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# EVALUATION OF MID-SYSTOLIC-CLICK SYNDROME

— with special reference to its apexcardiogram and left ventricular systolic time intervals —

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## Abstract

Clinical and polycardiographic observations conducted on 21 cases with mid-systolic-click syndrome showed the following results.

This syndrome was seen mostly in lean, young women, and most of them came to the hospital with complaint of palpitation. In addition, more than half of these cases had a past history of arrhythmia. Polycardiographically, the left ventricular function was maintained at normal level in most of the cases. Some form of "retraction" could be recognized on the apexcardiogram, and its nadir almost always coincided with the click. For the early detection of this syndrome careful auscultation at bedside and apexcardiography may serve as useful diagnostic aids.

## INTRODUCTION

Mid-systolic-click (MSC) syndrome is generally considered to be asymptomatic with benign prognosis, but because of its cardinal symptoms such as palpitation, nonspecific precordial pain or neuropsychiatric complaints there are some cases being treated as cardiac neurosis for a long period of time. On the other hand, there are reports on a patient resulting in a sudden death due to ventricular premature beat which is often seen in this syndrome[1], and on a case[2] with critical complication such as severe mitral regurgitation due to a rupture of the chordal tendon attached to the mitral valve.

We studied those 21 cases on which we conducted polygraphic examination with MSC syndrome in the past three years, and we investigated their clinical manifestations, apexcardiogram and the left ventricular systolic time intervals.

## SUBJECTS AND METHODS

The subjects, 21 cases in total, consisted of those whose click could

be heard in the mid- or late-systolic phase on physical examinations at the Division of Cardiology of our hospital. These were divided into two groups: those without any abnormality other than the click with or without systolic regurgitant murmur (Group A), and those complicated with some other cardiac diseases (Group B). With each group, sex, age, subjective symptoms, arrhythmia, actual body weight against the standard weight[3], pan-or late-systolic regurgitant murmur (LSM), number of clicks and electro-cardiogram were observed. Polygraphic recordings were made with simultaneous tracings of apexcardiogram (ACG), carotid artery pulses (CAP), phonocardiogram (PCG) and electrocardiogram (ECG).

On ACG the "retraction" of the systolic wave considered to be characteristic of the syndrome was divided into three groups (small, moderate and large) according to the classification by Epstein[4]. As shown in the upper portion of Fig. 1, the "small" is the one which has a notch on its descending limb coming from E point of ACG coincided with (or appeared near the timing of) the click (upper left), the "moderate" is the one where the retraction is recognized clearly (upper middle), and the "large" is the one where a large retraction is observable (upper right). In addition, as reported by other authors[4,5,6] the observation was carried out to see whether or not the nadir of retration coincided with click (the bottom of Fig. 1).

The left ventricular systolic time intervals (LVSTI)-the total systole (Q-II), the ejection time (ET) and the pre-ejection period (PEP)—were calculated from the combined tracings of CAP, ECG and PCG. Subsequently, differences from normal predictable values of LVSTI ($\Delta$Q-II, $\Delta$ET, $\Delta$PEP) as well as ET/PEP ratio were calculated. In this instance, $0 \pm 11$ msec for Q-II, $0 \pm 10$ msec for ET, $0 \pm 8$ msec for PEP, and $2.95 \pm 0.50$ for ET/PEP were taken as in the normal range. Further, the changes in the click and LSM were studied by such loading tests as respiration, postural changes, hand grip test, amyl nitrite inhalation, intravenous methoxamine and smoking.

## RESULTS

### 1. *Clinical findings*

Clinical manifestations are summarized in Table 1. Group A in the table consisted of 15 patients (Case 1 to 15) and Group B of 6 (Case 16 to 21). Case 16 had atrial septal defect (ASD), ventricular septal defect (VSD) and partial anomalous pulmonary venous return (PAPVR), and Case 17 was a surgically corrected ASD. Case 20 had a history of bacterial endocarditis.

