Factors responsible for normal splitting of first heart sound

High-speed echophonocardiographic study of valve movement

NICHOLAS BROOKS, GRAHAM LEECH, AND AUBREY LEATHAM

From St George's Hospital, Hyde Park Corner, London

SUMMARY Echocardiographic studies have confirmed that normal splitting of the first heart sound is a result of mitral valve closure preceding tricuspid valve closure. This fits in with contraction of the left ventricle before the right, but the width of splitting is usually greater than would be expected from the known ventricular asynchrony. The importance of atrial systole, which initiates closure of the atrioventricular valves, has not been considered. In this study of 67 normal subjects, high-speed echophonocardiograms were recorded and the timing of mitral and tricuspid valve closure was related to the PR interval and the beginning of left and right ventricular ejection.

The timing of mitral valve closure was strongly influenced by the PR interval; in patients with a long PR interval the valve leaflets were nearly apposed by atrial systole and closure was completed early after the Q wave on the electrocardiogram, while with a short PR interval the leaflets were still widely separated at the time of ventricular activation and closure was completed later. The timing of tricuspid closure was affected similarly but less strongly, and even when the PR interval was so long that mitral closure was complete before the onset of left ventricular systole, tricuspid closure occurred up to 48 ms later. The mean interval between mitral and tricuspid closure was 34 ms. Thus mitral closure was effected nearer the onset of left ventricular systole than was tricuspid closure in relation to the onset of right ventricular systole, and this accounts for the surprising width of splitting of the first sound. Variations in splitting of the first sound were mainly the result of variations in the timing of tricuspid rather than of mitral closure. When tricuspid closure was delayed, so was pulmonary valve opening, suggesting that the cause was delay in the onset of right ventricular systole or a slower rate of pressure development in the right ventricle.

It was postulated by Dock (1933) that the major components of the first heart sound were the result of tensing of the atrioventricular valves after the rise in ventricular pressure at the onset of systole. Simultaneous high frequency sound recordings from the apex and lower left sternal edge together with an indirect carotid pulse tracing led to the conclusion that splitting of the first sound into two components was commonly found in normal subjects, and that mitral closure preceded tricuspid (Leatham, 1954). This view has been challenged and tricuspid closure reported to be silent (Luisada *et al.*, 1974), but simultaneous echo- and phonocardiograms ('echophonocardiograms') have shown

exact coincidence between the final halt of the closing mitral valve and the onset of the first major component of the first sound, and between tricuspid valve closure and the onset of the second group of high-frequency vibrations (Burggraf and Craige, 1974; Leatham and Leech, 1974; Waider and Craige, 1975). Using echophonocardiography it is possible for the first time to identify the two components with certainty, and it is therefore opportune to re-examine the factors responsible for physiological splitting of the first heart sound.

Wide splitting of the first sound in bundle-branch block and during artificial pacing results from asynchronous ventricular contraction (Wolferth and Margolies, 1935; Haber and

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Leatham, 1965; Brooks *et al.*, 1979), but obvious splitting is also found in some normal subjects and it is not known whether or not this, too, is caused by ventricular asynchrony. Since atrioventricular valve closure is initiated by atrial contraction and relaxation (Henderson and Johnson, 1912; Little *et al.*, 1954; Zaky *et al.*, 1969), the timing of the two components of the first sound is also affected by the PR interval, and this important variable factor has not been taken into account in previous studies. In the present study high-speed simultaneous recordings of the echo- and phonocardiogram were used to assess the extent to which normal splitting of the first heart sound is affected by asynchronous ventricular contraction and by the effects of left and right atrial contraction on mitral and tricuspid valve closure, respectively.

Methods

We studied 67 normal subjects. Their ages ranged from 19 to 56 (mean 32) years and there were 27 men and 40 women. The three standard bipolar limb leads of the electrocardiogram were recorded simultaneously at four times normal calibration (1 mV=4 cm) and at a paper speed of 100 mm/s. The lead showing the earliest QRS deflection was selected for recording with the echophonocardiogram.

Echocardiograms were recorded on a Smith-Kline Ekoline 20 ultrasonoscope interfaced with a Cambridge six-channel photographic recorder. The system was modified to double its echo-depth magnification and increase the maximum paper speed to 200 mm/s. These adaptations permit resolution of tissue depth to 0.5 mm and time intervals to 2.5 ms.

