Systolic Time Intervals in Atrial Fibrillation*

Harisios Boudoulas, M.D.;** Richard P. Lewis, M.D.;†
Joel A. Sherman, M.D.;‡ Charles A. Bush, M.D.;§
George Dalamangas, M.D.;† and Wilbur F. Forester, P.E.‖

Forty patients with atrial fibrillation and 20 patients with congestive heart failure and sinus rhythm were studied. Patients were divided into two groups. Group A consisted of 20 patients with atrial fibrillation in whom systolic time intervals were measured. Twenty to 50 beats were analyzed. Five of the patients had high-fidelity measurements of left ventricular pressure simultaneous with determination of systolic time intervals. Analysis of the systolic time intervals for the entire group showed that the preejection period lengthened at faster heart rates and that the left ventricular ejection time was relatively constant at slower heart rates. This resulted in a progressive increase in the ratio of preejection period over left ventricular ejection time (PEP/LVET) as the heart rate increased. The rate of increase in PEP/LVET was minimal below a heart rate of 75 beats per minute. The increase in preejection period at faster heart rates is due to greater isovolumic developed pressure without a corresponding increase in left ventricular dp/dt. Group B consisted of 40 additional patients (20 with atrial fibrillation and 20 with sinus rhythm). In group B, the total electromechanical systole corrected for heart rate (QS, I) and the levels of digoxin in the blood were compared. The QS, I was significantly shorter in atrial fibrillation (497 ± 5 msec vs 528 ± 4 msec; P < 0.01), while the levels of digoxin in the blood were identical (0.9 ± 0.1 vs 1.0 ± 0.1 ng/ml). The results of this study must be considered when systolic time intervals are to be employed in patients with atrial fibrillation.

Systolic time intervals have achieved popularity as a noninvasive technique for the evaluation of left ventricular performance.14 In subjects with sinus rhythm, it is customary to calculate systolic time intervals by averaging ten or more successive beats.14 The same technique has been used when atrial fibrillation is present, except more beats are analyzed; however, there is wide beat-to-beat variation of the systolic intervals in atrial fibrillation.5-8 This can produce significant variability in the mean systolic interval, depending upon the nature of the beats analyzed. It is the purpose of this study to analyze the beat-to-beat variation of the systolic time intervals in atrial fibrillation and to determine the best method of analysis in the presence of this common arrhythmia.

Materials and Methods

Forty patients with atrial fibrillation and 20 patients with congestive heart failure and sinus rhythm were studied. The patients were divided into two groups.

In group A, the selection of 20 patients with atrial fibrillation was based upon the presence of a wide variation in beat-to-beat R-R intervals. Clinical information for the 20 patients is given in Table 1. Two of the patients had a history of congestive heart failure, but none had clinical evidence of failure at the time of the study. No attempts were made to standardize the medications that were receiving. Nine patients also had determinations of systolic time intervals available in sinus rhythm. Six underwent cardioversion, and in one patient, cardioversion was accomplished by administration of quinidine. The other two developed atrial fibrillation during cardiac catheterization. The systolic time intervals were recorded within 24 hours prior to and again within 24 hours after the change in rhythm. Five of the patients also underwent diagnostic catheterization.

Left ventricular pressure was recorded via a catheter with a high-fidelity manometer at the tip (Allard-Laurens) simultaneously with brachial arterial pressure recorded through a fluid-filled catheter, with both catheters connected to a pressure transducer (Statham P23Db). The high-fidelity left ventricular pressure pulse was then matched with the conventional pressure pulse recorded through the side hole of the micromanometer-catheter. The first derivative of left ventricular pressure was obtained through an RC differentiating circuit, previously calibrated to give the rate of the rise in pressure (or dp/dt).10 Recordings were made at a speed of 100 mm/sec using a photographic recorder (Sanborn 550). Left ventricular isovolumic developed pressure was determined by subtracting end-diastolic pressure from aortic pressure at valvular opening.11 Left ventricular end-diastolic pressure was measured using the micromanometer-catheter. Systolic time intervals were measured simultaneously with left ventricular and arterial pressures.

Systolic time intervals were measured as previously described.14 The preejection period, left ventricular ejection time, total electromechanical systole (QS, I), and the ratio of

Material and Methods

Forty patients with atrial fibrillation and 20 patients with congestive heart failure and sinus rhythm were studied. The patients were divided into two groups.

