Alteration of Systolic Time Intervals in Right Ventricular Failure

By Joseph S. Alpert, M.D., Frank D. Rickman, M.D., John P. Howe, M.D., Lewis Dexter, M.D., and James E. Dalen, M.D.

SUMMARY

Systolic time intervals (STI) were measured in matched patients with and without right ventricular failure (RVF). STI were calculated from brachial arterial pressure tracings obtained at cardiac catheterization in four groups of patients: 1) controls, without RVF; 2) acute pulmonary embolism with and without acute RVF; 3) mitral stenosis, with and without chronic RVF; 4) primary pulmonary hypertension, with chronic RVF.

In patients with pulmonary embolism without acute RVF, STI were normal. However, patients with acute RVF due to pulmonary embolism had significantly shortened left ventricular ejection times (LVETc) and significantly increased pre-ejection periods (PEPc) and increased PEPc/LVETc ratios ($P < 0.05$, $P < 0.001$, $P < 0.001$ respectively).

Similar results were obtained in patients with chronic RVF. In patients with mitral stenosis without RVF, STI were normal. However, in patients with chronic RVF due to mitral stenosis or primary pulmonary hypertension, PEPc and PEPc/LVETc ratios were lengthened and LVETc was shortened ($P < 0.003$, $P < 0.005$, and $P < 0.001$ respectively).

PEPc/LVETc ratios increased as stroke index decreased ($r = -0.55$). There was also an association between PEPc/LVETc and right atrial mean pressure ($r = 0.70$). These data demonstrate that patients with acute and chronic right ventricular failure have abnormal systolic time intervals possibly secondary to left ventricular dysfunction.

Additional Indexing Words:
Systolic time intervals Right ventricular failure Left ventricular function

Left ventricular failure is the commonest cause of right ventricular failure. The right heart fails in this circumstance due to the increased pressure work transmitted to it across the lung.

The impact of right ventricular failure on left ventricular function is not as clearly defined. Chronic right ventricular failure (RVF) has been shown to cause left ventricular dysfunction in animals.

Similarly there is some evidence that acute right ventricular overload may cause mild left ventricular dysfunction in dogs.

In man, there is only minimal direct evidence that right ventricular failure (RVF) may affect left ventricular function. Several autopsy studies have demonstrated unexplained left ventricular hypertrophy in patients with chronic cor pulmonale. It has long been suspected clinically that acute right ventricular failure, as in acute pulmonary embolism, may precipitate left ventricular failure. This observation has not been confirmed by objective measurements.

Weissler and his associates have demonstrated that systolic time intervals (STI) are sensitive indicators of the state of left ventricular (LV) function. The present work assesses STI in patients with acute or chronic right ventricular failure to determine if right ventricular failure can alter left ventricular function as measured by STI.

Materials

Patients

STI were calculated in four groups of patients (table 1). Group 1 (controls) consisted of ten patients who had been catheterized and found to have no evidence of organic heart disease.

Group 2 (pulmonary embolism with or without acute right ventricular failure) consisted of 20 patients, age and sex matched with Group 1, with angiographically proven acute pulmonary embolism. These patients were free of prior heart disease on the basis of history, physical examination, ECG, and chest X-ray. Ten of these patients had massive pulmonary embolism with acute right ventricular...
failure as judged by a right atrial mean pressure greater than 7 mm Hg and a stroke index less than 40 ml/beat/m². Six of these patients were studied a second time when their right ventricular failure had improved or resolved completely. The other ten patients with acute pulmonary embolism had no hemodynamic evidence of right ventricular (RV) failure (table 1).

Group 3 (mitral stenosis with or without chronic right ventricular failure) consisted of 20 patients with catheterization-proven pure mitral stenosis. These patients were free of other valvular defects nor did they have any evidence of coronary artery disease. They were age and sex matched with group 1. Ten of these patients had critical mitral stenosis with moderate to severe pulmonary vascular disease and chronic right ventricular failure as judged by a right atrial mean pressure greater than 7 mm Hg. The other ten patients with pure mitral stenosis were free of hemodynamic evidence of right ventricular failure.

