Left Ventricular Systolic Time Intervals as Indices of Postural Circulatory Stress in Man

By R. W. Stafford, M. D., W. S. Harris, M.D., and A. M. Weissler, M.D.

SUMMARY
The effects of graded increments of passive head-up tilt on the duration of the systolic time intervals corrected for heart rate were investigated in 15 normal subjects. Head-up tilt caused a prolongation of the pre-ejection period and a shortening of the left ventricular ejection time, while total electromechanical systole diminished minimally. The lengthening of the pre-ejection period and abbreviation of the left ventricular ejection time increased progressively with stepwise increments of head-up tilt. The application of venous occlusive tourniquets produced changes in the systolic intervals directionally similar to those observed with head-up tilt. In contrast to the normal subjects, three patients with congestive heart failure demonstrated no change in the systolic time intervals during head-up tilt. After diuresis in two of the patients with heart failure, the responses of their systolic time intervals to head-up tilt returned toward normal.

Additional Indexing Words:
Head-up tilt Electromechanical systole Left ventricular ejection time

The ONLY noninvasive measurements that are currently used to characterize gravitational circulatory stress in man are heart rate and arterial pressure. Previous studies in normal subjects and patients with heart disease have shown that changes in the systolic time intervals reflect, in a convenient and sensitive manner, alterations in left ventricular performance. To test the possible usefulness of these atraumatic measurements in assessing left ventricular responses to gravity, the present studies were performed in normal subjects and in patients with heart failure. These studies have delineated the effects of graded increments of head-up tilt on heart rate, arterial pressure, and the time intervals of left ventricular systole. In addition, the circulatory changes produced by head-up tilt were compared with those resulting from the application of venous occlusive tourniquets.

Methods
As described previously, the systolic time intervals were measured from simultaneous, fast-speed (100 mm per second) recordings of the electrocardiogram, phonocardiogram, and carotid arterial pulse tracing. Total electromechanical systole \((QS_2)\) was measured from the onset of ventricular depolarization to the initial high frequency vibrations of the second heart sound. The left ventricular ejection time \((LVET)\) was measured from the onset of the carotid upstroke to the trough of its incisura. The left ventricular pre-ejection period \((PEP)\) was derived by subtracting the left ventricular ejection time from total electromechanical systole. The intervals were calculated as the mean of measurements of at least 10 consecutive beats, each read to the nearest 5 msec. When sinus arrhythmia caused heart rate to vary more than 10 beats per minute, 20 consecutive beats were analyzed. Heart rate

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Supported in part by U. S. Public Health Service Grants HE-5546, HE-5786, HE-06737, Career Program Award HE-13971, and a grant from the Central Ohio Heart Association.
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Received September 15, 1969; accepted for publication November 19, 1969.

Circulation, Volume XLI, March 1970
(HR) was determined by dividing the average R-R interval into 60. Figure 1 shows schematically the relation of the measured systolic time intervals to the cardiac cycle.

Total electromechanical systole and the left ventricular ejection time are inversely related to heart rate; the pre-ejection period is minimally affected by heart rate. The following regression equations, derived from data previously obtained in 211 normal subjects, were used to correct the systolic time intervals in milliseconds for heart rate.

<table>
<thead>
<tr>
<th>Systolic interval</th>
<th>Sex</th>
<th>Regression equation</th>
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<tbody>
<tr>
<td>QS₂ (msec)</td>
<td>M</td>
<td>QS₂ = − 2.1 HR + 546</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>QS₂ = − 2.0 HR + 549</td>
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<td>LVET (msec)</td>
<td>M</td>
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<td>F</td>
<td>LVET = − 1.6 HR + 418</td>
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<td>PEP (msec)</td>
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</tr>
<tr>
<td></td>
<td>F</td>
<td>PEP = − 0.4 HR + 133</td>
</tr>
</tbody>
</table>

Deviations from these normal data were calculated as the difference between the observed interval and that predicted for heart rate from the normal regression equation. The difference in the deviations from the normal regression equation before and after tilt represents the tilt response and is expressed as ΔQS₂, ΔPEP, and ΔLVET. These values were calculated by subtracting the deviations from the normal regression equation after tilt from the immediately preceding supine control deviation from normal. The ratio of the pre-ejection period to left ventricular ejection time (PEP/LVET) was determined directly from the values uncorrected for heart rate. Arterial pressure was measured with a cuff sphygmomanometer. Statistical analysis was performed by the methods of Snedecor.