In group A, the selection of 20 patients with atrial fibrillation was based upon the presence of a wide variation in beat-to-beat R-R intervals. Clinical information for the 20 patients is given in Table 1. Two of the patients had a history of congestive heart failure, but none had clinical evidence of failure at the time of the study. No attempts were made to standardize the medications that were receiving. Nine patients also had determinations of systolic time intervals available in sinus rhythm. Six underwent cardioversion, and in one patient, cardioversion was accomplished by administration of quinidine. The other two developed atrial fibrillation during cardiac catheterization. The systolic time intervals were recorded within 24 hours prior to and again within 24 hours after the change in rhythm. Five of the patients also underwent diagnostic catheterization.

Left ventricular pressure was recorded via a catheter with a high-fidelity manometer at the tip (Allard-Laurens) simultaneously with brachial arterial pressure recorded through a fluid-filled catheter, with both catheters connected to a pressure transducer (Statham P23Db). The high-fidelity left ventricular pressure pulse was then matched with the conventional pressure pulse recorded through the side hole of the micromanometer-catheter. The first derivative of left ventricular pressure was obtained through an RC differentiating circuit, previously calibrated to give the rate of the rise in pressure (or dp/dt).10 Recordings were made at a speed of 100 mm/sec using a photographic recorder (Sanborn 550). Left ventricular isovolumic developed pressure was determined by subtracting end-diastolic pressure from aortic pressure at valvular opening.11 Left ventricular end-diastolic pressure was measured using the micromanometer-catheter. Systolic time intervals were measured simultaneously with left ventricular and arterial pressures.

Systolic time intervals were measured as previously described.14 The preejection period, left ventricular ejection time, total electromechanical systole (QS, I), and the ratio of

Material and Methods

Forty patients with atrial fibrillation and 20 patients with congestive heart failure and sinus rhythm were studied. The patients were divided into two groups.

In group A, the selection of 20 patients with atrial fibrillation was based upon the presence of a wide variation in beat-to-beat R-R intervals. Clinical information for the 20 patients is given in Table 1. Two of the patients had a history of congestive heart failure, but none had clinical evidence of failure at the time of the study. No attempts were made to standardize the medications that were receiving. Nine patients also had determinations of systolic time intervals available in sinus rhythm. Six underwent cardioversion, and in one patient, cardioversion was accomplished by administration of quinidine. The other two developed atrial fibrillation during cardiac catheterization. The systolic time intervals were recorded within 24 hours prior to and again within 24 hours after the change in rhythm. Five of the patients also underwent diagnostic catheterization.

Left ventricular pressure was recorded via a catheter with a high-fidelity manometer at the tip (Allard-Laurens) simultaneously with brachial arterial pressure recorded through a fluid-filled catheter, with both catheters connected to a pressure transducer (Statham P23Db). The high-fidelity left ventricular pressure pulse was then matched with the conventional pressure pulse recorded through the side hole of the micromanometer-catheter. The first derivative of left ventricular pressure was obtained through an RC differentiating circuit, previously calibrated to give the rate of the rise in pressure (or dp/dt).10 Recordings were made at a speed of 100 mm/sec using a photographic recorder (Sanborn 550). Left ventricular isovolumic developed pressure was determined by subtracting end-diastolic pressure from aortic pressure at valvular opening.11 Left ventricular end-diastolic pressure was measured using the micromanometer-catheter. Systolic time intervals were measured simultaneously with left ventricular and arterial pressures.

Systolic time intervals were measured as previously described.14 The preejection period, left ventricular ejection time, total electromechanical systole (QS, I), and the ratio of
Table 1—Clinical Data from 20 Patients with Atrial Fibrillation (Group A)

