A Simple Phonocardiographic Formula for Predicting Left Atrial Pressure in Mitral Stenosis

J. P. H. DAVIES*

From Cardiac Department, King's College Hospital, London, S.E.5

In 1862, Duroziez described the rhythm of pre-systolic reinforcement, split second sound, rumbling diastolic murmur, and absent systolic murmur in mitral stenosis. He likened the rhythm to "ffou-ta-ta-roù" and thought that the reduplication of the second sound, described originally by Bouillaud (1835), might be due to asynchronous closure of the aortic and pulmonary valves. But it was Guttman (1872), and later Sansom (1881), who first attributed the origin of the sound to vibration of the mitral valve. Then in 1888, Rouchés used the term "claquement d'ouverte de la mitrale". He suggested that the sound was produced by sudden limitation of the opening of the valve as blood flowed from the left atrium to the ventricle. Forty-four years later in a classic paper on the opening snap, Margolies and Wolferth (1932) reached the same conclusion.

Not until the advent of cardiac catheterization and phonocardiography has the importance of the opening snap been appreciated. In 1953 Mounsey described its characteristics and concluded that it was a useful diagnostic sign of mitral stenosis occurring 0.03 to 0.12 second (mean = 0.07 sec.) after closure of the aortic valve (A_2 -OS interval). Obviously in the absence of disease, the snap is inaudible but Luisada *et al.* (1958), using simultaneous tracings of the apex cardiogram, carotid arterial pulse, and phonocardiogram, found the normal A_2 -OS interval to be 0.09 to 0.14 second. Even when mitral stenosis is present, the opening snap may be absent if the valve is heavily calcified (Dack *et al.*, 1960), or severe pulmonary arterial hypertension or aortic incompetence is present (Wood, 1954).

Nevertheless the timing of the opening snap has

been used as an index to the severity of mitral stenosis (Wells, 1954, 1957; Bayer, Loogen, and Wolter, 1956; Julian and Davies, 1957). Thus in mitral stenosis, the raised left atrial pressure exceeds the falling left ventricular pressure earlier than normally. At this point the mitral valve opens (Fig. 1). In general, then, the shorter the A_2 -OS interval, or period of isometric relaxation, the tighter the stenosis.

The first heart sound in mitral stenosis is loud, short, and snapping. The sound is due probably to the anterior leaflet of the valve tensing and buckling with left ventricular contraction. In contrast to the shortened A_2 -OS interval in mitral stenosis, the mitral component of the first sound is delayed (Weiss and Joachim, 1911). Thus in mitral stenosis, the raised left atrial pressure is exceeded by the rising left ventricular pressure later than normally. At this point the mitral valve closes (Fig. 1). Clearly such a delay cannot be heard but can be timed from the onset of the Q wave of the electrocardiogram (Q-1 interval). Normally the Q-1 interval is 0.02 to 0.06 sec., but in mitral stenosis it may be increased to 0.04 to 0.10 sec. (Kelly, 1955).

Despite attempts by Wells (1954, 1957) and Craige (1957) to relate both the timing of the opening snap and the delay of the first heart sound to the severity of the mitral stenosis, Leatham (1958) thought that the factors responsible for the pressure relationships were too numerous to allow serious use of these intervals. Nevertheless the author has attempted to demonstrate a mathematical relation between the timing of the opening snap and the delay of the first heart sound to the left atrial pressure in mitral stenosis.

SUBJECTS AND METHODS

Studies were made of 50 patients (9 men, 41 women) with pure mitral stenosis. In 25, the pulmonary vascular

Received April 7, 1966.

* Present address: Redhill Central Hospital, Earlswood Common, Redhill, Surrey.

FIG. 1.—Timing of the mitral component of the first heart sound (IS) and the opening snap (OS). As the rising left ventricular pressure (LVP) exceeds the left atrial pressure (LAP) at Z, the mitral valve (MV) shuts, helping to produce the first heart sound. This can be timed from the Q wave of the electrocardiogram (ECG II), the Q-I interval. As the decreasing left ventricular pressure falls below the left atrial pressure at V, the mitral valve opens to produce the opening snap. This can be timed from the aortic valve (AV) component (A_2) of the second heart sound, the A_2 -OS interval, using the phonocardiogram (PCG).

resistance was greater than 2 units or 160 dynes per second per cm^{-5} , and of these 10 had resistances greater than 5 units. Twenty-five of the patients were in sinus rhythm, and atrial fibrillation was present in the remainder (25).

