The Echocardiogram of the Anterior Leaflet of the Mitral Valve

Correlation with Hemodynamic and Cineroentgenographic Studies in Dogs

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SUMMARY

The echocardiogram of the anterior leaflet of the mitral valve (ECHO) was compared to hemodynamic and cineroentgenographic data to evaluate its accuracy in timing mitral valve (MV) opening and closure, and to validate it as an indicator of MV motion. The ECHO, high speed cineroentgenography at 250 frames/sec, and/or measurement of intracardiac pressures allowed accurate timing of the events of MV motion in dogs on right heart bypass. The intersection of left ventricular and left atrial pressures in early diastole preceded the onset of rapid anterior motion of the ECHO (D' point) by 17 to 33 ± 7.6 msec; r = 0.98. The onset of left ventricular systole occurred before the termination of final rapid posterior motion of the ECHO in end diastole (C0 point) by 25 ± 10 msec; r = 0.96. Radiopaque clips were attached to the free edges of both leaflets of the MV. Cineroentgenographically determined plots of clip distance from the ultrasound transducer were morphologically similar to the simultaneously recorded ECHO. A delay of 23 ± 3 (0 to 40) msec was observed in the ECHO peaks of diastolic anterior excursion compared to clip motion. Contrast medium advances beyond the free edges of MV leaflets mixing with left ventricular blood 43 ± 3 msec after initial separation. These cineroentgenographic studies elucidate nonuniformity of leaflet motion responsible for ECHO delays.

Thus, ECHO D' and C0 correlate well with hemodynamic indicators of MV opening and closure. However, ECHO motion, although qualitatively similar, is unpredictably delayed compared to cineroentgenography of clips on the MV free edge. Since the ECHO correlates well with hemodynamic indices of MV opening and closure, this noninvasive technique can be used as a reference in the timing of intracardiac events and in the determination of systolic and diastolic time intervals.

Additional Indexing Words:
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ECHOCARDIOGRAPHY HAS PERMITTED non-invasive observation of a variety of intracardiac structures.1–2 One of the most distinctive echocardiographic patterns is that of the anterior leaflet of the mitral valve.1–3,4 In 1961 Edler concluded after advancing a long needle into a beef heart parallel to the ultrasound transducer4 that this characteristic echocardiogram originated from the anterior leaflet. Further documentation of the origin of this echo has been provided by injection of indocyanine green dye into the left ventricle during ultrasound recording.5 While studies relating echocardiographic mitral valve motion to hemodynamic data have been accomplished,8–10 most were performed in the presence of mitral valve disease or left ventricular dysfunction. Few studies are available relating normal mitral valve motion to the echocardiographic pattern.4 Furthermore, it is not known whether the mitral valve echocardiogram is capable of accurately defining opening and closure, although this has been suggested in a number of clinical studies.10,11 The purpose of the present study was to evaluate the echocardiogram of the anterior leaflet of the mitral valve in timing mitral valve opening and closure, and to validate it as an in-

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indicator of mitral valve motion. It was anticipated that this study would define the role of the echocardiogram of the mitral valve anterior leaflet as a reference in the timing of intracardiac events and in the determination of systolic and diastolic time intervals. Recent advances in the understanding and clinical application of these time intervals further emphasize the potential clinical value of this technique.12-18

Methods

Hemodynamic and Echocardiographic Correlation of Mitral Valve Opening and Closure

Ten mongrel dogs anesthetized intravenously with warmed chloralose (60 mg/kg) and urethane (600 mg/kg) were placed on right heart bypass as described in detail previously.19 Aortic pressure controlled by reservoir height, cardiac output determined by the input from the bypass pump, and heart rate controlled by atrioventricular pacing were varied over a wide range. Aortic, left ventricular, and left atrial pressures were measured through large bore short metal cannulae with Statham P23Db transducers and recorded simultaneously with epicardial electrograms, electronically differentiated left ventricular pressure, and the echocardiogram of the anterior leaflet of the mitral valve (ECHO) on a Beckman S-II oscillograph (fig. 1). Echocardiograms were obtained with an echograph* having a frequency output of 2.25 megacycles/sec and a repetition rate of 1000 pulses/sec equipped with an 0.5 inch diameter 10 cm focused transducer.† A time analog gate preamplifier was used to isolate the ECHO. The time delay in this ultrasound system is less than one millisecond, and the inherent frequency response limitation occurs above 500 Hz. ‡ The ultrasound transducer was held in contact with the epicardium of the anterior cardiac wall adjacent to the left anterior descending coronary artery. The transducer was oriented so as to maximize the amplitude of anterior mitral valve leaflet excursion. Anterior leaflet motion was observed at a depth between 3 and 5 cm in all preparations. The left atrial and left ventricular pressure crossover point in early diastole was selected as the hemodynamic indicator of mitral valve opening and was obtained by manually tracing the left atrial pressure superimposed onto the left ventricular pressure. The point of onset of left ventricular systole was