<table>
<thead>
<tr>
<th>Patient, Sex, Age (yr)</th>
<th>Diagnosis</th>
<th>Medications</th>
<th>Mean Heart Rate per minute (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, M, 25</td>
<td>Idiopathic atrial fibrillation</td>
<td>Digoxin</td>
<td>105 (61-160)</td>
</tr>
<tr>
<td>2, M, 19</td>
<td>Idiopathic atrial fibrillation</td>
<td>Digoxin</td>
<td>84 (48-122)</td>
</tr>
<tr>
<td>3, M, 40</td>
<td>Rheumatic heart disease; replacement of aortic and mitral valves</td>
<td>Digoxin; quinidine</td>
<td>97 (81-119)</td>
</tr>
<tr>
<td>4, M, 65</td>
<td>Rheumatic heart disease; mitral valvular replacement</td>
<td>Digoxin</td>
<td>91 (49-126)</td>
</tr>
<tr>
<td>5, F, 56</td>
<td>Aortic stenosis and regurgitation; congestive heart failure</td>
<td>Digoxin; triamterene + hydrochlorothiazide (Dyazide)</td>
<td>89 (65-111)</td>
</tr>
<tr>
<td>6, M, 51</td>
<td>Aortic stenosis and regurgitation</td>
<td>Digoxin</td>
<td>79 (49-100)</td>
</tr>
<tr>
<td>7, M, 45</td>
<td>Mitral regurgitation</td>
<td>Digoxin; quinidine</td>
<td>85 (67-119)</td>
</tr>
<tr>
<td>8, M, 47</td>
<td>Atherosclerotic heart disease</td>
<td>Digoxin</td>
<td>95 (71-141)</td>
</tr>
<tr>
<td>9, F, 60</td>
<td>Mitral regurgitation</td>
<td>Digoxin</td>
<td>95 (68-128)</td>
</tr>
<tr>
<td>10, F, 51</td>
<td>Aortic regurgitation and stenosis</td>
<td>Digoxin</td>
<td>82 (51-132)</td>
</tr>
<tr>
<td>11, M, 48</td>
<td>Rheumatic heart disease; mitral regurgitation; aortic valvular replacement</td>
<td>Digoxin; quinidine</td>
<td>56 (40-117)</td>
</tr>
<tr>
<td>12, M, 55</td>
<td>Atherosclerotic heart disease; mitral regurgitation</td>
<td>Digoxin; furosemide (Lasix)</td>
<td>74 (48-103)</td>
</tr>
<tr>
<td>13, F, 60</td>
<td>Atherosclerotic heart disease; mitral regurgitation</td>
<td>Digoxin</td>
<td>83 (51-121)</td>
</tr>
<tr>
<td>14, F, 74</td>
<td>Atherosclerotic heart disease</td>
<td>Digoxin</td>
<td>103 (67-176)</td>
</tr>
<tr>
<td>15, F, 40</td>
<td>Idiopathic hypertrophic subaortic stenosis; mitral regurgitation</td>
<td>Quinidine</td>
<td>72 (42-146)</td>
</tr>
<tr>
<td>16, F, 56</td>
<td>Pericardial disease</td>
<td>Digoxin</td>
<td>73 (44-115)</td>
</tr>
<tr>
<td>17, F, 71</td>
<td>Mitral regurgitation; congestive heart failure</td>
<td>Digoxin; quinidine; diuretics</td>
<td>87 (60-137)</td>
</tr>
<tr>
<td>18, F, 43</td>
<td>Atherosclerotic heart disease</td>
<td>Digoxin</td>
<td>68 (42-167)</td>
</tr>
<tr>
<td>19, M, 75</td>
<td>Atherosclerotic heart disease</td>
<td>Digoxin</td>
<td>62 (40-145)</td>
</tr>
<tr>
<td>20, M, 22</td>
<td>Rheumatic heart disease; mitral valvular replacement</td>
<td>Digoxin; quinidine</td>
<td>60 (43-92)</td>
</tr>
</tbody>
</table>

The pre-ejection period over left ventricular ejection time (PEP/LVET) were calculated for each beat. As many beats as possible were analyzed in each patient; and the number ranged from 19 to 52 beats (average, 33 beats). For purposes of this analysis, the preceding R-R interval was used to calculate the heart rate for each individual beat. We analyzed the data using the heart rate calculated from the preceding R-R interval, instead of the R-R intervals, in order to make the relationship between heart rate and the various systolic time intervals comparable to studies in sinus rhythm.

In group B, 20 additional patients with atrial fibrillation were matched for age and functional class (New York Heart Association) with 20 patients who were in sinus rhythm. None of them had valvular heart disease, and all were receiving long-term treatment with digoxin. In these 40 patients, systolic time intervals and the levels of digoxin in the blood were measured on the same day. The level of digoxin in the blood was determined at least eight hours after the last dose.

Statistical analyses were performed using regression analysis, analysis of variance, and Student’s t-test with the aid of a computer (Hewlett-Packard 9000B).

