

Clinical significance of early or mid-systolic apical murmurs: Analysis by phonocardiography, two-dimensional echocardiography and pulsed Doppler echocardiography

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Summary

The records of 2,000 consecutive patients who had been examined by auscultation, phonocardiography (PCG), two-dimensional echocardiography and pulsed Doppler echocardiography (PDE) were reviewed to assess the clinical significance of apical systolic murmurs which cease well before the aortic closure sound. Fifty-five patients were verified to have early or mid-systolic apical murmurs. Mitral regurgitation (MR) was detected in 32 patients by PDE (29/32) and/or PCG with methoxamine test (27/32). The degree of MR was judged to be mild by PDE in all cases. Apical systolic murmurs due to MR began mainly with the first heart sound (27/32), were confined to the apex (27/32), and high-pitched (25/32). Their intensity was grade III/VI or less in all cases. Mitral valve prolapse (12 patients) was the most common cause of MR. Other causes were rheumatic mitral involvement in seven patients, dilated or ischemic cardiomyopathy in five, mitral annular calcification in three, and hypertrophic cardiomyopathy in two. The causes of the MR in the remaining three patients could not be identified. Thus, early or mid-systolic apical murmurs are mainly attributable to mild MR which can be diagnosed by careful auscultation, PDE and/or PCG with the methoxamine test.

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Key words

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Introduction

When systolic murmurs of maximum intensity are audible at the apex, mitral regurgitation is regarded the most common cause. However, murmurs originating in the aortic valve or left ventricular outflow tract are sometimes best heard at the apex, and in older patients with well developed chests, or emphysema, the murmurs are often louder at the apex than in the second right intercostal space. In patients with idiopathic hypertrophic subaortic stenosis, a rough or harsh systolic murmur is sometimes loudest at the apex. If the murmur extends throughout systole, mitral regurgitation can be reliably diagnosed. However, a murmur which is not holosystolic, primarily early or mid-systolic, presents a problem.

To assess the clinical significance of the apical systolic murmurs which cease well before the second sound, we reviewed the records of 2,000 consecutive patients who had been examined by auscultation, phonocardiography, two-dimensional echocardiography, and pulsed Doppler echocardiography. The purpose of this study is to document the findings of 55 patients who were identified as having apical early or mid-systolic murmurs.

Subjects and Methods

The records of 2,000 consecutive patients who were examined by auscultation, phonocardiography, two-dimensional echocardiography and pulsed Doppler echocardiography were reviewed. The data of fifty-five patients who had apical early or mid-systolic murmurs were analyzed with special attention to their auscultatory findings.

Phonocardiography: Tracings were obtained using multifilter system phonocardiography¹⁾. Prior to the recordings, careful auscultation was made with special attention to the point of the maximum intensity, area of transmission, timing,

duration, intensity, pitch (high or medium), quality (blowing, harsh, rough, musical or vibratory and scratchy or clicky), and respiratory changes of the murmurs. The phonocardiographic tracings were analyzed in detail with particular reference to the timing and duration²⁾. Amyl nitrite inhalation was performed for all 55 patients, and the methoxamine test³⁾ was performed for 48 patients. Seven patients who were hypertensive, elderly, or diagnosed as having severe left ventricular dysfunction were not tested by methoxamine.

Pulsed Doppler echocardiography: An unidirectional ultrasonic pulsed Doppler echocardiograph was used in combination with a cross-sectional echocardiograph (Aloka SSD 910). The frequency of the pulsed Doppler transducer was 3 MHz, and the pulsed repetition rate was 4.4 KHz. The Doppler signal was recorded simultaneously with the M-mode echocardiogram, phonocardiogram and electrocardiogram using a strip chart recorder (Honeywell model 1219). The sampling site of the Doppler signal could be set at any depth from 0.5 to 15 cm from the transducer, and displayed on the simultaneously-recorded M-mode echocardiogram. The sampling volume dimension along the ultrasonic beam could be selected at 3, 4.5 or 6 mm. The Doppler signals were searched for by continuously moving the sampling site over a wide area around the mitral ostium in the left atrial cavity using two-dimensional display, and was also monitored by Doppler spectro-sound. The Doppler signal was recorded using real-time, on-line sound spectrography, showing flows toward and away from the transducer below and above the baseline, respectively. Mitral regurgitation was estimated on the basis of the location and area of distribution of abnormal systolic flow detected within the left atrium, according to the classification of Miyatake⁴⁾ et al. The appearance and duration of abnormal systolic flow has been noticed to be


