Myocardial lactate metabolism during isometric hand grip test

Comparison with pacing tachycardia

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Twenty-five patients with chest pain were studied by left ventriculography and coronary arteriography. Myocardial metabolic studies were done during control state, pacing tachycardia, isometric hand grip at 30 per cent of maximum force, and combined hand grip plus pacing tachycardia. Nine patients had myocardial lactate abnormality (group 1) as evidenced by myocardial lactate production or decreased extraction (less than 10%). Though tension time index and triple product (left ventricular ejection time $\times$ HR $\times$ systolic pressure) as determinants of myocardial oxygen consumption were highest during combined hand grip plus pacing tachycardia, myocardial lactate abnormalities were most frequent during pacing tachycardia. The present study indicates that isometric hand grip even if performed during pacing tachycardia is not a sensitive test for detection of myocardial lactate abnormalities. The rising level of arterial lactate during isometric hand grip is the most likely mechanism of positive myocardial arteriovenous lactate difference.

Isometric hand grip as a stress test for the cardiovascular system has been the subject of several reports (Helfant, DeVilla, and Meister, 1971; Lind *et al.*, 1964; Lindquist, Spangler, and Blount, 1973). Though the haemodynamic effects of isometric hand grip are well described, its value as a diagnostic stress test on myocardial metabolism is not known.

In this report we describe our findings of the effects of isometric hand grip on myocardial lactate metabolism. In addition, since tachycardia by right atrial pacing is one of the most common and effective stress tests used in the metabolic study of patients with coronary artery disease, the effects of pacing tachycardia *per se* are compared with those of isometric hand grip. Moreover, the combined effects of simultaneous hand grip and pacing tachycardia were also studied.

Subjects and methods

Twenty-five patients were studied, all of whom were referred to us for evaluation of chest pain. No patient had acquired valvular or congenital heart disease. All the patients had a routine history and physical examination, 12-lead resting electrocardiograms, and four-view chamber analysis with barium swallow. Informed

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consent was obtained from each patient for cardiac catheterization and angiographic studies. All the studies were performed in the postabsorptive state after premedication with diphenhydramine hydrochloride 50 mg and sodium pentobarbitone 50 mg intramuscularly each, one hour before catheterization.

The right brachial artery was used for retrograde catheterization of the left ventricle and coronary arteriography. Central aortic and left ventricular pressures were recorded at a paper speed of 25 and 100 mm/sec on Electronics for Medicine photographic recorder, model DR-8. Left ventriculogram in 30 degrees right anterior oblique view was obtained using a No. 7F NIH catheter. Methylglucamine diatrizoate (renografin 76) 40 ml was injected under pressure. Coronary cineangiography by Sones technique was performed in the posteroanterior, left anterior oblique, and right anterior oblique views on magnification mode of General Electric image intensifier, using a 35 mm camera at 60 frames/second. The total amount of radiopaque material used did not exceed 180 ml. After completion of angiographic studies, a No. 6F NIH catheter was introduced into the coronary sinus using an antecubital vein. This catheter was positioned in the middle part of the coronary sinus. A bipolar electrode catheter was introduced into the same vein and its tip was positioned high in the right atrium. Myocardial metabolic studies were performed in a 'randomized' fashion during control state, tachycardia by right atrial pacing, hand grip, and combined hand grip plus right atrial

pacing. A period of 15 minutes was allowed between each intervention. Right atrial pacing was performed using a Cordis generator (model Chronocor III) at threshold current and fixed mode. The patients were paced for 5 minutes at a rate at which chest pain occurred or just below the rate at which the Wenkebach phenomenon appeared. At the end of this period, arterial and coronary sinus blood samples were obtained and aortic pressure was recorded.

Isometric hand grip was performed by the left hand at 30 per cent of the maximal grip using a commercial hand grip (Stolting Co., Chicago 24, Ill., U.S.A.) for 5 minutes. Similarly combined hand grip plus right atrial pacing were performed at the same level of isolated hand grip (force) and right atrial pacing (rate). Blood samples and aortic pressures were similarly obtained in the 5th minute. Blood oxygen content and saturation were measured using a Beckman spectrophotometer. Arterial and coronary sinus blood lactate were measured by the enzymatic method. Left ventricular ejection time was measured from the upstroke of the arterial pressure to the dicrotic notch. Mean pressure was measured by electronic integration and mean systolic pressure was measured by planimetry of the area below the ejection phase of the aortic pressure. Tension time index (Sarnoff *et al.*, 1958) was calculated by multiplying the mean systolic pressure by ejection time in seconds per minute. In addition, the triple product, heart rate $\times$ aortic systolic pressure $\times$ left ventricular ejection time, was calculated (Redwood *et al.*, 1971). Myocardial oxygen extraction ratio was calculated using the formula: $\frac{\text{arteriovenous oxygen content} \times 100}{\text{arterial}}$

Ejection fraction was determined from the left ventriculogram (Greene *et al.*, 1967). The extent of coronary artery disease was considered significant if the lesion constricted the lumen by more than 50 per cent. The patients were divided into 2 groups. Group 1 consisted of 9 patients with myocardial lactate abnormality, i.e. lactate production or diminished extraction (less than 10 per cent of the arterial blood content). Group 2 consisted of 16 patients who had normal myocardial lactate extraction. Statistical analysis between the two groups was performed for the significance of the difference between the means of each group (Snedecor, 1956).

