Constancy of pressure-rate product in pacing-induced angina pectoris

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The pressure-rate product during anginal pain produced by right atrial pacing was studied in 12 patients before, during, and after an angiotensin infusion sufficient to produce a significant rise in blood pressure. During the infusion the pain occurred at a significantly lower heart rate ($P < 0.001$). However, the pressure-rate product was similar during anginal pain before and during the angiotensin-induced hypertension and after it wore off. Our studies support the concept that in each individual there is a constant level of myocardial oxygen consumption, as expressed by the pressure-rate product, at which anginal pain occurs.

Constancy of the pressure-rate product (heart rate $\times$ systolic blood pressure) or the triple product (heart rate $\times$ systolic blood pressure $\times$ ejection time) at the onset of exercise-induced pain has been observed in patients with exertional angina (Robinson, 1967; Redwood *et al.*, 1971). Both 'products' reflect myocardial oxygen consumption ($\dot{MVO}_2$). The duration of the ejection time is now thought to be of minor importance in estimating $\dot{MVO}_2$. The tension-time index has been found to correlate less well with $\dot{MVO}_2$ than the pressure-rate product or just the heart rate (Monroe, 1964; Kitamura *et al.*, 1972; Sheffield and Roitman, 1973; Nelson *et al.*, 1974).

It has been shown that with either exercise or atrial pacing patients develop ischaemic manifestations at a constant tension-time index (Sowton *et al.*, 1967; Bahler and Macleod, 1971) or pressure-rate product (O'Brien *et al.*, 1969). We have further investigated the constancy of the pressure-rate product in patients who developed anginal pain with rapid right atrial pacing.

Patients and methods

Twelve patients were studied. All had developed anginal chest pain in response to rapid right atrial pacing performed by the usual technique (Sowton *et al.*, 1967; Kelemen *et al.*, 1973). Atropine was given to three patients to reverse second degree atrioventricular block occurring at lower heart rates (Cokkinos *et al.*, 1973). All were premedicated with 5 to 10 mg diazepam intra-

muscularly. Blood pressure during the test was directly recorded in eight patients through an indwelling needle in the brachial artery and measured by a cuff sphygmomanometer in the remaining four patients. The pressure-rate product at the onset of pain was calculated in mmHg/min (Sheffield and Roitman, 1973) (1 mmHg/min = 0.133 kPa/min).

After pacing in the initial test had been stopped an intravenous infusion of angiotensin (2.5 mg in 1 litre normal saline) was started together with continuous monitoring of the blood pressure. When the systolic pressure had increased by 20 mmHg (2.7 kPa) or more rapid right atrial pacing was repeated and the pressure-rate product at the time of anginal pain was noted. After the angiotensin infusion had been stopped and the blood pressure had returned to initial levels pacing was repeated and the pressure-rate product at the onset of anginal pain recorded again. The heart rate, blood pressure, and pressure-rate product at the time of anginal pain before, during, and after angiotensin administration were compared by the paired *t* test.

Informed consent for the addition of an angiotensin infusion to the usual procedure of diagnostic rapid atrial pacing was obtained from all patients.

Results

Angiotensin produced the desired increase in systolic blood pressure in all 12 patients (see Table). The cardiac frequency at which each patient developed chest pain was significantly higher before and after the effect of the angiotensin wore off and lower during the infusion ($P < 0.001$). Thus, though there was a large rise in systolic pressure during angiotensin infusion, the fall in heart rate

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TABLE Heart rate, blood pressure, and pressure-rate product at onset of anginal pain in patients subjected to right atrial pacing before, during, and after angiotensin infusion

Case No.	Sex	Age	A Before angiotensin			B During angiotensin		
			HR (min)	BP mmHg (kPa)	PRP mmHg/min (kPa $\times 10^3$ /min)	HR (min)	BP mmHg (kPa)	PRP mmHg/min (kPa $\times 10^3$ /min)
1*	M	54	158	120/90 (15.96/11.97)	18.96 (2.52)	125	165/110 (21.94/14.63)	20.62 (2.74)
2*	M	68	165	150/90 (19.95/11.97)	24.75 (3.29)	140	170/100 (22.61/14.63)	23.80 (3.16)
3	M	51	175	165/100 (21.94/13.30)	28.87 (3.83)	148	190/130 (25.27/17.29)	28.12 (3.73)
4*	M	60	165	140/180 (18.62/10.64)	23.07 (3.06)	110	200/110 (26.60/14.63)	22.00 (2.92)
5*	M	47	152	150/90 (19.95/11.97)	21.02 (2.79)	125	175/120 (23.27/15.96)	21.87 (2.90)
6*	M	52	187(A)	136/80 (18.08/10.64)	25.43 (3.38)	140	190/110 (25.27/14.63)	26.60 (3.53)
7	M	44	160(A)	145/80 (19.28/10.64)	23.20 (3.08)	130	180/110 (23.94/14.63)	23.40 (3.11)
8*	M	62	175	135/85 (17.95/11.30)	23.62 (3.14)	130	180/105 (23.94/13.96)	23.40 (3.11)
9	F	54	166	140/90 (18.62/11.97)	23.24 (3.09)	135	175/100 (23.27/13.50)	23.62 (3.14)
10*	M	60	150(A)	125/80 (16.62/10.64)	18.75 (2.49)	120	160/105 (21.28/13.96)	19.20 (2.55)
11*	M	48	180	130/75 (17.29/9.97)	23.40 (3.11)	140	172/110 (22.87/14.63)	24.08 (3.20)
12*	M	61	156	135/80 (18.52/10.64)	21.06 (2.80)	130	160/100 (21.28/13.30)	20.80 (2.76)
Mean ($\pm$ SEM)			165.7 (± 3.31)	139.3/84 (± 3.20 (systolic))	22.94 (± 0.80) (0.10)	131.0 (± 2.99)	176.4/109.1 (± 4.01 (systolic))	23.12 (± 0.72) (0.09)
A vs B						$\Delta 34.7$ SED ± 2.82 P < 0.001	$\Delta 37.1$ (systolic) SED ± 3.36 P < 0.001	$\Delta 0.18$ SED ± 0.24 P > 0.05
B vs C								
A vs C								

*Ischaemic ST segment changes during pain.