The four heart valves were identified by standard echocardiographic techniques. Care was taken to record the moment of closure of the mitral and tricuspid valves, this being defined as the point of apposition of the anterior and posterior leaflets. Sometimes it was not possible to demonstrate two tricuspid valve leaflets, and a definite 'shoulder' on one was accepted. The technique for demonstrating tricuspid valve closure, and the typical appearance obtained, is described in detail elsewhere (Brooks *et al.*, 1979). For the aortic valve recording, the transducer position was adjusted to show separation of the valve cusps at the onset of ventricular ejection. It is usually possible to identify only one pulmonary valve cusp (the posterior), so that the moment of onset of right ventricular ejection cannot be defined precisely. For this reason recordings were made which showed the full extent of its opening movement. This point is often marked by a well-defined

'shoulder' as the rapid posterior movement is arrested and the cusp begins to move slowly anteriorly; when this shoulder was not seen the point at which the cusp echoes merge with those from the posterior wall of the right ventricular outflow tract was recorded. Previous studies have shown that this point can be defined consistently with little interobserver variation (Mills *et al.*, 1975).

A high-frequency phonocardiogram with the microphone positioned to detect both major components of the first sound was recorded simultaneously with the echocardiogram. The best microphone position was usually at the lower left sternal edge, but in a number of cases a site nearer to the apex was optimal. In subjects with a single first sound the left sternal edge position was used.

All recordings were made in shallow held expiration with maximal magnification of the echo display and at 200 mm/s paper speed.

MEASUREMENTS

The PR interval was measured on the simultaneous three-lead electrocardiogram from the onset of P to the onset of QRS using the leads which gave the earliest deflections. The mean of five cycles was expressed to the nearest 5 ms. Heart rate was measured on the echophonocardiogram. The following echocardiographic intervals were determined:

- (1) From the onset of the QRS complex to the earliest point of coaptation of the mitral leaflets at the moment of valve closure (Q-MC).
- (2) From the onset of the QRS complex to tricuspid valve closure (Q-TC).
- (3) From the onset of the QRS complex to the earliest separation of the aortic valve leaflets (Q-AO).
- (4) From the onset of the QRS complex to complete opening of the pulmonary valve (Q-POm).

Measurements were made with a hair-line cursor to the nearest 0.5 mm (2.5 ms) in a minimum of five cardiac cycles and the mean value was expressed to the nearest millisecond. When the Q wave was poorly defined for a particular beat, measurements were made from the peak of the R wave and the Q to R time was added.

Fig. 1 shows echocardiograms of all four heart valves with a simultaneous electrocardiogram and phonocardiogram from a single subject to illustrate the recordings and measurements.

Statistical calculations were carried out on a Hewlett-Packard 9810A calculator using standard formulae.

Results

TIMING OF MITRAL AND TRICUSPID VALVE CLOSURE

Technically satisfactory recordings of the mitral

valve were made in all 67 subjects, of the tricuspid valve in 63 subjects, and of the phonocardiogram in 58 subjects.

The mitral valve closed before the tricuspid valve in all cases. In 45 subjects there were two identi-

Fig. 1 Echocardiograms of the mitral, tricuspid, pulmonary, and aortic valves recorded with a simultaneous electrocardiogram and phonocardiogram from a normal subject. MC, mitral valve closure; TC, tricuspid valve closure; AO, onset of aortic valve opening; POm, maximal opening of pulmonary valve; M1, mitral component of first heart sound; T1, tricuspid component of first heart sound. Time lines 40 ms.

fiable high-frequency components of the first sound on the phonocardiogram; the onset of the first component (M1) coincided exactly with mitral closure on the echocardiogram and the onset of the second component (T1) coincided with tricuspid closure (Fig. 1). In seven out of the eight subjects with a single first sound its onset was synchronous with mitral closure and the tricuspid valve closed so soon afterwards that T1 was presumed to be superimposed on M1. In one individual with a PR interval of 220 ms, the mitral valve closed silently 27 ms after the Q wave; a single sound occurred 42 ms later and coincided with tricuspid valve closure (Fig. 2). In five subjects, all of whom had PR intervals of 190 ms or longer, neither M1 nor T1 could be recorded.

Mean Q-MC was 54 ms (SD 13), but the timing of mitral closure was influenced strongly by the PR interval. When the PR interval was long valve closure occurred soon after the QRS onset (short Q-MC) because of previous partial apposition of the cusps caused by atrial contraction and relaxation.

Fig. 2 Echocardiograms of the mitral and tricuspid valves with a simultaneous phonocardiogram from a subject with a PR interval of 220 ms. The recordings have been aligned on the QRS complex of the electrocardiogram and show early, silent mitral valve closure with the single first sound occurring synchronously with tricuspid valve closure. Abbreviations as in Fig. 1.

With short PR intervals the cusps were less closely apposed at the onset of ventricular contraction and Q-MC was long. There was a highly significant inverse linear correlation between Q-MC and PR interval (Fig. 3). The equation of the line is:

$$Q-MC = -0.67. PR + 158$$

($r = -0.72$, $P < 0.001$).

Fig. 3 The relation between PR interval and the timing of mitral valve closure (Q-MC).