*Echoline 20, Smith Kline Instruments Corporation.
†Aerotech C12.
‡Data provided by Smith Kline Instruments Corporation.

Figure 1

Representative recording of simultaneous aortic pressure (AP), echocardiogram of anterior leaflet of the mitral valve (ECHO), atrial electrogram, ventricular electrogram, left ventricular diastolic pressure (LVDP), left atrial pressure (LAP), left ventricular dP/dt (LV dP/dt), and left ventricular pressure (LVP). Note that the echocardiogram is inverted. P = posterior; A = anterior.
used as the hemodynamic indicator of mitral valve closure because the left atrial and left ventricular pressures often equilibrated in mid and end diastole at lower diastolic pressures.

In order to determine the timing error induced by the wide bore short metal cannula-Statham P23Db pressure measurement system used in the present study, recordings of left ventricular diastolic pressure measured with this system were compared with those measured through an SF-1 Statham catheter tip manometer. The pressure crossover point and the point of onset of left ventricular systole on the SF-1 preceded that of the P23Db curve by 4.5 msec (−2 to 10 msec) and 5.1 msec (0 to 8 msec), respectively. Echocardiograms were analyzed with respect to the timing of these points. The echocardiogram of the normal mitral valve anterior leaflet has an "M" shaped configuration and has been divided, by convention, into several segments by a series of points (fig. 2). Opening of the valve has been considered to occur between D and E, where the E point represents maximal anterior excursion. The E point is followed by posterior motion to point F during ventricular filling. Anterior motion again occurs after point F and reaches a second peak at point A during atrial contraction. Valve closure is thought to occur between points A and C. For the purpose of this analysis, additional points D' and C₀ were selected, representing the onset of most rapid anterior motion in early diastole and the end of final rapid posterior motion in late diastole respectively (fig. 2). Points D' and C₀ were easily defined echocardiographic events which could be determined most consistently and approximated mitral valve opening and closure, respectively.

Three intervals which relate to mitral valve opening and/or closure were compared echocardiographically and hemodynamically: 1) the isovolumic relaxation period (aortic dicrotic notch to echocardiographic D' point or left atrial and ventricular pressure crossover), 2) the electrocardiographic Q wave to valve closure interval (echocardiographic C₀ point or point of onset of left ventricular systole), and 3) the diastolic filling period (echocardiographic D' to C₀ or pressure crossover to point of onset of left ventricular systole). In addition to aortic pressure, cardiac input and heart rate, blood perfusion temperature was varied (table 1) to obtain a broad range of intervals. The intervals determined hemodynamically were compared to those obtained echocardiographically by calculation of a correlation coefficient, standard error, and plot of the best fit regression line on a Xerex Sigma 3 computer and Calcomp plotter.

Cineroentgenographic Studies of Mitral Valve Motion

Mitral valve motion in eleven additional dogs was studied by cineroentgenographic techniques. All experimental preparations underwent multiple injections of radiopaque contrast medium (meglumine diatrizoate and sodium diatrizoate) into the left atrium (10 cc) and/or the pulmonary artery (30 cc) with left-sided follow through with the dog in approximately 80° left anterior oblique position to maximize visualization of the mitral valve. High speed 16 mm cineangiograms (250 frames/sec) were obtained. An oscilloscopic image of the time-analog echocardiographic signal of the anterior leaflet of the mitral valve was simultaneously recorded on the cineangiogram. The delay in the oscilloscope was measured to be less than 0.1 msec, and the total delay in the ultrasound system was less than 1 msec. Thus mitral valve motion as shown by cineangiography could be accurately compared to simultaneously recorded echocardiographic pattern.