TABLE 1 Clinical Manifestations of MSC Syndrome

| | Case No. | Age | Sex | Subj. Symp. | Arrhy-thmia | BW % Δ | LSM | # of Clicks | ECG | Exercise ECG. |
|---|---|---|---|---|---|---|---|---|---|---|
| Group A | 1 | 30 | M | Chest pain Nervousness | PVC | -12.8 | (+) | 1 | LVHV | (-) |
| | 2 | 18 | F | Palpitation | (-) | | (-) | 1 | NL | |
| | 3 | 33 | M | None | (-) | | (-) | 1 | NL | |
| | 4 | 49 | F | None | (-) | | (-) | 1 | | |
| | 5 | 42 | F | Easy fatigability | (+) | -18.5 | (-) | 2 | NL | |
| | 6 | 43 | F | Palpitation Nervousness | (+) | -20.4 | (+) | 1 | LAD Nega. U | (+) |
| | 7 | 49 | F | Palpitation | (+) | -22.3 | holo SM | 1 | LVHV | |
| | 8 | 24 | F | Palpitation | (+) | -16.5 | (+) | 2 | NL | (±) |
| | 9 | 24 | F | Palpitation Chest pain | PAC | -19.0 | (-) | 1 | NL | (±) |
| | 10 | 60 | F | None | (+) | -22.0 | (+) | 3 | LVHV | |
| | 11 | 13 | F | None | PVC | -17.5 | holo SM | 1 | PVCs | (±) |
| | 12 | 18 | F | None | (-) | | (-) | 1 | NL | (-) |
| | 13 | 21 | F | None | (-) | | (-) | 1 | NL | (±) |
| | 14 | 54 | F | Palpitation | (-) | -12.0 | (-) | 2 | LAD flat T | |
| | 15 | 62 | M | None | (-) | -10.1 | (-) | 2 | Brady-cardia | |
| Group B | 16 | 30 | F | Easy fatigability | (-) | | (-) | 1 | NL | (-) |
| | 17 | 42 | F | Easy fatigability Palpitation | (-) | + 4 | holo SM | 1 | Inverted T | |
| | 18 | 52 | M | Anginal pain | (-) | - 3.6 | (-) | 1 | ST↓ | (+) |
| | 19 | 70 | F | None | (+) | -10.9 | (-) | 1 | ST↓ | |
| | 20 | 35 | F | Headache | (-) | -13.1 | holo SM | 1 | NL | (-) |
| | 21 | 63 | M | Precordial Oppression | Af PVC | + 5 | (-) | 1 | ST↓ Inverted T | |

Note : Case 1 ~ 15 : Without cardiac diseases
Case 16~21 : With cardiac diseases
(Case 16, 17 : Congenital heart disease,
18, 19 : Ischemic heart disease,
20 : Bacterial endocarditis
21 : Primary myocardial disease, probable)
LSM = Late systolic murmur, LVHV = Lt. ventricular high voltage,
PVC = Premature ventricular contraction,
PAC = Premature atrial contraction, NL = Normal,
LAD = Lt. axis deviation, SM = Systolic murmur

$$BW\ \%\ \Delta = \frac{\text{Acutual body weight - Standard body weight}}{\text{Standard body weight}} \times 100$$