Results

Left ventriculographic and coronary arteriographic findings

These are shown in Table 1. Generally patients in group 1 (lactate abnormality) had more extensive

TABLE 1 Coronary arteriographic and left ventriculographic data in 9 patients with myocardial lactate abnormality (group 1) and in 16 patients with normal lactate metabolism (group 2).

Vessel involvement	Group 1	Group 2
4 vessel disease	3	0
3 " "	1	2
2 " "	2	2
1 " "	1	3
Slight " "	2	8
Coronary spasm	0	1
Ejection fraction	0.44-0.96	0.32-0.87
Heart size		
Normal	7	15
Enlarged	2	1
Contractility		
Normal	5	9
Asynergy	4	7

disease than patients in group 2. Slight cardiomegaly was present in 2 patients in group 1, and one patient in group 2. Asynergy of contraction (localized abnormalities of vigour or temporal relation of contraction) by left ventriculography was present in 4 patients in group 1 and 7 patients in group 2.

Chest pain and electrocardiographic changes

These are shown in Table 2.

Group 1 - Four patients experienced angina during pacing tachycardia; however, only one of them developed chest pain during isometric hand grip. Three patients had chest pain during combined hand grip plus pacing tachycardia (of these patients, 2 had experienced chest pain during pacing). ST segment depression, which was present in 6 patients during pacing tachycardia and combined hand grip plus pacing tachycardia, was present in 3 patients during control state and hand grip.

Group 2 - Eight patients experienced chest pain during pacing tachycardia. Four of these patients developed chest pain during hand grip, and 5 patients during combined hand grip plus pacing tachycardia. There were no ST segment changes in this group.

The haemodynamic data are shown in Table 3.

TABLE 2 Chest pain and ST changes in group 1 and 2 patients.

		Control	Pacing tachycardia	Hand grip	Hand grip plus pacing tachycardia
Chest pain	Group 1	0	4	1	3
	Group 2	0	8	4	5
ST changes	Group 1	3	6	3	6
	Group 2	0	0	0	0

Heart rate

Group 1 Mean control heart rate was 74/min $\pm$ 4.4. During pacing tachycardia, mean heart rate was 132/min $\pm$ 4.0, during hand grip it was 90/min $\pm$ 5.5, and during combined hand grip plus pacing tachycardia it was 133/min $\pm$ 5.0.

Group 2 Mean control heart rate was 75/min $\pm$ 4.5. During pacing tachycardia, mean heart rate was 131/min $\pm$ 4.1, during hand grip it was 91/min $\pm$ 4.8, and during combined hand grip plus pacing tachycardia it was 131/min $\pm$ 5.0.

Left ventricular pressure

Left ventricular systolic and end-diastolic pressures before left ventriculography and coronary angiography in group 1 were 141 mmHg $\pm$ 8.8 and 14 mmHg $\pm$ 2.5, respectively. In group 2, these parameters were 128 mmHg $\pm$ 4.2 and 11 mmHg $\pm$ 1.4, respectively.

Aortic pressure

Group 1 Mean control aortic pressure was 142 mmHg $\pm$ 9.2 (systolic), 76 mmHg $\pm$ 3.2 (diastolic), and 102 mmHg $\pm$ 5.8 (mean). During pacing tachycardia, there was no significant change in systolic pressure, while there was a slight increase in diastolic and mean pressures. During hand grip, there was an increase in systolic, diastolic, and mean pressures. During the combined hand grip plus pacing tachycardia, there was no further increase in systolic pressures as compared to the hand grip data, while diastolic and mean pressures increased even further.

Group 2 Mean control aortic pressure was 128 mmHg $\pm$ 4.9 (systolic), 73 mmHg $\pm$ 2.0 (diastolic), and 97 mmHg $\pm$ 4.1 (mean). As with group 1, there was a slight increase in diastolic and mean pressures during pacing tachycardia. During hand grip and combined hand grip plus pacing tachycardia, systolic, diastolic, and mean pressures increased.

