

Post-extrasystolic potentiation without a compensatory pause in normal and diseased hearts

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Abstract

Variables derived from left ventricular volume were used to study post-extrasystolic potentiation. Left ventriculograms were obtained from 11 healthy individuals and 49 patients with coronary heart disease (30 with a previous myocardial infarction and 19 without any signs of myocardial damage). Post-extrasystolic potentiation was induced by a regularly driven right atrial rhythm that was interrupted by one atrial extrasystole in such a way that the post-extrasystolic RR interval was kept equal to the basic RR interval. The left ventricular end diastolic volumes of the pre-extrasystolic and post-extrasystolic beats were equal. In all groups there was evidence of post-extrasystolic potentiation in one or more of the indices of left ventricular function (ejection fraction, mean normalised systolic ejection rate, end systolic volume, and stroke volume). Potentiation was especially evident in patients with left ventricular damage; this suggests that a compensating mechanism is an intrinsic property of the myocardium.

The Frank-Starling mechanism does not contribute to the increased performance of the post-extrasystolic beat in normal individuals or in patients with coronary artery disease.

caused by chronic valve regurgitation.¹³ In these studies the consequence of the compensatory pause—that is the effect of the “rest contraction”—on the size of the post-extrasystolic beat was not taken into account.

Van der Werf *et al* showed that human post-extrasystolic potentiation can be elicited without a compensatory pause.¹⁴ They provoked controlled post-extrasystolic potentiation by altering the RR interval and by use of pressure-derived indices of contractility in normal and diseased hearts.

We used volume derived indices to investigate post-extrasystolic potentiation after a post-extrasystolic RR interval without a compensatory pause in healthy individuals and in patients with coronary heart disease.

Patients and methods

PATIENTS

We studied 60 patients. Each patient gave informed consent. The patients were divided into three groups: 11 with atypical chest pain, normal coronary arteries, and normal left ventricular pressure and volumes (group 1); 19 patients with typical angina pectoris without evidence of previous myocardial infarction (group 2); and 30 patients with enzymatic and electrocardiographic evidence of an earlier transmural myocardial infarction (group 3). We excluded patients with other forms of cardiac disease and patients who had had cardiac surgery.

STIMULATION PROCEDURE

We used a computed controlled stimulator to ensure that the duration of the post-extrasystolic RR interval was equal to the basic RR interval.¹⁴ The stimulation pattern was applied to the right atrium in such a way that variations in atrioventricular nodal delay caused by changes in the extrasystolic PR interval were compensated for. A test series of atrial stimulation pulses was generated and RR intervals were measured on line by computer. PR intervals were measured and atrial stimulus intervals were corrected by iteration so that the length of the post-extrasystolic RR interval was equal (inaccuracy < 1%) to that of the pre-extrasystolic cardiac cycle (figure). A stimulation series consisted of 20 basic intervals interrupted by one extrasystolic interval. The post-extrasystolic beat (P) was compared with the pre-extrasystolic or control beat (C).

QUANTITATIVE LEFT VENTRICULOGRAPHY

Left ventriculography (50 frames) was

A century ago Langendorff found that the force of contraction was stronger in the beat that followed an extrasystole.¹ Hoffman *et al* called this phenomenon post-extrasystolic potentiation.² Cohn in an editorial cited several investigators³ and attributed post-extrasystolic potentiation in vivo to the prolonged pause that follows the extrasystole, which would lead to increased ventricular filling,⁴⁻⁶ and reduced aortic impedance (resulting from a decline in aortic pressure during that compensatory pause).⁷ A third mechanism, which was seldom taken into account, is the phenomenon called “rest contraction”.⁸⁻¹⁰ This phenomenon, which is part of the so-called restitution curve,¹¹ is present after a compensatory pause.

