Continuous electrode monitoring of systolic time intervals during exercise

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SUMMARY Current systolic time interval techniques have limited clinical applicability since patient co-operation and attention to the carotid pulse and phonocardiogram transducers are required. Therefore only surface electrodes were used to monitor the electrocardiogram and electrical impedance cardiogram first derivative (dZ/dt) in the acquisition of the timing signals. dZ/dt motion artefacts were eliminated by computerised ensemble averaging, thus permitting uninterrupted data acquisition. We studied the continuous response of multistage treadmill exercise on 13 normal volunteers, since maximal distortion of noninvasive measurements occurs in dynamic exercise. The individual response trends were combined for 6 symbolic indices and each mean index had a high statistical significance ($P < 0.001$). This new method surveys continuously ventricular performance with surface electrodes and therefore has the potential of monitoring the ventricular performance of critically ill patients.

The physiological and clinical significance of the systolic time intervals have been reviewed extensively (Harris, 1974; Lewis *et al.*, 1974, 1976, 1977). The total electromechanical systole, left ventricular ejection time, and pre-ejection period are the intervals most frequently examined. Their high sensitivity to myocardial dysfunction has been clarified in exercise stress testing and has allowed classification of patients who had exhibited an ambiguous electrocardiographic response.

Both Pouget and co-workers (1971) and Lewis and co-workers (1976), measuring systolic time intervals before and after exercise, have shown a greater change in left ventricular ejection time, corrected for heart rate, in patients with angina pectoris than in normals. Lewis added such criteria to the ST depression on the electrocardiogram and reported a 74 per cent recognition of coronary artery disease. Both systolic time intervals (46%) and electrocardiogram (52%) were much less accurate when used separately. Furthermore, using continuous recording of systolic time intervals during bicycle ergometry, Van der Hoeven and co-workers (1977) were able to distinguish healthy men from patients (90%) and coronary insufficiency from ventricular dysfunction (86%). Thus, uninterrupted systolic time interval monitoring during exercise improved not only its previously tested

accuracy in recognising coronary artery disease, but it added the new diagnostic dimension of ventricular dysfunction.

In the traditional systolic time interval measurement 3 different waveforms must be obtained; the electrocardiogram, phonocardiogram, and carotid displacement pulse. The recording of the conventional transducers for heart sounds and the carotid pulse require patient co-operation and repeated attention by technicians to obtain adequate signals. Van der Hoeven and co-workers (1973) developed a carotid pulse transducer with a collar and used a large elastic band to attach the heart sound transducer to the chest. In this manner, these authors were able to record systolic time intervals during bicycle exercise with hardly any patient discomfort.

Electrical impedance cardiography, which employs surface electrodes, has been investigated as an alternative method. Labadidi and co-workers (1970) compared the time relation between the electrical impedance cardiogram first derivative (dZ/dt) and the phonocardiogram. In a comparative study to postural stress in normal and abnormal subjects, Zambrano and Spodick (1974) used the dZ/dt to determine the ejection time. Similarly, Hill and Merrifield (1976) and Smith and co-workers (1970) employed the impedance cardiogram to measure systolic time intervals during postural changes in man. Rasmussen and co-workers (1975) compared dZ/dt and aortic pressure systolic time interval

Table 1 Exercise stress test procedure

Control	Standing
Stage 0	1.0 mph, 0% grade
Stage 1	1.7 mph, 10% grade
Stage 2	2.5 mph, 12% grade
Stage 3	3.4 mph, 14% grade
Stage 4	4.2 mph, 16% grade

determinations using anaesthetised dogs. An excellent correlation for left ventricular ejection time ($r = 0.986$) and pre-ejection period ($r = 0.948$) was found.

In this present study on treadmill exercise stress testing in normal man we have expanded the role of the electrical impedance cardiogram for uninterrupted systolic time intervals determination by eliminating respiratory and motion artefacts with ensemble averaging and automated analysis.

Subjects and methods

Thirteen healthy, normally active, male volunteers, 18 to 37 years of age, mean 25.1 years, served as subjects for this study. Each subject had both a normal resting 12-lead electrocardiogram and exercise ST segment exercise response.