Right heart catheterization was done in all the patients, each having fasted and been given 200 mg. quinalbarbitone one hour before investigation. Pressures were recorded in mm. Hg, using a Statham strain gauge

(P23DB) and a New Electronics Products Photographic recorder with a paper speed of 25 mm. a second. The zero point of reference for all pressures was the sternal angle. The "wedged" pulmonary arterial pressure pulse was recorded during expiration, being assumed to be equivalent to that from the left atrium (Epps and Adler, 1953), and its mean was obtained by electronic integration. The pulmonary vascular resistance was calculated on each occasion using Poiseuille's formula,

FIG. 2.—Histogram of the Q-1 and A₂-OS intervals in the fifty patients with mitral stenosis. Q-1: range=0.06–0.12 sec.; mean=0.08 sec.; A₂-OS: range=0.04–0.12 sec.; mean=0.08 sec.

the cardiac output having been obtained by the Fick principle.

High frequency phonocardiograms, using a crystal microphone and a direct current amplifier, were recorded from the left fourth intercostal space close to the sternum in all patients at rest. Records were obtained during expiration, to distinguish the opening snap from splitting of the second sound, using a New Electronics Products Photographic recorder with a paper speed of 80 mm. a second.

Timing of events at both catheterization and phonocardiography was obtained by a simultaneous recording of lead II of the electrocardiogram. In addition at phonocardiography, the carotid arterial pulse was

recorded, the incisura being used to identify the aortic component of the second sound.

In all patients the height of the “Z” and “V” waves, corresponding respectively to the closing and opening of the mitral valve, and the mean pressure in the “wedged” pulmonary arterial tracing were measured in mm. Hg. The delay of the mitral component of the first heart sound was measured from the beginning of the QRS complex of the electrocardiogram to the first major component of the first heart sound (Q-1 interval). The timing of the opening snap was measured from the beginning of the aortic component of the second sound to the beginning of the opening snap (A₂-OS interval). The mean of five such measurements was used to obtain each interval.

FIG. 3.—Scattergram of the left atrial “Z” and “V” waves in mm. Hg plotted respectively against the Q-1 and A₂-OS intervals in seconds. No linear relation can be discerned. Key: ●=Q-1; ○=A₂-OS. The figure 2 or 3 alongside a particular point means that point represents 2 or 3 patients, respectively.

RESULTS

In the 50 patients the mean Q-1 interval was 0.08 sec. (0.06 to 0.12 sec.) as was the mean A₂-OS interval (0.04 to 0.12 sec.). Twelve patients had a Q-1 interval shorter than 0.08 sec. and 15 an A₂-OS interval longer than 0.09 sec. (Fig. 2).

Although the Q-1 interval varied directly with the left atrial "Z" wave, a wide scatter was present so that no linear relation could be discerned (Fig. 3).

Similarly, while the A₂-OS interval varied inversely with the peak of the left atrial "V" wave, a wide scatter was again present, so that no linear relation could be discerned (Fig. 3).

Since in mitral stenosis the Q-1 interval is prolonged and the A₂-OS interval shortened, it seemed reasonable to examine the relationship between the difference between these two parameters

$$\{(Q-1) - (A_2-OS)\}$$

and the mean of the sum of the left atrial "Z" and

"V" waves $\frac{(Z+V)}{2}$. A clear linear relation can be

observed between the difference between the A₂-OS and Q-1 intervals and the mean of the sum of the left atrial "Z" and "V" waves (Fig. 4). Accordingly the numerical data have been evaluated statistically.