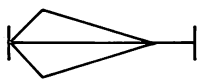


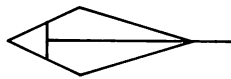
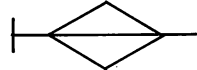
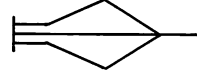
	Timing & peak	No.	Pitch	Quality	Transmission to 4L	Masking effect	Etiology
I		5	H 4 M 1	Blowing 1 Harsh 2 Rough 1	1		Rh 2 Scl 2 MVP 1
II		10	H 9 M 1	Blowing 2 Harsh 6 Rough 1	1 2 1	1 1 1	MVP 4 Rh 2 Nor 2 Scl 1 DCM 1
III		4	H 1 M 3	Blowing 1	1		MVP 2 Nor 1 DCM 1
IV		3	H 3 M 0	Blowing 1 Harsh 1 Rough 1		1	Rh 1 MVP 1 Scl 1
V		4	H 4 M 0	Blowing 1 Rough 3	1 1	1 1	OMI 1 MVP 1 Rh 2
VI		5	H 3 M 2	Harsh 2 Rough 2	1 1	1 1	HOCM 1 OMI 2 MVP 2 DCM 1
VII		1	H 1 M 0	Harsh 1	1	1	HOCM 1

Fig. 1. Diagram of phonocardiographic findings of mitral regurgitation thought to be the cause of early or mid-systolic apical murmurs.

Thirty-two patients in whom mitral regurgitation was detected by pulsed Doppler echocardiography and/or phonocardiography are subdivided into 7 groups according to the peak and timing of their systolic murmurs. Although the majority of the murmurs begin with the first heart sound and are crescendo-decrescendo in character, those of 5 patients are mid-systolic diamond- or spindle-shaped in character. The murmurs in question are localized at the apex in 27 of 32 patients.

H and M=high-pitched and medium-pitched murmurs; Rh=rheumatic heart disease; Scl=sclerotic mitral valve; MVP=mitral valve prolapse; Nor=normal mitral valve; DCM=dilated cardiomyopathy; OMI=old myocardial infarction; HOCM=hypertrophic obstructive cardiomyopathy.

changeable depending on the sampling site. A particular attention was paid, therefore, to get the holosystolic signal as possible as we do.

Two-dimensional echocardiography: Two-dimensional echocardiography was performed in the supine or slightly left lateral position using a commercially-available, real-time, wide-angle, phased-array-sector scanner (Aloka SSD 810) with a 2.25 MHz transducer. Two-dimensional echocardiographic records consisted of four

sectional images; namely, the long-axis, short-axis, apical four-chamber, and subxiphoid views. The images displayed in real-time at a rate of 30 frames/sec were recorded on a video tape, and simultaneous M-mode echocardiograms were recorded using a strip chart recorder (Aloka SSZ 91). Valve motion was carefully assessed to determine the lesions. Special attention was paid to the presence of mitral valve prolapse, according to the criteria of Yoshikawa et al⁵⁾.

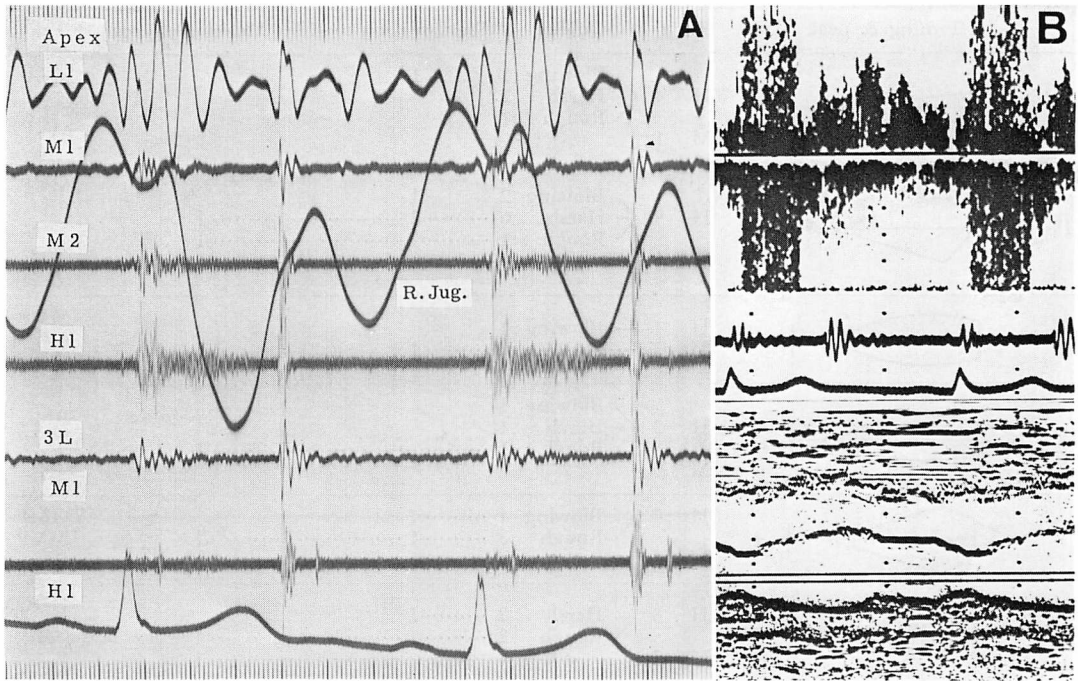


Fig. 2. Phonocardiogram and Doppler echocardiogram of a patient with chorea minor (11-year-old girl).

