Systolic Time Intervals
in Severe Aortic Valve Disease

Changes with Surgery and Hemodynamic Correlations

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and Eliot Schechter, Lt. Col., USAF, MC

SUMMARY
Systolic time intervals were recorded in 25 consecutive patients before and after aortic valve surgery. Ten patients with dominant aortic stenosis (AS) and 10 with dominant aortic insufficiency (AI) received a Starr-Edwards prosthesis; five underwent repair procedures for AS or subaortic lesions. Before operation, the mean rate-corrected left ventricular ejection time (LVETc) was prolonged; postoperatively LVETc decreased significantly. Conversely, preoperative mean rate-corrected preejection period (PEPc) was short and increased postoperatively. Serial measurement of LVETc in a patient who had two aortic valve replacements suggested its value in quantitating prosthetic malfunction.

In AS, preoperative LVETc correlated closely with cardiac index; normal ejection times were associated with the most severely depressed flows. Preoperative variations in PEPc in AS related inversely to the first derivative of the left ventricular pressure curve (maximal LV dp/dt). In AI, PEPc correlated with the quotient:

$$\frac{Adbp - LVed}{dp/dt}$$

where Adbp — LVed = transaortic end-diastolic pressure difference (aortic diastolic pressure minus LV end-diastolic pressure), and dp/dt = maximal LV dp/dt.

This study identifies the flow and pressure parameters which correlate with abnormalities of PEPc and LVETc, with severe AS and AI. The sensitivity of this technique to the hemodynamic changes of corrective surgery makes it a potentially useful noninvasive means to measure prosthetic valve function.

Additional Indexing Words:
Aortic insufficiency Aortic stenosis Aortic valve replacement
Left ventricular ejection time Preejection period

Systolic time intervals are an objective noninvasive means to assess left ventricular function and left ventricular outflow disorders. Prior study indicates left ventricular ejection time is prolonged when left ventricular outflow obstruction or aortic insufficiency (AI) occurs in the absence of congestive heart failure. Successful aortic valve surgery relieves much of the hemodynamic burden caused by these disorders. It was anticipated that their correction might be reflected by changes in systolic time intervals. This consideration led us to apply this technique to all patients undergoing aortic valve surgery at Wilford Hall USAF Medical Center since December 1968. The results of this study on 28 patients over a 2-year period are reported herein.
Methods

Systolic time intervals (STI) were defined according to the method of Weissler:2 (1) total electromechanical systole (Q-S2) is the interval from the onset of the Q wave in the electrocardiogram to the first high-frequency component of the aortic closure sound; (2) left ventricular ejection time (LVET) is the interval from the initial rapid rise of the carotid pulse to the trough of the incisura; (3) the preejection period (PEP) was derived by subtracting LVET from Q-S2. It is a function of the time interval from initial electrical depolarization of the ventricle to the aortic valve opening. An analysis of the components of PEP, the conduction time (Q-S1), and isovolumic contraction time (ICT) were not included in this report due to difficulty in identifying the mitral component of S1, particularly in patients with aortic insufficiency.

The phonocardiogram, carotid pulse, and electrocardiogram (lead II) were recorded simultaneously on an Electronics for Medicine photographic recorder at a paper speed of 150 mm/sec with time lines every 20 msec. With careful technique it was always possible to obtain records with a discernible second heart sound and clear incisura. In severe AI, the latter occasionally appeared as an abrupt change in slope on the descending limb of the indirect carotid pulse. The potential technical error of measuring the Q-S2 interval to the pulmonic component of S2 was avoided by selecting the first high-frequency component that preceded the incisura by 30-40 msec.5 To minimize beat-to-beat variation, systolic time intervals were measured at end-expiration. Under these circumstances the measured intervals of one cardiac cycle were representative of a sequence of 10 successive beats (coefficient of variation less than 1%).4

Systolic intervals corrected for heart rate (STL) were determined by dividing the observed measurement by that predicted from the regression equations of Weissler2 for the same heart rate:

\[ \text{STL} = \frac{\text{STI observed}}{\text{STI predicted}} \times 100 \]

Extrapolation to zero heart rate (STL index) was not used.

Additionally, the variation in msec from the predicted mean systolic interval for normal patients (ΔSTI) was calculated as follows:

\[ \Delta \text{STI} = \text{STI observed} - \text{STI predicted} \]

Preoperative determinations were performed in the resting state 24-48 hr before cardiac catheterization. Postoperative resting values were recorded 1-2 weeks after surgery during the ambulatory stage of each patient’s recovery, when any overt clinical signs of heart failure had disappeared. Patients receiving digitalis preparations preoperatively were maintained on the drug during the postoperative period of observation.