Group 4 (chronic right ventricular failure) consisted of four patients with primary pulmonary hypertension and right ventricular failure.

None of the patients, except for those with mitral stenosis were receiving digitalis preparations. Digoxin was given to nine of the ten patients with right ventricular failure and seven of the ten patients without right ventricular failure. All medication was held for 24 hours before catheterization. No patient was receiving β-blocking drugs or any catecholamine or similar agents.

Methods

Three indirect measurements of left ventricular function were obtained from ECG, brachial arterial, and left ventricular (LV) pressure tracings taken at the time of cardiac catheterization. Brachial artery pressure was obtained using fluid-filled Teflon catheters, 22 cm long with an internal diameter of 1.0 mm. Left ventricular pressures were obtained through standard fluid-filled USCI *5 medium-tip Lehman catheters. All pressures were recorded using Statham 29dp pressure manometers and an Electronics for Medicine recorder. The pre-ejection period (PEP) was derived from simultaneous brachial, arterial pressure and ECG tracings recorded at 50 mm/sec paper speed. PEP was defined as that interval from the onset of the QRS (lead II) to the onset of the upstroke of the brachial arterial pressure tracing. The left ventricular ejection (LVET) was derived from the brachial arterial pressure tracing recorded at 50 mm/sec and was defined as that interval from the start of the upstroke to the midpoint of the dicrotic notch. The Q-LV interval (analogous to the Q-1 interval) was measured in all patients with mitral stenosis from simultaneous left ventricular (LV) pressure and ECG tracings recorded at 50 mm/sec paper speed. The Q-LV interval was defined as that time from the onset of the QRS to the onset of the upstroke of the left ventricular (LV) pressure tracing.

The reported value for each interval was the average of 3-5 separate determinations for patients in normal sinus rhythm and ten determinations for patients in atrial fibrillation. Atrial fibrillation occurred only in patients with mitral stenosis. Nine of the ten patients with right ventricular failure and seven of ten patients without right ventricular (RV) failure were in atrial fibrillation. All values for PEP and LVET were corrected for heart rate.10,11

Systolic time intervals were measured in a group of ten patients who had two cardiac catheterization studies within the span of several days to determine the reproducibility of the systolic time intervals as calculated in the present work.

Patients were studied between 8:30 and 11 AM in the fasting state. The only premedication was diazepam 10 mg intramuscularly, a dosage shown to have minimal hemodynamic effects.10 All patients had QRS intervals of 0.10 sec or less. Means, standard deviations, and student’s t tests for paired and nonpaired variables were calculated using standard formulae.

Results

I. PEP corrected (PEPc)

A) Controls — PEPc in the ten controls without heart disease ranged from 0.16 to 0.20 seconds (mean

Table 1

<table>
<thead>
<tr>
<th>Hemodynamic Profiles of the Four Groups of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>1. Normal controls</td>
</tr>
<tr>
<td>n = 10</td>
</tr>
<tr>
<td>2. Pulmonary embolism</td>
</tr>
<tr>
<td>A. Without acute RVF</td>
</tr>
<tr>
<td>n = 10</td>
</tr>
<tr>
<td>B. With acute RVF</td>
</tr>
<tr>
<td>n = 10</td>
</tr>
<tr>
<td>3. Mitral stenosis</td>
</tr>
<tr>
<td>A. Without chronic RVF</td>
</tr>
<tr>
<td>n = 10</td>
</tr>
<tr>
<td>B. With chronic RVF</td>
</tr>
<tr>
<td>n = 10</td>
</tr>
<tr>
<td>4. Primary pulmonary hypertension with RVF</td>
</tr>
<tr>
<td>n = 4</td>
</tr>
</tbody>
</table>

Values are reported ± standard deviation.
Abbreviations: RVF = right ventricular failure; HR = heart rate; SI = stroke index; RA mean = right atrial mean pressure; PA mean = pulmonary artery mean pressure; BA diastolic = brachial artery diastolic pressure.