An apical systolic murmur begins with the first heart sound and radiates to the third left intercostal space. The pulsed Doppler echocardiogram shows bidirectional regurgitant flow signal behind the mitral valve, the duration of which is the same as the apical systolic murmur.

Results

1. Prevalence of mitral regurgitation in patients with early or mid systolic apical murmurs

Among 55 cases, mitral regurgitation was detected in 32 patients using pulsed Doppler echocardiography and/or pharmacodynamic phonocardiography using methoxamine. Pulsed Doppler echocardiography disclosed mitral regurgitation in 29 patients, but missed three patients whose regurgitation was detected by phonocardiography with pharmacodynamic maneuvers. The apical systolic murmurs of 27 patients were intensified by methoxamine infusion and decreased by amyl nitrite inhalation. Methoxamine infusion was not performed for four patients because of hypertension or very poor left ventricular function. In one patient with hypertrophic obstructive cardiomyopathy,

Table 1. Causes of apical early or mid-systolic murmurs

MR		No MR	
Mitral valve prolapse	12	Fish-bone murmur ⁶⁾	7
Rheumatic heart disease	7	Aortic valvular stenosis	6
Ischemic or dilated cardiomyopathy	5	Cardiorespiratory murmur	3
Sclerotic mitral valve	3	Hypertrophic cardiomyopathy	4
Hypertrophic cardiomyopathy	2	Others	3
Others	3		
	32		23

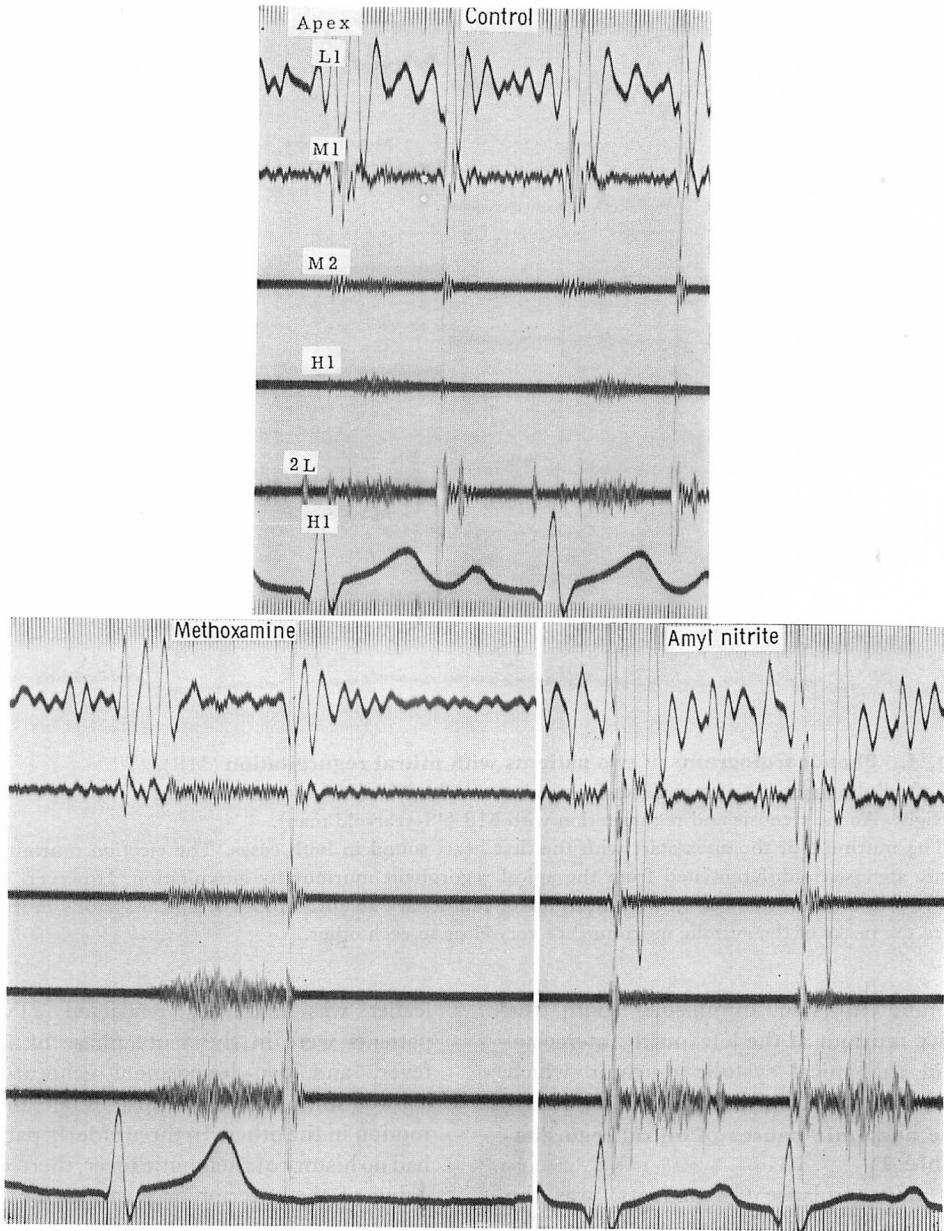


Fig. 3. Effects of pharmacodynamic maneuvers on systolic murmurs in a patient with mitral valve prolapse (24-year-old man).