Af = Atrial fibrillation

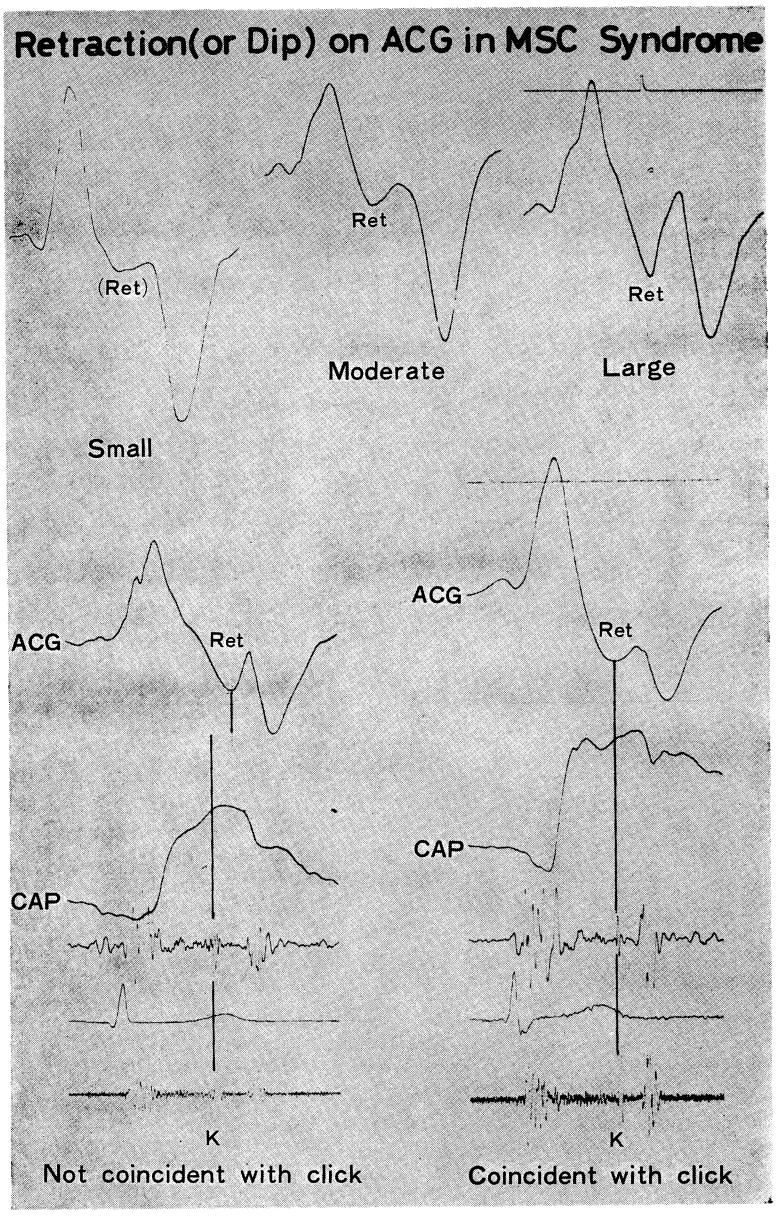


Fig. 1. Classification of "retraction" on ACG. Upper pannel: left; small, middle; moderate, right; large. Lower pannel; The nadior of retraction coincides with click (right), and does not (left). Ret; retraction K; click

Group A was in the age range of 13 to 62 years (36 in average), and of these 15 cases 7 had no subjective symptoms at all, but 6 had palpitation. Eight of them had arrythmia with 2 of ventricular premature beat (VPB) and 1 of atrial premature beat (APB). They gave -10.1 % to -22.3 % (the average being -17.1 %) in the deviation of the body weight against the standard weight. LSM was observed in 6 out of 15. Case 6 showed LSM only in expiration, and Case 13 had a click and holosystolic murmur only in VPB. ECG at rest was normal in 7 out of 14. The exercise ECG was positive in only one, and in 4 there could be observed non-specific ST-T change.

The age of Group B ranged 30 to 70 years with average of 48.7. Most of subjective symptoms and ECG changes in this group appeared to be due to the primary lesions.

2. *Apexcardiogram (ACG)*

ACG was obtainable in 20 out of 21 cases, and with exception of one showing the click only in VPB we studied on the remaining 19 cases (Table 2). In all the 19 there could be observed the retraction on ACG coinciding with or close to the click. There were 10 where the retration coincided with the click, and could be seen no close relationship between the size of the retraction and ET/PEP ratio.

TABLE 2

Retraction (or Dip) on ACG in MSC Syndrome

| Retraction (or Dip) | No. of Cases | =Click | Click > Dip | Dip > Click |
|---|---|---|---|---|
| Small | 5 | 4 | 1 | 0 |
| Moderate | 11 | 5 | 3 | 3* |
| Large | 3 | 1 | 2 | 0 |
| Total | 19 | 10 | 6 | 3 |

* 2 of 3 cases show late systolic bulge.

In Case 20 a pansynstolic murmur of Levine 4 with the click in the late systolic phase could be heard, and a nadir of retraction was also found on ACG (Fig. 2). This is the one in which cardiac murmur was pointed out after develop of bacterial endocarditis, and is presumed to be the subsequent rupture of the chordal tendon attached to the mitral valve.