The exercise stress test consisted of 6 stages incorporating a standing control (Table 1). The exercise portion, stages 0 to 4, consisted of successive increases in treadmill speed and tilt according to a modified Bruce procedure (Slack and Wright, 1977). Each stage lasted for 3 minutes allowing for equilibration of the cardiovascular response. If the subject's heart rate attained 85 per cent of age-predicted maximum, the stress test was terminated.

INSTRUMENTATION

The electrocardiogram precordial V5 lead was monitored with an exercise electrocardiogram computer (Avionics). One reference electrode was placed above the sternum and a second in the lower right thorax. ST segment response and beat-to-beat heart rate were continuously available.

Transthoracic electrical impedance was measured by a 4 electrode impedance cardiograph (Minnesota Model 202). Two aluminium band electrodes (3M Co.) were placed around the neck and 2 around the abdomen at the level of the xiphoid process. A carrier signal was applied to the outer electrodes and monitored with the inner electrodes to obtain the impedance cardiogram. An FM tape recorder was used to record continuously the electrocardiogram and impedance cardiogram first derivative (dZ/dt) for subsequent computer processing.

Digital signal processing and statistical analysis were performed on a digital PDP-12/40 mini-

Table 2 Summary of ensemble averaged waveform acquisition

Stage	Sampling period 0 minutes		2 minutes	
	Cycles	Time	Cycles	Time
C			44	40
0	62	49	54	41
1	62	39	60	37
2	59	32	62	32
3	64	30	64	28
4	64	27	64	24

Cycles, mean number of averaged cycles; Time, mean acquisition time in seconds.

computer with an FPP-12A floating point processor. The analogue-to-digital converters had a 10-bit accuracy and a 20 microsecond conversion time. The electrocardiogram was acquired at a 200 Hz sampling rate during mean heart rate analysis and then both electrocardiogram and dZ/dt were acquired at a 1000 Hz sampling rate for systolic waveform processing. The ensemble averaged

Fig. 1 Schematic diagram of the electrocardiogram (top) and electrical impedance cardiogram first derivative (bottom) features and measurements: onset of systole (Q); rapid upstroke of dZ/dt (up); time of peak dZ/dt (max); and end of systole (x). The dZ/dt amplitude is measured from up to max.

acquisition and automated systolic time interval analysis evaluation during treadmill exercise has been described previously (Kizakevich *et al.*, 1976, 1977).

DATA PROCESSING

Two sampling periods were processed for each exercise stage. Starting immediately and at 2 minutes after stage transition, the electrocardiogram and dZ/dt signals were acquired within a one-minute period. The mean heart rate over this period was calculated before ensemble averaging. A series

of 32 or 64 dZ/dt systolic waveforms, from cycles within 15 per cent of the mean heart rate, were then combined to obtain the ensemble average. The mean number of averaged cycles and mean acquisition time per determination was evaluated (Table 2). The averaged RR' interval was determined from the accepted cardiac cycles and used to calculate the average heart rate ($HR = 60000/RR'$).

The electrocardiogram and averaged dZ/dt waveform were automatically analysed for systolic feature determinations. The analysis algorithms identified 3 systolic events (Fig. 1): (1) the