Tension time index (mmHg sec/min)

Group 1 Mean control tension time index was 2591 mmHg sec/min $\pm$ 134, which increased to 3165 mmHg sec/min $\pm$ 191 during pacing tachycardia. During hand grip, tension time index was 3779 mmHg sec/min $\pm$ 172. The highest value of tension time index was during combined hand grip and pacing tachycardia (4299 mmHg sec/min $\pm$ 296).

Group 2 Mean control tension time index was 2393 mmHg sec/min $\pm$ 147 and, similar to that in group 1, increased during pacing tachycardia, hand grip, and combined hand grip plus pacing tachycardia.

Triple product

Group 1 Mean control triple product was 3206 $\pm$ 183, which increased during pacing tachycardia (4019 $\pm$ 189), hand grip (4484 $\pm$ 211), and combined hand grip plus pacing tachycardia (5347 $\pm$ 361).

Group 2 Mean control triple product was 2894 $\pm$ 198. Similar to group 1, there was an increase during pacing tachycardia (3861 $\pm$ 193), hand grip (4662 $\pm$ 338), and combined hand grip plus pacing tachycardia (4962 $\pm$ 322).

Left ventricular ejection time

Group 1 Mean control left ventricular ejection time was 320 msec $\pm$ 7. Pacing tachycardia and combined hand grip plus pacing tachycardia caused a pronounced shortening in left ventricular ejection time, while hand grip alone caused only insignificant shortening (300 msec $\pm$ 9).

Group 2 Mean control left ventricular ejection time was 300 msec $\pm$ 5. As with group 1, pacing tachycardia and combined hand grip plus pacing tachycardia caused a pronounced shortening in left ventricular ejection time, while hand grip alone did not cause any significant change (290 msec $\pm$ 5).

Myocardial arteriovenous O₂ difference and O₂ extraction

Group 1 Mean control myocardial arteriovenous oxygen difference was 12.82 vol per cent $\pm$ 0.36, which increased during pacing tachycardia (13.11 vol % $\pm$ 0.49), hand grip (13.89 vol % $\pm$ 0.44), and combined hand grip plus pacing tachycardia (13.9 vol % $\pm$ 0.87). Myocardial oxygen extraction ratio during control state was 65 per cent $\pm$ 2.74, with only a slight change during pacing tachycardia (66% $\pm$ 2.29), hand grip (69% $\pm$ 1.47), and combined hand grip plus pacing tachycardia (68% $\pm$ 3.04).

Group 2 Mean control myocardial arteriovenous oxygen difference was 11.76 vol per cent $\pm$ 0.44. There was a slight change during pacing tachycardia (11.31 vol % $\pm$ 0.47), while it increased during hand grip (12.36 vol % $\pm$ 0.53) and combined hand grip plus pacing tachycardia (12.04 vol % $\pm$ 0.58).

No statistically significant difference of the various parameters was found between the two groups.

Myocardial arteriovenous lactate difference

Group 1 (Fig.) During the control state, 3 patients had diminished lactate extraction (less than 10%) and one had lactate production. During pacing tachycardia, 5 patients had lactate production

TABLE 3 Haemodynamic data in group 1 and group 2 patients

		Age (yr)	Heart rate/min	Aortic pressure (mmHg)			TTI (mmHg sec/min)	Triple product HR × SP × ET
				S	D	M		
Group I: abnormal lactate								
Control	Mean	49.6	74	142	76	102	2591	3206
	±SE	2.4	4.4	9.2	3.2	5.8	134	183
Pacing	Mean		132	140	90	108	3165	4019
	±SE		4.0	7.5	2.2	4.6	191	189
Hand grip	Mean		90	167	97	125	3779	4484
	±SE		5.5	7.2	4.2	4.5	172	211
Pacing plus hand grip	Mean		133	169	109	131	4299	5347
	±SE		5.0	9.5	5.9	6.8	269	361
Group II: normal lactate								
Control	Mean	50	75	128	73	97	2393	2894
	±SE	2.3	4.5	4.9	2.0	4.1	147	198
Pacing	Mean		131	131	86	103	3303	3861
	±SE		4.1	5.0	2.1	2.7	241	193
Hand grip	Mean		91	177	99	131	3807	4662
	±SE		4.8	9.6	4.5	5.9	246	338
Pacing plus hand grip	Mean		131	160	102	127	4146	4962
	±SE		5.0	10.1	3.8	6.8	230	322

Abbreviations: D: diastolic; LVET: left ventricular ejection time; M: mean; S: systolic; TTI: tension time index. HR: heart rate; SP: systolic pressure; ET: ejection time.

and 1 had diminished lactate extraction. During hand grip alone, no patient developed lactate production but 2 patients had diminished extraction. During combined hand grip plus pacing tachycardia (8 patients), 3 developed lactate production while one had diminished extraction.

