Shortening of Electromechanical Systole as a Manifestation of Excessive Adrenergic Stimulation in Acute Myocardial Infarction

By Richard P. Lewis, M.D., Harisios Boudoulas, M.D., Wilbur F. Forester, B.S., and Arnold M. Weissler, M.D.

SUMMARY

The relationship between shortened electromechanical systole (QS₂₁) and 24-hour urinary catecholamine excretion (E + NE) was studied in 51 patients admitted to the coronary care unit with suspected acute myocardial infarction. Among these patients, 24 had a documented acute myocardial infarction while 27 had chest pain without evidence of recent myocardial infarction. Patients receiving cardioactive drugs or with impaired renal function were excluded. Initial elevation of catecholamine excretion was found in 22 of 24 subjects with myocardial infarction and 14 patients without documented myocardial infarction. A close linear correlation \((r = -0.82, P < 0.001)\) was noted between shortening of the QS₂₁ and catecholamine excretion among all patients irrespective of the presence of documented infarction. Patients with serious arrhythmias had significantly higher levels of catecholamine excretion. In 13 patients with a short QS₂₁, 2.5 mg of propranolol given intravenously produced a significant lengthening of the QS₂₁ while no change in the QS₂₁ occurred in normal controls. This test provided useful corroborative evidence that the short QS₂₁ was related to excessive adrenergic stimulation. In view of the current availability of effective beta-adrenergic blocking agents, these results may improve the selection of patients for antiarrhythmic therapy with these drugs.

Additional Indexing Words:

Propranolol 24-hour urinary catecholamine excretion Systolic time intervals

Acute myocardial infarction

Previous Studies have demonstrated that the duration of electromechanical systole is frequently shortened in patients with acute myocardial infarction.¹⁻⁸ It is known that beta-adrenergic stimulation shortens electromechanical systole in man and animals.⁹⁻¹⁴ Patients with acute myocardial infarction frequently exhibit excessive adrenergic activity as evidenced by an elevation of plasma and 24-hour urinary catecholamines.¹⁵⁻²³ It was therefore hypothesized that the abbreviated electromechanical systole characteristic of patients with myocardial infarction is a direct reflection of increased sympathetic nervous system activity. The present investigation was designed to test this hypothesis.

Material and Methods

Fifty-one consecutive patients admitted to the Ohio State University Hospital Coronary Care Unit with suspected acute myocardial infarction were studied. Patients who were taking drugs known to affect systolic time intervals or interfere
with the estimation of catecholamines were excluded. Subjects with left ventricular conduction defects producing a QRS complex in excess of 100 msec were excluded since this may of itself influence the duration of electromechanical systole.24 Systolic interval measurements were not made when ischemic pain was present.

Systolic time intervals were calculated from high-speed (100 mm/sec) simultaneous recordings of the phonocardiogram, electrocardiogram, and the externally derived carotid arterial pulse tracing obtained from a Statham P23Db strain gauge. The details of this method as performed in our laboratory are described elsewhere.24-26 From these tracings the preejection period (PEP), left ventricular ejection time (LVET), and total electromechanical systole (QS$_2$) are calculated. From the PEP and LVET the PEP/LVET ratio was calculated. Recently this ratio has been shown to be a useful measure of left ventricular performance which encompasses the two major subintervals of total electromechanical systole.26

The actual values of the measured time intervals are corrected for heart rate using previously derived regression equations.24 For example, the equation for the QS$_2$ in males is:

$$\text{QS}_2 = -2.1 \times \text{HR} + 546 \text{ msec}$$  \hspace{1cm} (1)

By transposition the equation can be expressed as:

$$\text{QS}_2 + 2.1 \times \text{HR} = 546 \text{ msec}$$  \hspace{1cm} (2)

The value of 546 msec represents the intercept of the regression equation at zero heart rate. It is termed the normal QS$_2$ index (QS$_2$I). By fitting the observed data for each patient to this form of the equation the individual QS$_2$I can be calculated. The increase or decrease in the QS$_2$I so calculated from 546 msec is a measure of the lengthening or shortening of the interval corrected for heart rate.