In four preparations on right heart bypass, radiopaque tantalum clips were attached to the mitral valve anterior leaflet free edge in all preparations, the posterior leaflet free edge in three preparations, and an anterior chorda tendinea adjacent to the anterior leaflet in one preparation. In one of these preparations two separate clips were placed on the free edge of the anterior leaflet (fig. 3). In the three preparations in which clips were attached to both leaflets, care was taken to insure that apposing clips would approximate one another when the mitral valve was closed. This methodology allowed visualization of mitral valve free edge motion and leaflet separation during high speed cineroentgenography with simultaneous echocardiographic recording. Heart rate ranged between 100 and 160 beats/min and cardiac output, aortic pressure and temperature were maintained within a similar range in all preparations.

Single frame analysis of appropriate segments of the cineroentgenographic studies were used to plot the

<table>
<thead>
<tr>
<th>Table 1: Range of Hemodynamic Variables</th>
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<tr>
<td>Heart rate</td>
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<tr>
<td>Mean aortic pressure</td>
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<tr>
<td>Peak left ventricular dP/dt</td>
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<td>Peak negative left ventricular dP/dt</td>
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<tr>
<td>Cardiac input</td>
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<td>Perfusion temperature</td>
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*Renografin-76, Squibb and Sons.

†Siemens Corporation.

Figure 2

Echocardiogram of the anterior leaflet of the normal mitral valve. Diastole occurs between points D and C. After D the leaflet moves anteriorly through D' to peak at E. This is followed by posterior motion between E and F and a second anterior peak associated with atrial contraction at point A. Valve closure occurs between points A and C. During systole (C to D) the valve slowly moves anteriorly. Points D' and C₀ are reference points related to opening and closure of the mitral valve respectively.

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chorda tendinea from the ultrasound transducer, and 4) simultaneously obtained echocardiogram. These data were scaled to match maximum and minimum amplitudes and plotted against time (4 msec for each data point or cine frame) on a Calcomp plotter driven by a Xerox Sigma 3 computer. The scaled echocardiogram of mitral valve motion was compared to clip motion on at least two plots representing a different transducer position from each of four experimental preparations. The time of maximal early diastolic anterior excursion and of maximal anterior excursion during atrial contraction were compared cinerently on graphically and echocardiographically. The clip which pivoted on the valvular end of the anterior chorda tendinea, and thus was flow-directed similar to a weather vane, provided an additional means for determination of the onset of diastolic filling.

Results

Mitral Valve Opening and Closure: Comparison of Echo-cardiographic and Hemodynamic Data

The isovolumic relaxation period (IRP) measured from the time of the aortic diastolic notch to the left ventricular and left atrial pressure crossover point (IRPH) and to D' on the echocardiogram (IRPκ) (fig. 4A) were closely related. This relationship is described by the regression equation:

\[
\text{IRPκ} = (1.1) \text{IRPH} + 8.6 \text{ msec};
\]

\[
0.98 (\text{SEM} = \pm 7.6 \text{ msec})
\]

The duration of the isovolumic relaxation period determined hemodynamically ranged between 30 and 190 msec. Substituting for IRPH, the range for IRPκ would be 42–218 msec. Thus, there is a 12–28 msec delay between the pressure crossover and echocardiographic D' points. Addition of the 5 msec delay in

Figure 3

Open heart display of position of tantalum steel clips on anterior (2 clips on the right side of the photograph) and posterior (1 clip on the left side of the photograph) leaflets of the mitral valve. This specimen is from the canine preparation used to obtain figures 7 and 8.

following: 1) distance of clips on the anterior leaflet from the ultrasound transducer, 2) points of separation and apposition of anterior and posterior mitral valve leaflet clips, 3) distance of the tip of the mobile clip on the anterior leaflet

Figure 4

A) Regression line relating isovolumic relaxation period (IRP) determined echocardiographically to that determined hemodynamically. B) Regression line relating the interval between the first transient of the electrocardiographic QRS and valve closure or Q to closure interval determined echocardiographically and hemodynamically. C) Regression line relating the diastolic filling period (DFP) determined echocardiographically and hemodynamically.
the pressure measuring system increases this delay to 17–33 msec.

