Brit. Heart J., 1967, **29**, 422.

Oxygen Extraction Rate of the Myocardium at Rest and on Exercise in Various Conditions

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The ability to study the oxygen arterio-venous difference in the heart and to measure coronary blood flow has led to a unique concept of the way in which oxygen demands of the heart are met. The coronary sinus oxygen content is low and apparently constant in health and in a wide variety of diseases (anæmia, arterio-venous fistula, hyperthyroidism), and oxygen demand is met by increased blood flow, not increased extraction (Bing *et al.*, 1949; Bing, 1951; Wégria *et al.*, 1958; Leight *et al.*, 1956). Only conditions in which coronary flow is restricted behave differently (Messer *et al.*, 1962). This is in marked contrast to the behaviour of skeletal muscle during exercise (Donald, 1959).

The unique nature of the myocardial response to exertion and the relatively few data on which these conclusions are based indicate the need for further study (Messer *et al.*, 1962; Lombardo *et al.*, 1953; Regan *et al.*, 1961).

The present study attempts to answer two questions.

(1) Is coronary venous oxygen content and oxygen extraction of the myocardium constant at rest in normal subjects and in patients with various diseases?

(2) Does the heart meet increased oxygen demand solely by increased coronary blood flow?

Subjects and Methods

Studies were done on 29 subjects (22 male and 7 female). Five had idiopathic hypertension, three had chronic anæmia, and three had chronic arterio-venous fistula. One patient had Takayasu disease with angina pectoris and one had moderate aortic stenosis. None of them had abnormal hæmodynamic findings indicating left ventricular insufficiency. The remaining sixteen were normal and had neither hæmodynamic nor clinical evidence of heart disease. Standard right heart and coronary sinus catheterizations were performed in all patients. A Cournand needle was inserted into the brachial artery for arterial sampling. Cardiac output was determined by the Fick principle (Fick, 1870) and coronary blood flow per 100 g. of left ventricle per minute was measured by the nitrous oxide desaturation method, utilizing blood-myocardial partition coefficient of 1·1. Myocardial oxygen consumption in ml. per 100 g. of left ventricle per minute was calculated as the product of coronary arterio-venous oxygen difference and coronary blood flow. Myocardial as well as skeletal muscle oxygen extraction coefficients were determined by the coronary arterio-venous oxygen difference/arterial oxygen vol. per cent, and peripheral arterio-venous difference/arterial oxygen vol. per cent formulæ, respectively (Messer *et al.*, 1962). Oxygen contents of the blood samples were determined by the method of Van Slyke and Neill (1924), and blood nitrous oxide volumes were determined by the method of Kety and Schmidt (1945). Pressures were recorded by Sanborn Strain gauge transducers and direct-writing polyviso.

After observations at rest, eight subjects were exercised on a bicycle ergometer for seven minutes, sufficient to raise the total body oxygen consumption 2–3 times above the resting values. All parameters were measured during the last four minutes of supine exercise.

Results

Observations at Rest. The resting hæmodynamic data of this group, consisting of 29 subjects, are given in Table I. With the normal resting subjects, coronary sinus oxygen content and myocardial oxygen extraction values were widely distributed (Fig. 1 and 2). Lowest coronary sinus oxygen content and saturation were 3·20 vol. per cent (saturation 20%) and 8 vol. per cent (saturation 45%), respectively. The mean value of coronary sinus content was 5·3 ∓ 1·7 vol. per cent and oxygen saturation was 29 ∓ 6·5 per cent. The mean oxygen extraction of the myocardium was 68 ∓ 6·5 per cent,

Received February 8, 1966.

TABLE I

MYOCARDIAL OXYGEN EXTRACTION RATE AND CORONARY OXYGEN SATURATION AT REST IN NORMAL SUBJECTS AND IN PATIENTS WITH VARIOUS DISEASE STATES