Normal volunteers, eight men and seven women, all active students, house staff, or laboratory technicians of average age 23 years, (range 18 to 28 years) were studied. Tilting was accomplished by use of an electrically-powered tilt table. The systolic time intervals, heart rate, and arterial pressure were measured in each subject in the supine position, and at 2°, 5, 10, 15, 20, 25, 30, 45, 60, and 90 degrees of passive head-up tilt. This sequence in head-up tilt was followed in all studies. Before each of the 10 applications of head-up tilt, supine control determinations of the time intervals, heart rate, and arterial pressure were obtained. The changes observed with each application of head-up tilt were calculated from the immediately preceding supine measurement. In preliminary studies it was determined that steady-state responses in heart rate, systolic intervals, and arterial pressure were achieved in from 3 to 15 minutes of head-up tilt. Control supine levels returned within 4 minutes after return to the horizontal position. Arterial pressure was determined during the fourth minute, and the systolic time intervals were recorded during the sixth minute of head-up tilt. Arterial pressure was then measured during the fourth minute, and the systolic time intervals were recorded during the sixth minute after the subject was returned to the supine position. There was no significant variation in pre-tilt supine control levels throughout the studies.

To determine the effects of venous pooling produced by nongravitational means, venous occlusive cuffs were applied to the arms and thighs of five normal men. The cuff pressures were kept 10 mm Hg below the arterial diastolic pressure. The systolic time intervals were recorded during the sixth minute of venous occlusion.

Three patients with severe congestive heart failure (New York Heart Association Classification III in each) due to primary myocardial disease in two and hypertensive and arteriosclerotic heart disease in one, were studied. Arterial pressure, heart rate, and the systolic time intervals were measured at 0, 30, 60, and 90 degrees of head-up tilt. After diuresis and clinical recovery from heart failure, these studies were repeated in two of the patients. Each of these patients lost 15 pounds of body weight between the studies.

The hydrostatic effect of head-up tilt is a function of the sine of the angle of tilt. For this reason, the changes in the systolic time intervals

Figure 1

Relation of the measured systolic time intervals to the cardiac cycle.
with head-up tilt were plotted against the sine of the angle of tilt in figures 2 and 3. For comparison, these figures also include the absolute angle of tilt.

**Results**

**Head-up Tilt**

The effects of head-up tilt on the systolic time intervals, heart rate, and arterial pressure in the 15 normal subjects are summarized in table 1 and in figure 2. These effects were determined by subtracting the value observed at each level of tilt from the immediately preceding control observation obtained in the supine position. The supine control determinations did not change significantly during the course of the study.

Table 1

**Effects of Head-up Tilt on Systolic Time Intervals in 15 Normal Subjects**

<table>
<thead>
<tr>
<th>Angle of tilt</th>
<th>BR (msec)</th>
<th>QS₂ (msec)</th>
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<th>LVET (msec)</th>
<th>ΔLVET (msec)</th>
<th>PEP (msec)</th>
<th>ΔPEP (msec)</th>
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* Data represent mean values plus standard error of the mean in parentheses.

The values for the systolic time intervals (QS₂, LVET, and PEP) and the ratio PEP/LVET are uncorrected for heart rate. The changes (Δ) in the systolic time intervals with head-up tilt were determined by subtracting the deviation from the normal regression equation after tilt from the immediately preceding supine control deviation from normal.

