Size and Motion of the Mitral Valve Annulus in Man

I. A Two-dimensional Echocardiographic Method and Findings in Normal Subjects

JOHN A. ORMISTON, M.B., CH.B., PRAVIN M. SHAH, M.D., CHUWA TEI, M.D., AND MAYLENE WONG, M.D.

SUMMARY Using wide-angle, phased-array, two-dimensional echocardiography, mitral leaflets and their annular attachments were recorded from a view close to the standard apical four-chamber view. The transducer was rotated and recordings were made at 30° rotational intervals around the circumference of the mitral valve annulus. To reconstruct the annulus, diameters (or chords) from each rotational interval were arranged around a reference point. This was done for 12 times during the cardiac cycle. Annular areas were planimetered and circumferences measured. Correlation was good for areas reconstructed and measured by the same observer on separate occasions (r = 0.963) and by two different observers (r = 0.987). In 11 normal subjects the annular area index (area divided by body surface area) increased during diastole to a maximum of 3.8 ± 0.7 cm²/m² (mean ± SD) in late diastole. There was presystolic followed by systolic narrowing to a minimum in mid-systole. The mean reduction in area was 26 ± 3%. The maximal annular circumference was 9.3 ± 0.9 cm and the mean reduction in circumference was 13 ± 3%. The overall motion pattern was similar to that reported in experimental studies in the dog. Mitral annular reconstruction may provide new information about normal and abnormal function of the mitral valve apparatus.

IN EXPERIMENTAL STUDIES and in human subjects on cardiopulmonary bypass, the size of the mitral valve annulus has been reported to change during the cardiac cycle. There has been no technique available to measure mitral annular areas during the cardiac cycle in human subjects. Little is known of the size and motion of the mitral annulus in intact man, although important observations relating to its size have been made at autopsy. Study of the mitral valve annulus may provide new insights into the overall function of the mitral valve apparatus in health and disease.

We used a two-dimensional echocardiographic technique to reconstruct the mitral valve annulus so that its area could be measured at different times during the cardiac cycle to examine phasic changes. The technique is described in detail and results in normal resting human subjects are reported.

Methods

Subjects were studied in the left lateral decubitus position. A Varian 3000 wide-angle, phased-array system was used to perform two-dimensional echocardiography. Studies were recorded on half-inch videotape using a Sanyo cassette recorder. The images could be redisplayed in real-time, slow motion or as single frames. Still frames were recorded on 90-mm film during real-time studies and are used as illustrations in this paper. Mounted on the echocardiographic transducer was an inclinometer, a circular, fluid-filled chamber containing an air bubble that allows measurement of 30° transducer rotational intervals.

Our method was designed to reconstruct the mitral valve annulus at 12 times during the cardiac cycle from diameters and chords measured at 30° rotational intervals. The transducer was held at the left ventricular apical impulse and the beam was directed toward the left atrium and the mitral valve leaflets to identify their annular hinge points. A view close to the standard apical four-chamber view was usually the initial plane of examination. Additional planes were obtained at 30° rotational intervals. Six planes were used to provide chords or diameters. The shaded area in figure 1 represents a plane of the two-dimensional beam that slices the mitral valve annulus in two places. At this rotation, the transducer was angled back and forth in an arc perpendicular to the plane of the beam to identify the maximal orifice diameter at a fixed time in the cardiac cycle. The time chosen was "end-isovolumic relaxation," defined as the moment just before the mitral leaflets opened. During held expiration, about 10 cardiac cycles were recorded on videotape. The transducer was then rotated 30° clockwise, the widest annular diameter at this rotation was identified and recordings were made. Recordings were made at 30° rotational intervals around the circumference of the annulus. No change in transmission power or receiver gain was made once recording had begun.

From the Department of Medicine, University of California School of Medicine and Wadsworth Veterans Administration Medical Center, Los Angeles, California.

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Address for correspondence: Pravin M. Shah, M.D., Cardiology Section (691/111E), Wadsworth Veterans Administration Medical Center, Wilshire and Sawtelle Boulevards, Los Angeles, California, 90073.