Case No., initials, sex, and age	Oxygen content (%)		O_2 saturation (%)		O_2 extraction (%)		Cardiac output (l./min.)	Myocardial O_2 consumption (100 g./ ml./min.)	Coronary blood flow (100 g./ ml./min.)
	Brachial artery	Coronary sinus	Brachial artery	Coronary sinus	Myocardium	Skeletal muscle			
				Normal Subjects					
1 N.R. F 25	16·0	4·6	90	16	70	22	5·9	9·3	83
2 F.C. M 24	16·6	5·0	92	27	70	24	5·8	7·7	67
3 E.A. M 19	15·0	5·1	91	30	66	25	5·7	8·5	85
4 G.O. F 54	13·4	6·7	87	43	51	30	4·4	6·8	101
5 L.E. F 32	14·8	4·4	93	27	73	25	5·3	7·3	70
6 V.Y. M 33	17·2	6·0	94	33	64	23	6·0	9·0	80
7 W.C. M 29	14·8	8·0	86	45	60	26	6·6	6·8	99
8 M.L. M 45	15·2	4·2	93	26	72	26	5·6	7·7	70
9 E.F. M 40	15·4	3·2	95	20	80	24	7·1	9·8	80
10 S.H. M 42	18·1	5·5	94	28	70	23	6·3	7·8	62
11 A.S. M 41	17·1	5·1	92	27	70	26	5·7	9·9	83
12 V.A. M 38	17·4	5·2	91	27	70	23	5·0	8·4	69
13 W.R. M 35	16·9	4·0	91	23	76	23	4·8	9·4	73
14 A.C. M 40	15·2	5·4	90	30	65	27	6·9	9·6	98
15 T.G. M 31	16·7	7·0	92	38	60	28	5·1	7·2	74
16 A.W. M 30	15·2	5·1	90	29	70	25	5·6	8·5	83
17 K.A. M 40	16·5	5·5	92	29	70	24	6·1	9·6	87
Mean	15·8	5·3	91	29	68	25	5·9	8·4	80
				High Cardiac Output State					
1 H.O. M 37	12·5	4·6	88	30	63	24	8·0	7·9	100
2 I.I. M 27	10·0	3·5	86	30	65	45	7·7	7·7	111
3 N.A. M 31	16·0	6·0	88	33	63	27	7·3	10·8	108
4 H.J. M 31	15·0	4·0	90	24	70	20	9·3	9·1	82
5 M.R. F 44	15·5	5·1	90	30	67	19	11·0	7·7	74
Mean	13·8	4·6	90	29	65	26	8·7	8·6	95
				Hypertension					
1 H.G. M 44	16·3	6·3	90	33	62	21	7·2	11·6	116
2 M.Ö. M 45	15·3	5·9	90	38	60	26	5·0	8·1	106
3 I.Y. M 21	17·1	7·1	90	37	60	26	5·0	12·6	121
4 H.G.* M 22	17·9	7·1	90	37	62	34	4·2	10·8	102
5 H.M. F 22	16·0	5·5	88	30	65	22	6·4	10·8	113
Mean	16·3	6·6	90	35	62	26	5·6	10·8	112
				Takayasu Disease					
1 S.Y.† F 30	16·6	8·2	90	44	51	19	7·0	8·5	101
				Aortic Stenosis					
1 M.K. F 20	18·2	6·4	93	32	65	22	5·0	13·8	118

* Heart failure was thought to be present.
† This patient had coronary insufficiency.

ranging from 51 to 80 per cent. The mean oxygen extraction rate of the skeletal muscle was $25 \mp 2{\cdot}2$. The coronary sinus oxygen content and saturation in the hypertensive group was higher than normal, the means for the two groups being 6·6 vol. per cent (saturation 35%) and 5·3 vol. per cent (saturation 29%), respectively (Table I, Fig. 1). Since the standard error in the determination of oxygen volumes in the Van Slyke method is less than $0{\cdot}2 \mp$ vol. in our laboratory, this difference was accepted as significant. As a result of this, the oxygen extraction of the myocardium in this group was somewhat lower than in normal subjects, values being 62 and 68 per cent respectively (Table I, Fig. 2).

The mean oxygen saturation of the coronary sinus was essentially similar, with both a normal and high cardiac output, though the mean coefficient of the oxygen extraction by the myocardium tended to be lower with a high cardiac output (Table I, Fig. 1 and 2). This reflected a somewhat lower hæmoglobin concentration in the high cardiac output group.