Abbreviations: HR = heart rate, QS₂ = QS₂ interval, LVET = left ventricular ejection time, PEP = pre-ejection period, SAP = systolic arterial pressure, DAP = diastolic arterial pressure.
Mean changes in the systolic time intervals and heart rate produced by head-up tilt in 15 normal subjects. The values for the systolic time intervals represent difference in deviation from the normal regression equation for heart rate before and after tilt. Above 15 degrees of head-up tilt, all changes in the systolic time intervals were significant (ΔPEP, ΔLVET, P < 0.001, ΔQS_2 < 0.05). Heart rate changes were significant beyond 25 degrees (P < 0.001).

**Venous Occlusive Cuffs**

In five normal supine male subjects, the application of venous occlusive tourniquets increased the heart rate from 54 (SE 6.8) to 61 (SE 8.5) beats per minute. Total electromechanical systole and the left ventricular ejection time diminished and the pre-ejection period lengthened. When corrected for the increase in heart rate, the ejection time shortened by 16 msec and the pre-ejection period lengthened by 14 msec, while electromechanical systole shortened by 3 msec (fig. 3).

**Heart Failure**

In three patients with severe congestive heart failure, head-up tilt produced only minimal changes in the systolic time intervals, heart rate, and arterial pressure. After diuresis...
in two of the patients, there was a return toward normal in the response of the systolic time intervals to head-up tilt (fig. 4).

Discussion

Previous investigations have defined the hemodynamic consequences of assuming the upright posture in man. By causing the venous pooling of blood below the heart,7-10 the gravitational stress incurred by head-up tilt diminishes ventricular filling, end-diastolic volume, stroke volume, and cardiac output.11-20 Owing to baroreceptor-mediated reflexes, mean arterial pressure increases slightly and peripheral resistance and heart rate rise significantly.19

The present results have demonstrated a quantitative relation between postural gravitational stress, expressed as the sine of the angle of head-up tilt, and the systolic time intervals corrected for heart rate. Earlier, Lombard and Cope21 showed that the left ventricular ejection time shortens when normal subjects sit or stand up. Raab and associates22 reported that standing up shortens total electromechanical systole and the left ventricular ejection time and prolongs the pre-ejection period. In neither of these two previous studies were the systolic time intervals corrected for the effects of heart rate, nor were graded increments of head-up tilt observed.

The changes observed in the systolic intervals with increasing degrees of head-up tilt parallel closely the hemodynamic changes with increasing tilt reported previously by Tuckman and Shillingford.19 In normal subjects these authors observed that cardiac output fell maximally at 30 degrees head-up tilt, failing to decrease further with greater tilt, although stroke volume fell at all angles of tilt through 60 degrees. Consonant with the data of these authors on stroke volume, the effects of gravity on the pre-ejection and ejection periods tended to continue with head-up tilt to 60 degrees. At 90 degrees head-up tilt, the changes in the systolic intervals were only slightly greater than at 60 degrees head-up tilt.

In studies of animals and man,1, 23-25 reductions of ventricular filling and stroke volume have been shown to prolong the pre-ejection period and shorten the duration of left ventricular ejection. During head-up tilt, the pattern of changes that occurs in the systolic time intervals most likely reflects the decreases of ventricular end-diastolic and stroke volume consequent to venous pooling. Probably operating through similar mechanisms, the application of venous occlusive tourniquets, which reduces stroke volume and cardiac output without significantly altering diastolic arterial pressure,18, 26, 27 also prolongs the pre-ejection period and shortens the left ventricular ejection time. The effects of this nongravitational stress on the systolic time intervals resemble those found with 15 to 20 degrees head-up tilt and approach 40% of that observed with 90 degrees head-up tilt.