Sung *et al* showed post-extrasystolic potentiation in healthy individuals without an increased end diastolic volume as a contributing factor.¹² Wisenbaugh *et al* found evidence of post-extrasystolic potentiation without an increased post-extrasystolic end diastolic volume in patients with volume overload

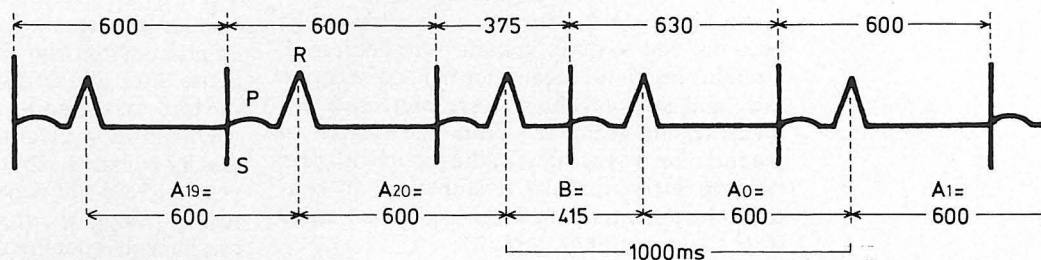
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Schematic presentation of the stimulation procedure used. Time intervals between stimulation spikes (S), P waves, and R waves are shown in ms. After 20 basic stimuli a shorter stimulus-stimulus interval (375 ms) was applied resulting in an RR interval of 415 ms (B). The difference between the RR interval and the stimulus-stimulus interval is caused by prolongation of the PR interval preceding the extrasystole. To correct for this prolongation, the post-extrasystolic stimulus-stimulus interval was chosen in such a way (630 ms) that it results in a post-extrasystolic RR interval (A0) equal to the basic interval (A20).

performed in the frontal and left lateral projection after injection of 40–56 ml metrizoate (Isopaque). The pulse for each cineframe was recorded on paper together with the electrocardiogram. We chose the peak of the R wave to mark end diastole. End systole was more difficult to identify, particularly in patients with coronary heart disease.¹⁵ The frame taken 80 ms before the opening of the mitral valve was taken as end systole. The end diastolic and end systolic ventricular silhouettes were traced by hand and biplane left ventricular volumes were calculated by Dodge's area-length method.¹⁶ Stroke volume, ejection fraction, and mean normalised systolic ejection rate were calculated from the volumes. The ejection rate was calculated by dividing the stroke volume by the duration of the ejection period. Because Van der Werf *et al* found no significant difference in end diastolic aortic pressure between pre-extrasystolic and post-extrasystolic beats, using an identical stimulation protocol,¹⁴ we did not measure aortic pressures in our study. Data are presented as mean (SD).

We used the Wilcoxon matched pairs signed ranked method for statistical analysis. Differences between groups were regarded as significant when p was <0.05 .

Table 1 Intra-observer variability of end diastolic and end systolic volumes measured twice by the same investigator at an interval of 3 months

Volume	n	Mean	Difference*	SD	Coefficients of:	
					Correlation (r)	Variation (%)†
End diastolic	53	77	0.53	5.4	0.98	7
End systolic	36	42	0.94	7.1	0.96	17

*Mean difference between the first and the second determinations.

† $\frac{SD}{mean} \times 100\%$

The first and second determinations of end diastolic and end systolic volumes were not significantly different.

Table 2 Mean (1 SD) calculated ventricular volumes and derived functional indices

	Group 1 (n = 11)		Group 2 (n = 19)		Group 3 (n = 30)		p
	Pre	Post	Pre	Post	Pre	Post	
Ejection fraction	0.64 (0.10)	0.66 (0.10) $p < 0.05$	0.64 (0.10)	0.66 (0.13)	0.46 (0.12)	0.52 (0.13)	<0.05
MNSER	147 (35)	150 (38)	155 (39)	164 (44) $p < 0.05$	142 (44)	166 (65)	<0.05
End systolic volume	24 (8)	23 (9)	25 (12)	24 (14)	51 (23)	45 (22)	<0.05
Stroke volume	40 (6)	42 (6) $p < 0.05$	43 (9)	45 (10)	40 (11)	46 (14)	<0.05
End diastolic volume	64 (8)	66 (9)	68 (17)	69 (17)	91 (24)	91 (26)	
Basic interval (ms)		754 (60)		734 (58)		750 (78)	
Extrasystolic interval (ms)		546 (81)		533 (71)		559 (76)	
Extrasystolic/basic $\times 100$		72 (5)		72 (6)		75 (7)	
Age (yr)		50.0 (8)		52.4 (7)		50.9 (10)	

MNSER, mean normalised systolic ejection rate.

