Mitral regurgitation in hypertrophic cardiomyopathy
Non-invasive study by two dimensional Doppler echocardiography

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SUMMARY Mitral regurgitation and its haemodynamic features were investigated non-invasively in cases of hypertrophic cardiomyopathy by means of two dimensional Doppler echocardiography. There were 28 patients, 14 of whom showed systolic anterior motion (SAM) of the mitral echo; the other 14 did not. The following results were obtained. (1) Mitral regurgitation was detected by the Doppler technique in all cases with systolic anterior motion of the mitral echo and in half of those without it. (2) Doppler signals of mitral regurgitation started immediately after the first heart sound. (3) Mitral regurgitant flow was often distributed from the entire mitral orifice over the entire or the posterior half of the left atrium in the cases with systolic anterior motion. In the cases without systolic anterior motion the regurgitation was usually localised near the mitral orifice. These features differ from those of regurgitation usually seen in rheumatic mitral valve disease and idiopathic mitral valve prolapse. (4) The Doppler technique and left ventriculography were equally efficient in detecting mitral regurgitation. (5) The early systolic component of the murmur of hypertrophic cardiomyopathy is considered to result in the main from concomitant mitral regurgitation, but not from turbulent blood flow in the left ventricular outflow tract, so that in cases with mitral regurgitation as a complication, mitral regurgitation may also contribute to the development of the midsystolic portion of the systolic murmur, while the main origin of this portion of the murmur is the left ventricular outflow obstruction.

It has been suggested that mitral regurgitation in hypertrophic cardiomyopathy, seen at angiography, may be in part artefactual, especially when ventricular premature beats are induced. This has not been confirmed, however. Whether or not mitral regurgitation is a natural complication in hypertrophic cardiomyopathy is a topic that requires further investigation. In the present study, mitral regurgitation in hypertrophic cardiomyopathy was investigated non-invasively by combined two dimensional echocardiography and the ultrasonic pulsed Doppler technique in order to determine if mitral regurgitation is present under conditions as near to natural conditions as possible. Based on the results obtained, the relation between mitral regurgitation and heart murmur in hypertrophic cardiomyopathy was also studied.

Subjects and methods

The subjects in this study were 28 cases of hypertrophic cardiomyopathy fulfilling the criteria in the WHO classification. They consisted of 21 men and seven women with an average age of 41 years. Hypertrophic cardiomyopathy was diagnosed in these patients by means of routine clinical examination, an electrocardiogram, an apex cardiogram, an M-mode echocardiogram, and a two dimensional echocardiogram. Fourteen cases out of the 28 cases examined showed systolic anterior motion of the mitral echo. Cardiac catheterisation was performed in nine of these 14 cases, and showed intracardiac pressure gradients in all nine cases, though the gradient was less than...
mmHg in two of them (Table 1). The other 14 cases of the 28 examined had asymmetric septal hypertrophy or asymmetric apical hypertrophy, but no systolic anterior motion of the mitral echo. Cardiac catheterisation was performed in six of these 14 cases, and no intracardiac pressure gradient was seen in these. Left ventriculography was also performed in all the cases who underwent cardiac catheterisation.

The equipment used was a commercially available two dimensional Doppler echocardiograph, Toshiba SSH-11A/SDS 10A. This system contained a pulsed Doppler flowmeter incorporated in a wide angle phased array system. The pulsed Doppler flowmeter had a 2-4 MHz transducer and the pulse repetition rate was 6 kHz. The sample volume was tear-drop shaped and was 2 mm in depth and 4 mm wide.

Before the intracardiac Doppler flowmetry, the static and dynamic morphology of the intracardiac structures, especially of the mitral valve, chordae, and papillary muscles, was examined by real time echocardiography. The Doppler examination was then performed while the location of the sampling volume was observed in the two dimensional echocardiogram as a monitor. The left atrial cavity was extensively searched for abnormal Doppler signals by continuously moving the sampling volume from the parasternal and apical approaches. When abnormal Doppler signals of mitral regurgitant flow, as previously reported in another paper, were detected, a two dimensional echocardiogram of the long axis view, including the beam direction for these abnormal Doppler signals, was recorded. The beam direction was recorded by a white line in the two dimensional image. The sampling volume was moved on this beam, and the range in which the abnormal Doppler signals are detected on this line was determined. Both ends of this range on the white line were indicated by two white dots in the two dimensional image. The beam direction was successively changed in this section and the above procedure was repeated. The range in which abnormal Doppler signals were detected in one section in the left atrium was drawn as the area surrounded by white dots on each line. This area was interpreted as the extension of mitral regurgitant flow.