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0.18 ± 0.01. The reproducibility of PEPc as herein measured was assessed in a group of ten patients with heart disease but without RV failure who had two hemodynamic studies within a period of several days. The average difference of this measurement in the same patient studied twice was 0.01 ± 0.01 seconds (fig. 1).

B) Patients with and without acute RVF secondary to acute pulmonary embolism — In the patients with acute pulmonary embolism without RVF, PEPc ranged from 0.16 to 0.21 sec (mean 0.18 ± 0.02). This is almost identical to the results in the control group (fig. 2; table 2). However, in the ten patients with acute RVF secondary to pulmonary embolism, PEPc was significantly prolonged (mean 0.23 ± 0.02 seconds). Six of these ten patients with RVF had a repeat study an average of 20 days after the initial study. PEPc values had decreased toward the normal range in four of the six patients (fig. 2; table 2).

C) Patients with and without chronic RVF — In ten patients with mitral stenosis without RVF, PEPc was comparable to that of the normal controls. It ranged from 0.17–0.20 (mean 0.18 ± 0.01 sec) (fig. 3; table 3). However, in patients with chronic RVF due to mitral stenosis, PEPc was significantly prolonged (mean 0.21 ± 0.02). Similarly in the small group of four patients with primary pulmonary hypertension PEPc was prolonged to a mean of 0.23 ± 0.03 seconds (fig. 3; table 3).

II. LVET corrected (LVETc)

A) Controls — LVETc in the ten controls without heart disease ranged from 0.39 to 0.47 (mean 0.43 ± 0.03) sec. In the ten patients who had repeat hemodynamic studies within days of each other LVETc did not change (fig. 1). LVETc averaged 0.42 ± 0.02 seconds at the time of the first study and 0.42 ± 0.03 sec at the second study. The average difference between the paired measurements was 0.02 ± 0.01 sec (fig. 1).

B) Patients with and without acute RVF — In patients with acute pulmonary embolism without RVF, LVETc was essentially the same as in the controls; it ranged from 0.38 to 0.46 (mean 0.42 ± 0.03) sec. However, in the patients with acute RVF secon-

### Table 2

**Effect of Acute Right Ventricular Failure (RVF) on Systolic Time Intervals**

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Pulmonary embolism without RVF</th>
<th>Pulmonary embolism with RVF</th>
<th>Pulmonary embolism with RVF-follow-up</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEPc (sec)</td>
<td>0.18 ± 0.01</td>
<td>0.18 ± 0.02</td>
<td>0.23 ± 0.02</td>
<td>0.21 ± 0.02</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>LVETc (sec)</td>
<td>0.43 ± 0.03</td>
<td>0.42 ± 0.03</td>
<td>0.40 ± 0.02</td>
<td>0.42 ± 0.01</td>
<td>P &lt; 0.03</td>
</tr>
<tr>
<td>PEPc/LVETc</td>
<td>0.42 ± 0.03</td>
<td>0.43 ± 0.04</td>
<td>0.58 ± 0.05</td>
<td>0.49 ± 0.03</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Values are reported ± 1 standard deviation.
P values reflect t test for parameters in the pulmonary embolism without RVF and the pulmonary embolism with RVF groups.

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dary to pulmonary embolism, LVETc was significantly reduced (mean 0.40 ± 0.02 sec). Of the six patients having a follow-up study, LVETc increased in five while the mean increased to 0.42 ± 0.01 sec (fig. 4; table 2).