Associated with the diminished left ventricular end-diastolic volume, other hemodynamic factors may contribute to the effects of gravity upon the pre-ejection and ejection periods in normal subjects. By increasing the isovolumetric pressure gradient, either a fall in left ventricular end-diastolic pressure or a rise in aortic diastolic pressure would tend to lengthen the pre-ejection period. The magnitude of the effect of a fall in left ventricular end-diastolic pressure per se cannot be assessed from the present results. However, in view of the relatively minor influence of peripheral venous pooling on left ventricular end-diastolic pressure in normal subjects,28 this would appear to be slight. Head-up tilt is responsible for the initiation of compensatory baroreceptor mediated reflex activity with a consequent increase in sympathetic cardiostimulatory activity and peripheral vasoconstriction.29 These changes of themselves might alter the systolic intervals. Sympathetic stimulation of the myocardium would tend to shorten the pre-ejection period by accelerating the isovolumic rise of left ventricular pressure.3, 30 When other variables are kept constant, acutely induced increases in peripheral resistance would tend to prolong the left ventricular ejection time.31 Despite the presence of these effects during head-up tilt, the pre-ejection period actually lengthened while the ejection time was abbreviated.
These reflex effects, hence, cannot explain the observed changes in systolic intervals with head-up tilt.

Patients with congestive heart failure who are studied in the supine position have systolic time intervals resembling those observed in normal subjects during head-up tilt: a long pre-ejection period, short left ventricular ejection time, and little change in total electromechanical systole.\textsuperscript{4, 5} In heart failure the long pre-ejection period and short ejection time are well correlated with the reduced stroke volume and cardiac output.\textsuperscript{4, 5} The two groups, patients in heart failure and normal subjects in the upright posture, differ markedly in their left ventricular end-diastolic volumes. These are large in patients with left ventricular failure\textsuperscript{32} and small in normal subjects undergoing upright tilt.\textsuperscript{20} Both in the supine patients with left ventricular failure and normal subjects during head-up tilt, the long pre-ejection period probably reflects a slower rise of left ventricular pressure during isovolumic contraction. In heart failure, it is the depressed myocardial function\textsuperscript{23, 34} that slows the rise of isovolumic pressure. In normal subjects during tilt, myocardial function is unimpaired, and it is the reduction in left ventricular end-diastolic volume and myocardial fiber length that most probably results in the slower rise of isovolumic pressure.\textsuperscript{35, 36} In both groups of subjects the shorter ejection time is associated with a reduction in stroke volume. The mechanism of shortening in the ejection time may be viewed in several ways. The shortened ejection time may simply reflect the reduction of stroke volume caused by either depressed ventricular function in heart failure or diminished end-diastolic volume during head-up tilt in normal subjects. On the other hand, the delay in aortic valve opening caused by the slower isovolumic rise of left ventricular pressure, at a time when total systole fails to lengthen, can explain the diminished duration of ejection in both heart failure and during head-up tilt.

When considered relative to the contractile properties of the myocardium, it is probable that in both hemodynamic states (heart failure and head-up tilt) the stroke volume and systolic temporal responses are but differing hemodynamic reflections of a common dynamic change in the myocardium, that of a decreased rate of developed force or myocardial contraction, or both, during the pre-ejection and ejection phases of the cardiac cycle. These changes are the result of depressed cardiac function in heart failure and diminished end-diastolic fiber length in the upright posture.

In our three patients with severe heart failure, head-up tilt failed to change the systolic time intervals, heart rate, or arterial pressure. This absence of postural responses is consistent with previous demonstrations that during upright tilt patients with heart failure or pulmonary congestion due to mitral valve disease fail to lower their right ventricular end-diastolic volume, cardiac output, and stroke volume.\textsuperscript{11, 37, 38} The inability of upright tilt to alter the systolic time intervals in patients with congestive failure may, in part, reflect the antigravitational effects of hypervolemia, elevated tissue pressure, and increased venomotor tone. By minimizing the shift of blood away from the central circulation, these extracardiac concomitants of heart failure may prevent the usual hemodynamic effects of gravitational stress. In support of this hypothesis is the observation that diuresis restored the responsiveness to head-up tilt in two of the patients with heart failure.

Current aerospace and deep-sea explorations have heightened the need to develop practical and effective noninvasive methods for monitoring circulatory changes in man. In the present study, the gravitational stress induced by head-up tilt was clearly shown to affect left ventricular performance. The measurement of the systolic time intervals would appear to provide a convenient, sensitive, and reliable method for rapidly assessing such gravitational effects upon the human circulation.

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Circulation. 1970;41:485-492
doi: 10.1161/01.CIR.41.3.485
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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