An apical high-pitched mid-systolic murmur becomes mid- to late systolic and transmits to the second left intercostal space after methoxamine infusion. Basal systolic murmur is buried in the new murmur. After amyl nitrite inhalation, the apical systolic murmur becomes trivial and the basal ejection systolic murmur is greatly intensified.

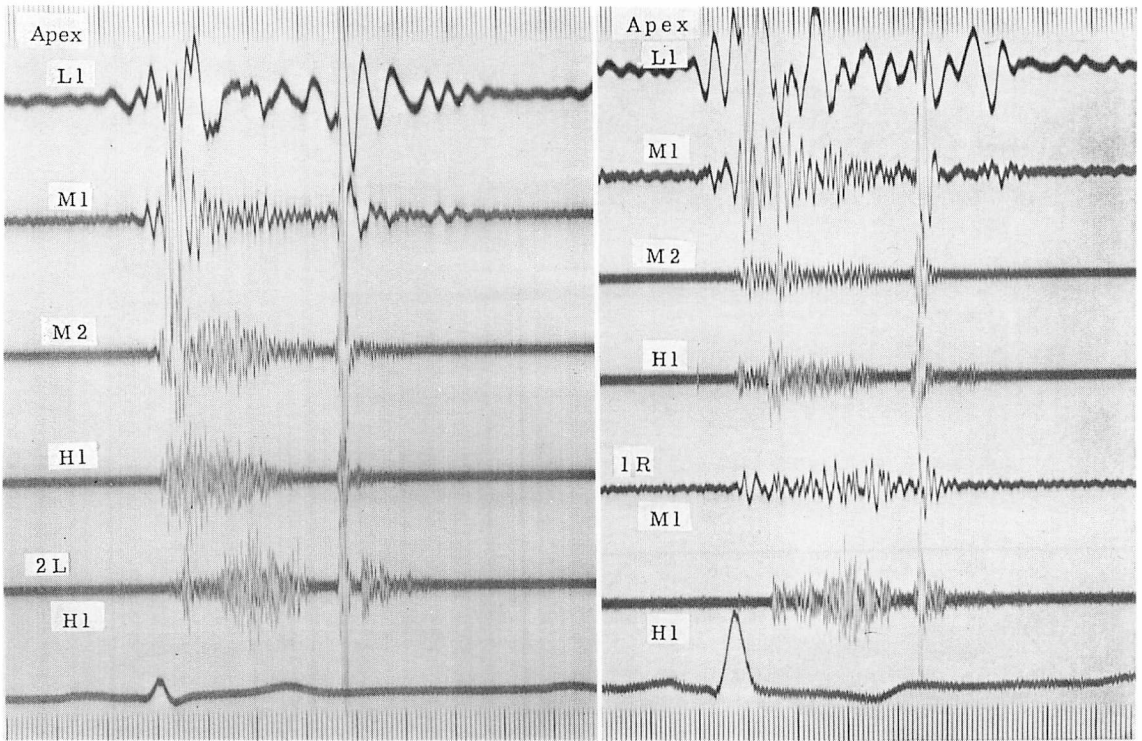


Fig. 4. Phonocardiograms of two patients with mitral regurgitation (MR).

Left: Pulmonary valve stenosis and regurgitation with MR (34-year-old woman).

Right: Aortic stenosis and regurgitation with MR (48-year-old man).

The murmurs at the apex start with the first heart sound in both cases. The ejection murmur of aortic stenosis is differentiated from the apical regurgitant murmur by auscultation. However, it is difficult to differentiate the ejection murmur of pulmonary stenosis from the apical systolic murmur since the peaks of the systolic murmurs are very close to each other.

methoxamine infusion diminished both the obstructive murmur at the left fourth intercostal space and the apical systolic murmur which commenced with the first heart sound.

2. The anatomic causes of mitral regurgitation (Table 1)

Mitral valve prolapse (12 patients) was the most common cause of mitral regurgitation. The leaflets bowing toward the left atrium beyond the mitral annulus was the characteristic two-dimensional echocardiographic finding. Rheumatic etiology was next in frequency (five patients). In three of the latter, both mitral leaflets were thickened; the anterior leaflet motion was reduced, and the diastolic motion of the posterior

leaflet was markedly restricted. Two other patients were in the acute phase of rheumatic fever, and two-dimensional echocardiography showed mitral valve prolapse in one and normal motion in the other. In three elderly patients who had no history of rheumatic fever, there was thickening of the anterior or posterior mitral leaflet with mild reduction of its motion, and we categorized this finding as sclerotic mitral valve (Table 1). Five patients had papillary muscle dysfunction due to coronary artery disease or dilated cardiomyopathy. Two-dimensional echocardiography showed diffuse or segmental wall motion abnormalities involving the base of one or both papillary muscles and the adjacent left ventri-