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Figure 1. The method and principle of recording annular diameters (or chords) at 30° rotational intervals. Attached to the transducer is an inclinometer, which has a fluid-filled circular chamber containing an air bubble and allows accurate measurement of 30° rotational intervals. The shaded area represents a plane of the two-dimensional echocardiographic beam that slices the annulus in two places. The transducer is angled back and forth at this rotation to identify the widest annular diameter at a fixed time in the cardiac cycle. After videotape recordings are made, the transducer is rotated 30° clockwise so that the beam lies along the next plane, the widest diameter is identified and recordings are made. Recordings are made in this fashion at 30° rotational intervals around the annular circumference.

Figure 2 shows still frames obtained in a normal subject from planes at 30° rotational intervals. The arrows indicate the mitral leaflet hinge points used to locate the annulus. Annular hinge points are shown in figure 3.

Preliminary observations showed that during the cardiac cycle, the mitral valve annulus moves with heart motion. To reconstruct the annulus, a reference line was selected. The annulus was considered to be elliptical; therefore, true diameters bisect each other at its center. As outlined above, recordings were made after identification of the maximal annular diameter at end-isovolumic relaxation. The diameters measured at different rotations at end-isovolumic relaxation bisect each other at the center of the annulus. Thus, the center of the annulus at end-isovolumic relaxation was chosen as a reference point and a line perpendicular to the plane of the annulus passing through the reference point and the left ventricular apex was chosen as a reference line. The reference line was made by drawing a line with wax pencil down a strip of transparent plastic, which was taped to the video monitor screen so that the line passed from the imaged cardiac apex down the long axis of the left ventricle and bisected the measured annular diameter at end-isovolumic relaxation. The reference line could be moved to ensure that before a cardiac cycle was analyzed, it did indeed bisect the annular diameter at end-isovolumic relaxation. A sheet of transparent mylar plastic was then placed over the video monitor screen and reference line. Using a fine-tipped pen, the plastic was marked over imaged mitral leaflet annular hinge points and the reference line. Care was taken to maintain constant head position and avoid parallax.
errors. Annular diameters (or chords) and distances moved from the reference line were measured at selected times during the cardiac cycle. The annulus was reconstructed for a particular time during the cardiac cycle by plotting around the reference line the diameters (or chords) from each rotational interval. The annulus was reconstructed for 12 selected times during the cardiac cycle. Figure 4 shows reconstruction for three of these times. Four cardiac cycles were analyzed at each rotation, so each diameter (or chord) represents the mean of data from four cardiac cycles.

The reconstructed mitral annulus at each selected time during the cardiac cycle was planimetered, and the resulting area was divided by the subject's body surface area and expressed as mitral annular index for each time in the cardiac cycle. Annular circumferences were measured from the reconstructed annuli using a wheel designed to measure distances on maps.

Variability of Measurements
To test intraobserver variability in measurements of annular size, the same observer on two occasions more than 3 weeks apart measured annular diameters from the same videotape recording, then reconstructed and planimetered areas for three subjects. Interobserver variability was tested by having two observers independently measure diameters from the same videotape recording, reconstruct and planimeter areas for four subjects. Linear regression analysis was performed and the standard error of the estimate was calculated. For each paired measurement, the percentage error from average was calculated. The mean percentages of intraobserver and interobserver error were then calculated. To test variability over a wide range of sizes, patients with cardiomyopathy and mitral valve prolapse were included in addition to normal subjects.
Figure 4. Reconstruction of a representative normal mitral valve annulus at selected times during the cardiac cycle showing changes in annular size and shape.

Subject Selection

Over an 8-month period, echocardiographic studies were performed on 40 normal subjects who were either medical staff members or medical students. In 11 of these subjects (all male), the quality of the apical views was good enough that we could clearly identify the mitral valve leaflets and their annular hinge points around the circumference of the annulus. These 11 subjects (mean age 25 years, range 23-38 years) are included in this study of normal subjects. We find it generally easier to obtain good-quality apical echocardiograms in subjects with heart disease than in normal subjects because cardiac enlargement offers a broader apical contact surface and the valve leaflets often exhibit greater echo reflectance.

