Alterations of Right Ventricular Systolic Time Intervals by Chronic Pressure and Volume Overloading

Edward I. Curtiss, M.D., P. Sudhakar Reddy, M.D., James D. O'Toole, M.D., and James A. Shaver, M.D.

SUMMARY Right ventricular (RV) systolic time intervals and hemodynamic parameters were determined by micromanometric techniques in 13 subjects with normal right ventricles (NRV). These data were compared to those of 16 patients with pulmonary hypertension (PH) or predominant pressure overloading and 13 individuals with uncomplicated secundum atrial septal defects (ASD) or predominant volume overloading.

In PH, the QP2 interval tends to remain within the normal range due to reciprocal changes in isovolumic contraction (ICT) and ejection (RVET) times. Elevations of pulmonary artery diastolic pressure are associated with increases in the mean rate of isovolumic pressure rise (MRIPR) ($r = 0.84$), but the latter change does not fully compensate for the widened ventriculoarterial diastolic pressure difference and ICT becomes prolonged ($P < 0.001$). Factors other than stroke index depression which may contribute to the decreased duration of RVET ($P < 0.001$) include tricuspid regurgitation and elevation of pulmonary vascular impedance.

In ASD, QP2 is significantly prolonged ($P < 0.025$) due to a significant increase in RVET ($P < 0.005$). In contrast to NRV, a linear correlation of RVET and stroke index was not present, which suggested an alteration of ejection dynamics in this group. Despite a high incidence of complete or incomplete right bundle branch block, the interval from QRS onset to rapid RV pressure upstroke was not prolonged. This is most probably the result of peripheral bundle branch block of genesis of the QRS pattern by right ventricular hypertrophy.

VALUES FOR LEFT VENTRICULAR SYSTOLIC TIME INTERVALS have been reported in the normal and a wide variety of disease states.$^{1-8}$ The ability to determine these intervals by noninvasive techniques has significantly contributed to their widespread use as an investigative tool. Although the right ventricular electromechanical interval has been assessed noninvasively using recording of the left parasternal pulsation,$^{6,7}$ the determination of right ventricular systolic time interval components usually requires cardiac catheterization. In the future, echocardiography may provide a noninvasive means for their determination.$^9$ At the present time, however, systematic investigations of these components have been rare.$^6,12$ The present study employed micromanometric techniques to examine right ventricular systolic time intervals in the normal state and attempted to ascertain how they might be altered by chronic diseases characterized by pressure and volume overloading of this chamber.

Methods and Materials

Forty-two patients undergoing diagnostic cardiac catheterization were the subjects of this investigation. Informed consent was obtained from all individuals prior to study. They were separated into three groups (table 1):

Group I — Normal Right Ventricle

This group was composed of 13 patients: four with functional systolic murmurs; five with audible expiratory splitting of the second sound, one of whom had complete right bundle branch block (CRBBB); one with hemodynamically insignificant mitral regurgitation; one with chest pain of noncardiac etiology who also manifested CRBBB and two with a patent ductus arteriosus — one had 1.2-to-1 and the other no detectable left-to-right shunt as determined by nitrous oxide inhalation and green dye curves, respectively.

All patients had normal resting right-sided hemodynamics; except for the two with a patent ductus arteriosus, none had evidence of intracardiac shunting. All were in sinus rhythm and none had electrocardiographic abnormalities except the two individuals with isolated CRBBB.

Group II — Pulmonary Hypertension

This group included 16 patients with mean pulmonary artery pressures greater than 28 mm Hg, diastolic pressures in excess of 22 mm Hg and no evidence of left ventricular disease. Diagnoses were isolated mitral stenosis in seven, primary pulmonary hypertension in five, pulmonary vascular disease due to progressive systemic sclerosis in two, and associated with chronic active hepatitis in one. The remaining patient had Lutembacher's syndrome with a 1.5-to-1 left-to-right shunt at the atrial level. Eleven patients were in sinus rhythm and five had atrial fibrillation. Since no significant differences in hemodynamic data, heart rate and systolic time intervals were found between the sinus rhythm and atrial fibrillation subgroups, their data were pooled. No patient in this group had CRBBB.