The interval between the onset of electrical activity and valve closure event (electrocardiographic Q wave to closure interval or QCI) was measured from the first transient of the ventricular electrogram to the point of onset of left ventricular systole (QClH) and to the C0 point on the echocardiogram (QClE). These intervals illustrated in figure 4B are related by the following equation:

\[
QClE = QClH + 20 \text{ msec;}
\]

\[
r = 0.96 \text{ (SEM = ± 10 msec)}
\]

Thus, there is a delay of 20 ± 10 msec between the hemodynamic and the echocardiographic valve closing event. The total delay including that incurred in the pressure measuring system is 25 ± 10 msec.

Finally, the diastolic filling period (DFP) was measured hemodynamically from pressure crossover to the point of onset of left ventricular systole (DFPH) and echocardiographically from D' to C0 (DFPE). These intervals illustrated in figure 4C are related by the regression equation:

\[
DFPE = DPH \text{ msec;}
\]

\[
r = 0.99 \text{ (SEM = ± 20 msec)}
\]

Therefore, the echocardiographically and hemodynamically determined diastolic filling periods are essentially equivalent.

Mitral Valve Opening and Closure: Cineroentgenographic and Echocardiographic Studies

The time relationships of the events described below are illustrated in figure 5.

Mitral Valve Opening: Three of the events constituting mitral valve opening as shown by cineroentgenography were compared with the echocardiogram: 1) the time of separation of apposing clips on the anterior and posterior leaflets, 2) the time of onset of rapid anterior motion of the anterior leaflet clip in early diastole (similar to ECHO D'), and 3) the time at which the advancing front of contrast medium within the left atrium mixes with left ventricular blood. The interval between the onset of mitral valve clip separation and the D' point on the ECHO was determined on 20 occasions in three canine preparations. Clip separation occurred 26 ± 5 msec before the echocardiographic D' point. The D' point occurs approximately 19–24 msec after pressure crossover within a physiologic range of IRP (50–100 msec).\(^8\) Thus, clip separation occurs within 2 to 7 msec of pressure crossover. This delay is not statistically significant. The time of onset of rapid anterior motion in early diastole of the anterior leaflet clip occurs an average of 6 msec after separation of anterior and posterior leaflet clips.

Contrast medium was observed to enter the left ventricle from the left atrium as a convex front behind the mitral valve until the valve opened widely in all cineangiographic studies. Disruption of this contrast medium front and mixture with left ventricular blood occurred 17 ± 2 msec after the D' point of the ECHO. Thus, an interval of approximately 43 msec between initial separation of mitral valve anterior and posterior leaflet and the flow of blood beyond the free edges of the mitral valve describes mitral valve opening. In one preparation, a mobile clip was attached to an anterior chorda tendinea near its insertion onto the anterior leaflet free edge. The distance of this "weather vane" clip and a clip on the anterior leaflet free edge from the ultrasound transducer and the simultaneous ECHO were plotted on the same scale (fig. 6). The flow directed "weather vane" clip changed direction 9 msec after the echo D' point, about 8 msec prior to the disruption of the contrast medium front.

Mitral Valve Closure: The C0 point on the ECHO

\(^8\) Substituting 50 to 100 msec for IRPA in the regression equation IRPE = 1.1 IRPA + 8.6 reveals a range of 64 to 119 msec for IRPE. Thus ECHO D' occurs 14 to 19 msec after the measured crossover point or 19 to 24 msec after the actual crossover point.
occurred 18 ± 2 msec after coaptation of free edge clips (fig. 5). We have shown that the onset of left ventricular systole occurred 25 msec before the echocardiographic C₀ point. Thus, clip coaptation occurs shortly after the onset of left ventricular systole (7 msec), an interval which is not statistically significant. The termination of rapid posterior motion of the anterior leaflet clip (similar to echocardiographic C₀) occurred within 2 msec of anterior and posterior leaflet clip coaptation.

Mitral Valve Motion: Cinerentgenographic and Echocardiographic Studies

The time relationship of mitral valve anterior leaflet motion determined cinerentgenographically and echocardiographically was analyzed by two additional methods: 1) comparison of the two points of maximal anterior leaflet excursion during early diastolic filling and during atrial systole, and 2) comparison of computer plots of distance of anterior leaflet clips from the ultrasound transducer with the simultaneous echocardiogram.