All patients who had correction of left ventricular outflow disorders at Wilford Hall USAF Medical Center from December 1968 to December 1970 were included in the study. Patients having additional cardiac procedures (mitral commissurotomy, other valve replacements) were not included.

Patients were classified as having dominant aortic stenosis (AS) if the calculated aortic valve area was 0.8 cm² or the peak transaortic systolic gradient was greater than 40 mm Hg with 1+ or less AI. Patients with dominant aortic insufficiency had 3 to 4+ AI on aortic root angiography, with a peak transaortic systolic gradient of less than 40 mm Hg. None of the patients included had complete left bundle-branch block (LBBB).

Pressure data at cardiac catheterization were recorded on an Electronics for Medicine photographic recorder using Statham P23Db strain gauge. Maximal LV dp/dt was recorded using the R/C differentiating circuit of an SGM pressure amplifier (Electronics for Medicine). This has a time constant of 1.0 msec and gives an output linearly proportional to input frequency, within 5%, up to the rated maximum frequency of 37 Hz. When care is taken to obtain undamped pressure traces and avoid use of those with excessive upstroke overshoot, it has been shown that maximal LV dp/dt so derived from a conventional catheter reasonably parallels that obtained with a catheter-tip transducer system.6

Cardiac output was determined by the Fick technique. Blood oxygen content was measured in duplicate for the method of Van Slyke and Neill.7 Expired gas was collected in a Tissot spirometer and oxygen content determined with a Beckman E-2 analyzer.

Statistical analyses were performed in accordance with standard formulae8 using a programmed Philco 2000 computer. Comparisons of a group with itself before and after surgery were done using the t-test for paired samples.

Results

Changes in Systolic Time Intervals with Surgery

During this study 28 patients had corrective surgery for left ventricular outflow disorders. Two patients died in the early postoperative period and a third was discharged without follow-up graphics. The remaining 25 had systolic time intervals recorded both before and after surgery.
Table 1

Systolic Time Intervals before and after Aortic Valve Surgery: Direct Measurements in Total Population Studied

<table>
<thead>
<tr>
<th>Group 1A: Aortic stenosis</th>
<th>Group 1B: Aortic insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative</td>
</tr>
<tr>
<td></td>
<td>HR (beats/min)</td>
</tr>
<tr>
<td>Pt.</td>
<td>Sex</td>
</tr>
<tr>
<td>WW</td>
<td>M</td>
</tr>
<tr>
<td>BG</td>
<td>M</td>
</tr>
<tr>
<td>TN</td>
<td>M</td>
</tr>
<tr>
<td>LB</td>
<td>M</td>
</tr>
<tr>
<td>CG</td>
<td>F</td>
</tr>
<tr>
<td>LR</td>
<td>M</td>
</tr>
<tr>
<td>IM</td>
<td>F</td>
</tr>
<tr>
<td>AW</td>
<td>M</td>
</tr>
<tr>
<td>BS</td>
<td>F</td>
</tr>
<tr>
<td>AF</td>
<td>M</td>
</tr>
<tr>
<td>LG</td>
<td>F</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2: Subaortic or aortic stenosis</th>
<th>Repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Er</td>
<td>53</td>
</tr>
<tr>
<td>Lm</td>
<td>23</td>
</tr>
<tr>
<td>Ml</td>
<td>32</td>
</tr>
<tr>
<td>Ml</td>
<td>32</td>
</tr>
<tr>
<td>Db</td>
<td>13</td>
</tr>
<tr>
<td>Rp</td>
<td>10</td>
</tr>
</tbody>
</table>

Abbreviations: M = myectomy; X = excision of subvalvular ring; V = valvuloplasty.

The systolic time intervals of this group are listed in table 1. There were 18 males and seven females with paired studies. Their ages ranged from 10 to 61 years (mean, 41 years).

These patients have been divided into two groups according to their mode of therapy. Group 1A consists of individuals with dominant aortic stenosis, and group 1B is comprised of individuals with dominant aortic insufficiency. Patients in both of these subgroups had their valves replaced by a Starr-Edwards prosthesis.

Group 2 consists of five individuals whose lesions were repaired directly. Patients ER and LM had a myectomy for idiopathic hypertrophic subaortic stenosis and patient MC had a subvalvular fibrous ring excised. DB and RP were the only patients in the study derived from the pediatric age group; they had valvuloplasties for congenital aortic stenosis.
Change in LVET before and after aortic valve surgery. Mean preoperative (black) and postoperative (white) values for groups 1A, 1B, and 2 are plotted on the horizontal axis. The vertical axis shows the deviation from the predicted normal in msec. The vertical lines extending above (or below) the mean indicate the standard error. Abbreviations: AS = aortic stenosis; AI = aortic insufficiency; (S) AS = subaortic and aortic stenosis.