In Vitro Study

Because echocardiography is a tomographic technique, true annular diameters and, ultimately, true annular sizes may be measured even when the plane of the annulus is not perpendicular to the echo beam. To test this concept experimentally in an oil bath, a wire ring of known size was imaged at 16 different orientations relative to the plane of the echo beam. The calibration grid of the two-dimensional echocardiographic equipment was checked by measuring the imaged diameters of the ring comparing them with the known diameter.

Results

The changes in mitral annular area index that occurred during the cardiac cycle in 11 normal subjects are shown in figure 5. There was a gradual increase in annular size during diastole to maximum in late diastole generally at or just after the P wave. There was some presystolic narrowing, followed by further systolic narrowing to the minimal size, which was reached in midsystole. Annular size increased in late systole and in isovolumic relaxation.

Maximal mitral annular area was 7.1 ± 1.3 cm² (mean ± SD) and maximal area index was 3.8 ± 0.7 cm²/m². The percentage reduction in size ([maximal area - minimal area] ÷ maximal area) was 26 ± 3%. The measured maximal annular circumference was 9.3 ± 0.9 cm and percentage reduction in circumference was 13 ± 3%. Annuli were elliptical, but in general were more circular in late diastole and flatter in systole.

During systole the annulus moved apically. It also moved to each subject’s right relative to the reference line.

Variability of Measurements

When the same videotape was analyzed by the same observer on separate occasions, the area measurements correlated well (r = 0.963) (fig. 6), and the mean percentage error was 2%. When two observers independently analyzed the data, the reconstructed areas correlated well (r = 0.987) (fig. 7), and the mean percentage error was 2%.

In Vitro Study

We imaged a 38.0-mm diameter wire ring in an oil bath at 16 different positions relative to the two-dimensional echocardiographic beam and found that (1) diameters (not chords) of the ring were equal in length irrespective of how the ring was positioned in the beam (fig. 8) and (2) the calibration grid overestimated length by 6%. When the 38.0-mm diameter wire ring was imaged echocardiographically, the diameter of the ring measured (from leading edge to leading edge of echoes) using the calibration grid was 40.3 ± 0.5 mm. Annular diameter measurements were corrected for this 6% overestimation of length.

Discussion

The mitral valve annulus is a junctional zone that separates and gives attachment to muscle of the left atrium and left ventricle and to the mitral valve
leaflet. It is not a rigid circumferential fibrous ring, but is pliable and incomplete anteriorly. The annulus has two major collagenous structures, the right and left fibrous trigones. The right fibrous trigone, or central fibrous body, lies in the midline of the heart and represents the confluence of fibrous tissue from the mitral valve, tricuspid valve, membranous septum and posterior aspect of the root of the aorta. The left fibrous trigone is composed of fibrous tissue at the confluence of the left margin of the aortic and mitral valves. Between the trigones ventrally, the anterior leaflet of the mitral valve is in direct fibrous continuity with the aortic root. There is, as a rule, no thickened fibrous ring in this region and the annulus is represented by a poorly defined, nontickened zone that gives attachment to the muscle fibers of the roof of the left atrium. Extending dorsally from the trigones on both sides of the mitral orifice are the tendon-like fila of Henle, which are usually thin. This part of the annulus, which gives attachment to the posterior leaflet of the mitral valve, varies considerably in thickness in different subjects. Photographs and diagrams show that the mitral valve annulus is elliptical or nearly elliptical.

Cardiac muscle fibers, blood vessels and nerves are present in the mitral valves of man, dog and cat.

Figure 6. Correlation of mitral annular areas measured by the same observer on two occasions at least 3 weeks apart. The measurements were made in three subjects at 12 different times during the cardiac cycle. Circles represent two normal subjects and closed triangles a subject with hypertrophic obstructive cardiomyopathy.

Figure 7. Correlation of mitral annular areas measured independently by two different observers. Circles represent two normal subjects, open triangles a subject with mitral valve prolapse, and closed squares a subject with dilated cardiomyopathy.