The peak anterior excursion of the anterior leaflet clips in early diastole occurred 24 ± 5 msec (0 to 40 msec) prior to the corresponding echocardiographic event (E point), while the peak anterior excursion during atrial contraction occurred 15 ± 4 msec (0 to 38 msec) before the A point of the echo. Considering both of these delays, a mean delay of 20 ± 3 msec has been demonstrated between clip motion and the ECHO.

The position of the ultrasound transducer and the clips on the free edge of the anterior and posterior leaflets is illustrated in eight frames of a representative cinerentgenographic sequence in figure 7. The simultaneous ECHO appears on the right-hand side of each cine frame. The configuration of the valve as determined by contrast medium injection during previous sequences is sketched into each frame. The computer plot of clip motion and echocardiographic motion for this sequence is illustrated in figure 8. The plots of clip motion are qualitatively similar to the echocardiogram. Note that peak anterior motion in early diastole occurred 20 msec before the echocardiographic E point and that peak anterior motion during atrial systole occurred 16 msec before the echocardiographic A point.

Figure 8 demonstrates the relationship of clip separation (point X) and the onset of rapid anterior motion in early diastole (clip D'), and of clip coaptation (point Y) and the termination of final rapid posterior motion in late diastole (clip C₀). Echocardiographic D' and C₀ are thus analogous to clip events which closely approximate separation and coaptation of the mitral valve free edges.

Discussion

Despite a large number of clinical studies in the use of diagnostic cardiac ultrasound, only a few studies of validation exist. Although numerous studies delineate normal mitral valve echocardiographic morphology, normal morphology has not been rigorously defined. Although the echocardiogram provides a convenient method of observing mitral valve motion, it has not been widely used as a means of timing opening or closure of the mitral valve, nor has the relationship of mitral valve opening and closure to the echocardiogram been accurately correlated.

The present study demonstrates an excellent correlation between hemodynamic and echocardiographic indexes of mitral valve opening and closure. However, a variable echocardiographic delay of up to 40 msec is evident in comparison to motion of anterior leaflet free edge radiopaque clips as shown by cinerentgenography. Plots of the simultaneously recorded echocardiogram of the anterior leaflet of the mitral valve and cinerentgenographic motion of radiopaque clips on the leaflet free edge are morphologically similar. Clips on two separate points of the free edge of the anterior leaflet display similar morphology, although a discrepancy in timing is evident. Thus, in figure 8, clip ALMV2 leads clip ALMV1 by up to 20 msec. The echocardiographic events occur 15–35 msec after comparable events of clip ALMV2 and 15–25 msec after comparable events of ALMV1. These delays are compatible with non-uniformity of motion of the free edge of the leaflet. Nonuniformity of mitral valve motion is evident upon inspection of the cinematographic studies by Edler.
Figure 7

Representative cineroentgenographic frames illustrating two radiopaque clips on the free edge of the anterior leaflet of the mitral valve (ALMV1, ALMV2), and a clip on the posterior leaflet of the mitral valve (PLMV), the position of the ultrasound transducer (T) and the cinetrace of the echocardiogram of the anterior leaflet of the mitral valve (ECHO). The anatomic structures have been drawn in and labeled for illustrative purposes. (Ao = aorta, LV = left ventricle, LA = left atrium.) 1 = mid systole, 2 = 8–12 msec prior to mitral valve clip separation, 3 = 8–12 msec after mitral valve clip separation, 4 = maximal anterior leaflet anterior excursion, 5 = maximal anterior leaflet excursion during atrial contraction, 6 = less than 4 msec prior to mitral valve clip apposition, 7 = less than 4 msec after mitral valve clip contact, 8 = early systole.
Thus, the edges at the midportion of the valve appear to separate before the edges closer to the commissures. The selective echocardiographic sampling of the free edge may account for a portion of the timing discrepancy between echocardiogram and cineroentgenography of anterior leaflet motion.