Statistical note:—Let x and y stand for the variates $\{(Q-1) - (A_2-OS)\}$ and $\frac{(Z+V)}{2}$ under investigation and

$\bar{x}$ and $\bar{y}$ their respective means given by the equations:

$$\bar{x} = \frac{\sum x}{n} \quad \text{and} \quad \bar{y} = \frac{\sum y}{n} \quad \text{I}$$

where n is the number of observations, then the coefficient of correlation (r) between the two variates is given by the equation:

$$r_{xy} = \frac{\sum \{(x - \bar{x})(y - \bar{y})\}}{\sqrt{\sum (x - \bar{x})^2 \sum (y - \bar{y})^2}} \quad \text{II}$$

Since the observations involved ungrouped numbers and decimals, deviations from the mean or $(x - \bar{x})$ have not been calculated. Instead the product xy has been used and a correction applied:

$$\sum \{(x - \bar{x})(y - \bar{y})\} = \sum (xy) - \left\{ \frac{\sum (x) \sum (y)}{n} \right\} \quad \text{III}$$

$$\text{Also} \quad \sum (x - \bar{x})^2 = \sum (x^2) - \frac{(\sum x)^2}{n} \quad \text{IV}$$

Substituting:

$$r_{xy} = \frac{\sum (xy) - \left\{ \frac{\sum (x) \sum (y)}{n} \right\}}{\sqrt{\left\{ \sum (x^2) - \frac{(\sum x)^2}{n} \right\} \left\{ \sum (y^2) - \frac{(\sum y)^2}{n} \right\}}} \quad \text{V}$$

its standard error being

$$\frac{1}{\sqrt{n-1}} \quad \text{VI}$$

The regression equation ($y = mx + c$) for the relationship between y and x is given by:

$$y - \bar{y} = r \left\{ \frac{\sigma y}{\sigma x} (x - \bar{x}) \right\} \quad \text{VII}$$

FIG. 4.—Relationship of the mean of the sum of the left atrial "Z" and "V" waves in mm. Hg to the difference between the Q-1 and A₂-OS intervals in seconds. A linear relation can be discerned.

Key:—The figure 2 or 3 alongside a particular point means that point represents 2 or 3 patients, respectively.

where σ is the standard deviation of the variate and is given by the equation:

$$\sigma = \sqrt{\left\{ \sum(x^2) - \frac{(\sum x)^2}{n} \right\} / n - 1} \quad \text{VIII}$$

using Fisher's correction ($n-1$) as the number of observations was only 50 and tests of significance were to be applied.

Substituting values for $\bar{y}$ and $\bar{x}$, their standard deviations, and r , the regression equation for the relationship between $\frac{(Z+V)}{2}$ and $\{(Q-1)-(A_2-OS)\}$

is $\frac{(Z+V)}{2} = 231 \{(Q-1)-(A_2-OS)\} + 17.4$, the mean of $\frac{(Z+V)}{2}$ being 18.8 ± 7.6 mm. Hg, and the mean of $\{(Q-1)-(A_2-OS)\}$ 0.0058 ± 0.024 second.

The coefficient of correlation (r) is 0.73 and is significant since r is at least five times as great as its standard error (0.14) and $p < 0.001$ for 50 observations and 48 degrees of freedom.

DISCUSSION

The assessment of the severity of mitral stenosis depends upon obtaining a number of symptoms, signs, and results of investigations and their correct

interpretation. Final evaluation requires the measurement of the gradient across the mitral valve which can only be obtained by left heart catheterization and in any case must be correlated with the cardiac output.

Wells (1954) was attracted first to the possibility of assessing the degree of mitral stenosis by the relatively simple technique of phonocardiography. Three years earlier Messer *et al.* (1951) had shown that in mitral stenosis complicated by atrial fibrillation, the Q-1 interval varied inversely and the A_2-OS interval directly with the preceding cycle length. Thus with a long diastolic pause, emptying of the left atrium can occur across the mitral valve, so reducing the gradient across the valve at the next beat. Consequently the Q-1 interval is shortened and the A_2-OS interval lengthened (Fig. 5). Uncontrolled atrial fibrillation with or without exercise with a resultant tachycardia, both of which shorten diastole, may not allow time for the left atrium to empty through a mitral valve that with normal rates is adequate. Thus the left atrial pressure rises as does the gradient across the mitral valve so that the first heart sound occurs later and the opening snap earlier (Fig. 6).

