Postural Changes in Left Ventricular and Mitral Valvular Dynamics in the Systolic Click – Late Systolic Murmur Syndrome

By Mary E. Fontana, M.D., Charles F. Wooley, M.D., Richard F. Leighton, M.D., and Richard P. Lewis, M.D.

SUMMARY
Marked changes in the auscultatory pattern with posture have been noted in patients with mid-systolic clicks and/or late systolic murmurs (MSC-LSM). MSC tend to move earlier in systole and LSM become longer and often louder when patients assume upright posture. Systolic prolapse of the mitral leaflets with mild regurgitation account for MSC-LSM; earlier and greater prolapse with more and prolonged regurgitation associated with a reduced left ventricular volume (LVV) in the upright position would explain the auscultatory changes.

Twenty-two patients with MSC-LSM were studied supine and at 45° head-up tilt, recording intracardiac pressures, cardiac outputs, systolic time intervals, and performing LV cineangiography. Systolic prolapse of one or both mitral leaflets was demonstrated in all patients. Left ventricular end-diastolic and end-systolic volumes both decreased significantly at 45° in all sixteen technically satisfactory studies. Greater mitral prolapse was noted upright in 12 of 14 studies with enough sinus beats to judge. The amount of mitral regurgitation was mild in all, and changes in amount from supine to upright posture could not be discerned angiographically. The findings suggest that the auscultatory changes occurring with upright posture in patients with MSC-LSM are related to greater prolapse of the mitral leaflets which is associated with a small LVV in the upright position.

Additional Indexing Words:
Mitral regurgitation
Mitral prolapse
Ventricular volume

Mid-systolic clicks and late systolic murmurs are associated with systolic prolapse of one or both mitral valve leaflets into the left atrium. Others have noted\textsuperscript{11-13} and we have previously emphasized\textsuperscript{14} the marked changes in the auscultatory pattern that occur with changes in posture. The systolic clicks tend to move toward and/or merge with the first sound; and the late systolic murmurs tend to become longer, often louder, and frequently holosystolic with the assumption of upright posture. We believe that the changes in auscultatory findings result from earlier and greater prolapse of the mitral leaflets, allowing longer and more pronounced mitral regurgitation, and that the primary determinant is the reduction in left ventricular volume that occurs in the upright position. Other authors have suggested this mechanism as well,\textsuperscript{1, 3, 5-7, 10} but objective proof is lacking. This study was designed to document the alterations in left ventricular and mitral valvular dynamics occurring in patients with mid-late systolic murmurs and/or clicks in the upright position.

Materials and Methods
Twenty-two symptomatic patients with mid-systolic clicks and/or late systolic murmurs were studied. The changes in auscultatory findings with changes in posture were documented in each patient by phonocardiograms recorded in the supine, sitting, standing, and squatting positions. The patients were then placed on the table in the catheterization laboratory and tilted upright until definite click mobility toward the first sound and/or murmur prolongation were produced. It became apparent that 45° head-up tilt was sufficient to produce obvious changes in the auscultatory findings, so this degree of tilt was routinely used. Although the auscultatory changes were not so dramatic as those occurring when the patients were standing, they were judged sufficient for the purpose of this study. It would have been technically difficult and would have increased patient risk to perform these studies in the standing position.

The day following the phonocardiographic studies, right and left heart catheterization with left ventricular cineangiography and systolic time intervals were performed in the supine and 45° head-up tilt positions. A microphone...
The amount of prolapse was determined by outlining the projected image of the cineangiogram frames where the prolapse appeared maximal. Lines were drawn connecting the point of intersection of the leaflets with the ventricular image. This area was then planimetered.

was placed on the chest to record the second sound for the systolic time intervals and also the clicks and murmurs whenever possible. Systolic time intervals were measured by the method of Weissler et al. Cardiac outputs were determined by the indicator dilution technique. Cineangiography was performed in the 30° right anterior oblique (RAO) and 35° left anterior oblique (LAO) positions supine, and in the 30° RAO position, upright, using meglumine diatrizoate and sodium diatrizoate.* Upright LAO injections were not done because the total amount of contrast medium required would have been excessive. All recordings were made on a Sanborn 550M recorder. Pressure measurements, cardiac outputs, and systolic time intervals were measured in the supine position first. Upright systolic time intervals, pressure measurements, and cardiac outputs were obtained beginning six minutes after the