The ultrasound transducer samples motion within a cylindrically shaped column with a diameter approximately equal to that of the transducer (fig. 9). Observation of the mitral valve during contrast medium injection demonstrated that following leaflet separation, the anterior leaflet free edge leads the remainder of the leaflet with a whipping motion progressing from free edge to base. The lag in motion of the remainder of the leaflet behind free edge could account for a portion of the time delay between cineroentgenographic and echocardiographic motion. The possibility that tantalum clips would alter mitral valve motion is recognized. However, mitral valve motion was similar in the studies performed with radiopaque contrast medium injection alone and in the studies with clips attached to the free edge(s) of the mitral valve.

Another factor in the observed delay is a parallax phenomenon. The transducer receives reflections only when the ultrasound beam interacts perpendicularly to an interface. As the mitral valve opens, the anterior leaflet free edge changes from a relatively perpendicular to a nearly parallel orientation with respect to the ultrasound transducer (fig. 6). Thus, as the mitral valve opens, a larger area of anterior leaflet is sampled by the ultrasound beam and relatively less of its echocardiogram is composed of leading leaflet free edge.

Finally, echocardiographic time resolution is related to the number of bursts of ultrasound energy emitted over a given time or the pulse repetition rate. The "echo dropout" phenomenon referred to by
Kingsley\textsuperscript{10} at a slow repetition rate (200/sec) would not be expected to be an important factor in delays greater than one millisecond at a repetition rate of 1000 as was employed in the present study. The results of the present study are consistent with data of other investigators who demonstrate in mitral stenosis that valve closure as determined hemodynamically occurs immediately before the most posterior motion of the anterior leaflet\textsuperscript{10} and that the opening snap on external phonocardiography occurs approximately 20 msec before the echocardiographic E point.\textsuperscript{22} Considering the delay demonstrated in the present study the opening snap would occur coincident with maximal anterior excursion in early diastole.

Since mitral valve leaflets separate nonuniformly, the time at which free edge clips separate depends upon their location. This nonuniform motion does not influence hemodynamic indicators of opening and closure, and is minimized by the echocardiogram due to the integrating properties of the ultrasound beam. Thus, echocardiographic indicators of mitral valve opening and closure correlate well with hemodynamic indicators of these events.

In the clinical setting, the mitral anterior leaflet is further from the ultrasound transducer (7–10 cm) than in the canine preparation used in the present study (3–5 cm). The area of anterior leaflet represented by the echocardiographic tracing in the clinical range with a focused or collimated transducer is approximately equivalent to the leaflet area represented in the present study (fig. 9). A good correlation with hemodynamic indicators of opening and closure similarly would be expected in a clinical study.

Inspection of cineroentgenography of mitral valves with clips on anterior and posterior leaflets and cineangiography elucidates the mechanism of mitral valve opening and left ventricular filling. Separation of the free edge clips begins 26 msec before D' on the echocardiogram (the point of onset of most rapid anterior mitral valve motion in early diastole) as the valve bulges into the left ventricle. An advancing front of contrast medium retains the convex configuration of the bulging mitral valve, while opening continues. The contrast medium does not begin to mix with left ventricular blood until the valve is almost fully opened. Hence, the onset of flow beyond the mitral valve free edges occurs considerably after the initial separation of anterior and posterior leaflets. Thus mitral valve opening is a complex sequence of events rather than a single event in time.

Mitral valve closure determined hemodynamically and cineroentgenographically correlated well with the echocardiographic C\textsubscript{0} point, although there was a delay of the C\textsubscript{0} point of approximately 20 msec (fig. 8). Hemodynamic and cineroentgenographic data demonstrate that the onset of left ventricular systole and coaptation of free edge clips occur at approximately the same time.

The interrelationship of events of mitral valve motion determined echocardiographically, hemodynamically, and cineroentgenographically has been demonstrated in the present study. Hemodynamic indicators of opening and closure correlate well with echocardiographic indicators, whereas a greater uncertainty (0 to 40 msec) is evident when comparing motion of anterior leaflet mitral valve free edge markers to the echocardiogram of the anterior leaflet. The echocardiogram provides a reliable noninvasive means of determining intervals which relate to hemodynamic indices of mitral valve opening and closure. The echocardiogram also provides a means of observing mitral valve motion qualitatively or quantitatively within the limits presented herein.

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