Accordingly Wells corrected his measurements in patients with atrial fibrillation for a cycle length of 0.8 sec. While admitting that the cardiac output

FIG. 5.—Simultaneous tracings of the left atrial (LAP) and ventricular (LVP) pressures in mitral stenosis complicated by atrial fibrillation. After a long diastolic pause, the gradient across the mitral valve falls.

Fig. 6. a and b.

FIG. 6.—Effect of exercise in two patients with mitral stenosis, one in sinus rhythm (a, b), the other with atrial fibrillation (c, d). In both (b, d) the left atrial pressure (LAP) rises so that the Q–I interval is lengthened and the A₂–OS interval shortened. In the patient in sinus rhythm (b), a low frequency diastolic murmur (MDM) with pre-systolic accentuation (PSM) appears at the lower sternal edge (PCG, LSE).

Fig. 6. c and d. Legend opposite.

and level of systemic arterial pressure might influence such observations, he found that values of -1 and greater for the difference between the A_2 -OS and Q-1 intervals suggested severe mitral stenosis. Three years later Wells (1957) suggested that the mean gradient across the mitral valve at operation

might be predicted from these measurements. From the duration of systole per minute he thought that a simpler but less accurate assessment might be made. In neither paper were any regression equations calculated, and from the scatter of his observations these would not be valid.

The same year, Julian and Davies (1957) in an analysis of the factors affecting the timing of the opening snap and the delay of the first heart sound pointed out that these were unrelated to the mean left atrial pressure. Neither the A_2 -OS or Q-1 intervals indicate the mean left atrial pressure or mean gradient across the mitral valve in ventricular diastole. Wells (1957) too had thought that this might be so, and Rich (1959) has shown that it is the level of the left atrial pressure at the onset of diastole that determines the timing of the opening snap. Left atrial and ventricular tracings combined with simultaneous intra- and extracardiac phonocardiograms show that the gradient across the mitral valve at the instant of the opening snap ranges from 2 to 9 mm. Hg, with a mean of 5 mm. Hg (Di Bartolo, Núñez-Dey, and Bende-zú-Prieto, 1962). Clearly, in routine studies, less direct reference tracings must be obtained, and for this purpose the left ventricular apex cardiogram has proved valuable (Ongley, Sprague, and Rappaport, 1955). The o-point of the apex cardiogram coincides with the opening of the mitral valve, while aortic valve closure can be identified by means of the incisura as seen in a carotid arterial pulse tracing.

The three factors upon which the timing of the opening snap depends are the rate of fall of the left ventricular pressure, and the height of the aortic and left atrial pressures (Fig. 1). Consequently systemic arterial hypertension prolongs (Julian and Davies, 1957) and mitral incompetence shortens (Rich, 1959) the A_2 -OS interval. Conversely, the timing of the mitral component of the first heart sound depends on the rate of rise of the left ventricular pressure and the height of the left atrial pressure (Fig. 1). Consequently a short electro-mechanical interval (Kelly, 1955) and mitral incompetence (Wells, 1954) may shorten the Q-1 interval.

In summary then, the A_2 -OS interval is inversely proportional and the Q-1 interval directly proportional to the left atrial "V" and "Z" waves, respectively. Successful mitral valvotomy by reducing the gradient across the mitral valve can restore the A_2 -OS and Q-1 intervals to normal (Kelly, 1955).

Despite the obvious limitation of phonocardiography in the assessment of mitral stenosis, an equation which is highly significant ($r=0.73$; S.E. = 0.14) can be predicted for assessing the mean of the left atrial "Z" and "V" waves in terms of the difference of the Q-1 and A_2 -OS intervals:

$$\frac{(Z+V)}{2} = 231\{(Q-1) - (A_2-OS)\} + 17.4.$$

Nevertheless where mitral stenosis is complicated by other valvular lesions such as mitral or aortic

incompetence, or systemic or pulmonary arterial hypertension, the equation is not valid, and further investigations such as catheterization and angiocardiography are required to assess the severity of the valvular obstruction.

SUMMARY

The severity of uncomplicated mitral stenosis can be predicted by the difference between the delay of the mitral component of the first heart sound and the timing of the opening snap. The expression

$$\frac{(Z+V)}{2} = 231\{(Q-1) - (A_2-OS)\} + 17.4$$

can be used to assess the degree of mitral stenosis.