Results

The precatheterization phonocardiograms demonstrated click mobility toward the first sound and/or murmur prolongation and/or intensification in all patients when they assumed the upright position (table 1). As can be seen in table 1, most of the patients developed pansystolic murmurs associated with merging of the click(s) with the first sound in the standing position. An example is shown in figure 2. Prompt squatting routinely reproduced the supine auscultatory findings. Upon standing from the squat-
### Table 1

**Auscultatory Findings**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Supine</th>
<th>Preclinical phonos</th>
<th>Standing</th>
<th>Catheterization, 45° tilt</th>
<th>Δ Heart rate</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RD</td>
<td>?MSC, II LSM (74)†</td>
<td>SC → S₁, IV HSM, Whoop (71)</td>
<td>—</td>
<td>—</td>
<td>77 → 68</td>
<td>Incomplete study, technically poor phon; symptomatic ↓ BP</td>
</tr>
<tr>
<td>MK</td>
<td>2 LSC, III LSM (92)</td>
<td>SC → S₁, IV HSM (95)</td>
<td>—</td>
<td>80 msec.</td>
<td>77 → 97</td>
<td>Complete study</td>
</tr>
<tr>
<td>EP</td>
<td>II LSM (81)</td>
<td>IV HSM (111)</td>
<td>—</td>
<td>120</td>
<td>72 → 91</td>
<td>Incomplete study, symptomatic ↓ BP</td>
</tr>
<tr>
<td>CVM</td>
<td>LSC, I-II LSM (71)</td>
<td>SC → S₁, II HSM (87)</td>
<td>—</td>
<td>110-140</td>
<td>71 → 83</td>
<td>Complete study, asymptomatic ↓ BP</td>
</tr>
<tr>
<td>RD</td>
<td>MSC, II LSM (94)</td>
<td>SC → S₁, IV HSM (124)</td>
<td>—</td>
<td>50</td>
<td>66 → 85</td>
<td>Complete study</td>
</tr>
<tr>
<td>AH</td>
<td>LSC, II LSM (79)</td>
<td>SC → S₁, II HSM, Whoop (113)</td>
<td>—</td>
<td>40</td>
<td>75 → 91</td>
<td>Complete study, asymptomatic ↓ BP</td>
</tr>
<tr>
<td>LB</td>
<td>MSC, I LSM (83)</td>
<td>SC → S₁, III HSM, Whoop (115)</td>
<td>—</td>
<td>140</td>
<td>92 → 109</td>
<td>Complete study</td>
</tr>
<tr>
<td>MC</td>
<td>LSC, II LSM (122)</td>
<td>SC → S₁, IV HSM, Whoop (143)</td>
<td>—</td>
<td>95 → N.D.</td>
<td></td>
<td>Incomplete study, symptomatic ↓ BP</td>
</tr>
<tr>
<td>DP</td>
<td>II MSM (79)</td>
<td>III MSM (115)</td>
<td>—</td>
<td>—</td>
<td>63 → 70</td>
<td>Murmur too soft to record; asymptomatic ↓ BP</td>
</tr>
<tr>
<td>BF</td>
<td>MSC, II LSM (Insp. Only) (94)</td>
<td>SC → S₁, II LSM (125)</td>
<td>—</td>
<td>30-70</td>
<td>92 → 105</td>
<td>Complete study</td>
</tr>
<tr>
<td>LH</td>
<td>LSC, I LSM (98)</td>
<td>SC → S₁, IV HSM (122)</td>
<td>—</td>
<td>90</td>
<td>97 → 111</td>
<td>Complete study</td>
</tr>
<tr>
<td>JS</td>
<td>ESC, II LSM (79)</td>
<td>ESC, II MSM (109)</td>
<td>—</td>
<td>—</td>
<td>77 → 80</td>
<td>Incomplete study, symptomatic ↓ BP</td>
</tr>
<tr>
<td>SM</td>
<td>II LSM (74)</td>
<td>III HSM (92)</td>
<td>—</td>
<td>—</td>
<td>66 → 81</td>
<td>Murmur too soft to record; asymptomatic ↓ BP</td>
</tr>
<tr>
<td>WW</td>
<td>I-II LSM (81)</td>
<td>III HSM (103)</td>
<td>—</td>
<td>85</td>
<td>73 → 77</td>
<td>Complete study</td>
</tr>
<tr>
<td>SS</td>
<td>I-II LSM (67)</td>
<td>II MSM (86)</td>
<td>—</td>
<td>—</td>
<td>61 → 72</td>
<td>Murmur too soft to record; Complete study</td>
</tr>
<tr>
<td>CP</td>
<td>II MSM (73)</td>
<td>III HSM (92)</td>
<td>—</td>
<td>—</td>
<td>59 → 74</td>
<td>Murmur too soft to record; Asymptomatic ↓ BP</td>
</tr>
<tr>
<td>ES</td>
<td>LSC (43)</td>
<td>LSC (49)†</td>
<td>—</td>
<td>65</td>
<td>36 → 41</td>
<td>Complete study</td>
</tr>
<tr>
<td>TEC</td>
<td>II LSM (72)</td>
<td>IV HSM (88)</td>
<td>HSM on Tilt</td>
<td>—</td>
<td>59 → 73</td>
<td>Complete study</td>
</tr>
<tr>
<td>RM</td>
<td>MSC, I-II LSM (85)</td>
<td>SC → S₁, III HSM (109)</td>
<td>—</td>
<td>120-170</td>
<td>83 → 95</td>
<td>Complete study</td>
</tr>
<tr>
<td>ST</td>
<td>II LSM (75)</td>
<td>III HSM (158)</td>
<td>—</td>
<td>—</td>
<td>71 → 92</td>
<td>Technically poor upright phon; Complete study</td>
</tr>
<tr>
<td>BJ</td>
<td>Normal (73)</td>
<td>ESC (122)</td>
<td>ESC upright only</td>
<td>—</td>
<td>77 → 98</td>
<td>Complete study</td>
</tr>
<tr>
<td>SR</td>
<td>Normal (95)</td>
<td>ESC (107)</td>
<td>ESC upright only</td>
<td>—</td>
<td>78 → 98</td>
<td>Complete study</td>
</tr>
</tbody>
</table>