3. *Left ventricular systolic time intervals (LVSTI)*

LVSTI of our MSC syndrome are shown in Fig. 3. In Group A,

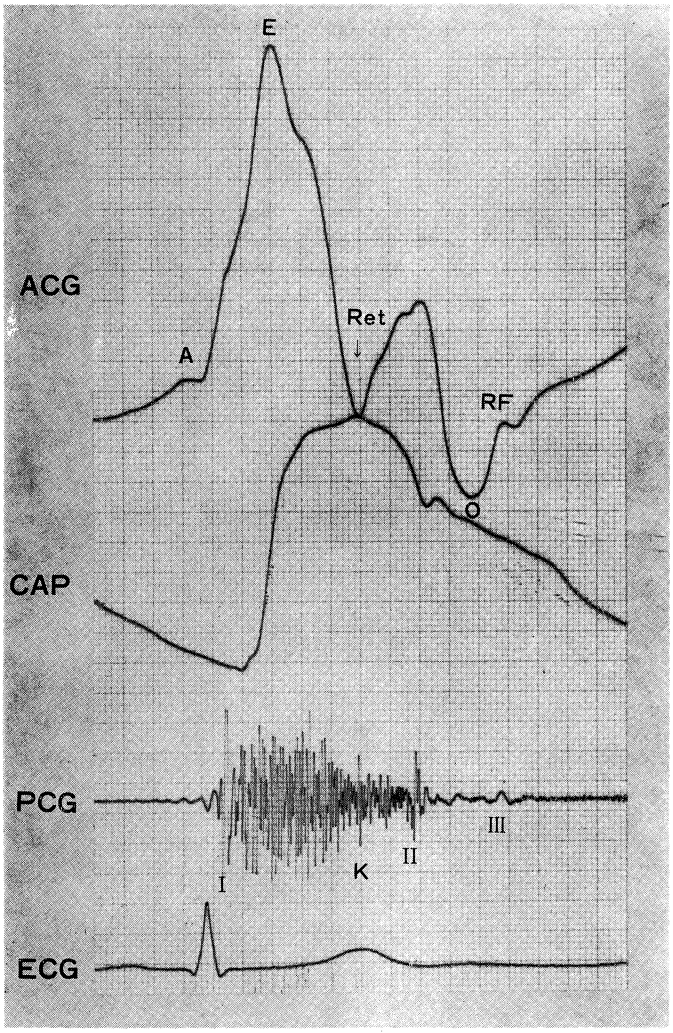


Fig. 2. Case 20 with holosystolic murmur and late systolic click (K) by ausculation, and with large retraction (Ret) on ACG. CAP; carotid artery pulse. PCG; phonocardiogram.

⊿Q-II and ⊿ET ranged in the normal value in the majority of them, while in Group B these values were mostly low. The ET/PEP ratio was in the normal value or close to the normal in most of them, and there were only 4 showed the value below the normal.

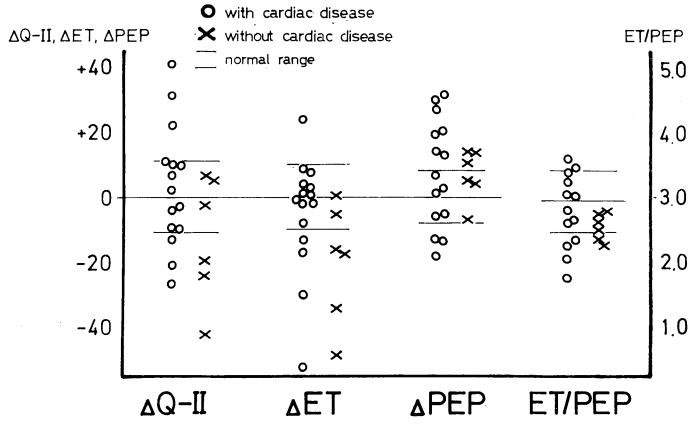


Fig. 3. LVSTI in MSC syndrome. ET/PEP showsng normal value in most of the cases. See the text.

*4. Loading tests*

The results of various tests are given in Table 3. Amyl nitrite inhalation was conducted on 8 cases, and it was found that the click after the inhalation shifted forward in every case. The click became much louder in 2, slightly louder in 3 and fainter in 3. The retraction on ACG became marked after the inhalation, and it shifted forward with the click (upper part of Fig. 4). After intravenous methoxamine given to one patient there appeared late systolic murmur (LSM) (the lower part of Fig. 4).

## DISCUSSION

*1. Clinical observations*

According to Pocock[8], out of 104 cases with MSC and LSM 33 % of them did not have any other cardiac lesions, but in our experiences as high as 74 % of them had some form of other cardiac lesions. It is said[9,10] that atrial septal defect (ASD) is accompained relatively often by this syndrome, and in our groups two cases with congenital heart disease had ASD. On the other hand, we did not see any Marfan's syndrome as pointed out by many authors[1,8], nor was there any case suggesting that the click was extracardiac in origin.

In considering the nature of this syndrome, since in the Group B the clinical feature seems to be greatly modified by the primary lesion, and the following discussions will be limited only in the Group A.