Previous investigations from our laboratory have indicated that there is a diurnal variation in QS$_2$I in ambulatory patients.27 However, patients in this study were at complete bed rest. To test whether diurnal variation in QS$_2$I occurs in the patients of this study, 11 patients had systolic interval determinations three times daily (9AM, 12 noon, 4PM). There were no statistically significant differences in the QS$_2$I values at these three time periods. It was concluded that the determination of the QS$_2$I in the morning could be employed as representative of the QS$_2$I for the 24-hour period in subjects at complete bed rest.

In several instances a significant shortening of the QS$_2$I was noted when a lidocaine infusion was discontinued. Therefore five subjects in this series, in whom the QS$_2$I was initially short, were studied serially following the administration of an intravenous dose of 100 mg of lidocaine. The mean QS$_2$I prior to therapy was 489 msec and increased to 510 msec (at 10 or 15 min). This change is highly significant ($P < 0.001$). In view of this finding, no studies were accepted when patients were receiving this agent at the time of the QS$_2$I determination.

Twenty-four hour urinary excretion of epinephrine (E) and norepinephrine (NE) was measured by a modification of the trihydroxyindole fluorometric technic employing a Turner fluorometer.28 Employing this method the mean percentage recovery for NE was 91 ± 2% (1 sd), and for E was 96 ± 5% when six standard samples were analyzed. The values of E and NE excretion were not corrected for this recovery. The normal range for 24-hour excretion was obtained from 11 hospitalized subjects with normal renal function and no obvious emotional or physical stress. This was 10.4 ± 5.2 µg for E and 37.7 ± 15 µg for NE. A creatinine clearance was calculated during each catecholamine collection period. Any subject with a creatinine clearance of less than 60 ml/min during the day of study was excluded. This virtually excluded subjects with cardiogenic shock or significant reduction of the cardiac output.

The patients were divided into two groups based on the presence or absence of myocardial infarction documented by both the electrocardiogram and serum enzymes. Group I consisted of 24 patients with acute myocardial infarction (13 posterior, 11 anterior), 21 of whom were transmural by electrocardiographic criteria. There were 19 males (age 40-67 years, mean 53 years) and five females (age 59-79 years, mean 66 years). There were a total of 48 determinations;

Table 1

<table>
<thead>
<tr>
<th></th>
<th>E (msec)</th>
<th>P</th>
<th>NE (msec)</th>
<th>P</th>
<th>E + NE (msec)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>-0.50</td>
<td>&lt;0.001</td>
<td>-0.73</td>
<td>&lt;0.001</td>
<td>-0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group II</td>
<td>-0.40</td>
<td>&lt;0.025</td>
<td>-0.75</td>
<td>&lt;0.001</td>
<td>-0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Both</td>
<td>-0.42</td>
<td>&lt;0.001</td>
<td>-0.76</td>
<td>&lt;0.001</td>
<td>-0.82</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: E = epinephrine; NE = norepinephrine. See text for discussion.

Correlation Matrix

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The relationship of 24-hour excretion of E + NE and the QS₂I in patients with documented acute myocardial infarction (group I).

Each patient was studied during the first 3 days of hospitalization, and in most patients a follow-up study was obtained prior to discharge.

Group II consisted of 27 patients admitted to the coronary care unit who were found not to have sustained an acute myocardial infarction. There were 19 males (age 40–78 years, mean 57 years) and eight females (age 40–78 years, mean 51 years). Fifteen of these subjects had established coronary heart disease. There were 33 determinations of urinary catecholamines and QS₂I in these subjects, all of which were performed during the first 3 days of hospitalization. In none of these subjects was clinically conspicuous heart failure present.

Standard statistical analyses were performed with the aid of a Hewlett-Packard 9100 A calculator and the OMNITAB program developed at the statistical laboratory, Iowa State University, by R. L. Chamberlain, in conjunction with an IBM 360/75 computer.

Results

The relationship between the QS₂I and the excretion of E, NE, and E + NE for groups I and II is shown in table 1. It is apparent that the best correlation exists when QS₂I is related to the combined value of E + NE.* The correlation between E + NE and QS₂I was similar for both groups. When the PEPI and LVETI for the combined groups were correlated with E + NE, significant but small correlations were found (r = −0.37, P < 0.001, and r = −0.42, P < 0.001, respectively).