Figure 8. (top) Two-dimensional echocardiographic still frames of a metal ring imaged in an oil bath. The ring is placed parallel to the beam in B and obliquely in A and C. (bottom) Diagram showing that the imaged diameter (x) of the ring is the same irrespective of the orientation of the ring in the echo beam.
The muscle is arranged mainly perpendicularly to the annulus, but a less prominent group of fibers is arranged parallel to the valve margin. Muscle in the leaflets is a direct extension of left atrial muscle. The valve leaflet in dogs possesses intrinsic contractility that may play a role in the function of the mitral valve apparatus.\textsuperscript{21, 22}

Cyclic changes in primary mitral orifice size (i.e., the area at the level of the mitral annulus) have been directly observed in isolated animal hearts,\textsuperscript{1} in the perfused hearts of open-chested dogs\textsuperscript{9} and in human subjects on cardiopulmonary bypass.\textsuperscript{8} In patients with mitral valve disease, changes in silhouettes of the mitral annulus have been measured from cineangiocardiograms.\textsuperscript{20} In normal subjects and in patients with dilated left ventricles, maximal and minimal tomographic annular diameters have been measured from the two-dimensional echocardiographic parasternal long-axis view.\textsuperscript{28} The relationship between changes in a single tomographic annular diameter and changes in annular area is uncertain because the annulus not only moves, but also changes shape during the cardiac cycle.

Davis and Kinmonth\textsuperscript{2} and Tsakiris et al.\textsuperscript{4} cineradiographically studied dogs with lead beads sutured to their mitral annuli. The changes in size and the motion of the mitral annuli in these two studies in dogs are very similar to those in our study of human subjects. During systole, in all three studies annuli moved apically and to each subject's right relative to an axis passing from the left ventricular apex through the primary mitral orifice. In all three studies, the annulus gradually increased in size after mitral valve opening to a maximum in late diastole. There was presystolic narrowing, followed by further narrowing in ventricular systole so that minimal size was reached in mid-systole. In our study and that of Davis and Kinmonth, annular size began increasing in the latter half of ventricular systole and increased further during isovolumic relaxation. It is possible that this increase in annular size during the latter half of systole was caused by the increased left atrial size associated with left atrial filling. Tsakiris et al. reported a rapid increase in size of the annulus during ventricular isovolumic relaxation.

Tsakiris et al.\textsuperscript{4} attributed the presystolic annular narrowing to atrial contraction because they found that narrowing was gradually reduced when the PR interval was progressively shortened and that it was abolished by induced atrial fibrillation. This concept is supported by our findings in a patient with first-degree atrioventricular block (not included in the present analysis) in whom presystolic narrowing occurred just after the P wave, which was earlier than otherwise would be expected.

The maximal diastolic annular area in dogs on cardiopulmonary bypass was reduced by 30\% (range 24–54\%) during the cardiac cycle.\textsuperscript{2} In five anesthetized intact dogs, reductions were 19–34\% in the “control” state and 10–36\% during different hemodynamic conditions. The mean reduction in our resting human subjects was 26\% (range 23–31\%).

In the present study, annuli were elliptical and changed shape during the cardiac cycle, being more circular in late diastole and flatter in systole. However, area reduction was not due to shape change alone because there was a coincident 13 \pm 3\% reduction in annular circumference.

It is difficult to relate mitral annular sizes measured at autopsy to those measured during life. In life, there is a wide variation in annular size not only during the cardiac cycle, but also under different hemodynamic conditions. Maximal diastolic annular area in a dog varied from 2.9–5.0 cm\textsuperscript{2} under different conditions.\textsuperscript{4} Different methods of specimen preparation may produce different annular sizes. It is possible that in formalin-preserved hearts, the annuli are in the systolic state, whereas if hearts are fresh or examined after perfusion fixation,\textsuperscript{10} annuli may be in the diastolic state.