In 15 of the 21 cases in which abnormal regurgitant Doppler signals were detected on the long axis image, as described later, the short axis cross-section of the mitral orifice was also recorded and the distribution of regurgitant signals in this section was assessed in the same manner as in the long axis section.8
The left ventricular outflow tract was also searched for abnormal Doppler signals by the Doppler technique. The Doppler signals were subjected to a fast Fourier transform analysis. The instantaneous flow velocity components were continuously displayed in reference to the time axis. Here, the flow velocity components toward the transducer were displayed above the baseline and those away from the transducer below the baseline. Flow velocity spectrograms and the M-mode echocardiogram by one of the Doppler beams were recorded polygraphically with the electrocardiogram and the phonocardiogram obtained in the upper sternal area. The site of the sampling volume was also indicated on the M-mode echocardiogram. A thorough examination with phonocardiography was performed in a sound-proof room on the same day.

Results

DETECTION OF MITRAL REGURGITANT DOPPLER SIGNALS AND MODE OF REGURGITATION

Abnormal Doppler signals were detected in the left atrium in all 14 cases with systolic anterior motion of the mitral echo and in seven of the 14 cases without systolic anterior motion. These 21 cases showed a wide band frequency spectrum composed of uni- or bidirectional frequency components in systole. Such a wide band frequency spectrum was considered to indicate disturbed flow. These abnormal Doppler signals were interpreted as originating from mitral regurgitation. The abnormal signals started immediately after the Doppler signal of the mitral valve closure. In 17 of the 21 cases, the abnormal Doppler signals were pansystolic, but among these 17 cases they appeared prominent in early systole in two, in mid-systole in three, and in late systole in one. In the remaining four of the 21 cases, the abnormal Doppler signals were prominent in early systole and only continued for a short time. These cases showed a lesser extension of mitral regurgitation as in (c) described in the next paragraph.

Distribution of abnormal Doppler signals in the long axis cross-section was classified into the following three types: (a) wide distribution from the mitral orifice over the whole left atrium (Fig. 1), (b) distribution over the posterior half of the left atrium (Fig. 2) and (c) distribution limited to the narrow region near the mitral orifice (Fig. 3). There were no cases in which the regurgitant flow was distributed only in the anterior half of the left atrium.

Fig. 1 Distribution of mitral regurgitant flow in the left atrium. Abnormal pansystolic Doppler signals resulting from mitral regurgitation are recorded in the left atrium. Left: long axis view of the left side of the heart. Ao, aorta; LA, left atrium. White lines indicate the beam directions for the Doppler examination. White dots which are pointed by the small arrows on each beam direction indicate the ends of the segment where abnormal Doppler signals are detected, so that the distribution of mitral regurgitant flow is shown by an area encircled by the white dots, as indicated by the large white arrow. Right: the M-mode echocardiogram, which was recorded by a beam for the Doppler examination, is above, the phonocardiogram is in the middle, and the Doppler signal is below. SV, depth of the sampling volume. Doppler signals of flow toward and those away from the transducer are displayed above and below the baseline, respectively. (Case 10, a 52 year old man, with systolic anterior motion.)
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Fig. 2 Distribution of mitral regurgitant flow in the left atrium. Left: long axis view of the left side of the heart above and short axis view at the level of the mitral orifice below, showing the areas where the abnormal Doppler signals are detected. In this case the mitral regurgitant flow is distributed over the posterior half of the left atrium. Right: M-mode echocardiogram which indicates the depth of the sampling volume, phonocardiogram, and Doppler signals. (Case 21, a 33 year old woman, with systolic anterior motion.)