Table 3 Summary of mean systolic time interval data

	Control 2 min	Stage 0 0 min	2 min	Stage 1 0 min	2 min	Stage 2 0 min	2 min	Stage 3 0 min	2 min	Stage 4 0 min	2 min
Heart rate											
X	76	85	82	99†	102*	115*	122*	134*	142*	152*	166*
SD	13.9	15.7	17.4	16.5	19.4	20.5	23.8	24.4	25.5	24.5	20.3
ΔC		+8*	+6†	+22*	+26*	+38*	+46*	+58*	+66*	+77*	+88*
SD		5.7	7.1	9.2	13.8	15.9	19.0	20.0	19.5	20.9	18.2
%C		111*	108*	130*	135*	152*	162*	178*	189*	205*	216*
SD		7.9	9.7	14.7	22.2	27.5	31.6	35.0	32.8	35.1	31.7
EMS											
X	331	330	332	302	295‡	279†	266*	253*	236*	226*	207*
SD	35.1	37.3	37.5	35.6	38.5	37.1	39.6	36.1	31.7	33.9	19.2
ΔC		-1	-1	-29*	-36*	-52*	-65*	-76*	-93*	-104*	-116*
SD		17.3	15.5	21.6	28.0	28.3	33.8	36.5	30.8	38.7	33.0
%C		100	100	91*	89*	84*	81*	77*	72*	69*	64*
SD		5.5	4.9	6.5	8.1	8.1	9.6	10.1	8.1	10.5	7.7
PEP											
X	87	63‡	63†	44*	44*	35*	35*	34*	31*	29*	30*
SD	22.7	21.0	18.6	18.5	12.1	13.2	8.7	7.3	6.9	4.4	6.5
ΔC		-24*	-25*	-43*	-43*	-52*	-52*	-53*	-56*	-56*	-58*
SD		18.3	19.1	19.8	19.7	20.0	20.2	19.2	20.6	18.6	17.8
%C		74*	74*	53*	52*	43*	42*	41*	38*	35*	35*
SD		19.0	19.3	14.3	14.0	13.7	12.8	9.3	9.6	8.0	7.1
LVET											
X	244	267	269‡	258	251	244	231	219‡	205†	196*	177*
SD	22.7	33.4	31.6	28.7	31.0	35.7	36.5	33.5	29.2	34.2	20.2
ΔC		+23†	+24*	+14‡	+7	0	-12	-23†	-38*	-45*	-59*
SD		25.4	21.4	21.3	26.9	27.5	29.3	26.2	20.2	27.2	20.8
%C		109†	110†	106‡	103	100	95	90†	84*	81*	75*
SD		10.6	9.1	9.0	11.1	11.3	12.1	11.0	8.4	11.7	8.3
LVET/PEP											
X	3.0	4.8†	4.7‡	6.1*	6.1*	7.3*	6.8*	6.6*	6.7*	6.8*	6.1*
SD	1.10	1.87	1.82	1.51	1.57	2.25	1.51	1.41	1.14	1.52	1.44
ΔC		+1.7†	+1.6†	+3.1*	+3.0*	+4.3*	+3.8*	+3.5*	+3.7*	+3.9*	+3.3*
SD		1.75	1.77	1.60	1.62	2.41	1.75	1.10	0.99	1.35	1.11
%C		162†	162†	215*	213*	257*	241*	227*	235*	242*	218*
SD		61.3	58.5	68.5	67.3	81.6	63.8	43.5	51.2	51.2	38.8
LVET%EMS											
X	74	81†	81†	85*	85*	87*	87*	86*	87*	87*	85*
SD	5.4	5.8	5.0	2.9	3.4	3.1	2.3	2.4	2.0	3.1	3.3
ΔC		+7*	+7*	+11*	+11*	+13*	+13*	+12*	+13*	+13*	+12*
SD		5.4	5.4	5.2	5.4	5.2	5.1	4.0	4.5	3.9	3.3
%C		110*	110*	116*	116*	118*	118*	117*	118*	118*	117*
SD		7.5	7.5	7.7	7.9	7.6	7.4	6.2	7.0	6.0	5.0
n	13	13	12	13	13	13	13	12	12	09	08

Heart rate, in bpm; EMS, electromechanical systole in ms; PEP, pre-ejection period in ms; LVET, left ventricular ejection time in ms; LVET/PEP, ratio of LVET to PEP; LVET%EMS, LVET as per cent of EMS; X, actual data; ΔC, difference from control; %C, percentage of control; SD, standard deviation of mean; n, number. The following symbols indicate a significant difference from control: * $P < 0.001$, † $P < 0.01$, ‡ $P < 0.05$.

beginning of ventricular depolarisation (Q), (2) the rapid upstroke of the electrical impedance cardiogram first derivative (dZup) and (3) the closure of the aortic valve (dZx). The waveforms and the 3 feature markers were presented on a computer display for validation before acceptance. From these features the following systolic time intervals and indices were derived: EMS = Q to dZx; PEP = Q to dZup; LVET = dZup to dZx; LVET/PEP; and LVET per cent EMS = $100 \times \text{LVET}/\text{EMS}$.