C) Patients with and without chronic RVF — In the patients with mitral stenosis without RVF, mean LVETc was the same as in the control group (0.43 ± 0.03 sec). In patients with RVF due to mitral stenosis, however, LVETc was significantly shortened (0.39 ± 0.03 sec). Similarly, in the small group of patients with primary pulmonary hypertension LVETc was shortened to a mean of 0.36 ± 0.02 sec (fig. 5; table 3).

III. PEPC/LVETc Ratio

A) Controls — PEPC/LVETc ratios ranged from 0.38 to 0.46 (mean 0.42 ± 0.03) in the group of normal controls. In the ten patients studied twice PEPC/LVETc ratios did not change, with a mean difference of 0.02 ± 0.01 units between the first and second studies (fig. 1).

B) Patients with and without acute RVF — In patients with pulmonary embolism without RVF, PEPC/LVETc ratios were the same as in the normal controls, ranging from 0.40 to 0.51 (mean 0.43 ± 0.04). In patients with acute RVF secondary to pulmonary embolism, however, PEPC/LVETc ratios were significantly increased (mean 0.58 ± 0.05). In the six patients with acute RVF who underwent follow-up study, PEPC/LVETc ratios decreased toward normal (mean 0.49 ± 0.05) in all six (fig. 6, table 2).

C) Patients with and without chronic RVF — In the patients with mitral stenosis without RVF mean PEPC/LVETc ratios were the same as in the normal controls (mean 0.43 ± 0.04). In patients with mitral stenosis and right ventricular failure, however, PEPC/LVETc ratios were significantly increased (mean 0.54 ± 0.06). Likewise, patients with primary pulmonary hypertension PEPC/LVETc ratios were significantly increased (mean 0.51 ± 0.05). In all cases PEPC/LVETc ratios were significantly increased compared to controls.

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Mitral stenosis without RVF</th>
<th>Mitral stenosis with RVF</th>
<th>Primary pulmonary hypertension with RVF</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEPC (sec)</td>
<td>0.18 ± 0.01</td>
<td>0.18 ± 0.01</td>
<td>0.21 ± 0.02</td>
<td>0.23 ± 0.03</td>
<td>P &lt; 0.005/P &lt; 0.001</td>
</tr>
<tr>
<td>LVETc (sec)</td>
<td>0.43 ± 0.03</td>
<td>0.43 ± 0.03</td>
<td>0.39 ± 0.03</td>
<td>0.36 ± 0.02</td>
<td>P &lt; 0.005/P &lt; 0.001</td>
</tr>
<tr>
<td>PEPC/LVETc</td>
<td>0.42 ± 0.03</td>
<td>0.43 ± 0.04</td>
<td>0.54 ± 0.06</td>
<td>0.61 ± 0.05</td>
<td>P &lt; 0.001/P &lt; 0.001</td>
</tr>
<tr>
<td>Q-LV (sec)</td>
<td>0.04 ± 0.01</td>
<td>0.04 ± 0.01</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>ICT (sec)</td>
<td>0.11 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td></td>
<td></td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Values are reported ± 1 standard deviation.

The first P value reflects t test for parameters in mitral stenosis without RVF and mitral stenosis with RVF groups. The second P value reflects t test for parameters in primary pulmonary hypertension and control groups.

ICT = isovolumic contraction time.

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**Figure 3**

PEPC in patients with and without chronic right ventricular failure. MS without RVF = patients with mitral stenosis without right ventricular failure; MS with RVF = patients with mitral stenosis with right ventricular failure; PPHT = patients with primary pulmonary hypertension and right ventricular failure.

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**Figure 4**

LVETc in patients with and without acute right ventricular failure. (abbreviations as in figure 2)
pulmonary hypertension had significantly increased (mean 0.61 ± 0.05) PEPc/LVETc ratios (fig. 7, table 3).