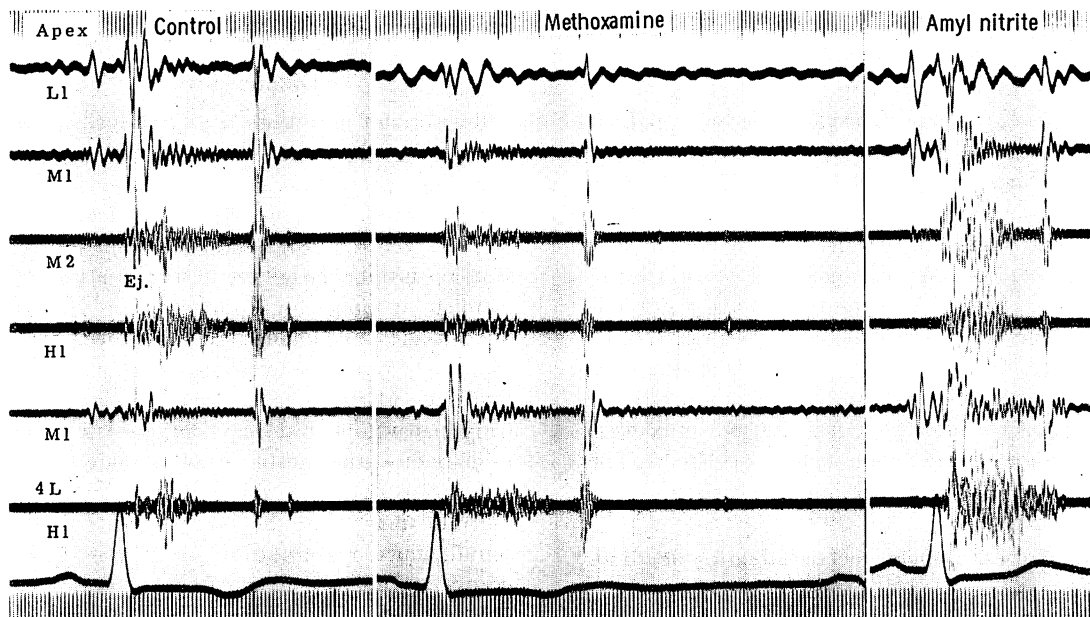


Fig. 5. Phonocardiograms of a patient with an apical systolic murmur in whom mitral regurgitation was not detected (63-year-old man).

A loud ejection sound precedes the apical systolic murmur which decreased with methoxamine infusion and increases with amyl nitrite inhalation. This is an example of an ejection systolic murmur loudest at the apex.

cular wall. Two patients had hypertrophic obstructive cardiomyopathy. The causes of mitral regurgitation in three patients could not be identified.

3. The phonocardiographic characteristics of apical systolic murmurs

The apical systolic murmurs of 32 patients in whom mitral regurgitation was detected were classified in seven types according to their timing and peak amplitude, as shown in **Fig. 1**. The murmurs commenced with the first heart sound (**Fig. 2**) in 27 patients, whereas they were mid-systolic in five. The murmurs were localized at the apex in 22 patients, and radiated to the 4th left intercostal space in 10 patients. The murmurs were high-pitched and blowing, and harsh or rough in 25 patients. In another seven patients they were medium-pitched. The murmurs were of 2/6 or 3/6 intensity in all patients. Methoxamine infusion provoked pansystolic (**Fig. 3**) or late systolic murmurs in 26 patients. In one

patient with hypertrophic obstructive cardiomyopathy, methoxamine infusion markedly decreased an apical systolic murmur with disappearance of a Doppler signal of MR.

Despite meticulous auscultation, mitral regurgitation was not diagnosed before the phonocardiography in eight patients, because the loud murmurs of combined valvular disease (**Fig. 4**) or hypertrophic cardiomyopathy masked the stray vibrations after the first heart sounds and the apical systolic murmurs sounded as though they began after the first heart sound and ceased well before the second heart sound.

The relationship of the timing and peak of the apical systolic murmurs to the etiology of mitral regurgitation is shown in **Fig. 1**. Configuration of apical systolic murmurs did not suggest their etiologies.

The apical systolic murmurs of 23 patients in whom mitral regurgitation was ruled out by all the diagnostic means began after the two compo-

nents of the first heart sound (**Fig. 5**). Ejection sounds preceded the murmurs in 12 patients. The murmurs radiated to the 4th left intercostal space in 22 patients. One exception was a patient with a localized musical apical systolic murmur in which an anomalous band in the left ventricle was regarded the cause. The murmurs of 11 patients had a characteristic pitch and quality which facilitated differentiating the systolic murmurs from the murmurs of mitral regurgitation. There were seven fishbone murmurs⁹⁾, three cardiorespiratory murmurs and one innocent vibratory systolic murmur (Still's murmur). In seven of 12 other patients, the murmurs were high-pitched and either rough or harsh. The murmurs of the remaining five patients were medium-pitched.