Results

TREND ANALYSIS

The mean systolic time interval data are presented in three ways (Table 3): (1) actual data (X), (2) difference from control (ΔC), and (3) percentage of control (%C). All mean statistics of actual data indices were significant ($P < 0.001$). The significance of the exercise response to control was ob-

tained by the difference of mean t test employing a two-tailed significance table.

Heart rate (Fig. 2a)

While the actual heart rate showed no significant increase until stage 1, both the delta and percentage groups indicated a small increase during stage 0. All 3 groups showed an accelerated response at stage 1 which continued to increase through stage 4 and resulted in a 115 per cent total increase.

EMS (Fig. 2b)

The electromechanical systole had no significant response until stage 1. At this level electromechanical systole shortened by 35 ms (10%) and continued to decrease by 20 to 30 ms per stage through stage 4.

PEP (Fig. 2c)

The pre-ejection period had an immediate decrease of 24 ms (26%) during stage 0 and continued to shorten significantly through stage 2. At this level a 58 per cent reduction in pre-ejection period had occurred, followed by less than 4 ms further reduction through stage 4.

Fig. 2 Composite of actual data trend response: (a), heart rate; (b) EMS, electromechanical systole; (c) PEP, pre-ejection period; (d) LVET, left ventricular ejection time; (e) LVET/PEP, ratio of LVET to PEP; (f) LVET%EMS, LVET as per cent of EMS.

Table 4 Summary of regression analysis

	a	b	r	n
EMS vs HR				
Stages 0-4	-1.52	455	0.96	118
Stages 2-4	-1.53	457	0.95	67
LVET vs HR				
Stages 0-4	-1.18	373	0.92	118
Stages 2-4	-1.27	387	0.93	67
PEP vs HR				
Stages 0-4	-0.34	82	0.66	118
Stages 2-4	-0.11	48	0.45	67
PEP vs RR				
Stages 0-4	0.08	0	0.74	118
Stages 2-4	0.03	18	0.47	67

HR, heart rate in bpm; RR', RR' interval in ms; EMS, electro-mechanical systole in ms; LVET, left ventricular ejection time in ms; PEP, pre-ejection period in ms; STI = $a \cdot \text{HR} + b$ with a , slope in ms/bpm; b , intercept in ms; r , correlation coefficient; n , number.

LVET (Fig. 2d)

The left ventricular ejection time increased by 23 ms (10%) during stage 0. Left ventricular ejection time shortened at stage 1 and thereafter decreased by 20 ms per stage.

LVET/PEP (Fig. 2e)

The LVET/PEP ratio increased 62 per cent during stage 0 and continued to rise to an increase of 156 per cent at stage 2. From then on no significant changes in LVET/PEP occurred.

LVET/EMS (Fig. 2f)

Left ventricular ejection time as a percentage of electromechanical systole showed an increase (13%) at the beginning of exercise and then remained stable.

REGRESSION ANALYSIS

The results of the trend analysis indicated a biphasic exercise response. Therefore, two regression analyses relating systolic time intervals to heart rate were performed (Table 4). The first analysis included all exercise data (stages 0-4) and the second included data accompanying the accelerated response (stages 2-4). Both analyses combined the actual data from all subjects.

Electromechanical systole vs heart rate

The relation of electromechanical systole to heart rate during exercise was the same by both analyses and had a high correlation ($r = 0.95$).

Left ventricular ejection time vs heart rate

The relation of left ventricular ejection time to heart rate during exercise was slightly different in the two analyses. Though the analysis of stages 2-4 had a greater slope and intercept, both analyses had the same high correlation ($r = 0.93$).

Pre-ejection period vs heart rate

The relation of pre-ejection period to heart rate

showed considerable differences between analyses. Limiting the data to stages 2-4, the already low correlation ($r < 0.66$) was further reduced ($r < 0.47$) showing no relation.

