Coronary Hemodynamics and Myocardial Oxygen Metabolism during Oxygen Breathing in Patients with and without Coronary Artery Disease

By William Ganz, M.D., C.Sc., Roberto Donoso, M.D., Harold Marcus, M.D., and H.J.C. Swan, M.B., Ph.D.

SUMMARY
Oxygen in high concentration (arterial pO₂ over 400 mm Hg), administered for 7-10 minutes to six subjects with normal coronary arteries and nine subjects with coronary artery disease caused the following significant changes: The heart rate and cardiac index decreased in both groups. The mean arterial pressure increased in the coronary group. The coronary sinus blood flow fell from 158 ± 11 (mean ± SEM) to 131 ± 13 in the noncoronary and from 151 ± 14 to 138 ± 14 ml/min in the coronary group, due to an increase in coronary resistance. The coronary sinus oxygen tension increased from 19 ± 1 to 22 ± 1 in the noncoronary and from 19 ± 1 to 24 ± 1 mm Hg in the coronary group. The coronary arteriovenous oxygen difference decreased from 13.2 ± 0.6 to 12.5 ± 0.6 ml/100 ml in the coronary group. Left ventricular oxygen consumption fell from 21.5 ± 2.1 to 18.2 ± 2.4 in the noncoronary and from 19.9 ± 2.0 to 16.7 ± 1.7 ml/min in the coronary group. Myocardial lactate extraction increased from 40 ± 9 to 60 ± 4 and from 4 ± 6 to 28 ± 3%, respectively. In four patients with severe coronary artery disease, oxygen breathing reverted myocardial lactate production to extraction. It would appear that oxygen breathing might be beneficial in myocardial ischemia by increasing coronary arterial oxygen tension and reducing myocardial oxygen consumption.

Additional Indexing Words:
Coronary sinus blood flow
Cardiac output and oxygen
Myocardial lactate metabolism

Oxygen in high concentrations has been widely administered to patients with symptomatic coronary artery disease, including those with acute myocardial infarc-
because of known or suspected coronary artery disease were studied. They were fasting and premedicated with 100 mg of secobarbital. Their relevant clinical and arteriographic data are summarized in table 1. The coronary arteriography confirmed the diagnosis of coronary artery disease in nine subjects. In six subjects the coronary arteriogram was normal and consistent with the clinical history.

The hemodynamic and metabolic measurements were obtained first with the patient breathing room air and then after 7 min of oxygen breathing. Oxygen was applied by means of a close-fitting face mask with a reservoir bag at flow rates of 10–15 liters/min. The oxygen concentration in the inspired air using this system and flow rate has been reported to be approximately 90–95%. The following measurements were performed.

1. Arterial blood pressure by means of an 18-gauge thin-wall Cournand needle, placed percutaneously into the left femoral artery.

2. Coronary sinus blood flow by the continuous thermodilution method. In brief, a special 7F-size thermistor catheter was inserted from the left antecubital vein into the coronary sinus. A 5% solution of dextrose at room temperature was injected into the coronary sinus at a constant rate of between 35 and 40 ml/min for 20–30 sec. The temperatures of the injectate, of the blood, and of the mixture of injectate and blood were measured by two thermistors mounted in the lumen and on the outside of the catheter. The resistance of the thermistors was determined by separate Wheatstone bridges, balanced prior to the injection of dextrose. The off-balance output of the bridges during injection was amplified and recorded. The change in resistance was calibrated by a resistance in series with each thermistor. The temperature change represented by the calibrating resistance was obtained from the temperature-resistance relationship of each thermistor.

The coronary sinus blood flow was calculated by the following formula:

\[ \text{Blood flow} = F_v \times \left( \frac{T_H - T_I}{T_H - T_M} - 1 \right) \times 1.08 \]

where: \( F_v \) = volume of injectate (ml/min); \( T_H \), \( T_I \), \( T_M \) = temperatures of blood, of injectate, and of mixture of blood and injectate (°C); and 1.08 = constant derived from the density and specific heat of the dextrose solution and of the blood.

3. Cardiac output by the dye-dilution technique with injection of indocyanine green into the coronary sinus and sampling from left femoral artery.