The mean deviations from normal in rate-corrected systolic time intervals for these 25 patients were compared before and after surgery (figs. 1–3). Significant decreases in LVETc occurred in all groups studied. In group 1A, LVETc decreased from 113.8% predicted to 93.6% predicted, a mean change of 58.2 msec (P < 0.001). In group 1B, LVETc decreased from 124.6% predicted to 101.0%, a mean fall of 63.8 msec (P < 0.001). Group 2 showed a mean decrease of 54.4 msec from 119.4% predicted to 101.1% predicted (P < 0.05).

The patients who received a Starr-Edwards prosthesis also showed a significant increase in

Figure 1

Change in QS2c before and after aortic valve surgery. Mean preoperative (black) and postoperative (white) values are shown as in figure 1.

PEPc. In group 1A, PEPc rose from 64.2% predicted to 84.5% predicted, a mean increase of 22.7 msec (P < 0.01). In group 1B, PEPc increased from 46.0% predicted preoperatively to 105.8% predicted postoperatively, a mean increase of 59.5 msec (P < 0.001). In group 2 the mean increase of 26.7 msec from 71.8% predicted to 98.3% predicted was not statistically significant.

In group 1A, Q-S2c decreased significantly from 100.8% predicted to 91% predicted, an average fall of 35.5 msec (P < 0.05). In group

Figure 2

Change in PEP before and after aortic valve surgery. Mean preoperative (black) and postoperative (white) values are shown as in figure 1.

Figure 3

Serial rate-corrected left ventricular ejection times in patient H. B. who underwent two aortic valve replacements, the first on 11/25/64, the second on 7/22/70, for aortic insufficiency. The year is shown on the horizontal axis and the rate-corrected LVET (% predicted) on the vertical axis. AVR = aortic valve replacement; SBE = bacterial endocarditis. See text for details.
SYSTOLIC TIME INTERVALS

Table 2

Preoperative Hemodynamic Data in Patients Undergoing Aortic Valve Surgery

<table>
<thead>
<tr>
<th>Pt.</th>
<th>CI (liters/min/m²)</th>
<th>LV(s/ed) (mm Hg)</th>
<th>A(s/d) (mm Hg)</th>
<th>Adp–LVed (mm Hg)</th>
<th>LV dp/dt (mm Hg/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WW</td>
<td>3.1</td>
<td>205/29</td>
<td>120/75</td>
<td>46</td>
<td>2390</td>
</tr>
<tr>
<td>BG</td>
<td>1.9</td>
<td>200/12</td>
<td>132/80</td>
<td>68</td>
<td>2020</td>
</tr>
<tr>
<td>TN</td>
<td>3.2</td>
<td>235/25</td>
<td>110/66</td>
<td>41</td>
<td>1410</td>
</tr>
<tr>
<td>LB</td>
<td>1.5</td>
<td>140/34</td>
<td>90/70</td>
<td>36</td>
<td>1180</td>
</tr>
<tr>
<td>CG</td>
<td>2.2</td>
<td>165/13</td>
<td>125/50</td>
<td>37</td>
<td>1070</td>
</tr>
<tr>
<td>LR</td>
<td>2.0</td>
<td>227/28</td>
<td>131/58</td>
<td>30</td>
<td>2610</td>
</tr>
<tr>
<td>IM</td>
<td>1.8</td>
<td>240/21</td>
<td>140/65</td>
<td>44</td>
<td>2550</td>
</tr>
<tr>
<td>AW</td>
<td>3.3</td>
<td>210/31</td>
<td>117/81</td>
<td>50</td>
<td>n.d.</td>
</tr>
<tr>
<td>BS</td>
<td>2.4</td>
<td>210/14</td>
<td>110/70</td>
<td>56</td>
<td>1530</td>
</tr>
<tr>
<td>AF</td>
<td>2.9</td>
<td>240/23</td>
<td>160/90</td>
<td>67</td>
<td>2540</td>
</tr>
<tr>
<td>LG</td>
<td>2.5</td>
<td>170/8</td>
<td>128/65</td>
<td>57</td>
<td>2600</td>
</tr>
</tbody>
</table>

Group 1A: Aortic stenosis

Group 1B: Aortic insufficiency

Group 2: Subaortic or aortic stenosis

Abbreviations: CI = cardiac index; LV (s/ed) = peak left ventricular systolic and end-diastolic pressures; A (s/d) = aortic systolic and diastolic pressures; Adp–LVed = transaortic end-diastolic pressure difference; LV dp/dt = maximal rate of left ventricular pressure rise; n.d. = not determined.