Fig. 3 Distribution of mitral regurgitant flow in the left atrium. In this case, the mitral regurgitant flow is distributed only near the mitral orifice. (Case 26, a 52 year old man, without systolic anterior motion.)
Regurgitant flow in the short axis cross-section of the mitral orifice level was distributed in the centre of the mitral orifice or throughout the entire orifice (Fig. 2). There were, however, no cases of mitral regurgitant flow which was localised in the vicinity of the anterior commissure or the posterior commissure.

MITRAL REGURGITATION AND ECHOCARDIOGRAPHIC CONDITIONS OF MITRAL VALVE

There was a correspondence between the mode of mitral regurgitation and the presence of systolic anterior motion of the mitral echo. Mitral regurgitation widely distributed throughout the left atrium ((a) above) was seen in only eight cases with systolic anterior motion, and this mode of regurgitation was not found in any of the cases without systolic anterior motion. Mitral regurgitation distributed over the posterior half of the left atrium ((b) above) was seen in five cases with systolic anterior motion and in only two cases without. Mitral regurgitation localised near the centre of the mitral orifice ((c) above) was seen in only one case with systolic anterior motion but in five cases without it (Table 2).

Dislocation between the anterior and posterior mitral leaflets was noted in only two cases with systolic anterior motion (cases 1 and 11 in Table 1).

Efficacy of Two Dimensional Doppler Echo Technique and Left Ventriculography in Detection of Mitral Regurgitation

Mitral regurgitation was seen in 14 of 15 cases undergoing left ventriculography. In 13 of these 14, regurgitation was also detected by two dimensional Doppler echocardiography. In the remaining case, no regurgitation was detected by the Doppler technique, while mild regurgitation was found by left ventriculography. Regurgitation was found by left ventriculography in all of the cases in which regurgitation was seen with the Doppler technique. There was one case in which no regurgitation was observed with either left ventriculography or the Doppler technique (Table 3).

The degree of mitral regurgitation detected by left ventriculography was grade 1 or 2 in 11 of the 14 cases and grade 3 in the other three cases based on the classification of Sellers et al.9 There were no cases of grade 4 regurgitation. In the left ventriculograms, mitral regurgitant flow extended from the centre of the mitral orifice toward the centre or the posterior half of the left atrium. There were, however, no cases of regurgitant flow toward the anterior half of the left atrium. Therefore, the features of mitral regurgitation seen in the left ventriculograms coincided closely with the findings obtained by the Doppler technique.

RELATION BETWEEN MITRAL REGURGITATION AND EARLY PART OF SYSTOLIC MURMUR

Systolic murmurs were recorded in 25 out of the 28 subjects in the present study (Table 1). In eight of these cases (Table 1, cases 1 to 8), the systolic murmur was noted at the apex (Table 2).

Table 2 Modes of mitral regurgitation in reference to the form of hypertrophic cardiomyopathy

<table>
<thead>
<tr>
<th>Distribution of mitral regurgitant flow</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>With systolic anterior motion</td>
<td>8</td>
</tr>
<tr>
<td>Without systolic anterior motion</td>
<td>0</td>
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</tbody>
</table>

Fig. 4 Phonocardiogram in a case of hypertrophic cardiomyopathy with mitral regurgitation. High pitched murmur (black arrows) is recorded in the early phase of systole, and is followed by a murmur of the ejection type. (Case 22, a 49 year old man, with systolic anterior motion.)
Fig. 5 Mitral regurgitant Doppler signals in the left atrium and Doppler signals of the turbulent flow in the left ventricular outflow tract. The mitral regurgitant Doppler signal is shown at the top and the Doppler signal of turbulent flow in the left ventricular outflow tract at the bottom. The mitral regurgitant Doppler signal arises immediately after the first heart sound. The Doppler signal of turbulent flow in the left ventricular outflow tract starts with a short interval after the first heart sound and shows its peak in mid-systole. (Case 5, an 18 year old man, with systolic anterior motion.)

