Clin. Cardiol. 9, 545-549 (1986)

Relationship Between Systolic Time Intervals and Arterial Blood Pressure

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Summary: It has been suggested that systolic time intervals (STI) can be used to monitor the cardiac effects of antihypertensive treatments and also to evaluate hypertensive patients. STI changes observed in hypertensives have been ascribed to myocardial disease, although they could be due to the existence of a relationship between STI and blood pressure. A group of 37 subjects (18 normotensives and 19 hypertensives) with no signs of heart failure and left ventricular dysfunction were studied to examine the relationship of STI to blood pressure. Pacing with an external battery pulse generator was performed at the rate of 95 beats/min in order to eliminate differences in heart rate. STI were measured from good quality high speed (100 mm/s) recordings and the average value of 10 consecutive cardiac cycles was used for statistical analysis. Normal subjects showed significantly lower values of pre-ejection period (PEP), electromechanical systole (QS_2), and pre-ejection period/left ventricular ejection time ratio (PEP/LVET). Moreover, a significant inverse relationship between diastolic pressure and LVET and significant direct relationships between diastolic pressure and PEP, systolic pressure and PEP, diastolic pressure and PEP/LVET, and between systolic pressure and PEP/LVET were demonstrated. We suggest to consider the relation of STI to blood pressure to provide regression equations to best appreciate and use STI.

Key words: systolic time intervals, hypertension, diastolic pressure, systolic pressure

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Received: January 29, 1986
Accepted: March 21, 1986

Introduction

The analysis of systolic time intervals (STI) is a simple, inexpensive, noninvasive, and reliable technique to assess cardiac function (Lewis, 1975; Lewis *et al.*, 1977; Weissler *et al.*, 1972). At present, though echocardiography is preferred in evaluating left ventricular function, STI are still subjects of papers in well-known international journals (Buch and Rasmussen, 1983; Kyle and Freis, 1985; Mitake *et al.*, 1984; Randazzo *et al.*, 1983; Ulmer *et al.*, 1982; Vanhees *et al.*, 1984; Waldorff *et al.*, 1982). STI are also applied clinically to provide quantitative estimates of the effect of coronary artery disease on the left ventricle (Randazzo *et al.*, 1983; Vanhees *et al.*, 1984), to evaluate hypertensive patients (Alves Da Silva *et al.*, 1981; Heymsfield *et al.*, 1975; Radice *et al.*, 1976), and to monitor antihypertensive therapy (Buch and Rasmussen, 1983; Dodek *et al.*, 1975; Kyle and Freiss, 1985). Since blood pressure (BP) may affect STI, changes in their values due to variations of BP may erroneously be ascribed to left ventricular disease (Armstrong *et al.*, 1973; Harris, 1974; Spodick *et al.*, 1972; Tarazi *et al.*, 1969). Therefore, we should improve our knowledge of the relationship existing between STI and BP in order to provide them with higher sensitivity.

It has been appreciated that STI vary inversely with the heart rate, and the simple linear regression equation of Weissler represents a widely used method of properly interpreting their variations related to differences in resting heart rate (Lewis *et al.*, 1977; Weissler *et al.*, 1972).

This study has been designed to examine the relationship of STI to BP. In fact, if it is true that hypertensive subjects with no evidence of ventricular failure and/or coronary artery disease show significantly different STI in comparison with healthy subjects, a correction must be made for variations related to differences in BP.

Materials and Methods

The study population consisted of 18 normotensives (4 females and 14 males, mean age 55 $\pm$ 11) and 19 patients with essential hypertension (11 females and 8 males, mean age 47 $\pm$ 10). The diagnosis of essential hypertension was

made when serum electrolytes, urinary catecholamines, renal function, and pyelography were within normal limits and BP was above 140/90 mmHg as the average of the last 3 measurements. Subjects were included in the study if the following criteria were met: (1) no clinical or radiological (chest x-ray) signs of heart failure; (2) normal left ventricular internal dimensions and contractility pattern; (3) peak velocity of circumferential fiber shortening (VCF), evaluated by M-mode echocardiography, within the normal range of our laboratory (1.8 ± 0.4 circ/s); (4) no conduction disturbances; (5) no clinical or instrumental (stress test) signs of coronary artery disease. Hypertensive subjects with left ventricular hypertrophy were admitted to the study. In fact, cardiac contractility does not seem to be affected by hypertrophy (Suga *et al.*, 1984). Each subject was informed of the purpose of this research and gave written consent before participating in the experiment. They did not take any drug for 10 days before the test. The procedure, always performed between 9 a.m. and 12 noon, consisted of positioning a bipolar pacing electrode catheter in the right atrium through an arm vein. Pacing with an external battery-powered pulse generator (Siemens-Elema 146F) was performed at the rate of 95 beats/min. During pacing, humeral blood pressure was measured by sphygmomanometer and simultaneous high speed recordings (100 mm/s) of the electrocardiographic lead best displaying the onset of left ventricular depolorization (usually DII), a carotid pulse tracing, and a phoncardiogram best displaying the initial high frequency vibrations of the aortic closure sound, were obtained (Polygraph Mingograf 34, Siemens-Elema).