In this group the male to female ratio was 1 to 4, and this syndrome

TABLE 3

Changes in Click & LSM by Various Stress Testing

| | Position | | | Amplitude | | | |
|---|---|---|---|---|---|---|---|
| | Unchanged | Forward | Backward | Unchanged | Increased | Decreased | ↓→↑ |
| A. Amyl Nitrite | | | | | | | |
| Click (8 cases) | | 8 | | | 2 | 3 | 3 |
| L S M (5 cases) | | | | 1 | 1 | 1 | 2 |
| B. Methoxamine | | | | | | | |
| Click (1 case) | | 1 | | | | 1 | |
| L S M (1 case) | | | | | 1* | | |
| C. Respiration | | | | | | | |
| Click (9 cases) | 7 | 2 (insp.←, exp.→) | | | | | |
| D. Squatting | | | | | | | |
| Click (2 cases) | 1 | | 1 | | | | |
| E. Sitting | | | | | | | |
| Click (2 cases) | | 2 | | | | | |
| F. Standing | | | | | | | |
| Click (1 case) | | | 1 | | | | |
| G. Hand-Grip | | | | | | | |
| Click (2 cases) | 1 | 1 | | | | | |
| H. Cigarett smoking | | | | | | | |
| Click (1 case) | 1 | | | | 1 | | |

Note : ( ) = Number of observed cases
↓→↑ = Initially decreased, then increased at 30～90 sec. after amyle nitrite inhalation.
* Newly developed after methoxamine intravenous infusion

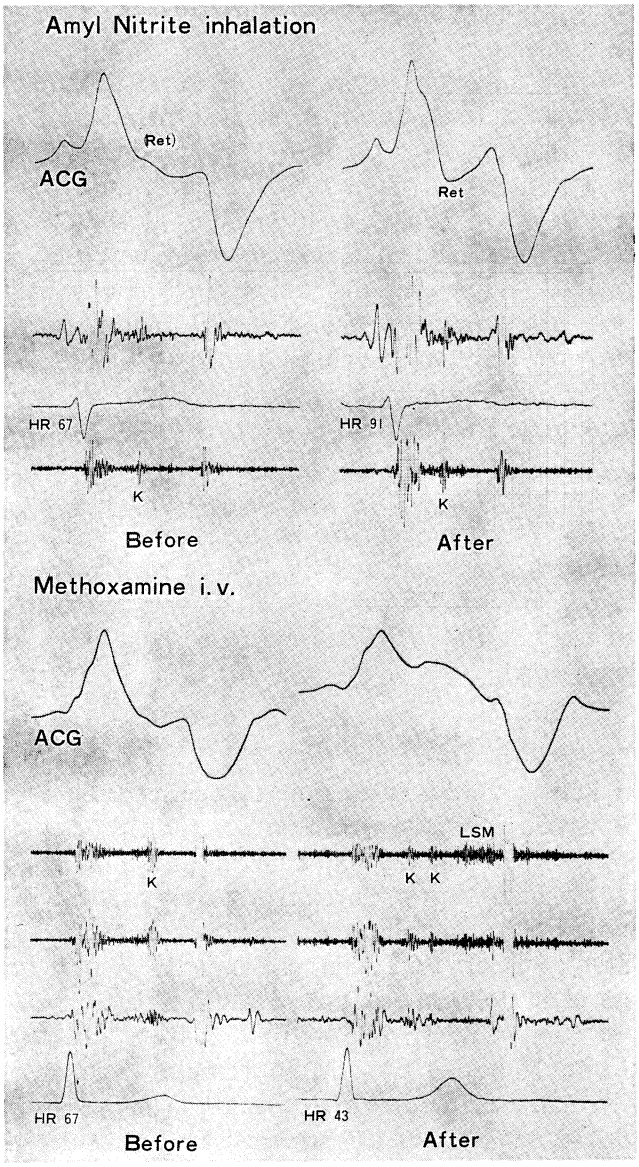


Fig. 4. Upper pannel; Case 8. Polycardiographic tracings before and after amyl nitrite inhalation. The click shifted foreward and "retraction" on ACG became more deep after the inhalation. Lower pannel; Case 9. Polycardiographic tracings before and after intravenous methoxamine. LSM appeared after methoxamine.

has been observed predominantly in young females, as found in available reports[1].