I wish to thank Dr. Samuel Oram for his advice and criticism in the preparation of this paper, and the technicians of the Cardiac Department at King's College Hospital for their help.

REFERENCES

- Bayer, O., Loogen, F., and Wolter, H. H. (1956). The mitral opening snap in the quantitative diagnosis of mitral stenosis. *Amer. Heart J.*, **51**, 234.
- Bouillaud, J. (1835). *Traité Clinique des Maladies du Cœur, Précédé de Recherches Nouvelles sur l'Anatomie et la Physiologie de cet Organe*. Baillière, Paris.
- Craige, E. (1957). Phonocardiographic studies in mitral stenosis. *New Engl. J. Med.*, **257**, 650.
- Dack, S., Bleifer, S., Grishman, H., and Donoso, E. (1960). Mitral stenosis. Auscultatory and phonocardiographic findings. *Amer. J. Cardiol.*, **5**, 815.
- Di Bartolo, G., Núñez-Dey, D., and Bende-zú-Prieto, J. (1962). Left heart studies in mitral stenosis with special reference to intracardiac phonocardiography. *Amer. J. Cardiol.*, **10**, 93.
- Duroziez, P. L. (1862). Essai sur les maladies du cœur, du rythme pathognomonique, du rétrécissement mitral. *Arch. gén. Med.*, **20**, 385.
- Epps, R. G., and Adler, R. H. (1953). Left atrial and pulmonary capillary venous pressures in mitral stenosis. *Brit. Heart J.*, **15**, 298.
- Guttmann, P. (1872). *Lehrbuch der Klinischen Untersuchungs, Methoden für die Brust- und Unterleibs-Organen*, p. 257. A. Hirschwald, Berlin.
- Julian, D., and Davies, L. G. (1957). Heart sounds and intracardiac pressures in mitral stenosis. *Brit. Heart J.*, **19**, 486.
- Kelly, J. J. (1955). Diagnostic value of phonocardiography in mitral stenosis: mode of production of first heart sound. *Amer. J. Med.*, **19**, 862.
- Leatham, A. (1958). Auscultation of the heart. *Lancet*, **2**, 703.
- Luisada, A. A., Liu, C. K., Aravanis, C., Testelli, M., and Morris, J. (1958). On the mechanism of production of the heart sounds. *Amer. Heart J.*, **55**, 383.
- Margolies, A., and Wolferth, C. C. (1932). The opening snap (claquement d'ouverture de la mitrale) in mitral stenosis, its characteristics, mechanism of production and diagnostic importance. *Amer. Heart J.*, **7**, 443.

- Messer, A. L., Counihan, T. B., Rappaport, M. B., and Sprague, H. B. (1951). The effect of cycle length on the time of occurrence of the first heart sound and the opening snap in mitral stenosis. *Circulation*, **4**, 576.
- Mounsey, P. (1953). The opening snap of mitral stenosis. *Brit. Heart J.*, **15**, 135.
- Ongley, P. A., Sprague, H. B., and Rappaport, M. B. (1955). The diastolic murmur of mitral stenosis. *New Engl. J. Med.*, **253**, 1049.
- Rich, C. B. (1959). The relationship of heart sounds to left atrial pressure. *Canad. med. Ass. J.*, **81**, 800.
- Rouchés, F. J. M. (1888). *Du claquement d'ouverture de la mitrale, étude clinique, séméiologique et pathogénique*. Thesis, Paris.
- Sansom, A. E. (1881). On the causes and significance of reduplication of the sounds of the heart. *Proc. med. Soc. Lond.*, **5**, 191.
- Weiss, O., and Joachim, G. (1911). Registrierung von Herztönen und Herzgeräuschen mittels des Phonoskops und ihre Beziehungen zum Elektro-cardiogramm. *Z. klin. Med.*, **73**, 240.
- Wells, B. (1954). The assessment of mitral stenosis by phonocardiography. *Brit. Heart J.*, **16**, 261.
- (1957). Prediction of mitral pressure gradient from heart sounds. *Brit. med. J.*, **1**, 551.
- Wood, P. (1954). An appreciation of mitral stenosis. Part I. Clinical features. *Brit. med. J.*, **1**, 1051.