Electromechanical systole (QS_2) was measured from the beginning of the depolorization in the electrocardiographic lead chosen to the first high frequency vibrations of the aortic component of the heart sound. Left ventricular ejection time (LVET) was measured from the beginning of the upstroke of the carotid tracing through to the incisura. Pre-ejection period (PEP) was calculated by subtraction of LVET from QS_2. Pre-ejection period/left ventricular ejection time ratio (PEP/LVET) was calculated too. The values for STI to be used in the statistical analysis were calculated, for each recording, by averaging 10 consecutive cardiac cycles.

Simple linear regression by the least-squares method was used to assess the possible existence of statistically significant relationships between both systolic and diastolic pressure and STI. The *t*-test for unpaired data was used for statistical analysis with a probability value of less than 0.05 considered statistically significant.

Results

PEP, LVET, QS_2, and PEP/LVET values are presented in detail in Table I. Table II shows the results of statistical analysis by unpaired *t*-test. It can be seen that normal subjects have significantly lower values of PEP ($p<0.001$), QS_2 ($p<0.025$), and PEP/LVET ($p<0.001$). On the contrary, no statistically significant difference was demonstrated in LVET between the two groups. In order to have a wider rage of BP values, we pooled both normotensives and hypertensives, thus obtaining a single group of 37 subjects. Table III includes all possible statistical data obtained by simple linear regression equation performed on pooled data. We demonstrated the existence of a significant direct relationship between diastolic pressure and PEP($r=.754$, $p<0.001$), systolic pressure and PEP ($r=.686$, $p<0.001$), diastolic pressure and PEP/LVET ($r=.756$, $p<0.001$), and between systolic pressure and PEP/LVET ($r=.659$, $p<0.001$). A statistically significant inverse relationship was demonstrated between diastolic pressure and LVET ($r=.502$, $p<0.01$).

In the following section, we will discuss the relationships between diastolic pressure and PEP and between diastolic pressure and PEP/LVET. In fact, these show the highest correlation coefficients (Table III). Figures 1 and 2 illustrate the linear relationship existing between diastolic pressure and PEP and PEP/LVET, respectively.

Discussion

Numerous studies have demonstrated that STI show variations related to both acute and chronic changes in BP (Dodek *et al.*, 1975; Heymsfield *et al.*, 1975; Radice *et al.*, 1976; Tarazi *et al.*, 1969). We pointed out that PEP is longer in a group of hypertensives with normal left ventricular function, assessed by peak VCF, than in a group of normotensives. Furthermore, we showed the existence of a highly significant direct relationship between diastolic pressure and PEP and PEP/LVET.

Our results agree with those of Dodek *et al.* (1975) and Tarazi *et al.* (1969) who found higher PEP values in hypertensive patients and also with findings of Heymsfield *et al.* (1975) who demonstrated that PEP and PEP/LVET correlate well with diastolic pressure. Tarazi *et al.* (1975) ascribed the prolonged PEP to myocardial disease found in patients with arterial hypertension. Prolongation of PEP is commonly used for identification of left ventricular dysfunction, and a reduction in contractility is frequently invoked as the underlying mechanism (Chen and Gibson, 1979). VCF is a noninvasive and easily measured index of myocardial performance and is capable in certain situations of distinguishing between normal and impaired myocardial function (Fortuin *et al.*, 1972; Karliner *et al.*, 1971; Paraskos *et al.*, 1971). However some limitations do apply, since VCF is dependent on cardiac loading conditions (Mahler *et al.*, 1975; Quinones *et al.*, 1975). Yet, measurements of peak VCF have been validated against angiocardiography and showed close relationship with peak left ventricular dP/dt in patients with coordinate contraction pattern (Gibson and Brown, 1975, 1976). Since all the subjects studied showed normal peak VCF, we believe that longer PEP values found in our hypertensives should be ascribed to higher diastolic pressure only. This is supported also by the demonstration

TABLE I Systolic time intervals and blood pressure in patients with essential hypertension and in normal subjects