Hancock et al.[1] observed some form of cardiac symptoms in 75% of the cases and stated that 19 out of 40 had palpitation, 14 chest pain, and 15 neurotic complaints. Compared with our cases the occurrence of subjective symptoms in their's was higher, but the frequency of palpitation in ours was comparable to their's. It is said that this syndrome is more often observed in Marfan's syndrome or in cases with the skeletal stigmata. While we did not encounter any patients showing such features, this syndrome was observed more frequently in lean, young females with body weight 20 % less than the standard weight.

Humphries et al.[12] designated this syndrome as "electrocardiographic ausculatory syndrome" on account of patients with late-systolic murmur showing abnormal T-wave on ECG. In contrast, in cases reported by Bitter et al.[13] the majority of them revealed normal ECG, while Hancock et al.[1] found the T-wave abnormality to be high in 40 cases. In our 7 out of 14 showed completely normal ECG at rest, and the abnormality of T-wave as pointed out by various author was found in only one.

Pocock[8] observed the VPB after strenous exercise. However, we could not observe any onset or increase of VPB in Master's double 2-step tests.

2. *Apexcardiogram (ACG)*

It is well known that a retraction coinciding with the click can be seen on ACG in this syndrome. The cause for this phenomenon is not yet clarified, but it is variously explained as due to a sudden tension of chorda tendinea which draws the left ventricular wall instantaneously inferiorly, or as due to an abnormal contraction of the left ventricle[4]. Spencer et al.[5] consider that this phenomenon is brought about by a sudden change of systolic impedance of the left ventricle.

Epstein et al.[4] observed the retraction in 31 out of 38 cases, and Spencer et al.[5] in 16 out of 24. In our cases are included 5 cases classified as the "small" retraction and 4 out of 5 showed a dip coinciding with the click. A majority of cases reported in literatures[4,5,6] reveal the retraction coinciding with the click. This peculiar feature on ACG, especially as observed in Case 20 would serve as a useful point for distinguishing MSC syndrome from other types of mitral insufficiency (Fig. 2).

3. *Left ventricular systolic time intervals (LVSTI)*

$\Delta$Q-II and $\Delta$ET were found in normal range in most of the cases,

and ⊿PEP tended to be prolonged. On the other hand, there were 4 cases that showed ET/PEP ratio, considered to be well correlated to the ejection fraction, to be below the normal value. Two out of these 4 revealed a late-systolic bulge on ACG, and the other showed frequent VPB while the last one had left ventricular high voltage on ECG. These last two, however, were completely free from subjective symptoms. Therefore, it can be true that, judging from the LVSTI, the cardiac function of this syndrome is maintained in the majority of cases. Whereas even in those having no cardiac complaints, there were cases whose cardiac function was decreased.

*4. Loading tests*

It is postulated that the left ventricular endodiastolic volume after amyl nitrite inhalation is diminished so that the click shifts[14] in a early part of systole, and in our 8 cases the click moved forward. It is variously reported that LSM is decreased[4,13], or increased[14], or it is decreased immediately after the inhalation and then increased after 20-50 seconds[15]. In our cases we also found three kinds or responses: those with increased LSM, those with decreased LSM, and those with decreased LSM immediately after the inhalation and increased 30 or 90 seconds later. In the two cases last mentioned, the co-existing click shifted in a similar manner. The increase of LSM after amyl nitrite is interpreted to be due to the lengthening of the cardiac long axis in consonant to chorda tendinea. The increase in LSM 20 or 50 seconds after the inhalation is understood to be due to the fact[15] that the intraventricular pressure at this phase becomes low but the stroke volume falls, so that the systolic murmur intensifies at an early part of the systole.

In Case 9 where LSM could not be heard at control period is appeared after intravenous methoxamine. This phenomenon is explained[15] as due to a rise in the intracardiac pressure.

The early detection of this syndrome may be possible in most cases without performing invasive procedures such as left ventricular cineangiography if careful auscultation and apexcardiogram are employed at bed-side. In addition, the introduction of echocardiography may serve as the most useful aids discovering this condition non-invasively.

## ADDENDUM

Five more patients with mid-systolic-click syndrome have been experienced since we made this manuscript. These clinical manifestation are listed as follows:

| case # | Age | Sex | Symptoms | Underlying heart disease |
|---|---|---|---|---|
| 22 | 37 | F | none | none |
| 23 | 66 | M | none | none |
| 24 | 39 | F | Chest pain VPBs | none |
| 25 | 25 | M | none | none |
| 26 | 24 | M | VPBs | none |

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