Table 1 shows annular measurements in normal hearts prepared in different ways in an autopsy series.

\begin{table}
\centering
\caption{Mitral Annular Circumferences and Areas in Autopsy Studies of Normal Hearts}
\begin{tabular}{|l|c|c|c|c|}
\hline
Investigator & Number of hearts & Sex & Preparation of specimens & Annular circumference (cm)\textsuperscript{a} & Annular area (cm\textsuperscript{2}) \\
\hline
Bulley and Roberts\textsuperscript{8} & 24 & † & Preserved & 9 (7–11) & — \\
Rusted et al.\textsuperscript{8} & 25 & M & Formalin & 9.9 (8.5–11.0) & — \\
 & 25 & F & Formalin & 8.5 (7.5–10.5) & — \\
Chiechi et al.\textsuperscript{7} & 60 & M & Formalin & 10 (8.5–11.5) & — \\
 & 45 & F & Formalin & 9 (6–10.5) & — \\
Chiechi et al.\textsuperscript{7} & 8 & M & Fresh & — & 7.93 (5.72–10.20) \\
 & 8 & F & Fresh & — & 6.42 (4.90–8.75) \\
DuPlessis and Marchand\textsuperscript{8} & 10 & † & Fresh & 10.2 & 8.2 \\
McAlpine\textsuperscript{10} & † & † & Perfusion fixation & 13.4 & — \\
\hline
\end{tabular}
\textsuperscript{a}Mean and range.
\textsuperscript{†}Information not available.
\end{table}
TABLE 2. Echocardiographic Maximal and Minimal Mitral Annular Areas and Circumferences

<table>
<thead>
<tr>
<th></th>
<th>Mean annular circumference (cm)</th>
<th>Mean annular area (cm²)</th>
</tr>
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<tbody>
<tr>
<td>Maximal</td>
<td>9.3 (8-10.5)</td>
<td>7.1 (5.3-8.9)</td>
</tr>
<tr>
<td>Minimal</td>
<td>8.0 (7-9)</td>
<td>5.2 (3.6-6.8)</td>
</tr>
</tbody>
</table>

The range is given in parentheses.

and table 2 shows measurements from our echocardiographic study. If formalin preservation produces annuli in the systolic state, then sizes measured at autopsy are similar to or somewhat larger than systolic sizes measured echocardiographically in the present study. If annuli in fresh hearts or after perfusion fixation are in the diastolic state, then sizes measured at autopsy are similar to or somewhat larger than diastolic sizes measured echocardiographically in the present study.

Changes in a single echocardiographic annular diameter may not predict changes in annular area because the annulus moves during the cardiac cycle. This is schematically shown in figure 9A, in which a hypothetical annulus does not change in size, but moves sideways. We overcame this problem by measuring six diameters (or chords). In figure 9B, despite the motion, the annulus is accurately reconstructed from the diameters (or chords) and the measured size is unchanged. Another reason that changes in one annular diameter may not accurately predict annular area changes is that the annulus changes shape during the cardiac cycle.

There is no foreshortening of annular diameters, even if the plane of the annulus is not perpendicular to a line passing from the echocardiographic transducer through the center of the annulus. Diameters (not chords) of a metal ring are the same regardless of the orientation of the ring relative to the echocardiographic beam (fig. 8).

The mitral apparatus is a complex, finely coordinated mechanism that, to perform normally, requires the functional integrity of its anatomic elements: the mitral annulus, valve leaflets, chordae tendineae, papillary muscles, posterior left atrial wall and left ventricular wall. The annulus has been inaccessible to noninvasive examination, but echocardiographic study may provide new information about the overall function of the mitral valve apparatus in normal and disease states. There are situations in which noninvasive measurements of mitral annular size and function at rest and under different hemodynamic conditions would be of interest. The contribution of mitral annular size and dysfunction to the mitral regurgitation of dilated cardiomyopathy is uncertain. Borgenhagen et al. and Yoran et al. have suggested that in dogs with experimentally induced acute mitral regurgitation, the size of the subvalvular cavity of the ventricle and size of the mitral annulus greatly influence the size of the regurgitant orifice and regurgitant flow. Radiologic studies of the mitral valve prolapse syndrome suggest abnormalities of annular function, and Bulkle and Roberts reported annular dilatation in an autopsy series. The function of the mitral valve annulus in hypertrophic cardiomyopathy is also unknown. Clinical studies of mitral annular size and function are currently in progress in our laboratory. Additional validation of the method will also require serial studies in the same subject under basal conditions. The new echocardiographic method described in this report appears promising and the findings in normal subjects will form the basis for comparisons with pathologic states.

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