Group III — Normotensive Atrial Septal Defect

Thirteen patients had an isolated secundum atrial septal defect with pulmonary to systemic flow ratios of 1.7–3.3 determined by the nitrous oxide inhalation method.$^9$ Mean pulmonary artery pressure was less than 21 mm Hg in all members of this group. All were in sinus rhythm.

Nine had incomplete right bundle branch block and three complete right bundle branch block QRS patterns. In two of
## Table 1. Clinical, Hemodynamic and Systolic Time Interval Data

<table>
<thead>
<tr>
<th>PT/Age/SEX</th>
<th>Dx</th>
<th>RA &amp; V (mm Hg)</th>
<th>RV END (mm Hg)</th>
<th>S (mm Hg)</th>
<th>D (mm Hg)</th>
<th>M (mm Hg)</th>
<th>MPSR/ECG (mm/s)</th>
<th>MSER/ECG (mm/s)</th>
<th>MRRP/ECG (mm/s)</th>
<th>MIR/ECG (cycles/min)</th>
<th>HR/RR</th>
<th>RV systolic time intervals</th>
</tr>
</thead>
</table>

**Group I — Normal Right Ventricle**

| D.M., 51/M | AES | 0 | 4 | 28 | 12 | 16 | 57 | 155 | 85 | 15 | 51 | 15 | 15 | 201 | 6.0 | 2.3 | 35 |
| D.W., 51/M | AES | 0 | 4 | 28 | 12 | 16 | 57 | 155 | 85 | 15 | 51 | 15 | 15 | 201 | 6.0 | 2.3 | 35 |
| D.W., 51/M | AES | 0 | 4 | 28 | 12 | 16 | 57 | 155 | 85 | 15 | 51 | 15 | 15 | 201 | 6.0 | 2.3 | 35 |

**Group II — Pulmonary Hypertension**

| E.L. / 44/F | PPH | 7 | 11 | 83 | 36 | 52 | 21 | 30 | 63 | 19 | 44 | 33 | 57 | 103 | 12 | 88 | 53 |
| E.M. / 50/F | PPH | 7 | 11 | 83 | 36 | 52 | 21 | 30 | 63 | 19 | 44 | 33 | 57 | 103 | 12 | 88 | 53 |
| J.S. / 67/F | PPH | 9 | 7 | 69 | 35 | 48 | 62 | 107 | 69 | 35 | 48 | 62 | 107 | 69 | 35 | 48 | 62 |

**Group III — Atrial Septal Defect**

| T.K. / 25/M | AES | 3 | 6 | 16 | 8 | 10 | 67 | 188 | 65 | 14 | 94 | 41 | 135 | 56 | 37 | 49 |
| T.K. / 25/M | AES | 3 | 6 | 16 | 8 | 10 | 67 | 188 | 65 | 14 | 94 | 41 | 135 | 56 | 37 | 49 |

**Mean**

<table>
<thead>
<tr>
<th>PT/Age/SEX</th>
<th>Dx</th>
<th>RA &amp; V (mm Hg)</th>
<th>RV END (mm Hg)</th>
<th>S (mm Hg)</th>
<th>D (mm Hg)</th>
<th>M (mm Hg)</th>
<th>MPSR/ECG (mm/s)</th>
<th>MSER/ECG (mm/s)</th>
<th>MRRP/ECG (mm/s)</th>
<th>MIR/ECG (cycles/min)</th>
<th>HR/RR</th>
<th>RV systolic time intervals</th>
</tr>
</thead>
</table>

**Abbreviations:** RA = right atrium; V = ventricle; MPSR = mean pulmonary systolic pressure; MSER = mean right ventricular systolic pressure; MRRP = mean rate of inotropic pressure rise; MIR = mean right ventricular systolic ejection rate; MVP = mitral stenosis; NCCP = non-coronary sinus pressure; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PPH = primary pulmonary hypertension; PVS = progressive severe sclerosis; RV = right ventricular; S = sphygmonanometer; S = systolic; T = terminal.

*In years.

Complete right bundle branch block.