The timing of valve closure was not significantly affected by heart rate, the correlation coefficient between Q-MC and heart rate being -0.27 and the partial correlation coefficient (keeping PR interval constant) -0.41 .

The PR interval had a similar effect on the timing of tricuspid valve closure, but there was an important difference from the mitral valve. There was a highly significant correlation between Q-TC and PR interval (Fig. 4) given by the equation

$$Q-TC = -0.45. PR + 155$$

($r = -0.6$, $P < 0.001$), but the slope of this line is significantly less steep than that of the Q-MC/PR interval relation ($P < 0.05$). In other words, right atrial contraction and relaxation was less effective than that of the left in closing its atrioventricular valve. Like the mitral valve the timing of tricuspid closure was unaffected by heart rate.

In order to compare the timing of mitral and tricuspid valve closure between subjects with different PR intervals, Q-MC and Q-TC indices, in which the timing of valve closure is corrected to an arbitrary PR interval of 160 ms, were calculated from the regression coefficients using the equations:

$$\text{Q-MC index} = \text{Q-MC} + 0.67. \text{ PR} - 107$$

$$\text{Q-TC index} = \text{Q-TC} + 0.45. \text{ PR} - 72.$$

Mean Q-MC index was 48 ms (SD 10 ms) and mean Q-TC index was 84 ms (SD 13 ms).

Mean MC-TC, the interval between closure of the mitral and tricuspid valves, was 34 ms (SD 10 ms). Though the timing of mitral and tricuspid closure was affected unequally by variations in the PR interval there was no significant correlation between MC-TC and PR interval because of the wide scatter of the results. MC-TC showed no tendency to shorten at longer PR intervals. Fig. 5 shows the Q-MC and Q-TC intervals in seven subjects with PR intervals of 180 ms or longer: MC-TC ranged from 18 to 48 ms.

TIMING OF AORTIC AND PULMONARY VALVE OPENING

Satisfactory recordings of the aortic valve were made in 45 subjects and of the pulmonary valve in 47 subjects.

Mean Q-AO was 94 ms (SD 16 ms). There was

Fig. 4 The relation between PR interval and the timing of tricuspid valve closure (Q-TC).

Fig. 5 The Q-MC, Q-TC, and MC-TC intervals in seven subjects with PR intervals equal to or exceeding 180 ms.

no significant correlation between the timing of aortic opening and heart rate.

Mean Q-POM was 126 ms (SD 13 ms) and there was a weak ($r = -0.51$) but highly significant ($P < 0.001$) linear correlation between the timing of pulmonary valve opening and heart rate (Fig. 6). The equation of the line is:

$$\text{Q-POM} = -0.58 (\text{heart rate}) + 165.$$

To compare the timing of pulmonary opening between subjects with different heart rates Q-POM was therefore corrected to a heart rate of 60/min (Q-POM index) from the equation:

$$\text{Q-POM index} = \text{Q-POM} + 0.58 (\text{heart rate}) - 35.$$

Mean Q-POM index was 129 ms (SD 11 ms).

RELATION BETWEEN ATRIOVENTRICULAR VALVE CLOSURE AND AORTIC AND PULMONARY VALVE OPENING

There was a highly significant linear correlation between MC-TC and Q-TC index ($r = 0.74$, $P < 0.001$) which is shown in Fig. 7. There was no significant correlation between MC-TC and Q-MC index.

Tricuspid valve closure, whether timed from the Q wave of the electrocardiogram (Q-TC index) or from closure of the mitral valve (MC-TC), was significantly related to the timing of pulmonary valve opening. Fig. 8 shows the correlation between Q-TC index and Q-POM index ($r = 0.71$). The

Fig. 6 The relation between heart rate and the timing of complete opening of the pulmonary valve (Q-POm).

correlation between MC-TC and Q-POm index was less close ($r=0.59$) but still highly significant ($P<0.001$). By contrast there was no significant correlation between the timing of mitral closure (either MC-TC or Q-MC index) and the timing of aortic opening (Q-AO).

The results are summarised in the Table.

Discussion

Previous studies on the first heart sound have been impeded by the inability to identify its two major components with certainty in all subjects. The exact coincidence of mitral and tricuspid valve closure with the corresponding sound components M1 and T1 has been established both by haemodynamic and echocardiographic techniques (Burggraf and Craige, 1974; Leatham and Leech, 1974; O'Toole *et al.*, 1976). High-speed echocardiograms recorded simultaneously with the phonocardiogram thus made it possible to study the factors determining the timing of M1 and T1 in normal subjects, since accurate measurement is possible even when the valves close nearly synchronously and the two components are merged into each other on the sound recording.

