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Reduction of Myocardial Contractility by 100% Oxygen in Patients with Coronary Disease[1] (37756)

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Oxygen inhalation therapy in patients with myocardial ischemia has been one of the routine procedures in clinical medicine. Experimental studies showed prolonged survival in animals with acute myocardial infarction while breathing oxygen (1, 2), and increased exercise tolerance has been demonstrated in patients with coronary artery disease (3, 4). Other workers have shown an elevation of coronary venous oxygen saturation and an increase in myocardial lactate extraction rate in the ischemic myocardium, although coronary blood flow and myocardial oxygen supply diminish during the administration of oxygen (5, 6). Decreased myocardial oxygen demand during oxygen administration could account for the beneficial effect of oxygen. Experimental studies in open chest preparations in dogs revealed a decrease in myocardial contractility by administration of oxygen (6–8). Since myocardial oxygen demands are in part dependent on myocardial contractility (9), a study was undertaken to determine the effect of oxygen on myocardial contractility in patients with coronary artery disease.

Methods. Diagnostic heart catheterization and coronary arteriography by Judkins technique (10) were carried out on 14 patients (10 males and 4 females), ages 34–63, with clinical diagnosis of coronary artery disease, after premedication with seconal 100 mg and local anesthesia using 2% xylocaine 5–10 ml. After the procedure, a catheter-tip manometer (MIKRO-TIP pressure transducer, Model PC-350 5F, Millar Instruments, Inc., Houston, TX) was inserted into the right femoral artery, and the tip of the catheter was advanced into the left ventricle. The first derivative of left ventricular pressure (dp/dt) using an RC differentiator output from the pressure channel (Carrier amplifier Model SGM, Electronics for Medicine, Inc., White Plains, New York) was recorded simultaneously with left ventricular pressure. Maximum value of left ventricular dp/dt (max dp/dt), velocity of the shortening of the contractile element of the muscle at zero load (V_{max}) (11), were calculated as indices of contractility of left ventricular muscle. Heart rate, left ventricular systolic and end-diastolic pressures, and tension-time index per min (12) were calculated. All indices were measured as averages of 10 cardiac cycles. The measurements were performed first during air breathing and were repeated 5 min after breathing 100% oxygen at 1 atm using a mouthpiece connected to a Douglas bag. Oxygen tension in the arterial blood was measured during air and oxygen breathing. A total of 19 studies were performed; in eight of these, heart rate was maintained constant by right atrial pacing using a bipolar pacing catheter in the right atrium. All patients were in fasting condition, and the medications were discontinued 1 day prior to the study. A total of 100 ml of 76% meglumine diatrizoate (Renografin) and nitroglycerin 0.4 mg were given during catheterization for diagnostic purposes. The measurement of myocardial

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contractility was made at least 20 min after administration of these drugs. Five out of 14 patients showed narrowing of the lumen of the major coronary arteries of less than 50%, and the remaining nine patients had narrowing of more than 50% in one or more of the major coronary arteries. No patient was in heart failure, shock, or complaining of chest pain at the time of the study, and no patient had left ventricular aneurysm, mitral insufficiency, or intraventricular conduction defect. The results were statistically evaluated using Student's t test in paired samples (13).

Results. Arterial oxygen tension during oxygen breathing was significantly elevated (Table I). Heart rate, when not controlled by right atrial pacing, was slightly reduced during oxygen breathing in 8 out of 11 studies. In eight studies, heart rate was maintained at 95 ± 6 beats/min (mean ± 1 standard deviation) by right atrial pacing, and it remained constant during the study. Left ventricular systolic pressure increased in 16 studies out of 19 during oxygen breathing, the average elevation in left ventricular systolic pressure was 8% (Table I), while left ventricular end-diastolic pressure showed no significant change. Tension-time index inceased during oxygen breathing due to a significant rise in left ventricular systolic pressure. In 13 studies out of 19, reduction in max dp/dt was observed, but this change was not statistically significant. In all studies, V_{max} was significantly reduced during oxygen administration (Table I, Fig. 1). This occurred even in the presence of constant heart rate (Fig. 1). This change was not statistically different between the patients with and without coronary artery lesions. Accordingly, all 14 patients were tabulated as a single group in Table I.

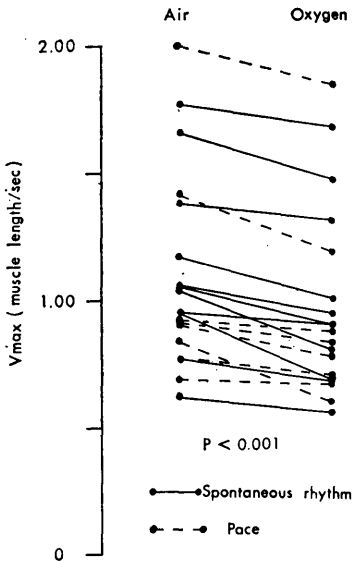

FIG. 1. Effect of oxygen breathing on V_{max} of left ventricular muscle. In 11 studies with spontaneous heart rate (solid line) and eight with heart rate controlled by right atrial pacing (broken line), V_{max} showed a significant decrease with oxygen breathing.