Subject	Age (yrs)	PEP (ms)	LVET (ms)	QS_2 (ms)	PEP/LVET	Pressure (mmHg)
Normotensives						
1	43	68.0	274.8	342.8	.247	124/70
2	53	74.0	278.5	352.5	.266	130/85
3	41	90.0	214.8	304.8	.419	138/88
4	62	91.5	263.5	355.0	.347	130/75
5	49	115.5	243.0	358.5	.475	130/90
6	43	89.0	247.0	336.0	.360	138/84
7	48	100.0	255.0	355.0	.392	130/80
8	33	83.5	214.0	297.5	.390	135/85
9	62	83.5	279.0	362.5	.299	135/85
10	35	91.0	235.0	326.0	.387	128/94
11	30	66.0	278.0	344.0	.237	110/70
12	45	73.5	271.0	344.5	.271	110/80
13	41	73.5	264.5	338.0	.278	115/85
14	54	68.0	259.0	327.0	.263	133/80
15	51	90.6	256.3	346.9	.353	120/80
16	37	83.5	271.5	355.0	.308	138/85
17	44	76.5	262.5	339.0	.291	110/70
18	67	117.7	247.0	364.7	.477	140/90
Mean ± SD	46.6 ± 10.3	85.2 ± 14.8	256.4 ± 19.9	341.7 ± 18.4	.340 ± .07	128.6/82.0 ± 12.4/7.1
Hypertensives						
19	62	94.7	260.3	355.0	.364	170/120
20	76	85.2	258.0	343.2	.330	190/90
21	69	125.2	239.3	364.5	.523	210/115
22	53	114.5	247.0	361.5	.464	180/115
23	53	115.2	236.8	352.0	.486	135/105
24	67	110.0	252.0	362.0	.437	160/80
25	35	113.5	251.0	364.5	.452	190/115
26	60	135.7	204.8	340.5	.663	205/140
27	55	98.3	239.0	337.3	.411	170/100
28	47	120.5	277.0	397.5	.435	210/110
29	60	115.5	216.5	332.0	.533	200/115
30	37	103.0	263.7	366.7	.551	160/100
31	38	129.0	245.5	374.5	.525	153/105
32	57	100.2	253.8	354.0	.395	158/113
33	60	104.0	240.0	344.0	.433	145/95
34	58	120.5	231.0	351.5	.522	190/110
35	53	98.5	258.5	357.0	.381	152/90
36	49	89.5	254.0	343.5	.352	180/105
37	48	105.0	241.5	346.5	.435	180/105
Mean ± SD	54.6 ± 10.8	109.4 ± 13.5	245.8 ± 16.7	355.1 ± 15.2	.460 ± .08	175.7/106.7 ± 22.4/13.2

Abbreviations: LVET: left ventricular ejection time; PEP: Pre-ejection period; QS_2: electromechanical systole.

of a significant direct relationship between diastolic pressure and PEP in normotensives (Fig. 3). Therefore, parameters providing an estimate of left ventricular performance, like PEP, should be freed from the influence of afterload conditions (in this case represented by the diastolic pressure).

Thus, for PEP values to be properly interpreted, correction should be made for variation related to differences in resting diastolic pressure. With such a correction PEP could improve its potential for assessing left ventricular performance and its value as quantitative noninvasive technique for evaluating the therapy of hypertensive disease.

Our results demonstrated that the ratio of PEP to LVET is significantly related to diastolic pressure too. Consequently, also the values of this parameter should be revised.

We did not distinguish between hypertensives with and without left ventricular hypertrophy, since it has been demonstrated that the force-length relations of unit mass

TABLE II Results of statistical analysis by unpaired *t*-test

Parameter	t-Value	p-Value
PEP	5.161	<0.001
LVET	1.748	>0.1
QS_2	2.426	<0.025
PEP/LVET	4.686	<0.001

Number of subjects: 37

Abbreviations: LVET: left ventricular ejection time; PEP: Pre-ejection period; PEP/LVET: pre-ejection period/left ventricular ejection time ratio; QS_2: electromechanical systole.

TABLE III Results of analysis by correlation coefficient

Parameters	r-Value	p-Value
DAP vs PEP	.754	<0.001
SAP vs PEP	.686	<0.001
DAP vs LVET	.502	<0.01
SAP vs LVET	.410	<0.05
DAP vs QS_2	.253	>0.1
SAP vs QS_2	.279	>0.05
DAP vs PEP/LVET	.756	ₓ0.001
SAP vs PEP/LVET	.659	ₓ0.001

Degrees of freedom : 35.