4. Pulsed Doppler echocardiographic findings

Mitral regurgitation of 29 patients was detected by pulsed Doppler echocardiography (PDE). The Doppler signals detected by PDE had a wide frequency range, and were either unidirectional or bidirectional. They were pansystolic regurgitant in 20 patients. In 13 of them the flow signals were immediately posterior to the mitral valves, and in another seven the signals were recorded over a wider area except for the area below the aortic root. Early to mid-systolic regurgitant flow signals were observed in six patients and they were localized immediately posterior to the mitral leaflets. In the remaining three patients, the flow signals were late systolic and localized posterior to the mitral valves.

In 12 patients with mitral valve prolapse, the relation between the prolapsing phase of the mitral valve as examined by two-dimensional and M-mode echocardiography and the mitral systolic flow patterns were as follows: Among seven patients who had pansystolic prolapse, there were six pansystolic regurgitant flow patterns and one late systolic regurgitant flow patterns. In five patients who had late systolic prolapse by two-dimensional and M-mode echocardiography, three had pansystolic regurgitant flow patterns (**Fig. 6**) and two had

late systolic patterns.

Discussion

Regurgitant murmurs are produced by the retrograde flow from a cardiac chamber of relatively high pressure to the one of lower pressure. Since there is a high pressure difference between the left ventricle and left atrium throughout systole, mitral regurgitant murmurs are usually pansystolic and high-pitched, and usually plateau-like in configuration. However, as previously reported by some investigators, the murmurs of mitral regurgitation may not be truly pansystolic but may end in late systole well before the aortic or pulmonic closure sound⁷⁻⁹⁾. In acute mitral regurgitation the murmur may cease before the aortic second sound, since regurgitation of a large volume occurs in the case of a left atrium of normal size and poor distensibility; then, an unusually high left atrial pressure occurs in late systole and the ventriculo-atrial pressure gradient is resolved there⁷⁾. Early systolic murmurs are sometimes heard in patients with severe mitral stenosis and mild mitral regurgitation⁹⁾, and mid-systolic murmurs can occur in mitral regurgitation due to papillary muscle dysfunction⁹⁾. On the other hand, aortic systolic murmurs often radiate to the apex or may occasionally be maximal at this site¹⁰⁾, and systolic murmurs due to hypertrophic cardiomyopathy are likewise sometimes loudest at the apex¹¹⁾, providing a differential diagnostic problem.

Development of the ultrasonic pulsed Doppler techniques and cross-sectional echocardiography has facilitated the noninvasive analysis of dynamics of intracardiac flow and its spatial and temporal relations to intracardiac structures. Using these techniques we studied the genesis of apical systolic murmurs which cease well before the second heart sound.

1. The cause of mitral regurgitation

In the present results, neither severe acute mitral regurgitation nor severe rheumatic mitral valve involvement was observed; mitral valve prolapse was the most common cause. In 1979, Mintz et al¹²⁾ reported that mitral valve