It is of interest that in the patient with Takayasu disease, where angina pectoris was diagnosed clinically and confirmed electrocardiographically, coronary sinus oxygen saturation was unexpectedly higher than in the normal group, values being 8·2 vol. and 39 per cent saturation. Myocardial oxygen

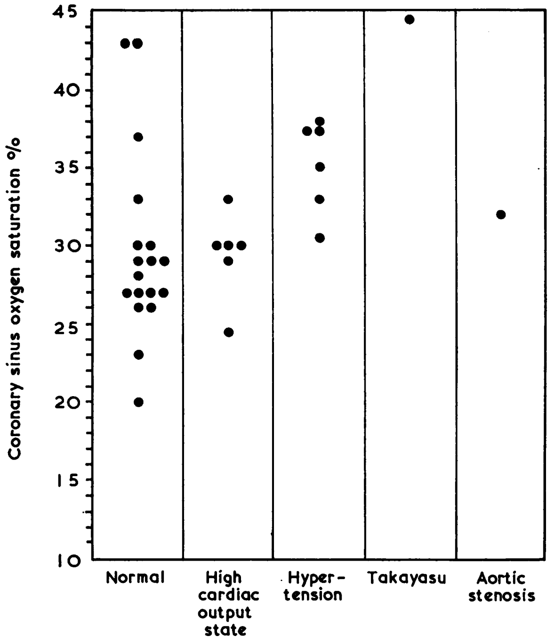

FIG. 1.—Distribution of the coronary sinus oxygen saturation at rest in normal subjects and in patients with various diseases.

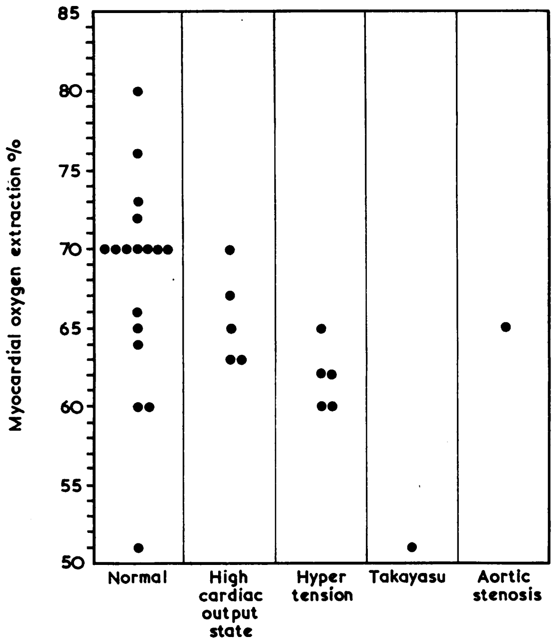

FIG. 2.—Distribution of the myocardial oxygen extraction rate at rest in normal subjects and in patients with various diseases.

extraction in this patient and in the normal group also showed striking differences of 51 and 68 per cent respectively. The oxygen demand of the myocardium in this patient was obviously met by raised coronary blood flow (Table I, Fig. 1 and 2).

One patient studied at rest had moderately severe aortic stenosis. Coronary sinus oxygen content and saturation were somewhat higher than in the normal group, while oxygen extraction of the myocardium was slightly lower (Table I, Fig. 1 and 2).

Observations during Exercise. Exercise data presented in Table II were obtained from 4 normal subjects (Cases 1, 2, 3, 4), two patients with chronic arterio-venous fistula (Cases 5, 6), one with chronic anæmia (Case 7), and one with aortic stenosis. In all subjects except two (A.W. and M.K.) exercise did not alter the oxygen extraction of the myocardium (Fig. 4), though in some cases coronary sinus oxygen saturation slightly decreased (Fig. 3).

An interesting point was that in 6 patients the

TABLE II

MYOCARDIAL OXYGEN EXTRACTION RATE AND CORONARY SINUS SATURATION AT REST AND DURING EXERCISE IN NORMAL SUBJECTS, IN PATIENTS WITH HIGH CARDIAC OUTPUT STATE, AND AORTIC STENOSIS