Pre-ejection period vs RR'

The relation of the pre-ejection period to the RR' interval had even larger differences between analyses. The direct analysis with cyclic interval improved the correlation ($r = 0.74$); however, limiting the data to stages 2-4 again reduced the correlation significantly ($r = 0.47$).

Discussion

The cardiovascular response to treadmill exercise has been extensively investigated by invasive as well as noninvasive procedures and therefore the changes are reasonably predictable. Our data confirmed the expected results by both trend and regression analysis.

The inotropic response phase was clearly shown in the stepwise pre-ejection period shortening which accompanied the increasing work load to stage 2. At submaximal work loads of 50 to 150 watts, comparable to stages 0-2, Nandi and Spodick (1977) also found that the degree of pre-ejection period shortening followed the load. In supine bicycle ergometry, Maher and co-workers (1974) reported that the inotropic effect increased slightly throughout submaximal exercise but reached saturation early in maximal exercise. Our data correlate with this finding in that the pre-ejection period remained unchanged after stage 2 in spite of further increases in load and heart rate. As the overall pre-ejection period shortening was independent of the heart rate response, it is not surprising that our regression analysis had a low correlation ($0.45 < r < 0.74$).

The mean values of the pre-ejection period were somewhat shorter than expected, which could not be attributed to an instrumentation error. In a previous study (Kizakevich *et al.*, 1977) we examined the effects of changing posture in the same set of subjects and likewise the pre-ejection periods were also shorter than expected. The mean pre-ejection values in supine and standing positions at rest, however, were the same as reported by Smith and co-workers (1970) who also employed dZ/dt for postural systolic time interval changes.

At the beginning of exercise (stage 0), heart rate and electromechanical systole essentially remained constant, left ventricular ejection time increased slightly, and, expressed as a percentage of control, it conspicuously increased. This implies an increase in stroke volume probably caused by adrenergic effects (Xenakis *et al.*, 1975). At higher work loads,

stages 2 to 4, heart rate rose and progressively shortened left ventricular ejection time. The stronger heart rate influence was also shown in the steeper regression slope found for stages 2 to 4.

The application of pre-ejection period (PEP) and left ventricular ejection time (LVET) as a ratio (LVET/PEP or PEP/LVET) was initiated by Weissler and co-workers (1969) who described the lengthening pre-ejection period and the shortening of left ventricular ejection time caused by heart failure. Consequently the PEP/LVET ratio has been correlated to stroke volume (Weissler *et al.*, 1961, 1968; Leighton *et al.*, 1971; Lewis *et al.*, 1976) and ejection fraction (Garrard *et al.*, 1970; McConahay *et al.*, 1972). Xenakis and co-workers (1975) found an immediate decrease in PEP/LVET to exercise and relatively little change thereafter. The PEP/LVET ratio has been shown to be independent of load in the immediate (Xenakis *et al.*, 1975) and post-exercise (Nandi and Spodick, 1977) response. In our study, however, a progressive increase in LVET/PEP for stages 0 to 2 was evident which coincided with the progressive decrease in pre-ejection period.

Both regression analyses of electromechanical systole and heart rate resulted in the same slope and intercept. In addition, the electromechanical systole trend response virtually mirrored the heart rate trend response. This uniform relation indicates that left ventricular ejection time may be adjusted for heart rate changes on a cyclic basis by computing the left ventricular ejection time percentage of electromechanical systole. A clear advantage of this approach is the elimination of predetermined regression coefficients for heart rate adjustment. For instance, when LVET per cent EMS was correlated with heart rate and with the RR' interval, the correlation coefficients were only 0.27 and 0.35, respectively. Furthermore, the LVET per cent EMS trend remained stable whereas left ventricular ejection time progressively shortened in stages 2 to 4.

The LVET per cent EMS response confirms the direct measurements of Rushmer and Smith (1959) who showed the preponderant heart rate role in raising cardiac output during supine exercise. This however was preceded by an immediate inotropic stroke volume increase to accommodate the reduced preload in the standing position. Thereafter raising the degree of exercise resulted in an increase in heart rate rather than in stroke volume.

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