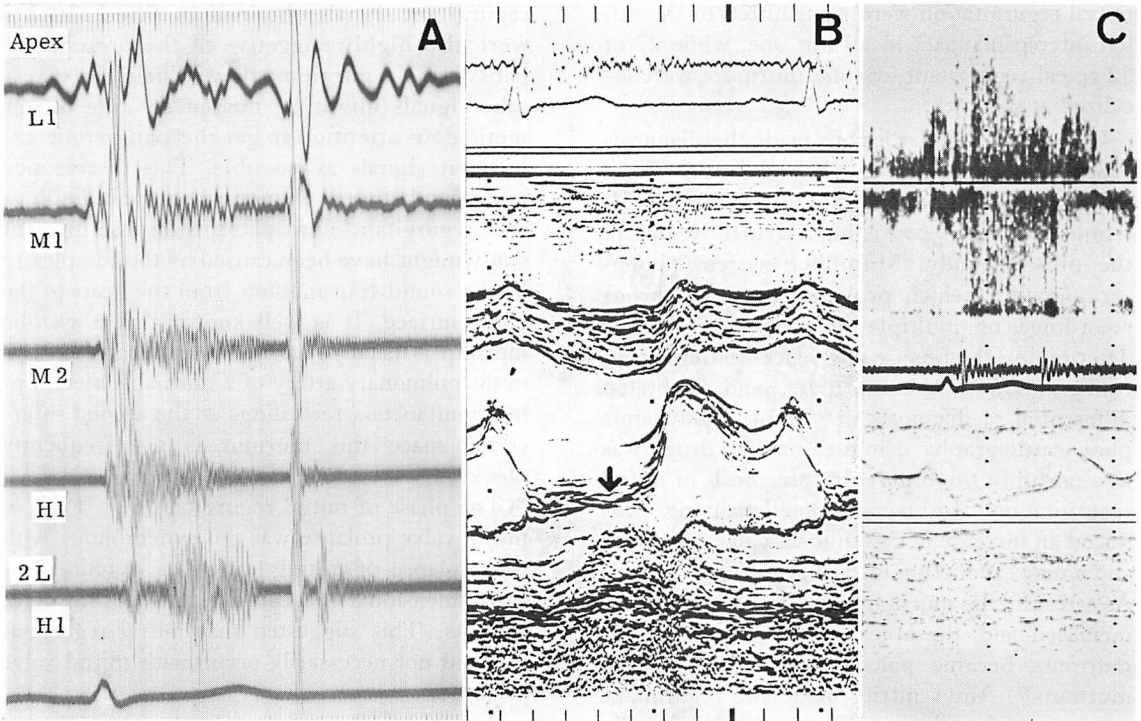


Fig. 6. Phonocardiogram, M-mode echocardiogram and pulsed Doppler echocardiogram of a patient with mitral valve prolapse (34-year-old woman).

An apical systolic murmur starts with the first heart sound and ends well before the second heart sound (A). M-mode echocardiogram shows mid-systolic buckling of the mitral valve which appeared in late systole (B). Pulsed Doppler echocardiogram shows a pansystolic decrescendo regurgitant flow signal behind the mitral valve.

prolapse was the most common cause of mitral regurgitation which was diagnosed by the presence either of pansystolic or late systolic murmurs. Actually, after the development of two-dimensional echocardiography, patients thought to have mitral regurgitation of other than rheumatic etiology have often been elucidated as having mitral valve prolapse.

2. Phonocardiographic findings

Auscultation by well-trained cardiologists is an accurate, simple and innocuous method for making the diagnosis. In our series, 21 early systolic apical murmurs were diagnosed as mitral regurgitant murmurs by auscultation with strict attention to the fact that these systolic murmurs begin with the first heart sound. Ravin¹³⁾

stressed that, in placing great emphasis on the timing and phonocardiographic shape of murmurs, many physicians have lost sight of the important differences in pitch and quality of these murmurs which can more easily be recognized than the finer details of timing. However, among 21 apical systolic murmurs mentioned above, only six were high-pitched and blowing; the others were high-pitched but rough or harsh in character. Rough or harsh early systolic murmurs were difficult to differentiate from the murmurs of aortic origin without paying attention to their timing. Localization of murmurs at the apex was highly suspicious of mitral regurgitation in the present study, since apical systolic murmurs without evidence of

mitral regurgitation were transmitted to the 4th left intercostal space in all but one, while 27 of 32 apical regurgitant systolic murmurs were localized at the apex.

Coexisting valvular lesions made the diagnosis of mitral regurgitation more difficult. Eight apical systolic murmurs were missed by auscultation because of coexisting valvular lesions in the present study. Multifilter system phonocardiography, which provided us simultaneous recordings of multiple areas, was useful in determining the precise differences in timing and configuration of the murmurs, and facilitated differential diagnosis¹⁾. Pharmacodynamic phonocardiography using vasoactive drugs was also useful in the differential diagnosis of mitral regurgitation. Intravenous methoxamine produced an increase in systemic vascular resistance and a reflex reduction in cardiac rate and output. As a result, the murmurs of mitral regurgitation increased and the apical early or mid-systolic murmurs became pansystolic or late systolic murmurs²⁾. Amyl nitrite made the regurgitant murmurs softer, but an increased basal systolic ejection murmur started earlier and was transmitted well to the apex, so that in some cases, it became difficult to decide whether an apical systolic murmur truly decreased in intensity.

3. Pulsed Doppler findings

It is now recognized that pulsed Doppler echocardiography (PDE) is very useful to diagnose mitral regurgitation noninvasively by detecting reverse flow through the mitral valve. In a recent study¹⁴⁾, it was demonstrated that in all but one patient the phase of mitral regurgitation detected by PDE coincided well in timing with a regurgitant murmur recorded on the PCG. Furthermore, in patients whose regurgitant murmurs were intensified by Angiotension II, abnormal Doppler signals were detected even at rest, and these signals coincided with newly-developed regurgitant murmurs on provocation. The present results were much different from that report. The regurgitant murmurs of our patients were early or mid-systolic, whereas most of the regurgitant flow patterns by PDE were pansystolic (20 of 29 cases). The late systolic

regurgitant signals obtained in three patients were also highly suggestive of the presence of pansystolic regurgitant flow. Their early systolic signals might be missed in spite of our meticulous attention to get the pansystolic regurgitant signals as possible. This discrepancy in timing between phonocardiographic findings and regurgitant flow patterns in the present study might have been caused by the complexity of the sound transmission from the heart to the chest surface. It is well known that a systolic murmur is usually recorded by intracardiac PCG in the pulmonary artery of a normal subject, but in simultaneous recordings at the second intercostal space this murmur is not frequently observed.

The phase of mitral regurgitation on PDE in mitral valve prolapse was not synchronous with the prolapse of mitral leaflets as examined by two-dimensional echocardiography in four of 12 patients. This suggested that mitral regurgitation did not necessarily occur with mitral valve prolapse.