	Rest				Exercise				Oxygen extraction (%)				Cardiac output (l./min.)		Coronary blood flow (100 g./ml./min.)		Myocardial O_2 consumption (100 g./ml./min.)	
	Brachial artery		Coronary sinus		Brachial artery		Coronary sinus		Myo-cardial		Skeletal muscle							
Case No., initials, sex, and age	Vol. (%)	Sat. (%)	Vol. (%)	Sat. (%)	Vol. (%)	Sat. (%)	Vol. (%)	Sat. (%)	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
1 T.G. M 31	16·7	92	7·00	38	17·00	92	6·70	37	60	60	28	40	5·1	8·1	74	108	7·2	11·1
2 A.W. M 30	15·2	90	5·10	29	15·50	92	3·80	22	66	76	25	33	5·6	9·2	83	169	8·5	19·8
3 K.A. M 43	16·5	92	5·50	29	17·00	94	5·20	28	70	70	24	30	6·1	17·4	87	132	9·6	16·6
4 N.R. F 25	15·0	90	3·80	23	15·10	90	3·80	23	75	75	23	45	5·9	6·0	83	108	9·3	12·2
5 H.J. M 31	15·0	90	4·00	24	15·50	93	4·50	27	70	70	20	35	9·3	16·4	82	108	9·1	11·9
6 M.R. M 44	15·50	90	5·10	30	14·90	88	4·90	29	67	67	19	33	11·0	16·5	74	111	7·7	11·1
7 H.O. M 37	12·5	88	4·60	30	13·00	90	4·80	33	63	63	24	34	8·0	13·5	100	142	7·9	11·5
8 M.K. F 20	17·2	93	6·40	32	17·80	92	5·20	26	65	71	22	29	5·0	7·6	118	128	13·8	16·1

Note: In no case was either coronary insufficiency or congestive heart failure found to be present.

myocardial oxygen extraction did not change during exercise, regardless of the condition of the subjects (Tables II and III and Fig. 4). Since this degree of exercise did not produce any significant change in the oxygen extraction, increase in myocardial oxygen consumption was met by a rise in coronary blood flow. On the other hand, exercise produced a rise in the skeletal muscle oxygen extraction in all subjects of 57 per cent above resting values (Tables III and IV).

The left ventricular oxygen extraction increased in two subjects (A.W. and M.K.) ranging from 7 to 9 per cent (Table II and IV, Fig. 4). As a result of this increment in oxygen extraction the coronary sinus oxygen saturation decreased markedly in both cases (Fig. 3).

The other finding, which showed the difference between subjects who did not alter their myocardial oxygen extraction, was a slight increment of arterial oxygen saturation in the first group during exercise (Tables III and IV).

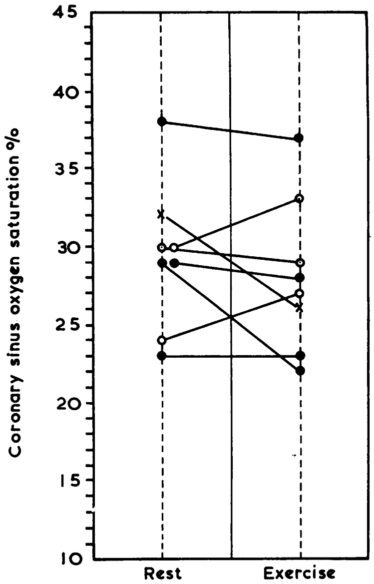

FIG. 3.—The effect of exercise on the coronary sinus oxygen saturation in normal subjects and in patients with various diseases.
● = Normal subjects
○ = High cardiac output state
× = Aortic stenosis

DISCUSSION

The oxygen extraction rate of the myocardium at rest varies widely in normal subjects. A claim, therefore, that the coronary arterio-venous difference remains constant in disease can only be based on statistical calculation from many patients; such claims for any individual patient must be accepted with caution.

The highest resting coronary sinus oxygen saturation was observed in the case of Takayasu disease in which angina pectoris was present. This seemingly paradoxical finding was also reported by Messer *et al.* (1962) who suggested that generalized reflex dilatation of the remaining normal vessels may exist as an inappropriate response to areas of localized myocardial ischæmia. In addition, arterio-venous shunts may develop around the scar tissue. These factors could be responsible for the higher oxygenation of the coronary sinus blood, which occurs in this condition. Reduction in the coronary sinus oxygen saturation during exertion, observed in coronary atherosclerosis, was suggested by Messer *et al.* (1962) to confirm this hypothesis.