Table 3 Doppler echocardiography and left ventriculography in detecting mitral regurgitation in hypertrophic cardiomyopathy

<table>
<thead>
<tr>
<th>Left ventriculogram</th>
<th>Doppler</th>
<th>Mitral regurgitation (+)</th>
<th>Mitral regurgitation (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral regurgitation (+)</td>
<td>13 cases</td>
<td>1 case</td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation (-)</td>
<td>0 cases</td>
<td>1 case</td>
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</table>

mur had early systolic components following the first heart sound, which were recorded most distinctly near the apex. These components were high pitched (Fig. 4). Seven of the eight cases showed systolic anterior motion of the mitral echo (cases 1 to 7). In these cases, mitral regurgitation was seen by the Doppler technique. The regurgitant Doppler signals started just after the first heart sound and soon reached their full scale (Fig. 1, 2, and 5). In these cases, turbulent Doppler signals in systole were detected in the left ventricular outflow tract, and were thought to originate from the outflow obstruction (Fig. 5). The start of these turbulent Doppler signals was a little later than the end of the first heart sound and their peak was about 0.1 s later than the end of the first heart sound. In one case without sys-
systolic anterior motion which was not seen in the left atrium, but no turbulent Doppler signals were detected in the left ventricular outflow tract. In the remaining four cases (cases 16 to 19), however, mitral regurgitant Doppler signals reached a peak in the early part of systole. No systolic murmurs were seen in three cases without systolic anterior motion of the mitral echo (cases 26 to 28).

Discussion

In the present study, mitral regurgitation was detected by the Doppler echo technique in all cases with systolic anterior motion of the mitral echo and in half of the cases without. The presence of mitral regurgitation in so high a proportion of cases with hypertrophic cardiomyopathy makes a study of pathophysiological features of this disease worthwhile.

MECHANISM OF MITRAL REGURGITATION

It is well known that systolic anterior motion of the mitral echo is one of the characteristic phenomena in hypertrophic cardiomyopathy. Some have shown that the echo sources of systolic anterior motion were the mitral chordae tendineae. Others showed that the distal end of the anterior mitral leaflet was oriented perpendicularly to the interventricular septum in systole, manifesting systolic anterior motion in the M-mode echocardiogram. One of us has already reported that the position, shape, and movement of the hypertrophied papillary muscle play essential roles in causing the abnormal motion and orientation of the mitral valve and the chordae tendineae, resulting in systolic anterior motion in the M-mode echocardiogram. The abnormalities in the anatomy and motion of the mitral valve, chordae tendineae,
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and papillary muscles are considered to be mild or absent in patients who do not show this.

These abnormalities may also cause the deformation of the mitral orifice, resulting in distorted coaptation of the valve, as well as systolic anterior motion of the mitral echo. This is probably why all the cases with systolic anterior motion showed mitral regurgitation in the present study. The abnormalities of the mitral apparatus are mild or absent in patients of the non-obstructive form. This is considered to be why the mitral regurgitant signals were localised near the mitral orifice or were absent in the cases without systolic anterior motion in the present study.

The mitral regurgitant signals started immediately after mitral valve closure. They were prominent, however, in the first half of systole in some cases, in the latter half of systole in others, and in mid-systole or pansystole in the remainder, while systolic anterior motion was usually maximal in mid-systole. Thus, systolic anterior motion and mitral regurgitation do not seem to be closely related and appear to be different effects of the abnormalities in the anatomy and motion of the mitral apparatus. These, in many instances, produce localised narrowing between the mitral apparatus and papillary muscles and the hypertrophied septum, resulting in an intraventricular pressure gradient. Thus, patients with systolic anterior motion are usually considered to have obstruction, even though some have no intraventricular pressure gradient. The obstructive and non-obstructive forms are considered to be a continuous spectrum. One can generalise that mitral regurgitation is usually present in the obstructive form of hypertrophic cardiomyopathy, but is mild or absent in the non-obstructive form.