Abbreviations: AES = audible expiratory splitting of the second heart sound; CAH = chronic active hepatitis; D = diastole; Dx = diagnosis; EPI = electrosympathetic interval; FS = functional systolic murmur; HR = heart rate; Lu = Lutembacher's syndrome; M = mean; MR = mitral regurgitation; MRRP = mean rate of inotropic pressure rise; MSER = mean right ventricular systolic ejection rate; MS = mitral stenosis; NCCP = non-coronary sinus pressure; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PPH = primary pulmonary hypertension; PVS = progressive severe sclerosis; RA = mean right atrial pressure; RV = right ventricular; RVEND = right ventricular end-diastolic pressure; RV = right ventricular stroke index; S = systolic; SD = standard deviation.

the latter three patients, abnormal terminal QRS slowing was documented vectorcardiographically (>45 msec).

Hemodynamic data for the three groups are presented in table 1.

Right heart catheterization was performed using standard techniques. Retrograde or transseptal left heart study was done if warranted by the clinical circumstances in each case. Cardio output determinations were performed by the Fick or dye dilution methods. In Group III, estimations of pulmonary blood flow were obtained in ten subjects by the Fick method using Van Slyke determinations of brachial and pulmonary arterial oxygen contents; none of these subjects had evidence of significant right-to-left shunting by green dye curves (vena caval injection with brachial arterial sampling).

Right ventricular systolic time intervals were determined using cather-tipped micromanometers placed in the right ventricle and proximal main pulmonary artery (fig. 1). Catheter equisensitivety was determined according to previously described methods. Electrocardiographic and external phonocardiographic traces were obtained with the pressure.
records. Respiratory phase was determined by a nasal thermistor.

Simultaneous high fidelity recordings of right ventricular (RV) and pulmonary artery (PA) pressure were obtained in 11 of 13 group I, 13 of 16 group II and 12 of 13 group III subjects. In the remainder, sequential recordings of RV and PA pressure were used.

Right ventricular systolic time intervals were measured according to the following definitions (fig. 1).

1) Electropressor interval (EPI)† — the onset of QRS to the onset of rapid ventricular pressure rise.

2) Isovolumic contraction time (ICT) — the onset of rapid ventricular pressure rise to the onset of rapid pressure rise in the PA pressure trace.

3) Pre-ejection period (PEP) — the addition of EPI and ICT.

4) Right ventricular ejection time (RVET) — the onset of rapid PA pressure rise to the incisura of the PA pressure trace.

5) QP₂ — since the pulmonic component of the second sound was always coincident with the incisura of the PA pressure trace, this interval represents the addition of PEP and RVET.

Tracings were obtained on an oscillographic recorder* at a paper speed of 100 mm/sec with 20 msec timeline markers. Intervals were measured to the nearest 5 msec. The mean of at least 20 consecutive cardiac cycles was determined for each patient. Statistical analysis was performed on an Olivetti desk top computer. The difference between group means was assessed for statistical significance using the two-tailed Student’s t-test. A P value of less than 0.05 was considered to be significant. Regression analysis and Pearson’s correlation coefficient were obtained according to standard statistical methods.¹⁷

There were no statistically significant differences in heart rate or respiratory rate between the three groups (table 1). Pre-ejection period and its components demonstrated no significant correlation with heart rate. However, RVET and QP₂ intervals were significantly related to heart rate. In order to eliminate the possible bias introduced by the minor intergroup differences in heart rate, the significance of group differences in RVET and QP₂ intervals was evaluated by an analysis of covariance.¹⁷ Since no statistically significant intergroup differences in the slope of the respective intervals on heart rate were found, a pooled regression coefficient was used to adjust the observed group mean intervals. Inter-group comparison of intervals was also performed using only end expiratory values; this did not change the comparative results. Therefore, the interval values reported represent the mean of consecutive cardiac cycles. In group I, the EPI, PEP and QP₂ intervals of the subjects with CRBBB were excluded from analysis.

The mean rate of isovolumic pressure rise (MRIPR) was calculated as (fig. 2):

\[
\text{MRIPR} = \frac{\text{Developed pressure}}{\text{RVICT}}
\]

where the units of MRIPR are mm Hg/sec; RVICT = right ventricular isovolumic contraction time; and developed pressure equals PA end-diastolic minus RV end-diastolic pressure.