RESULTS

Group A

Analysis of various systolic time intervals for the entire group showed that the pre-ejection period lengthened at faster heart rates, instead of the shortening that is expected in sinus rhythm. The left ventricular ejection time was relatively constant at slower rates, in contrast to sinus rhythm. This resulted in a progressive increase in the PEP/LVET as the heart rate increased (Fig 1). The PEP/LVET dramatically increased above a heart rate of 75 beats per minute.

The data from the five patients who underwent left cardiac catheterization were used to help determine the physiologic basis for the unusual changes in the systolic time intervals with increasing heart rate. Figure 2 shows the relationship of the various systolic time intervals to heart rate in these patients. The diagonal lines represent the 95 percent confidence limits of the normal regression equations for QS2, left ventricular ejection time, and pre-ejection period.12 Data are presented separately for individual patients, and the various systolic time intervals are plotted against the calculated heart rate for each individual beat. (Similar plots [not shown] were made for the remaining 15 patients, which indicated that the five subjects who underwent catheterization were representative of the entire group.)

In all instances the pre-ejection period increased with the heart rate. Linear correlation coefficients ranged from 0.86 to 0.90 (P < 0.01). The left ventricular ejection time and the Q5 showed relatively constant at rates of less than 75 beats per minute; however, good relationships were found between the left ventricular ejection time and the heart rate (r ranging from 0.70 to 0.91; P < 0.01) and between the Q5 and heart rate (r ranging from 0.60 to...
0.87; P < 0.01) at rates faster than 75 beats per minute.

Figure 3 shows the relationship between heart rate and left ventricular isovolumic developed pressure. The correlation coefficients ranged from 0.83 to 0.97 (P < 0.01). Thus, the isovolumic developed pressure varies directly with heart rate in atrial fibrillation.

Figure 4 shows the relationship between the pre-ejection period and the left ventricular isovolumic developed pressure. The correlation coefficients ranged from 0.77 to 0.89 (P < 0.01). Thus, the duration of the pre-ejection period varies directly with the pressure developed during the isovolumic systole.

The maximal left ventricular dp/dt (not shown) was constant in four of the five patients at heart rates ranging from 40 to 160 beats per minute. In

---

**Figure 1.** In patients with atrial fibrillation, PEP/LVET increases as heart rate increases but is relatively constant at heart rates under 75 beats per minute. Beats were grouped by decades of heart rate, and number of beats analyzed for each decade is indicated.

**Figure 2.** Relationship between various systolic time intervals and heart rate in five patients with atrial fibrillation who underwent catheterization. Diagonal lines represent 95 percent confidence limits of normal regression equation for QS, left ventricular ejection time (LVET), and pre-ejection period (PEP).
one patient, there was a slight decrease at faster heart rates.

The left ventricular end-diastolic pressure was greater at slower heart rates and decreased as the heart rate increased. Thus, the mean left ventricular end-diastolic pressure was 18 ± 1 mm Hg when only beats with an R-R interval greater than 800 msec were included, was 12 ± 1 mm Hg when beats with an R-R interval of 500 to 800 msec were included (P < 0.05), and was 7 ± 1 mm Hg when beats with an R-R interval less than 500 msec were included (P < 0.05).

In the nine patients in whom determinations of systolic time intervals were available in both sinus rhythm and atrial fibrillation, the PEP/LVET obtained by averaging only beats with a heart rate of 75 beats per minute or less (0.35 ± 0.02) was identical to that in sinus rhythm (0.37 ± 0.02). This is in contrast to the PEP/LVET of 0.46 ± 0.03 (P < 0.01) that was obtained when all beats in atrial fibrillation were averaged.

Group B

The QS2 corrected for heart rate (QS2I) in the group with atrial fibrillation was significantly shorter than in the patients with sinus rhythm (497 ± 5 msec vs 528 ± 4 msec; P < 0.01). Only beats with a heart rate of less than 75 beats per minute were analyzed in the patients with atrial fibrillation. The levels of digoxin in the blood were identical in both groups (0.9 ± 0.1 vs 1.0 ± 0.1 ng/ml).

