of cases.

pable of a high degree of reproducibility in human subjects (23), and even compares favorably with the Fick method (15,16,30-32).

Gorlin and Gorlin (23), introduced their well known hydraulic formula for the calculation of the area of the stenotic mitral valve. Whitley *et al* (29), described a radioisotopic approach to the estimation of mitral valve size. They suggested a special quotient -A-:

$$A = \frac{M.T.}{FCO/P.}$$

where M.T. or the mean transit time is the time interval between the mean appearances of the radioactive bolus in the heart and in the abdominal aorta, expressed as the number of ventricular systoles occurring in the interval (obtained from a simultaneous electrocardiographic tracing) and FCO/P is the fractional stroke volume.

These workers determined the fractional cardiac output by the same technique that we adopted in the present work. Their quotient could only separate mitral valve areas less than 1.5 cm² from mitral valve areas above that level in patients with mitral stenosis.

Our suggested radiocardiographic formula was shown to be able to calculate the mitral valve area in patients with mitral stenosis within the reasonable standard error of 0.2 cm² and showed a reasonable reproducibility on duplicate estimations. These levels compare favorably with those ascribed to the Gorlin's formula (33). Our suggested formula is, however, simpler than Gorlin's, which entails determination of the cardiac output by the direct Fick method, involving cardiac catheterization, arterial puncture and the collection of expired air, procedures that are all time-consuming and subject to technical difficulties (31). The

TABLE IV

Ser. Case No.	Actual M.V.A. Cm ²	1st Calc. M.V.A. Cm ²	2nd Calc. M.V.A. Cm ²	Difference between 1st & 2nd Calc. M.V.A. Cm ²
1	0.9	0.74	0.82	-0.08
6	1.6	1.60	1.54	+0.06
9	0.2	0.42	0.34	+0.08
13	0.8	1.11	0.91	+0.20
21	0.3	0.78	0.50	+0.28

Table IV: Duplicated calculations of the mitral valve Area (M.V.A.), computed from duplicate radiocardiograms performed on five patients prior to mitral commissurotomy.

M.V.A. = Mitral valve area as estimated by the surgeon during operation.

1st Calc. M.V.A. = Mitral valve area as calculated from the first radiocardiogram.

2nd Calc. M.V.A. = Mitral valve area as calculated for the same patient from a second radiocardiogram.

present technique entails only the simple intravenous injection of a radioisotope and precordial recording of the radiocardiogram, procedures that are non-disturbing, convenient and time-saving for both the patient and the investigator. With regard to the question of risk to the patient from irradiation, the dose administered by the isotope technique is much less than that from the fluoroscopic screening needed for cardiac catheterization (31) necessary to determine the different parameters of the Gorlin's formula. The practical clinical applications of the suggested formula for the selection of cases of mitral stenosis for surgery and for the appraisal of operative procedures on the mitral valve are obvious.

It must be noted, however, that neither the increase in the P.C.T., nor the decrease in the fractional stroke volume are diagnostic of mitral stenosis. Similar changes are expected to occur in other affections, e.g., in any of the conditions associated with pulmonary hypertension. The radiocardiogram is therefore not intended to be used for the diagnosis of the presence or absence of mitral stenosis in any case. The formula suggested is applied to estimate the mitral valve area only in cases in whom the diagnosis of pure mitral stenosis has been established on clinical and other grounds.

TABLE V

<i>Serial Number</i>	<i>FCO/P/m²</i>	<i>P.C.T. Secs.</i>	<i>Quotient (Q)</i>	<i>Calculated M.V.A. cm²</i>
1	1.92	4	48	3.09
2	1.95	4.6	42.4	2.73
3	2.38	5	47.6	3.08
4	2.44	4	61	3.93
5	2.02	3.4	59.2	3.82
6	1.85	3	61.7	3.97
7	1.63	4	40.75	2.62
8	2.37	4.5	52.7	3.39
9	1.57	4	39.25	2.52
10	3.16	5	63.2	4.09
11	4.20	4.5	93	5.99
12	3.37	4	84.25	5.44

Table V: Showing the calculated M.V.A. in 12 normal subjects using the suggested radiocardiographic formula.

FCO/P/m²: Fractional stroke volume per square metre body surface area.

P.C.T.: Peak to peak pulmonary circulation time.

Quotient (Q): $\frac{\text{FCO/P/m}^2}{\text{P.C.T.}} \times 100$.

M.V.A.: Mitral Value Area.

SUMMARY AND CONCLUSIONS

Twenty-three patients with pure mitral stenosis were studied with radiocardiography and their mitral valve area (M.V.A.) measured by the surgeon during commissurotomy. A significant correlation existed between two radiocardiographic informations and the mitral valve area. These were the fractional stroke volume per square metre of body surface area ($FCO/P/m^2$) and the pulmonary circulation time (P.C.T.). Since these two parameters vary in opposite directions, a quotient (Q) combining them as:

$$\frac{FCO/P/m^2}{P.C.T.} \times 100$$

was suggested and was found to show a higher and more significant correlation with the mitral valve area. From this quotient, a radiocardiographic formula for the calculation of the area of the stenotic mitral valve was worked out. This formula is:

$$M.V.A. (cm^2) = 0.0645 Q - 0.01$$

The formula was shown to be able to calculate the mitral valve area in patients with mitral stenosis within the reasonable standard error of 0.2 cm² and showed a reasonable reproducibility on duplicate estimations. Although it could not be checked, it could also calculate the mitral valve area in the 23 patients studied after commissurotomy and in 12 normal subjects within a reasonable range.

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