†The term, “electropressor” rather than “electromechanical,” is used since right ventricular mechanical systole usually precedes upstroke of the ventricular pressure pulse by a small interval.¹⁴

*DR-12, Electronics for Medicine, White Plains, New York.
Mean right ventricular systolic ejection rate was obtained by dividing stroke index by right ventricular ejection time.

**Results**

The mean electropressor interval was $42 \pm 8$ msec (sd) in the group with normal right ventricles (table 1). Based upon two standard deviations from the mean, the upper limit of normal for EPI is 58 msec. This interval was not significantly different from normal in the atrial septal defect and pulmonary hypertensive groups. The EPI was 39 and 39 msec respectively, in two group III subjects (S.R., E.K.) with vectorcardiographic evidence of complete right bundle branch block. This contrasted with abnormal EPIs of 81 and 94 msec in two group I subjects (R.K., J.K.) who had complete right bundle branch block as an isolated defect.

Isovolumic contraction time was $43 \pm 11$ msec in group I subjects and not significantly different in patients with atrial septal defects. These two groups manifested no significant differences in right ventricular or pulmonary artery diastolic pressures although systolic pressures in group III were significantly higher (table 1). This indicates that the group with chronic volume overloading of the right ventricle did not manifest an increased mean rate of isovolumic pressure rise (MRIPR) detectable by the methods employed in this study.

In the pulmonary hypertensive group, the rise in pulmonary artery diastolic pressure (PADP) increased the mean amount of pressure development required during isovolumic systole (developed pressure) to 27 mm Hg or approximately five and a half times that found in the normal group. Although ICT was significantly prolonged, to $75 \pm 15$ msec, similar values for this interval were found despite variations in developed pressure from 20 to 43 mm Hg; there was no linear relationship between ICT and the absolute level of PADP or developed pressure. The reason for these findings is illustrated in figure 3. Although rises in PADP were strongly associated with rises in the amount of pressure development required during isovolumic systole, they were also strongly associated with increases in the mean rate of pressure development.

Two patients (E.I. and J.W.) had ICTs which were within the normal range despite significant elevations of pulmonary artery diastolic pressure. Their developed pressures were smaller than expected from the observed levels of PADP. Normalization of ICT duration in these two patients was apparently related to a significant elevation of right ventricular end-diastolic pressure.

The significant increase in right ventricular pre-ejection period found in the pulmonary hypertensive group was due to prolongation of isovolumic contraction time. Groups I and III were examined individually and in combination to detect the relationship between PEP or ICT and resting heart rate. No significant correlation was found; hence, no rate corrections for these intervals were employed.

Ejection time correlated with heart rate in all three groups (fig. 4 and table 2). The right ventricular ejection time was significantly decreased in pulmonary hypertension ($P < 0.001$) and significantly increased in atrial septal defect ($P < 0.001$).

A strong linear correlation of stroke index and ejection time was found only in the normal group. In the pulmonary hypertensive subjects, the decrease in RVET generally paralleled the degree of stroke index depression (fig. 5). However, four patients, (C.H., Z.D., E.D., C.M.) had ejection times which were strikingly lower than that predicted from the observed stroke indices. All four had auscultatory or intracardiac phonocardiographic evidence of tricuspid regurgitation.

In patients with atrial septal defect, prolongation of RVET was accompanied by a significant increase in mean...
stroke index (table 1). However, increases in stroke index were not accompanied consistently by proportionate increases in ejection time (fig. 5). Ejection time generally increased to a lesser extent than stroke index, especially when the latter rose above 100 cc/m². Above this level, the tendency toward increasing ejection duration was no longer apparent consistent with significant increases in the mean rate of systolic ejection.

The QP₂ interval was not significantly different from normal in pulmonary hypertension patients due to the reciprocal changes in pre-ejection period and ejection time (fig. 6). However QP₂ was significantly prolonged in atrial septal defect patients (P < 0.025); this prolongation could be attributed to increased duration of the ejection period.