Results of the present study showed that apical early or mid systolic murmurs are mainly due to mild mitral regurgitation, that mitral valve prolapse is the most common cause, and that pulsed Doppler echocardiography and/or phonocardiography using the methoxamine test is valuable for confirming mitral regurgitation.

要 約

心尖部収縮早期および中期雑音に対する心音図, 心エコー図, パルス・ドップラー法による検討

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II音大動脈成分に到らずに終り, 心尖部に最強点を有する心尖部収縮早期および中期雑音の臨床的意義を検討する目的で, 聴診, 心音図, 心エコー図, パルス・ドップラー法による検査を施行した連続2000例につき検討を加えた。55例の心尖

部収縮早期および中期雑音を呈する症例が認められ、うち 32 例にパルス・ドプラー法および薬物負荷心音図法、あるいはその一方によって僧帽弁閉鎖不全の存在が確認された。パルス・ドプラー法によると、僧帽弁逆流の程度は全例で軽度であった。僧帽弁閉鎖不全に起因する心尖部収縮期雑音は、主として I 音に引き続いて開始しており (27/32)、心尖部に限局し (27/32) また高調であった (25/32)。雑音の強さは全例で Levine III 度以下であった。僧帽弁閉鎖不全の成因としては、僧帽弁逸脱症がもっとも多く、12 例に認められた。その他、リウマチ性 7 例、拡張型ないしは虚血性心筋症 5 例、僧帽弁輪部石灰化 3 例、肥大型心筋症 2 例を認めた。残る 3 例については、僧帽弁閉鎖不全の成因を明らかにし得なかった。これらのことにより、心尖部収縮早期ないし中期雑音は主として僧帽弁閉鎖不全に起因するものであり、注意深い聴診により診断可能であるが、パルス・ドプラー法ならびに薬物負荷心音図法が確定診断に強力な武器となる。僧帽弁閉鎖不全の成因としては僧帽弁逸脱症が最も頻度が高いと考えられる。

References

- 1) Sakamoto T, Uozumi Z, Kaito G, Ueda H: Better resolution in clinical phonocardiography—The use of simultaneously recorded multi-filter system phonocardiograms synchronously taken from various auscultatory areas. *Jpn Heart J* 7: 154, 1966
- 2) Sakamoto T: Mitral insufficiency: Role of phonocardiography in the etiological diagnosis. *J Cardiography* 6: 213-236, 1976
- 3) Ueda H, Sakamoto T, Uozumi Z, Inoue K, Kawai N, Yamada T: The use of methoxamine as a diagnostic aid in clinical phonocardiography. *Jpn Heart J* 7: 204-226, 1966
- 4) Miyatake K, Kinoshita N, Nagata S, Beppu S, Park Y, Sakakibara H, Nimura Y: Intracardiac flow pattern in mitral regurgitation studied with combined use of the ultrasonic pulsed Doppler technique and cross-sectional echocardiography. *Am J Cardiol* 45: 155, 1980
- 5) Yoshikawa J, Kato H, Yanagihara K, Okumachi F, Takagi Y, Yoahida K, Asaka T, Inanami H: Criteria for the diagnosis of prolapsed mitral valve using phonocardiography and echocardiography. *J Cardiography* 12: 773, 1982
- 6) Sakamoto T, Yamaguchi T, Hada Y, Amano K, Takenaka K, Takikawa R: Fishbone murmurs in presumably healthy persons and in functional disorders: A description and phonocardiographic features. *Acta Cardiol* 40: 41, 1985
- 7) Sutton GC, Craige E: Clinical signs of severe acute mitral regurgitation. *Am J Cardiol* 20: 141, 1967
- 8) Surawicz B, Mercer C, Chlebus H, Reeves JT, Spencer FC: Role of the phonocardiogram in evaluation of the severity of mitral stenosis and detection of associated valvular lesions. *Circulation* 795, 1966
- 9) Burch GE, DePasquale NP, Phillips JH: Clinical manifestations of papillary muscle dysfunction. *Arch Intern Med* 112: 112, 1963
- 10) Burch GE, Phillips JH: Murmurs of aortic stenosis and mitral regurgitation masquerading as one another. *Am Heart J* 66: 439, 1963
- 11) Braunwald E, Lambrew CT, Rockoff SD, Ross J Jr, Morrow AG: Idiopathic hypertrophic sub-aortic stenosis. I. A description of the disease based upon an analysis of 64 patients. *Circulation* 30 (Suppl IV): 3, 1964
- 12) Mintz GS, Kotler MN, Segal BL, Parry WR: Two-dimensional echocardiographic evaluation of patients with mitral insufficiency. *Am J Cardiol* 44: 670, 1979
- 13) Ravin A: *Auscultation of the Heart*. 2nd ed, London, Year Book Medical Publ, 1977, p 87
- 14) Yamamoto M, Fukuda N, Asai M, Ohshima C, Kusaka Y, Tominaga T, Ishimoto T, Oki T, Niki T, Mori H: Phase analysis of mitral regurgitation in mitral valve prolapse: Comparison of pulsed Doppler echocardiography with phonocardiography. *J Cardiography* 13: 467, 1983