Abbreviations: HR=heart rate; BP=blood pressure; PRP=pressure-rate product; SEM=standard error of mean; SED=standard error of difference; Δ =difference.

was such that the product of rate and pressure was almost exactly the same. The heart rate and blood pressure at the onset of pain were not significantly different before and after angiotensin ($P > 0.05$).

Ten of our patients developed ischaemic ST segment changes at the time of anginal pain (see Fig.). No untoward reactions to angiotensin were noted. Its hypertensive effect wore off in 4 to 11 (mean 6.9) minutes.

Discussion

Our results support the hypothesis that there is a constant myocardial oxygen consumption for each patient at which angina will develop. Each of our patients experienced anginal pain at a constant pressure-rate product regardless of whether this was produced by a relatively greater increase of the heart rate or of the systolic blood pressure.

We chose atrial pacing and angiotensin infusion

C
After angiotensin

HR (min)	BP mmHg (kPa)	PRP mmHg/min (kPa × 10 ³ /min)	Angiotensin effect ceased after : (min)
160	118/80 (15.69/10.64)	18.88 (2.51)	5.5
160	150/100 (19.95/13.30)	24.00 (3.19)	4.0
170	170/100 (22.61/13.30)	28.90 (3.84)	8.5
170	130/100 (17.29/13.30)	22.10 (2.93)	6.5
160	140/95 (18.62/12.63)	22.40 (2.97)	10.0
180	140/80 (18.62/10.64)	25.20 (3.35)	11.0
155	148/90 (19.68/11.97)	22.94 (3.05)	5.5
180	130/90 (17.29/11.97)	23.40 (3.11)	4.5
160	142/85 (19.68/11.30)	22.72 (3.02)	6.5
150	120/80 (15.96/10.64)	18.00 (2.39)	6.0
170	128/70 (17.02/9.31)	22.40 (2.97)	7.0
158	130/75 (17.29/9.97)	20.54 (2.73)	8.0
164.8 (±2.85)	137.1/88.7 (±4.17 (systolic))	22.62 (±0.819)	6.9

Δ33.8 Δ39.3 Δ0.50
 SED ± 3.14 SED ± 2.92 SED ± 0.31
 P < 0.001 P > 0.05

Δ0.9 Δ2.2 Δ0.32
 SED ± 1.06 SED ± 2.16 SED ± 0.30
 P > 0.05 P > 0.05 P > 0.05

for manipulating the pressure-rate product for various reasons. Rapid pacing, in contrast to muscular exercise (Piggott *et al.*, 1971), does not produce any significant change in adrenergic activity provided diazepam is given to prevent undue anxiety (Voridis *et al.*, 1974). Nevertheless, Nelson *et al.* (1974) found that the pressure-rate product correlated very well with $\dot{M}V\text{O}_2$ in exercising patients. We chose angiotensin for raising the

blood pressure because, in contrast to sympathomimetic pressor amines, it does not alter myocardial contractility in man (Ross and Braunwald, 1964; Perloff, Binnion, and DeLeon, 1967), though Koch-Weser (1964) and Fowler and Holmes (1964) have described a positive inotropic effect in animals. Moreover, venous tone, venous return, and heart volume, which are considered to influence $\dot{M}V\text{O}_2$ (Simaan, 1974), are only minimally affected by angiotensin (Rose *et al.*, 1962). Patients exercising after nitroglycerin develop anginal pain at a higher pressure-rate product than controls, presumably because of reduced ventricular dimensions, which lower the $\dot{M}V\text{O}_2$. Conversely, after propranolol the pressure-rate product at the onset of angina is reduced, possibly as the result of increased ventricular size, which tends to augment $\dot{M}V\text{O}_2$ (Wolfson, Phillips, and Schecter, 1970; Detry and Bruce, 1971; Goldstein and Epstein, 1973; Nelson *et al.*, 1974).

Angiotensin has been found to increase coronary arterial resistance (Fowler and Holmes, 1964) but Perloff *et al.* (1967) believed this action to be of no practical significance. Angiotensin has also been used to evaluate contractility in patients with coronary artery disease without any evidence of coronary constrictive effect (Parmley *et al.*, 1975). Anginal chest pain was taken as the criterion of a positive response to atrial pacing. It has been repeatedly stressed that ST segment changes are not specific enough, especially at high atrial pacing rates (Kelemen *et al.*, 1973; Rios and Hurwitz, 1974). Nevertheless, 10 of our 12 patients developed such changes coincidentally with the pain.

Our observations suggested that in addition to other possible haemodynamic modifications drugs preventing increases in blood pressure during exercise may be expected to ameliorate exertional angina.

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FIG. Case 1. Anginal pain and ischaemic ST changes occur at about the same pressure-rate product before and after angiotensin administration.

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