The individual data are shown in figures 1 and 2. Twenty-two of 24 patients (92%) in group I had an initial elevation of NE + E while initial values were elevated in only 14 of

*Inasmuch as two variables are not perfectly correlated and carry independent information and are both negatively (or both positively) correlated to a third variable, their sum will be more negatively correlated (or more positively correlated) to the third variable than either one alone. A rigorous proof will be provided by the authors upon request.

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27 (52%) in group II. The E + NE and QS₂I returned toward or became normal by the time of discharge in those subjects with a follow-up study.

An abnormally increased PEP/LVET suggesting left ventricular dysfunction was initially present in 10 subjects in group I and 14 in group II. However, the correlations between E + NE and PEP/LVET for each group (r = 0.02 and r = -0.14) as well as for the combined group (r = -0.09) were not significant.

Although several patients with elevated urinary NE + E excretion exhibited clinical signs of increased adrenergic tone, these signs were not consistently present. This was particularly true after the first day of hospitalization. Thus, no relationship between E + NE excretion and either heart rate or blood pressure could be demonstrated in either group I or II.

Figure 3 illustrates serial studies in one patient with an acute myocardial infarction who suffered an extension of his infarction on the seventh hospital day. It can be seen that the changes in QS₂I and E + NE excretion were closely associated.

The effect of a small intravenous dose (2.5 mg) of the beta-adrenergic blocking agent propranolol upon the QS₂I was studied in 13 patients in whom the QS₂I was short and urinary catecholamines elevated (seven from group I and six from group II). These results were contrasted to results from eight normal volunteers (fig. 4). In normal subjects this dose of propranolol caused no significant change in the QS₂I. However, in the 13 patients with a short QS₂I there was a lengthening in each instance, although the QS₂I remained abnormally short (less than 2 SD of normal QS₂I) in four of 13. The mean increase after 15 min was 14 msec ± 5.3 (P < 0.001).

The catecholamine excretion of patients with acute myocardial infarction accompanied by serious arrhythmia (multiple PVCs, ectopic tachycardia of any type) during the time of study is contrasted to those without arrhythmia in figure 5. In most instances the study was performed prior to the development of the arrhythmia since antiarrhythmic therapy usually excluded the patient from study. Both the total E + NE and E were significantly higher in the arrhythmia group.

\[ \text{Figure 4} \]

The effect of 2.5 mg of propranolol administered intravenously on the QS₂I in 13 patients from groups I and II, and in eight normal volunteers. The mean change in QS₂I after 15 min is illustrated for both groups. A significant lengthening occurred in the patients while none occurred in normals.
of adrenergic activity may not be appropriate in all patients with acute myocardial infarction. It is not clear from our data to what extent increased sympathetic nervous system activity was needed to maintain a normal cardiac output. However, clinical evidence of significant circulatory deterioration was not present in any of the group I subjects.

In view of the greater frequency of serious arrhythmias in patients with the highest catecholamine excretion, it is possible that excessive adrenergic activity is deleterious to some of these patients. It should also be stressed that clinical criteria for catecholamine excess were not reliable after the first day of hospitalization.

It must be emphasized that certain important constraints were placed upon patients selected for this study. Patients with impaired renal function were excluded in an effort to insure that urinary excretion accurately reflected sympathetic activity. This virtually excluded patients in cardiogenic shock at the time of the study. Furthermore, patients receiving digitalis, exogenous catecholamines, sympathetic blocking agents, lidocaine, or with left bundle-branch block were also excluded. These restrictions tended to make the infarction group relatively homogenous and may in part account for the high correlation found between the QS2I and catecholamine excretion in this study. In this regard it is notable that in a similar study Samson was unable to demonstrate a clear-cut relationship between QS2I and either E or NE excretion. However, this author employed only mean data for QS2I and catechol excretion and did not observe the constraints employed in our patient selection.

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References

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RICHARD P. LEWIS, HARISSIOS BOUDOULAS, WILBUR F. FORESTER and ARNOLD M. WEISSLER

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