The results of the present study show that the PR interval is a major determinant of the timing of mitral and tricuspid valve closure in normal subjects. At a PR interval of 180 ms Q-MC is about 30 to

40 ms (Fig. 3). This is approximately the time between electrical depolarisation and the onset of the left ventricular pressure pulse (Braunwald *et al.*, 1956; Luisada and Cortis, 1970), and so it may be concluded that when the PR interval is longer than this the mitral valve is closed entirely by atrial contraction and relaxation. Zaky *et al.* (1969) drew similar conclusions, though Shah *et al.* (1970) and Burggraf and Craige (1974) in their studies of patients with complete atrioventricular block found evidence of presystolic valve closure only when the PR interval exceeded about 200 ms. With shorter atrioventricular conduction times mitral closure, though initiated by atrial contraction and relaxation, is completed by ventricular contraction.

The tricuspid valve, however, does not close before the onset of the right ventricular pressure pulse unless the PR interval is considerably longer than 180 ms. In the subjects with PR intervals equal to or exceeding 180 ms, tricuspid closure still followed mitral closure by an interval of up to 48 ms (Fig. 5). In one subject (Fig. 2) with a PR interval of 220 ms, the mitral valve must have closed before the beginning of left ventricular contraction since Q-MC was 27 ms and no M1 was recorded. The tricuspid valve, however, closed 42 ms later (69 ms after the Q wave) and was associated with a definite T1 on the phonocardiogram. The time between the Q wave of the electrocardiogram and the onset of

Fig. 7 The relation between MC-TC and Q-TC index.

the right ventricular pressure upstroke is said to be about 50 ms (Luisada and Cortis, 1970) and so it is probable that, despite the very long PR interval in this individual, tricuspid closure was completed after the onset of right ventricular contraction. These observations, together with the finding of a steeper slope of the Q-MC/PR interval relation compared with the Q-TC/PR interval relation, indicate that contraction of the right atrium has a less powerful valve-closing action than contraction of the left atrium. Since the right atrium starts to contract before the left (Braunwald *et al.*, 1956), the difference is substantial. This explains the apparent discrepancy pointed out by Luisada *et al.* (1974) that the average interval between the two components of the first sound, M1 and T1, is over 30 ms, whereas the interval between the onset of left and right ventricular contraction is less than 20 ms. It seems that over the physiological range of PR interval the mitral valve is more nearly closed when left ventricular contraction begins than is the tricuspid valve at the start of right ventricular contraction, so that the time from right ventricular contraction to tricuspid valve closure and T1 is longer than the time from left ventricular contraction to mitral valve closure and M1.

Mean MC-TC in the present study was 34 ms,

Fig. 8 The relation between the timing of tricuspid valve closure corrected for PR interval (Q-TC index) and the timing of maximal pulmonary valve opening corrected for heart rate (Q-POm index).

but there was wide variation between subjects. The strong correlation between MC-TC and Q-TC index suggests that this variation in MC-TC (and splitting of the first sound) is mainly the result of differences in the timing of tricuspid rather than mitral valve closure. This variability in the timing of tricuspid closure has a number of possible

Table Mean echocardiographic intervals

Interval	Mean (ms)	Standard deviation	No.
PR	151	25	67
Q-MC	54	13	67
Q-MC index	48	10	67
Q-TC	87	17	63
Q-TC index	84	13	63
MC-TC	34	10	63
Q-AO	94	16	45
Q-POm	126	13	47
Q-POm index	129	11	47

explanations. The difference might be in the valve-closing action of right atrial contraction from one person to another, in the rate of rise of right ventricular pressure imparting a variable closing force on the valve, or in the timing of right ventricular contraction. One or both of the second two possibilities is supported by our demonstration of a correlation between the timing of tricuspid valve closure and the timing of pulmonary valve opening, since delayed pulmonary opening could reflect either delayed onset of right ventricular contraction or a slow-rising pressure upstroke, and early opening either early contraction or a rapid upstroke. Both Braunwald *et al.* (1956) and Luisada and Cortis (1970) showed that there was considerably more variation in the timing of right ventricular contraction (measured as the time from the Q wave to the start of the right ventricular pressure pulse) than in the timing of left ventricular contraction, and so we believe that it is this which is principally responsible for variations in the timing of tricuspid valve closure between one normal person and another. No significant correlation was found between the timing of mitral valve closure and aortic valve opening, and this seems to indicate that variations in timing of mitral closure and M1 are not caused primarily by differences in timing of left ventricular contraction, or the rate of pressure rise.

By extrapolation from the echocardiographic findings, we have shown that normal splitting of the first heart sound, which is wider than expected from the known degree of asynchronous ventricular contraction, is determined by a difference in the effects of left and right atrial contraction on mitral and tricuspid valve closure. Variations in the timing of the tricuspid component are probably the result of variations in the timing of right ventricular

activation and contraction, despite the absence of evidence of electrical delay on the electrocardiogram.

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Requests for reprints to Dr Nicholas Brooks, Cardiac Department, London Chest Hospital, Bonner Road, London E2 9JX.