*Shortening of Q-systolic click or murmur interval.
†Heart rate in parentheses.
Δ Q-SC = 40 msec.
Abbreviations: ESC = Early systolic click; MSC = Midsystolic click; LSC = Late systolic click; MSM = Midsystolic murmur; LSM = Late systolic murmur; S₁ = First heart sound; HSM = Holosystolic murmur; ND = Not done.
ting position, the clicks could be heard to migrate to their early systolic position accompanied by prolongation of the murmur.

Table 1 illustrates the amount of movement of the click toward the first sound during 45° head-up tilt in the patients in this study where precise measurements could be made. The clicks did not merge with the first sound in any patient. One person who had a late systolic murmur without a click supine (T.E.C.) did develop a pansystolic murmur at 45° tilt. Several patients who had murmurs recorded before the catheterization no longer had them at the time of the study, although the clicks were still present. In several cases the murmurs were too soft to record, but could still be heard with a stethoscope. Figure 3 illustrates the auscultatory findings with upright tilt during the catheterization in the same patient whose phono is shown in figure 2.

Complete studies were obtained in 18 of 22 patients. Four patients developed symptomatic

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**Figure 4**

The changes in cardiac index, stroke volume index, and heart rate are shown here. In each instance the dots on the left of the panel are the supine values and those on the right of each panel are the values at 45° head-up tilt. The majority of the supine values are normal. The patient with the high stroke volume index and slow heart rate had congenital complete heart block.
hypotension upon passive tilt which obviated complete upright studies. Asymptomatic reduction in systemic blood pressure occurred in five others, which tended to diminish the auscultatory changes. Some of the hemodynamic changes with upright tilt are shown in figure 4. The cardiac index was normal or elevated in all and decreased an average of 21%. Stroke volume decreased an average of 29%. The average heart rate increase was 12 beats/min, but several patients had an exaggerated heart rate response to upright tilt. These patients tended to have the most dramatic changes in auscultatory findings as well. A significant increase in the PEP/LVET ratio routinely occurred.