IV. Q-LV and ICT

Q-LV intervals were calculated in the patients with mitral stenosis. They were the only patients in whom left heart catheterization had been performed. The Q-LV interval was the same (0.04 ± 0.01 seconds) in patients with and without RVF due to mitral stenosis. Q-LV intervals were subtracted from PEP intervals in these patients to obtain an estimate of the true left ventricular isometric contraction time (ICT). Mean left ventricular ICT was significantly longer in patients with RV failure than in those without it (table 3).

V. Relation of Systolic Time Intervals (STI) to Stroke Index (SI) and Right Atrial Mean Pressure (MRAP)

As noted in table 4, modest correlations were present between the various systolic time intervals (PEPc, LVETc, and PEPc/LVETc) and the two hemodynamic measurements, stroke index, and right atrial mean pressure. These associations were strongest in patients with pulmonary embolism and weakest in patients with mitral stenosis (table 4, figs. 8, 9).

Discussion

Systolic time intervals have been reported to be sensitive indicators of left ventricular function.7–9, 11–14 They are capable of detecting acute or chronic changes in ventricular function caused by pathological conditions or drugs.7, 8

Usually these parameters are measured noninvasively; however, systolic time intervals measured with catheters in the left ventricle and aorta have correlated very closely with externally derived indices.11, 12 The present work derives systolic time intervals from pressure tracings recorded from the brachial artery and the left ventricle. These internally derived indices are highly reproducible as seen in a group of ten patients catheterized twice several days apart (fig. 1). Moreover, the systolic time intervals as derived in the present work correlated with stroke index in all patient groups except those with mitral stenosis. Similar correlations have been noted previously, employing externally derived systolic time intervals.7, 8, 13, 14 In the present work, STI were also noted to correlate with right atrial mean pressure.

The pre-ejection period (PEP) is composed of two separate events, the electromechanical delay and the isometric contraction period of the left ventricle. The electromechanical delay period can be estimated by measuring the Q-LV interval. In those patients who had left ventricular catheterization, the Q-LV interval

Figure 5

LVETc in patients with and without chronic right ventricular failure. (Abbreviations as in figure 3)

Figure 6

PEPc/LVETc ratios in patients with and without acute right ventricular failure. (Abbreviations as in figure 2)

Figure 7

PEPc/LVETc ratios in patients with and without chronic right ventricular failure. (Abbreviations as in figure 3)
was unaffected by the presence or absence of RV failure. When the Q-LV interval was subtracted from the PEP an estimation of the isovolumic contraction time was obtained which was significantly prolonged in the patients with RV failure as compared with patients without RV failure.

PEP and LVET as reported here were corrected for heart rate employing the regression equations of Weissler.\(^7\) The uncorrected values for PEP and LVET, however, showed the same significant differences between the groups with and without RV failure, as did the values corrected for heart rate.

The fact that the present internally derived values for PEP are longer than the externally derived indices is the result of two factors: first, aortic to brachial arterial pulse delay and second, pressure wave delay in the fluid-filled catheter system. Values for internal LVETc are similar to those obtained externally since pulse and catheter delay affect both measurement points of this parameter equally. Similar observations on internally and externally derived values for PEP and LVET have been made previously.\(^11\) Therefore, we believe that STI as measured here reflect left ventricular function to the same degree as externally derived indices.

Four possible mechanisms exist to explain the abnormal systolic time intervals in patients with acute and chronic right ventricular failure. First, left ventricular preload is decreased secondary to a reduced stroke output from the failing right ventricle. A decrease in left ventricular preload can result per se in abnormalities in various left ventricular function parameters including systolic time intervals.\(^15\, 16\)

A second explanation for the findings presented is suggested by Braunwald's finding\(^17\) that acute increases in peripheral resistance result in shortened left ventricular ejection times. In the same manner, increased right ventricular afterload, such as that seen in our patients with right ventricular failure, may cause alterations in right ventricular systolic events. Given the close interplay between right and left ventricular systolic events, the measured changes in left heart systolic time intervals may in part reflect alterations in right ventricular systolic time intervals.