Abbreviations: DAP: diastolic arterial pressure; LVET: left ventricular ejection time; PEP: Pre-ejection period; PEP/LVET: pre-ejection period/left ventricular ejection time ratio; QS_2: electromechanical systole; SAP: systolic arterial pressure; r-Value: correlation coefficient; p-Value: significance level.

of myocardium are comparable in different-sized hearts (children's and adults' hearts, normal hypertrophied and dilated hearts) (Suga *et al.*, 1984). Furthermore, our hypertensives were significantly older than our normotensives ($p<0.05$). This could be considered responsible for the longer PEP of the hypertensives, but, according to Colan *et al.* (1984), age does not seem to affect the end-systolic wall stress/velocity of shortening relation, generally accepted as a reliable index of myocardial contractility, over the broad range of 3–75 years.

Finally, we did not study the sympathetic tone of our subjects. It is well known that some patients with essential hypertension may show an increased sympathetic nervous activity which affects cardiac mechanics. We believe that an increased sympathetic tone, though present in some of our hypertensives, should not be considered responsible for prolongation of PEP, since its effect is expressed by shortened PEP.

In spite of these limitations, we think that the worth of this study is the demonstration of a significant direct relationship between diastolic pressure and PEP in a group of subjects undergoing atrial pacing at a rate of 95 beats/min to eliminate the effect of different heart rates on PEP.

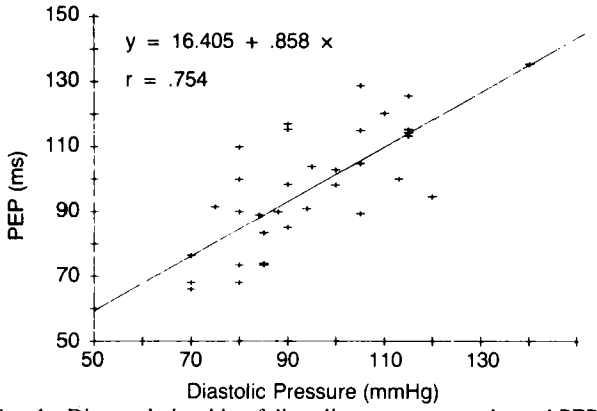

FIG. 1 Direct relationship of diastolic pressure to prolonged PEP values. Hypertensive patients exhibited higher PEP values.

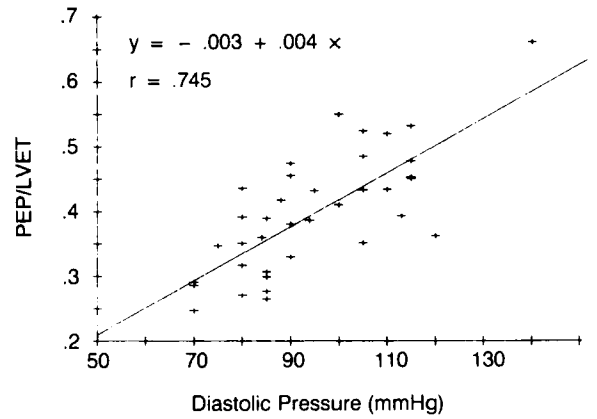

FIG. 2 Ratio of PEP/LVET is significantly related to diastolic pressure.

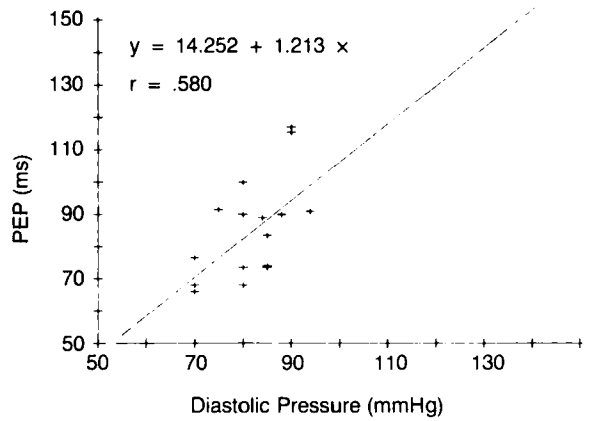

FIG. 3 Diastolic pressure-PEP values are directly related innormotensive subjects in our study.

We suggest to consider this relationship as has likewise been done with heart rate, to provide a multiple regression equation to best appreciate and correct PEP for variation related to differences in resting heart rate and blood pressure.

Acknowledgment

We are indebted to Dr. Joseph Lindsay Jr., Chairman, Department of Cardiology, The Washington Hospital Center, Washington D.C., for assistance in revision of this paper.

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