Discussion. The effect of oxygen on contractility of heart muscle has been previously

TABLE I. Effect of Oxygen Breathing on Left Ventricular Pressure, dp/dt, and V_{max}.

	Air breathing (1)	Oxygen breathing (2)	Difference (2)−(1)/(1) × 100	Statistical significance of difference
Arterial pO_2 (mm Hg)	79 ± 8[a]	461 ± 44	488 ± 169	$P < 0.001$
Heart rate[b] (beats/min)	81 ± 16	80 ± 16	−1 ± 9	NS[c]
LV[d] end-diastolic pressure (mm Hg)	12 ± 9	13 ± 9	8 ± 24	NS
LV systolic pressure (mm Hg)	120 ± 17	129 ± 16	8 ± 6	$P < 0.005$
Tension-time index (mm Hg • sec/min)	2703 ± 536	2951 ± 514	10 ± 10	$P < 0.001$
Max dp/dt (mm Hg/sec)	1298 ± 347	1274 ± 335	−2 ± 9	NS
V_{max} (muscle length/sec)	1.10 ± 0.37	0.95 ± 0.37	−11 ± 8	$P < 0.001$

[a] Mean ± one standard deviation.
[b] Values for heart rate controlled by right atrial pacing were not included.
[c] NS = not significant ($P > 0.05$).
[d] LV = left ventricular.

determined in isolated muscle preparation (14, 15). Lentini demonstrated in the isolated muscle preparation, that developed tension increased during hyperoxia (14); however, this result is not applicable to the heart *in vivo* in which oxygen availability does not increase by giving oxygen, since coronary blood flow diminishes (6, 7). Daniell and Bagwell in 1968 (7) demonstrated that 100% oxygen breathing in an open chest dog caused a decrease in force development of the left ventricle. Kioschos *et al.* (8) showed in dogs that 100% oxygen breathing at 3.6 atm absolute of oxygen pressure caused a decrease of dp/dt by 14% and the ratio of max dp/dt to integrated isometric tension (dp/dt/IIT) by 31%. More recently it was demonstrated that contractile force measured in the local ischemic myocardium in dogs decreased by from 4–6% after oxygen administration (6). However, this has not been shown in man. There was an average 2% reduction in max dp/dt during oxygen breathing in the present study and this was statistically not significant. Horvat *et al.* (4), using a saline-filled catheter, also failed to demonstrate any change in contractility of the left ventricle in patients with coronary artery disease breathing 100% oxygen, possibly because only maximum left ventricular dp/dt was determined. This measurement is known to be a less specific index than other indices of contractility (11). Elevation of left ventricular systolic pressure occurring during oxygen breathing might mask the reduction of contractility when only max dp/dt is determined, since max dp/dt depends on afterload (11). In this regard, V_{max} (11) was calculated. This value was reduced during oxygen breathing in all studies.

Oxygen demand of the heart is determined by the velocity of the contraction of the myocardium and by myocardial wall tension (9). Consequently, as myocardial contractility diminishes, oxygen demand of the heart decreases. Therefore, a significant fall in contractility of 11% (Table I) during oxygen breathing suggests a reduction in myocardial oxygen demand. This fall is not secondary to a slowing of the heart rate (Fig. 1). However, one must also consider the fact that left ventricular wall tension increases, since left ventricular systolic pressure rises (Table I), thus increasing myocardial oxygen demands. A study performed by Graham *et al.* (16) demonstrated that, in order to produce a 50% increase in myocardial oxygen consumption, an 83% increase in peak-developed stress was required; however, at constant wall stress or tension, only a 42% increase in V_{max}, i.e., contractile state, was required (16). Graham's study (16) suggests that an 11% decrease in contractility (Table I) has a greater effect on myocardial oxygen demand than an 8–10% increase in left ventricular wall tension (Table I). However, without determination of myocardial oxygen consumption, no definite conclusion on myocardial oxygen demands can be drawn. It is likely, however, that myocardial oxygen demand diminishes, since myocardial oxygen consumption calculated in animals (6, 7, 17), as well as in man (4, 5, 18), is shown to be decreased during oxygen inhalation. However, it cannot be stated with certainty that a reduction in myocardial contractility observed here is the only reason for the diminution in myocardial oxygen demand induced by oxygen inhalation.

Summary. Changes in contractility indices for left ventricular muscle were calculated during air and oxygen breathing in 19 studies on 14 patients with coronary artery disease. The following significant changes were observed on oxygen breathing: rises in pO_2 of arterial blood, in left ventricular systolic pressure, and in tension-time index, and a fall in the velocity of the shortening of the contractile element of the left ventricular muscle at zero load (V_{max}). The fall in V_{max} was similar even when heart rate was maintained constant. These observations suggest that oxygen breathing diminishes myocardial contractility and consequently may reduce myocardial oxygen demand. It is recognized that the reduction in myocardial contractility may be only one of the factors responsible for the decrease in myocardial oxygen demand induced by oxygen administration.

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