Group 2 Mean control arterial lactate during control state was $1.48 \text{ mEq/l.} \pm 0.08$, which increased to $1.64 \text{ mEq/l.} \pm 0.09$ during pacing tachycardia. During hand grip alone, mean arterial lactate was $1.84 \text{ mEq/l.} \pm 0.11$, which increased to $2.00 \text{ mEq/l.} \pm 0.15$ during combined hand grip plus

FIG. Arterial, coronary sinus, and myocardial arteriovenous lactate difference during control state, pacing tachycardia, hand grip, and combined hand grip plus pacing tachycardia in the individual subjects in Group 1. Percentage figures denote the myocardial lactate extraction as a percentage of arterial content.

LVEF (msec)	Myocardial arteriovenous O ₂ diff. (vol %)	Myocardial O ₂ extraction ratio (%)
320	12.82	65
7	0.36	2.74
220	13.11	66
9	0.49	2.29
300	13.89	69
9	0.44	1.47
240	13.9	68
8	0.87	3.04
300	11.76	64
5	0.44	1.51
240	11.31	60
2	0.47	2.05
290	12.36	65
5	0.53	1.56
240	12.04	65
8	0.58	2.31

pacing tachycardia. Myocardial lactate extraction during control state was 33.8 per cent $\pm$ 4.58. During pacing tachycardia, extraction was 27.5 per cent $\pm$ 2.58. During hand grip, it was 33 per cent $\pm$ 3.33 and during combined hand grip and pacing tachycardia, it was 32 per cent $\pm$ 3.54.

Discussion

Isometric hand grip testing causes an increase in cardiac output, heart rate, and blood pressure (Helfant *et al.*, 1971; Kivowitz *et al.*, 1971; Lind *et al.*, 1964; Lindquist *et al.*, 1973). The rise in blood pressure which can be quite significant will expose the heart to pressure load and its effect on myocardial oxygen consumption. Helfant *et al.* (1971) and Kivowitz *et al.* (1971) have used this test to differentiate patients with abnormal ventricular function from those with normal myocardium. While these findings were of definite haemodynamic value in separating normal patients from those with impaired ventricular function, our study shows that isometric hand grip is not a reliable test when lactate studies are used as metabolic indicators of myocardial ischaemia.

In group 1 (lactate abnormality), pacing tachycardia caused lactate abnormality in 6 patients (lactate production in 5 patients and diminished extraction in one). However, during hand grip none of these patients developed lactate production,

while 2 patients showed diminished lactate extraction (Cases J and A) (see Fig.). From these 2 patients, 1 (A) had normal lactate extraction during control state and pacing tachycardia, while during hand grip he had 3 per cent lactate extraction. In addition, during combined hand grip plus pacing tachycardia, 3 patients developed lactate production and 1 patient had diminished extraction. From the above-mentioned patients, only 1 (N), who had lactate production, had normal extraction ratio during hand grip, pacing tachycardia, and control state. Hence hand grip alone is not a sensitive test for myocardial metabolic studies. In addition, combined hand grip plus pacing tachycardia does not have the 'yield' of pacing tachycardia alone. However, when hand grip alone and combined hand grip plus pacing tachycardia are added to pacing tachycardia in metabolic studies of patients with coronary artery disease, a small additional yield is gained.

It is generally agreed that myocardial oxygen consumption is related to tension time index or triple product (though other factors, such as the inotropic state of the heart muscle, the rate of rise of pressure and heart size are of major importance). Since tension time index, triple product, and presumably myocardial oxygen consumption were highest during combined hand grip plus pacing tachycardia, while lactate abnormality was more frequently observed during pacing tachycardia, it may be deduced that a steady state of lactate is not established during the period of hand grip; hence though parts of the myocardium may be ischaemic and producing lactate, the rising levels of arterial lactate produced by the hand-grip exercise overcome the myocardial lactate production and thus a positive myocardial arteriovenous difference is obtained.

In the present study, hand grip was performed by the left hand (since coronary arteriography was carried out through the right brachial artery), though all the patients were right handed. However this does not affect the results since the haemodynamic effects of hand grip are dependent upon the 'percentage' of maximum force generated by a group of muscles and not on the maximum force (Lind and McNicol, 1967).

Conclusions

- 1 - The present reports indicates that the hand grip test, even if combined with pacing tachycardia, has a low 'yield' for myocardial lactate abnormality when compared to pacing tachycardia alone.
- 2 - Pacing tachycardia remains the most reliable stress test as far as lactate metabolism is concerned. However, in a small number of patients,

hand grip and combined hand grip plus pacing tachycardia will reveal myocardial lactate abnormalities which were not present during control state or pacing tachycardia.

- 3 - Previous work by other investigators has shown that hand grip is a satisfactory test for haemodynamic differentiation of patients with normal cardiac function from those with impaired ventricular function.

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