Discussion

In micromanometric pressure recordings from the supravalvular aorta, the aortic component of the second sound and the aortic incisura are coincident,⁴ ¹³ these events are frequently used as markers for the termination of left ventricular mechanical systole. While the pulmonic component of the second sound and the pulmonary artery incisura are also coincident, these analogous events cannot be similarly taken to signal the conclusion of right ventricular mechanical systole. As can be appreciated from figure 1, which was obtained in a young male without cardiopulmonary disease, the pulmonary artery incisura is separated from the right ventricular pressure trace by a significant interval of 45 msec. In the normal systemic circulation, this interval, descriptively labeled “hangout” by Shaver et al.,¹³ amounts to less than 15 msec; hence, the aortic incisura or the aortic component closely approximates the end of ventricular mechanical systole. This close approximation is usually not present in the normal pulmonary circulation where the hangout interval varies from 30 to 80 msec.¹⁸ The duration of the right-sided hangout interval appears to be a reflection of the status of pulmonary vascular impedance; it narrows to 15 to 25 msec when impedance is elevated as in pulmonary hypertension, and increases in situations where increased capacitance of the pulmonary vascular bed is found such as idiopathic dilatation of the pulmonary artery.¹⁵ ¹⁸ The events transpiring in the hangout interval include 1) conclusion of ventricular mechanical systole, 2) cessation of flow into the pulmonary artery, and 3) the occurrence of P₂ or the pulmonic incisura. The relationship between these events is complex and incompletely understood at present but it is evident they cannot be assumed to be synchronous.¹⁵ ¹⁶ ¹⁹

RVET was found to correlate significantly with heart rate in each group, and at any given rate, the duration of this interval was significantly abbreviated in pulmonary hypertension and significantly prolonged in atrial septal defect. The significant correlation of RVET and stroke index in the group with normal right ventricles suggests only that similar determinants affect both parameters. It is evident from an inspection of figure 5 that the relationship between RVET and stroke index in the pressure and volume overloaded groups deviates significantly from the one established in the group with normal right ventricles. The changes in RVET in the pulmonary hypertensive group are only partially associated with parallel changes in forward stroke index. Ejec-

![Figure 5](http://circ.ahajournals.org/)

**TABLE 2. Regression Data**

<table>
<thead>
<tr>
<th>Group</th>
<th>Equation</th>
<th>N</th>
<th>SD (msec)</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRV</td>
<td>−2.18 HR + 503</td>
<td>13</td>
<td>15</td>
<td>−0.854</td>
</tr>
<tr>
<td></td>
<td>1.77 SI + 262</td>
<td>13</td>
<td>15</td>
<td>0.845</td>
</tr>
<tr>
<td>PH</td>
<td>−2.35 HR + 469</td>
<td>16</td>
<td>28</td>
<td>−0.739</td>
</tr>
<tr>
<td>ASD</td>
<td>−2.69 HR + 574</td>
<td>13</td>
<td>21</td>
<td>−0.834</td>
</tr>
<tr>
<td></td>
<td>−1.63 HR + 546</td>
<td>11</td>
<td>15</td>
<td>−0.782</td>
</tr>
<tr>
<td></td>
<td>−2.44 HR + 590</td>
<td>16</td>
<td>23</td>
<td>−0.818</td>
</tr>
<tr>
<td>ASD</td>
<td>−2.48 HR + 637</td>
<td>13</td>
<td>25</td>
<td>−0.767</td>
</tr>
</tbody>
</table>

Abbreviations: HR = heart rate (cycles/min); SI = stroke index (cc/beat/m²); NRV = normal right ventricle; PH = pulmonary hypertension; ASD = atrial septal defect.

![Figure 6](http://circ.ahajournals.org/)
tion duration was decreased below the expected value in subjects with overt manifestations of tricuspid regurgitation. The alternate ejection route, having a significantly lower impedance than the pulmonary arterial tree, may alter the pattern and rate of ejection, analogous to the changes demonstrable in mitral regurgitation. A portion of the decrease in ejection duration in pulmonary hypertension may also be due to the elevation of pulmonary vascular impedance, which uniformly narrows the hangout interval. The reduction in stroke volume and ejection duration would be concomitant results of the impedance elevation rather than representing cause and effect.