Left ventricular cineangiography demonstrated systolic prolapse of one or both mitral leaflets in all 22 patients. Eighteen had posterior leaflet prolapse only, and 4 had prolapse of both leaflets. The cineangiograms were technically satisfactory for volume determinations in 16 patients. The left ventricular end-diastolic volume varied from 48 to 100 ml/m², (normal = 70 ± 20 ml/m²) and decreased significantly (P < .001) at 45° head-up tilt, an average of 16.5% (fig. 5). The left ventricular end-systolic volume likewise decreased significantly (P < .005) in the upright position, an average of 18% (fig. 6).

The amount of mitral regurgitation was mild in all patients. Five patients had only systolic clicks at the time of study; no mitral regurgitation was seen in these patients although leaflet prolapse was evident. In two patients, the amount of mitral regurgitation was clearly greater in the upright position compared to supine. Differences in amount of regurgitation in the remainder of the cases could not be discerned primarily because the small amount of regurgitated contrast quickly dissipated into the nonopacified blood in the left atrium. No objective means of comparison sensitive enough to detect small differences in regurgitation is currently available. Our available timing devices were also inadequate to detect the precise timing of the onset of prolapse. Visual estimation of onset of prolapse was not reproducible by the observers with enough precision to give meaningful results. It has been shown by others, however, that the systolic click occurs at the point of maximum prolapse of the mitral leaflets, so the earlier clicks likely mean earlier prolapse. The amount of prolapse, determined by planimetry as previously described, was sig-

![Figure 5](image1.png)

*The changes in LV end-diastolic volume occurring with upright tilt are shown. The supine values are represented by the black dots on the left and are connected to the upright values on the right for each patient.*

![Figure 6](image2.png)

*The changes in LV end-systolic volume from supine, on the left, to upright, on the right, are shown. The net change in end-systolic volume was similar to that of the end-diastolic volume.*

*Circulation, Volume 51, January 1975*
significantly greater ($P < 0.05$) in 12 of 14 studies in which there were enough sinus beats to judge and in which the clarity of the cineangiogram was sufficient to outline the prolapsed leaflet (fig. 7). In the remaining two cases, no difference could be measured between supine and upright cineangiograms. In one patient, who had a solitary early systolic click audible only in the upright position, prolapse was identified only in the upright cineangiogram. An example of the volume and prolapse changes is shown in figures 8 and 9, which are from the study of the same patient whose phonocardiograms are shown in figures 2 and 3.

Discussion

The click migration toward the first sound and the murmur prolongation and frequent intensification that occurred with the assumption of upright posture in the patients in this study is similar to that reported by us$^{13}$ and others.1'13 Passive tilt to 45° produces similar auscultatory changes, although not so marked as with active standing. These changing auscultatory phenomena are associated with significant increases in the amounts of mitral valve prolapse which are associated with significant reductions in left ventricular end-diastolic and end-systolic volumes.

No data are available on the quantitation of the left ventricular volume changes with upright tilt by the angiographic method with which to compare our results. Paley et al.21 noted approximately a 25% decrease in ventricular volumes by the thermodilution technique at 60° tilt. Rushmer has also documented the reduction of volume in the upright position in dogs.$^{17,18}$ The determination of left ventricular volume by the area-length method from single plane supine angiograms is a well established technique. There is no reason to believe that it would not be equally appropriate for upright cineangiography performed in the same projection. The twenty minute interval between the upright and supine cineangiograms used for volume calculation has been shown by others to be sufficient to allow the increase in plasma volume induced by a contrast injection to dissipate.22-24 The increased plasma volume produced by the previous contrast injection could have exaggerated the supine ventricular volume if the blood volume change had not been taken into account. The changes in ventricular volumes occurring with upright tilt in the patients in this study are presumed to be normal since the other hemodynamic and systolic time interval changes agreed with previously obtained values in normal individuals.$^{17-20}$

The greater prolapse demonstrated in the upright position was reproducible in multiple beats in a given patient, and by separate observations. The method used quantitates only posterior leaflet prolapse, since only 30° RAO cineangiograms were compared. Greater prolapse in the upright position might have been evident if left anterior oblique cineangiography had also been performed in the upright tilt position, since anterior leaflet prolapse is usually better seen in this projection.