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Patients with mitral stenosis</th>
<th>Patients with pulmonary embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEPc/SI</td>
<td>(r = -0.48)</td>
<td>(r = -0.43)</td>
<td>(r = -0.64)</td>
</tr>
<tr>
<td>LVETc/SI</td>
<td>(r = 0.45)</td>
<td>(r = 0.24)</td>
<td>(r = 0.37)</td>
</tr>
<tr>
<td>PEPc/LVETc/SI</td>
<td>(r = -0.55)</td>
<td>(r = -0.39)</td>
<td>(r = -0.66)</td>
</tr>
<tr>
<td>PEPc/RA mean</td>
<td>(r = 0.62)</td>
<td>(r = 0.26)</td>
<td>(r = 0.79)</td>
</tr>
<tr>
<td>LVETc/RA mean</td>
<td>(r = -0.47)</td>
<td>(r = -0.55)</td>
<td>(r = -0.59)</td>
</tr>
<tr>
<td>PEPc/LVETc/RA mean</td>
<td>(r = 0.70)</td>
<td>(r = 0.45)</td>
<td>(r = 0.84)</td>
</tr>
</tbody>
</table>

Abbreviations: SI = stroke index; RA mean = right atrial mean pressure.
Actual alteration of the contractile function of the left ventricle is the third possible explanation for the present observations. Kelly et al. observed reduced left ventricular peak systolic pressure, peak systolic wall stress, peak dp/dt, peak contractile element velocity and myocardial concentration of norepinephrine in dogs with chronic right ventricular failure. Left ventricular force velocity curves were also markedly abnormal. Salel et al. noted abnormal left ventricular contractility indices in a mixed group of patients most of whom had chronic right ventricular overload. Moreover, Machida and Rapaport observed altered left ventricular compliance and decreased left ventricular contractility parameters in dogs whose pulmonary circulation had been embolized with barium sulfate.

A fourth possible explanation for abnormal systolic time intervals in right ventricular failure is the so-called "reversed Bernheim phenomenon", or septal encroachment on the left ventricular cavity. The septal "bulge" is said to result in an alteration in left ventricular geometry and hence contractile function. Taylor et al. found that left ventricular distensibility was considerably reduced during right ventricular diastasis. Dogs with acute or chronic right ventricular overload have been noted to have decreased left ventricular compliance as measured by pressure/volume curves. Stool et al. quantitated canine left ventricular septal to lateral wall diameter changes caused by septal bulging secondary to right ventricular pressure overload. Increasing pulmonary arterial pressure to a mean of 60 mm Hg resulted in a 23% decrease in septal-lateral left ventricular wall diameter as well as concomitant decreases in left ventricular end-diastolic volume and stroke volume. In a single clinical observation, Harken noted a decreased left ventricular cavity secondary to septal bulging in a patient with mitral stenosis and severe right ventricular failure.

It is concluded that left ventricular function, insofar as it can be measured by systolic time intervals, is altered in acute and chronic right ventricular failure. Four possible mechanisms exist to explain the alteration in left ventricular function noted in patients with right ventricular failure: decreased left ventricular preload, alteration in right ventricular systolic time intervals, decreased left ventricular contractility, and altered left ventricular geometry and compliance. The present data do not suggest which mechanism is actually responsible for the abnormal systolic time intervals noted in patients with right ventricular failure.

References

8. Weissler AM, Garrard CL Jr: Systolic time intervals in cardiac disease II. Mod Conc Cardiovasc Dis 40: 5, 1971
16. Spodick DH, Khan AH, Querry VM: Systolic and diastolic time intervals in pulsum alternans. Am Heart J 87: 5, 1974
18. Salel A, Mason DT, Amsterdam EA, Zelis R: Depression of left ventricular contractility in primary right ventricular overload: the 'reverse Bernheim phenomenon'. Circulation 43, 44 (suppl II): II-220, 1971
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