1B, Q-S₂ₑ was 103.6% predicted before surgery and 102.3% predicted after surgery. The mean decrease of 4.3 msec was not significant. Group 2 had a mean Q-S₂ₑ of 106.9% predicted preoperatively and this decreased to 99.8% predicted postoperatively. The mean decrease of 27.7 msec was not statistically significant for this group of five patients.

The course of one patient (HB) whose left ventricular ejection time was recorded on multiple occasions in relation to two aortic valve replacements is illustrated in figure 4. His LVETₑ was 159% expected in 1965 when he underwent initial valve replacement for severe aortic insufficiency secondary to bacterial endocarditis. His LVETₑ fell to 40% postoperatively, but gradually increased as he developed a mild perivalvular leak. In October 1969, Streptococcus viridans endocarditis occurred on the prosthetic valve. Despite bacteriologic cure he became fatigued and stopped working. Concomitantly, his LVETₑ increased from 115% to 137%. Severe aortic regurgitation was again documented angiographically and his loose prosthesis was replaced. Subsequently, his LVETₑ again fell to normal. He is currently asymptomatic and has returned to work.

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Hemodynamic Correlations with Preoperative Systolic Time Intervals

The flow and pressure data obtained in these patients during their preoperative cardiac catheterization are listed in table 2. The patients in group IA (dominant AS) had lower cardiac indices and higher peak left ventricular pressures than those in group IB (dominant AI). In group IA, maximal LV dp/dt varied from 1,070 to 2,610 mm Hg/sec. Group IB patients had higher left ventricular end-diastolic pressures, lower aortic diastolic pressures, and their peak LV dp/dt showed less variation, ranging from 1,120 to 1,750 mm Hg/sec. It is noteworthy that the transaortic end-diastolic pressure difference (aortic diastolic – LV end-diastolic) showed no overlap between the AS and AI subgroups (≥30 mm Hg in AS, mean 51; <30 mm Hg in AI, mean 18).

The relation of LVETc and PEPc to flow and pressure data is illustrated in figures 5 and 6, respectively. Additionally, correlations of LVETc and of PEPc with these parameters are shown in table 3. Correlations of identical statistical significance were obtained if the alternative rate corrections, ΔLVET and ΔPEP, were used.

Variations in LVETc had a significant positive correlation with cardiac index in group IA (r = +0.90, P < 0.01) but not in group IB. Similarly, stroke index had a significant correlation with LVETc in the AS subgroup (group 1A) only. A significant
inverse correlation between PEP<sub>e</sub> and these parameters of flow was not obtained.

PEP<sub>e</sub> showed a highly significant correlation with maximal LV dp/dt in group IA (r = -0.79, P < 0.01). This correlation was not improved by further manipulations with aortic or left ventricular pressures or by inclusion of the mean aortic gradient in the formulation. In group IB, PEP<sub>e</sub> correlated poorly with any single hemodynamic parameter. The correlation improved when the transaortic end-diastolic pressure difference (Adbp - LVed) (r = 0.51) was considered, but became statistically significant for this group only when these values were divided by their respective LV dp/dt (r = 0.76, P < 0.05). The correlation of (Adbp-LVed)/dp/dt with PEP<sub>e</sub> (fig. 6) remained highly significant when all groups were considered (r = 0.70, P < 0.01).

Discussion

A prolonged left ventricular ejection time has previously been noted in severe aortic stenosis and insufficiency. These observations are extended herein. We have documented a short preejection period with these lesions and a normalization of both these systolic intervals after successful operative intervention. The decrease in LVET was striking, being in excess of 50 msec in all groups studied. In a serial study of carotid pulse traces before and after insertion of fascia lata valves a similar decrease in LVET was noted in the first postoperative month in aortic stenosis and insufficiency. Similarly, Benchimol and Matsuo have recently reported decreases in ejection time after aortic valve replacement with a Starr-Edwards prosthesis.

A question may be raised as to whether the inertia of the prosthesis poppet significantly influences STI. Since the postoperative changes in STI in group 2 patients who received no prosthesis are identical in direction and comparable in magnitude to those in patients who did receive prostheses, one must conclude that the prosthesis has no major effect on the results. Laboratory studies using pulse duplicator systems indicate that Starr-Edwards valves have an opening delay of the order of 10 msec and a closing delay of about 25 msec. Assuming no delay for a normal aortic valve (not necessarily the case for a diseased valve) this effect would lengthen LVET approximately 15 msec and PEP 10 msec. Thus, theoretically, decreases in LVET after insertion of a Starr-Edwards prosthesis may tend to underestimate the results of surgery by this small amount. Conversely, increases in PEP may overestimate the operative result.