In the atrial septal defect group, the degree of RVET prolongation progressively decreased relative to the increase in calculated stroke index, compatible with increasing rates of mean right ventricular systolic ejection. At stroke indices above 100 cc/beat/m², RVET began decreasing, suggesting that the right ventricle adapts to these extreme volume loads by increasing the velocity of contraction; however, this conclusion is uncertain since the number of data points is limited and errors inherent in the method used to calculate stroke index would tend to be large at these high levels of cardiac output. It must also be emphasized that increased ejection duration in selective volume overloading of the right ventricle does not necessarily mean the duration of mechanical systole is prolonged. O'Toole et al. found the duration of right ventricular systole, as estimated from the QP₂ interval minus the right-sided hangout interval, was essentially equal to the QA₂ interval in atrial septal defect. Thus, prolongation of RVET in this condition is primarily due to the hangout interval which, in turn, appears related to a low pulmonary vascular impedance.

Since the determinants of isovolumic contraction time include pulmonary artery diastolic pressure, right ventricular end-diastolic pressure, and the rate of isovolumic pressure rise, this interval may be viewed as the base of a right triangle (fig. 2). The other leg of the triangle is the pressure developed during isovolumic systole and the hypotenuse represents the mean rate of pressure rise during this period. In predominant chronic pressure overloading of the right ventricle, PEP was significantly prolonged solely due to lengthening of ICT. While it might be anticipated that the increase in ICT would be linearly related to the degree of pulmonary artery diastolic pressure elevation, this was not the case. Increases of PADP resulted in increases of both determinants of ICT — the increase in the amount of developed pressure tended to prolong ICT while the increase in the mean rate of pressure rise tended to shorten the interval. Since the increase in MRIPR was proportionately less than the increase in developed pressure, the net result was prolongation of ICT.

In predominant chronic volume overloading of the right ventricle, as typified by patients with uncomplicated atrial septal defect, PEP and its component intervals were not significantly different from normal. While most patients in this group had electrocardiographic patterns of incomplete or complete right bundle branch block, prolongation of the electropressor interval was not found. This finding was documented in two normal subjects with CRBBB as an isolated defect; the normal EPI in atrial septal defect is thus most probably due to a peripheral site of block in the right bundle branch or genesis of the electrocardiographic pattern by right ventricular hypertrophy. Analogously, minimal or absent prolongation of the left ventricular electromechanical interval in complete left bundle branch block has been attributed to "arborization" block. With regard to ICT in atrial septal defect, no significant change in this interval and its determinants could be detected. A characteristic change in the rate of isovolumic pressure rise is not excluded by these observations since our method of detecting this change may be too insensitive. Gleason and Braunwald have previously demonstrated a moderate increase of right ventricular dp/dt in patients with chronic volume overloading of this chamber. However, in contrast to peak left ventricular dp/dt which usually occurs near the onset of ejection, peak right ventricular dp/dt in pulmonary normotensive patients occurs well after the onset of ejection (fig. 7). Hence, minimal changes in MRIPR and PEP are not incompatible with the findings of Gleason and Braunwald.

In chronic pressure and volume overloading of the right ventricle, the QP₂ interval tends to be within the normal range and prolonged, respectively. In the former situation, this result is produced by the tendency of PEP and RVET to change in opposite directions. In the latter situation, the change is due to prolongation of ejection time.

**Figure 7.** Simultaneous micromanometric pressures in the right ventricle and pulmonary artery. The trace above the pressure recordings is right ventricular dp/dt. Arrows indicate the onset of right ventricular ejection. Panel A) Subject from Group I (J.D.) with audible expiratory splitting of the second sound. Panel B) Subject from Group III (E.K.). In these subjects peak right ventricular dp/dt occurs approximately 50 msec after the onset of ejection. In contrast to the systemic circulation where peak dp/dt generally occurs with the onset of ejection, peak right ventricular dp/dt usually occurs during the ejection phase of systole in subjects with normotensive pulmonary values. PA = pulmonary artery pressure; RV = right ventricular pressure; Resp = respiration; Ej = onset of ejection.
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