There was strong evidence of potentiation in all four systolic variables in the group of patients with documented transmural myocardial infarction (group 3).

INTRA-OBSERVER VARIABILITY

End diastolic and end systolic volumes were calculated twice by the same investigator at an interval of about 3 months (table 1). The degree of intra-observer variability was affected by the stage (end diastolic or end systolic) at which the volume was measured. Nevertheless, the first and second determination at both end systole and diastole were not statistically different (Student's paired t test) ($p < 0.05$).

Results

Table 2 shows the calculated ventricular volumes and derived functional indices in the three groups of patients. There was no statistically significant difference between the left ventricular end diastolic volume of the post-extrasystolic (P) beat and the control (C) beat in all three groups. The only pre-extrasystolic values that were significantly different from those in the controls were the increased end diastolic and end systolic volumes and decreased ejection fraction found in group 3.

Although the end diastolic volume preceding the post-extrasystolic beat was unchanged and the contribution of a compensatory pause was excluded, several indices of left ventricular function indicated enhanced performance of

that beat (table 2). In the post-extrasystolic beat the end systolic volume was decreased; ejection fraction, mean normalised ejection rate, and stroke volume were increased significantly in group 3. Thus the degree of potentiation was greatest in the group with pre-existing left ventricular dysfunction. In contrast, the potentiation effects in groups 1 and 2 were slight or absent (table 2).

Discussion

We found that volume derived variables indicated little or no post-extrasystolic potentiation of left ventricular performance in controls and in patients with coronary heart disease without myocardial infarction. In these two groups only one of the three indices of left ventricular performance indicated the presence of post-extrasystolic potentiation. In patients with previous myocardial infarction, however, potentiation was evident in all the measured indices and reference values for left ventricular function were abnormal (table 2). This potentiation was independent of preload—as it was in healthy individuals in an earlier study¹² and in animals.¹⁷ Potentiation may be attributed to an increased contractile reserve in non-infarcted areas, which compensates for the loss of contractile power in the infarcted myocardium. Van der Werf *et al* reported post-extrasystolic potentiation of the left ventricular performance when they used the same stimulation protocol in healthy individuals and in patients with coronary heart disease without infarction.¹⁴ They were studying pressure derived variables, and they too found no significant difference between the preloads of the post-extrasystolic beats and the pre-extrasystolic beats.

In most studies^{18–20} the contribution of the prolonged pause after an extrasystole to the enhanced myocardial contractile performance was attributed to an increase in end diastolic volume and an increase in the active state mediated by calcium.²¹ These two effects were avoided in the present study by preventing augmented diastolic filling and by keeping the post-extrasystolic interval equal to the basic interval. So the Frank-Starling mechanism²² and/or “rest contraction”^{23–10} do not necessarily participate in or contribute to the increase of the post-extrasystolic contraction.

The role of the compensatory pause and its contribution as part of the interval-force relation to the increased performance of the post-extrasystolic beat has been overlooked by many investigators of post-extrasystolic potentiation.^{4 5 12 13 18–20 23 24} In these studies the so-called post-extrasystolic beat is a beat potentiated by the prepreceding shorter interval and at the same time augmented by the longer interval that immediately preceded it.⁸ Sung *et al* showed post-extrasystolic potentiation with a compensatory pause in healthy individuals—as in our study without an increased left ventricular volume.¹² Compar-

ison of the results of this study with ours emphasises the contribution of the prolonged pause after the extrasystole to the increase in the force of the post-extrasystolic beat.

Our study of volume derived indices showed that post-extrasystolic potentiation of the left ventricle did not depend on the preload. Our results suggest that the Frank-Starling mechanism is not involved in post-extrasystolic potentiation in normal and diseased human hearts.

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