The possibility that the change in leaflet prolapse occurring upright may have been related to a change in the position and axis of the heart must be considered. The orientation appeared similar to supine by visual inspection and it is doubtful that this is a significant factor.

The demonstration of a reduction in left ventricular volumes and an increase in the amount of mitral prolapse does not necessarily mean that they are related as cause and effect. That the volumes decreased in every case in which the amount of prolapse increased suggests that they are related. The explanation for the greater prolapse of the mitral leaflets in the upright position compared to the supine, based on ventricular volume changes, is likely
as follows: with a smaller end-diastolic volume, the supporting structures of the mitral valve, i.e., ventricular wall and papillary muscles, are physically closer to the mitral valve ring at end-diastole. There would be less tension on the chordae tendineae and the leaflets would, therefore, be closer to a position of

Figure 8

End-diastolic frames from 30° RAO cineangiograms done in the supine position, on the left and in the 45° head-up tilt position, on the right, from a patient in this series are shown. The end-diastolic volume (EDV) in the upright frame is clearly smaller (70 ml/m² vs 98 ml/m² in the supine position).

Figure 9

End-systolic cine frames with accompanying reference figures for the supine position, on the left, and the upright position, on the right, are shown. The characteristic appearance of contrast underlying the posterior leaflet is apparent. The end-systolic volume is significantly smaller in the upright study (27 ml/m² vs 34 ml/m² in supine position). The area under the prolapsed leaflet (AP) is larger in the upright cine (19.6 cm² vs 18.6 cm² in supine position).
prolapse. With ventricular systole, which results in a smaller end-systolic volume, the leaflets then prolapse more and likely earlier, which would permit more prolonged and greater regurgitation. Considering the relative inelasticity of the mitral leaflets and chordae tendineae, changes in the relationship of the supporting structures of the valve, i.e., papillary muscles and ventricular wall, to the point of attachment of the leaflets (i.e., valve ring) would logically explain the alterations in mitral valve function seen in patients with mitral valve prolapse. Changes in ventricular volumes would clearly be the major determinant of this relationship.

Standing up resulted in a marked tachycardia in many of these patients (table 1). This was associated with the development of pansystolic murmurs in the majority of them (table 1). The greater changes in auscultatory findings with the greater increase in heart rate would be explained by the further reduction in ventricular volume because of marked reduction in the diastolic filling period, which would be additive to the peripheral pooling that occurs on assuming upright posture. The inotropic stimulus of the increased sympathetic activity that occurs with upright tilt,25,26 which is likely greater in the standing position, and with increases in heart rate, may contribute to the reduction in both end-systolic and end-diastolic volumes seen in this study.

The major determinant of the greater prolapse seen in this study appears to be ventricular volume reduction resulting primarily from peripheral pooling. In four patients the heart rate during the filming of the cineangiograms was the same or slower during the upright injection as during the supine injection, presumably related to the deep, held inspiration. The ventricular volume still decreased and the amount of mitral valve prolapse did increase in these patients. The changes in volume and prolapse were greater in those with increases in heart rate, although not statistically significant, consistent with the additive effects of heart rate on ventricular volume reduction as previously discussed.

Further support for the volume theory can be deduced from the response to prompt squatting. Prompt squatting routinely results in movement of the clicks and murmurs back to a later systolic position, similar to supine (fig. 2). Prompt squatting increases venous return and slows the heart rate, which results in lengthening of the diastolic filling period.27,28 An increase in ventricular volume would then result,18 which would produce more tension on the mitral valve leaflets and chordae by increasing the distance between the ventricular wall and papillary muscles and the valve ring. Later and less leaflet prolapse would then result during systole.

In conclusion, the movement of the systolic clicks toward the first sound and the murmur prolongation and intensification that occur in the upright position in patients with mid-systolic clicks and late systolic murmurs are associated with greater prolapse of the mitral leaflets, which could allow greater and more prolonged regurgitation. A primary determinant of the greater prolapse appears to be the reduction in left ventricular volume that occurs in the upright position.

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POSTURAL CHANGES IN MSC-LSM SYNDROME

Postural changes in left ventricular and mitral valvular dynamics in the systolic click - late systolic murmur syndrome.
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Circulation. 1975;51:165-113
doi: 10.1161/01.CIR.51.1.165
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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