Our observations in hypertensive cases differ from those of Lombardo *et al.* (1953) and Bing (1951). In four of the five cases we found that both myocardial oxygen consumption and coronary blood flow were increased and that myocardial oxygen extraction rate was decreased. The discrepancy between our results and those of Lombardo *et al.* and Bing can only be explained by the wide variations in these parameters usually found at rest. We believe that comparison of results obtained only at

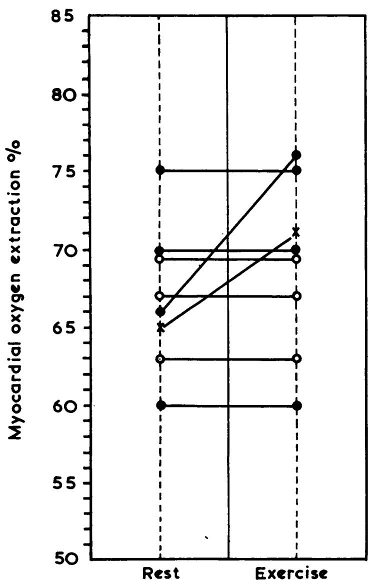

FIG. 4.—The effect of exercise on the oxygen extraction rate of the myocardium in normal subjects and in patients with various diseases
● = Normal subjects
○ = High cardiac output state
× = Aortic stenosis

TABLE III

MEAN VALUES IN 6 SUBJECTS IN WHOM MYOCARDIAL OXYGEN EXTRACTION WAS NOT INCREASED DURING EXERCISE

	No. of patients	Volume (%) Brachial artery	Volume (%) Coronary sinus	Saturation (%) Brachial artery	Saturation (%) Coronary sinus	Myocardial O_2 extraction (%)	Skeletal muscle O_2 extraction (%)	Cardiac output (l./min.)
Rest	6	15·20	5·00	92	29	67	23	7·6
Exercise	6	15·42	4·98	90	31	67	36	13·0
Change (%)	—	+1·4	0	−2·2	+7	0	+57	+71

TABLE IV

MEAN VALUES IN 2 SUBJECTS IN WHOM MYOCARDIAL OXYGEN EXTRACTION INCREASED DURING EXERCISE

	No. of patients	Oxygen volume (%) Brachial artery	Oxygen volume (%) Coronary sinus	Oxygen saturation (%) Brachial artery	Oxygen saturation (%) Coronary sinus	Myocardial O_2 extraction (%)	Skeletal muscle O_2 extraction (%)	Cardiac output (l./min.)
Rest	2	16·70	5·75	91	30	67	23	5·3
Exercise	2	16·65	4·50	92	25	73	31	8·4
Change (%)	—	0	−22	+1·1	−17	+9	+35	+ 60

rest in healthy subjects and in those with disease would lead to faulty conclusions.

We consider that exercise studies are a much more accurate way of studying the myocardial circulation and myocardial oxygen extraction capacity. Three of our normal subjects did not increase their sinus oxygen saturation and myocardial oxygen extraction. This, then, is the usual myocardial response to exercise (Messer *et al.*, 1962; Lombardo *et al.*, 1953). An occasional subject, however (Table II Case: A.W.), without detectable heart disease will increase oxygen extraction. Patient A.W. showed this response, and Messer *et al.* (1962) reported 3 similar cases. Patients with chronic anæmia (Lombardo *et al.*, 1953) and arterio-venous fistula (Wégria *et al.*, 1958), likewise did not increase myocardial oxygen extraction during exercise nor meet increased oxygen demand by increased blood flow. Subject M.K. (Table II) with aortic stenosis also increased his myocardial oxygen extraction on exercise. This finding, we feel, is explained by the high intraventricular tension leading to an increased intramural tension compressing the smaller coronary vessels. In addition, low perfusion pressure above the stenotic valve may alter the flow/extraction ratio of the myocardium.

Conclusion

Since coronary sinus oxygen saturation and myocardial oxygen extraction are so widely distributed at rest in individual cases, definite conclusions should not be drawn comparing normal and disease states.

Although myocardial oxygen extraction capacity is limited in many conditions, in some disease states where coronary blood flow is considerably restricted, extraction may increase in an attempt to compensate for the oxygen deficit of the myocardium.

Summary

Oxygen extraction rate of the myocardium at rest and on exercise has been studied in normal subjects and in various disease states by the technique of coronary sinus catheterization and measurement of coronary arterio-venous oxygen difference. Twenty-nine observations were made at rest and eight during exercise. In both normal subjects and patients at rest, coronary sinus oxygen content and myocardial oxygen extraction values were widely distributed. In six subjects, exercise did not produce any change in the oxygen extraction of the myocardium. This, then, is the usual response to the exercise, regardless of the condition of the subjects. Although this is true in many conditions, in some disease states where coronary blood flow is restricted extraction may increase in an attempt to compensate for the oxygen deficit of the myocardium.

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