Mitral regurgitant flow in the cases with systolic anterior motion of the mitral echo usually showed a wide distribution over the central part and the posterior half of the left atrial cavity. In the short axis cross-section at the level of the mitral orifice, regurgitant flow was detected over the entire extent of the coaptation line or in the centre of the orifice. In idiopathic valve prolapse caused by the floppy mitral valve, mitral regurgitant flow is, in general, located either at the anterolateral or posteromedial commissures. In the present study, only two cases showed mitral leaflet prolapse towards the left atrium. In rheumatic mitral valve disease, regurgitation does not often occur along the left atrial posterior wall. The distribution pattern of mitral regurgitant flow in hypertrophic cardiomyopathy appears to be different from the patterns in idiopathic mitral valve prolapse and rheumatic mitral valve disease. This difference in the haemodynamic features of mitral regurgitation between these diseases suggests that the underlying valve condition of mitral regurgitation is different. It seems also to support the idea that mitral regurgitation in hypertrophic cardiomyopathy results from the distorted coaptation of the valve caused by the abnormalities in anatomy and motion of the mitral apparatus.

RELIABILITY OF DOPPLER TECHNIQUE IN DETECTION OF MITRAL REGURGITATION

In the present study, a satisfactory correspondence was seen between the Doppler technique and angiocardiography in sensitivity for detecting mitral regurgitation, and the information obtained by both methods was similar. This agreement appears to support the reliability of the Doppler method in the detection of mitral regurgitation.

Doubts have existed of course concerning angiocardiography which, until recently, was the main way of detecting mitral regurgitation in hypertrophic cardiomyopathy. It has been argued that mitral regurgitation may be artefactually induced, especially by premature ventricular contractions or by the injection of contrast material itself. The results we have obtained non-invasively by the Doppler technique confirm the reality of the mitral regurgitation previously observed by angiocardiography and deny the importance of these artefacts.

Thus, the good correspondence between the Doppler technique and angiocardiography shows that mitral regurgitation occurs frequently in hypertrophic cardiomyopathy.

SIGNIFICANCE OF MITRAL REGURGITATION IN DEVELOPMENT OF SYSTOLIC MURMUR

The cause of the systolic murmur in hypertrophic cardiomyopathy has been variously attributed to obstruction of the left ventricular outflow tract, to the concomitant regurgitation, or to the obstruction of the right ventricular outflow tract and so far no satisfactory analysis of the cause of this murmur exists. In the present study, we tried to determine if obstruction of the left ventricular outflow tract or mitral regurgitation was more closely related to the systolic murmur. The early part of the systolic murmur has the following characteristics: (1) the maximum point is at the apex (Fig. 7), (2) it has a high-pitched quality, and (3) in cases in which the murmur is clearly recorded, mitral regurgitation is detected by the Doppler technique and the Doppler signals started just after the first heart sound (Table 1, cases 1 to 8). These features suggest that the early part of the systolic murmur is closely related to mitral regurgitation. Turbulent Doppler signals in the left ventricular outflow tract occur a little later than the first heart sound and the peak of these signals was during or after mid-systole. In one case without systolic anterior motion of the mitral echo, the early part of the systolic mur-
mur was detected together with mitral regurgitation even though no turbulent flow was found (Table 1, case 8). From these results, it appears that the early part of the systolic murmur in this disease results mainly from mitral regurgitation rather than from the turbulence of blood flow in the left ventricular outflow tract.

Even though the Doppler signals of mitral regurgitation were detected in the early systolic phase, there were cases where the early part of the systolic murmur was not recorded. In such cases, the distribution of regurgitation was localised in the vicinity of the mitral orifice and the degree of regurgitation was mild. Therefore, they do not seem to be detected by phonocardiography because of unsatisfactory sensitivity.

The cause of the midsystolic and late parts of the systolic murmur in this disease are thought to be obstruction in the left ventricular outflow tract, but mitral regurgitation may also contribute at these stages.

Conclusion

The high incidence of mitral regurgitation in hypertrophic cardiomyopathy is confirmed non-invasively by two dimensional Doppler echocardiography. Mitral regurgitation is more frequent and more severe in the obstructive form than in the non-obstructive form. It is thought to be attributable to the distortion of the mitral orifice which may be inevitable in hypertrophic cardiomyopathy. The early part of the systolic murmur is generated mainly by mitral regurgitation but this also contributes to the mid and late systolic parts of the murmur.

References

Mitrval regurgitation in hypertrophic cardiomypathy


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