Of note is the decrease in LVET<sub>e</sub> in group 1A to 93.6% predicted. The drop in LVET in the remaining groups did not fall below the predicted mean postoperatively. This may reflect a difference in response of the left
ventricle in patients with dominant AS and those with dominant AI to insertion of prosthetic valves. It is difficult to glean information bearing on this observation from reports of hemodynamic studies done early following aortic valve replacement. Cardiac index and pressure data are usually normal 48–72 hr after successful insertion of a Starr-Edwards prosthesis, regardless of whether the preexisting dominant lesion is AS or AI. However, left ventricular ejection times were not reported in these studies. It may be speculated that in AS, with prominent ventricular hypertrophy, marked diminution of afterload is followed by high ejection rates and a short LVET for some time postoperatively. The alternative explanation invoking heart failure as a cause of the short postoperative LVET in AS is not supported by the short postoperative PEP in this group. Long-term evaluation of systolic time intervals in relation to clinical and hemodynamic findings, currently in progress in these patients, may help to elucidate this further.

Weissler et al. have previously indicated that the duration of left ventricular ejection in normal men and in patients with congestive heart failure correlates with cardiac output and stroke index. Using a direct flow measuring technique, Greenfield, Harley, and coworkers emphasized that LVET was primarily flow dependent. The correlation of rate-corrected LVET and the cardiac and stroke indices in aortic stenosis in this study verifies that this interpretation can be extended to cases with predominant obstruction of left ventricular outflow. In aortic insufficiency, the correlation of the duration of left ventricular ejection and output measured by the Fick technique is poor. Since it is likely that LVET reflects total transaortic flow, while the Fick output measures only net forward flow irrespective of the degree of regurgitation, this finding is not surprising.

PEP increased postoperatively in all groups. This rise was highly significant in groups 1A and 1B. This response, however, showed more individual variability than changes in LVET (table 1). Out of 25 patients, 24 showed a postoperative decrease in LVET, (patient LB was the exception). PEP is considerably less rate dependent than LVET, and direct inspection of table 1 shows several exceptions to the trend of increase in PEP in groups 1A and 2, but no exceptions in group 1B.

Metzger et al. have shown that in normal animals the duration of the preejection period correlates inversely with maximal LV dp/dt. Our results indicate a similar significant inverse correlation in dominant aortic stenosis in man (table 3, group 1A; \( r = -0.79, P < 0.01 \)). Variations in aortic diastolic pressure are a known determinant of the preejection period, and the correlation of the preejection period in dominant aortic insufficiency with maximal LV dp/dt is poor for at least this reason. Table 3 indicates that, when the lesion is dominant aortic insufficiency, left ventricular end-diastolic pressure becomes an additional important determinant of the duration of preejection. Thus, the correlation of PEP with either left ventricular end-diastolic or aortic diastolic pressures is poor (table 3), but there is an improved positive correlation when the transaortic end-diastolic pressure difference (Adbp – LVEDp) is considered. A significant correlation, however, was achieved only when this pressure difference was divided by the maximal left ventricular dp/dt. Since aortic diastolic pressure and left ventricular end-diastolic pressure showed little variation in the patients with dominant outflow obstruction, the expression \( \frac{Adbp - LVEDp}{dp/dt} \) correlated with the duration of PEP in left ventricular outflow disease whether the dominant lesion was stenosis or insufficiency.

The correction of aortic regurgitation with restoration of normal aortic diastolic blood pressures and presumably improved left ventricular end-diastolic pressure is an extremely likely explanation for the universal improvement and restoration of a normal preejection period (group 1B). Relief of afterload, an establishing potentiating factor in maximal LV dp/dt may be invoked to explain the improvement in PEP in those patients with
dominant obstructive lesions. The fact that this normalization was not complete may indicate that elevated peak LV dp/dt does not resolve fully immediately after relief of chronic obstruction.

The data herein establish a pattern of response in systolic time intervals seen in patients undergoing initially successful aortic valve surgery and indicate the hemodynamic parameters these systolic intervals most likely reflect. The potential usefulness of this technique in the long-term management of patients with aortic valve replacements is suggested by the serial changes in LVETc in figure 4. Study is currently in progress evaluating systolic time intervals in the assessment of prosthetic valve dysfunction and quantitation of perivalvular leaks.

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References

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