DISCUSSION

This study has demonstrated that the systolic time intervals in atrial fibrillation behave differently with respect to heart rate than is the case in sinus rhythm.1-4 The pre-ejection period increases at faster heart rates, instead of shortening. The left ventricular ejection time shortens at heart rates greater than 75 beats per minute, but it is relatively constant under a heart rate of 75 beats per minute. The SQ2, which is the summation of the pre-ejection period and the left ventricular ejection time, was relatively constant at heart rates less than 75 beats per minute and was shortened less than normal with increasing heart rates. The PEP/LVET significantly lengthens at faster heart rates. This is in contrast to the normal subjects in whom the PEP/LVET is independent of
the size of the heart.14

It should be emphasized that an isolated beat of a heart rate of 120 beats per minute in atrial fibrillation is not necessarily comparable to a sinus beat of the same rate. In the case of the latter, there is presumably a steady state; and circulatory adjustments in the preload, afterload, and inotropic state for the fast rate have occurred. This is not true in the case of a single beat at a fast rate in atrial fibrillation. Thus, these two beats cannot be directly compared.

On the basis of our data, we propose the following explanation for the different behavior in preejection periods with faster heart rates in atrial fibrillation. At a faster heart rate, diastole is shorter. Central aortic pressure has less time to fall and is higher at the time of opening of the aortic valve. There is less time for diastolic filling and, hence, a lower left ventricular end-diastolic pressure. Thus, the isovolumic developed pressure increases as the heart rate increases (Fig 3). Finally, the left ventricular maximal dp/dt remains relatively constant, in spite of variations in heart rate and increases in afterload. Therefore, at higher heart rates the left ventricle must develop a greater isovolumic pressure at a constant rate of development of pressure. This results in a prolongation of the preejection period. Although the mechanism of the relatively constant maximal dp/dt is not clear, it may be the net result of opposing changes in preload and contractility at varying R-R intervals.

The prolongation of the preejection period was entirely related to isovolumic time and not to electromechanical delay.8

The left ventricular ejection time in atrial fibrillation also does not behave as in sinus rhythm. Below a heart rate of 75 beats per minute, there is no progressive lengthening of the ejection time. This most likely occurs because the fibrillating left atrium is unable to produce a further significant increase in ventricular filling after the rapid filling phase.13-16 Therefore, stroke volume becomes relatively fixed at slower rates in atrial fibrillation. Whether the same phenomenon would occur in normal subjects in whom left ventricular diastolic compliance might be greater is not known. Of interest is the observation that in patients with mitral stenosis and atrial fibrillation, the left ventricular ejection time does not reach a plateau at slower heart rates,5,17 presumably due to obstruction in the rapid filling phase.

Regardless of the underlying valvular heart disease or the status of left ventricular function (or both), the changes observed in the systolic time intervals with changes in heart rate were similar. It should be noted that identical changes were observed in patients with idiopathic atrial fibrillation and no other obvious heart disease. Thus, the variations in heart rate (and not the nature of the underlying heart disease) appear to be the basis for the response of the systolic time intervals in atrial fibril-
We conclude that if the systolic time intervals (or, for that matter, any measure) are to be employed to estimate left ventricular performance in patients with atrial fibrillation, the effect of heart rate must be considered. Inclusion of beats with heart rates above 75 beats per minute will result in a mean PEP/LVET that is higher than would be obtained if the subjects were in sinus rhythm. Thus, it is desirable to slow the heart rate before determining systolic time intervals and then to exclude all beats with a heart rate above 75 beats per minute. Failure to recognize this phenomenon may lead to the erroneous conclusion that greater left ventricular dysfunction is present than is actually the case.

Finally, it should be noted that calculation of the systolic time intervals by employing only beats of a heart rate less than 75 beats per minute will shorten the QS I. This is largely due to the flat left ventricular ejection time below a heart rate of 75 beats per minute, but the preejection period also slightly decreases at slower rates. Thus, the QS I employing only beats of a heart rate less than 75 beats per minute was significantly shorter in patients with atrial fibrillation, compared to 20 patients with sinus rhythm, in spite of the fact that the serum levels of digoxin were identical for the two groups. This must be considered when the QS I is used to judge excessive inotropic stimulation in patients with atrial fibrillation.\textsuperscript{4,18-22}

ACKNOWLEDGMENT: We thank Arnold Weissler, M.D., for his critique of this manuscript and also Mrs. Janice Whitmire for typing the manuscript.

REFERENCES


834 BODDOULAS ET AL

CHEST, 74: 6, DECEMBER, 1978