4. Blood samples were obtained simultaneously from the femoral artery and the coronary sinus and immediately analyzed for pH, pCO2, and pO2 by a pH/gas analyzer (model 113

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical and Angiographic Data</th>
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<tr>
<td>No.</td>
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<td>Subjects with normal coronary arteries</td>
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<td>F</td>
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<td>2</td>
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<td>6</td>
<td>M</td>
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<tr>
<td>Subjects with coronary artery disease</td>
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</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>Number of major vessels involved</td>
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<td>15</td>
<td>M</td>
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Instrumentation Laboratory, Inc., Boston). The reproducibility of pO₂ determinations from successive samples in this laboratory is ± 0.5 mm Hg in the 15–25-mm Hg range, ± 2 mm Hg in the 60–100-mm Hg range, and ± 10 mm Hg in the range over 300 mm Hg. Hemoglobin saturation was obtained from the oxyhemoglobin dissociation curve with correction for pH and temperature, as described by Severinghaus.4

Samples of arterial and coronary sinus blood were also taken for determination of lactate concentration by the enzymatic method of Hohorst.5 The following calculations were made:

Oxygen content (ml/100 ml) = hemoglobin saturation (%) x hemoglobin content (g/100 ml) x 1.34 + 0.0031 x P0₂ (mm Hg)

Left ventricular oxygen consumption (ml/min) = (arterial – coronary sinus oxygen content [ml/100 ml]) x coronary sinus blood flow (ml/min) x 10⁻²

Myocardial lactate extraction (%) = arterial – coronary sinus arterial lactate

Left ventricular coronary resistance (units) =
mean arterial blood pressure (mm Hg)
coronary sinus blood flow (ml/min)

Results

Table 2 summarizes the data on the hemodynamic and metabolic effects of oxygen breathing. The reduction in heart rate and cardiac index and the increase in arterial blood pressure in patients with coronary artery disease is in accord with previous reports.6–8 Data on changes in coronary circulation and myocardial oxygen and lactate metabolism in single subjects is presented in figures 1 and 2. Oxygen breathing caused a decrease in coronary sinus blood flow both in subjects with normal coronary arteries (from 158 ± 11 to 131 ± 13 ml/min) and coronary artery disease (151 ± 14 to 138 ± 14 ml/min) by increasing left ventricular coronary resistance. The arterial pO₂ rose to over 400 mm

Figure 1

Changes in coronary sinus blood flow, coronary resistance, and coronary sinus oxygen content during oxygen breathing in subjects with normal coronary arteries (open circles) and subjects with coronary artery disease (solid circles). Abbreviations: = coronary artery disease; normal = subjects with normal coronary arteries; I = standard error of the mean.

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Hemodynamic and Metabolic Effects of Oxygen Breathing

Table 2

<table>
<thead>
<tr>
<th>HR (beats/min)</th>
<th>MABP (mm Hg)</th>
<th>CI (liters/min/m²)</th>
<th>CSBF (ml/min)</th>
<th>LV CR (mm Hg/ml/min)</th>
<th>A pO₂ (mm Hg)</th>
<th>CS pO₂ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Air</strong></td>
<td>79 ± 10</td>
<td>106 ± 6</td>
<td>3.6 ± 0.3</td>
<td>158 ± 11</td>
<td>0.68 ± 0.03</td>
<td>77 ± 3</td>
</tr>
<tr>
<td><strong>O₂</strong></td>
<td>72 ± 7</td>
<td>107 ± 5</td>
<td>3.2 ± 0.4</td>
<td>131 ± 13</td>
<td>0.85 ± 0.06</td>
<td>425 ± 43</td>
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<td><strong>P</strong></td>
<td>0.01–0.05</td>
<td>NS</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
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</tbody>
</table>

**Subjects with normal coronary arteries (N = 6)**

**Subjects with coronary artery disease (N = 9)**

<table>
<thead>
<tr>
<th>HR (beats/min)</th>
<th>MABP (mm Hg)</th>
<th>CI (liters/min/m²)</th>
<th>CSBF (ml/min)</th>
<th>LV CR (mm Hg/ml/min)</th>
<th>A pO₂ (mm Hg)</th>
<th>CS pO₂ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Air</strong></td>
<td>75 ± 5</td>
<td>93 ± 9</td>
<td>2.9 ± 0.1</td>
<td>151 ± 14</td>
<td>0.65 ± 0.06</td>
<td>75 ± 2</td>
</tr>
<tr>
<td><strong>O₂</strong></td>
<td>69 ± 5</td>
<td>99 ± 4</td>
<td>2.6 ± 0.1</td>
<td>138 ± 14</td>
<td>0.79 ± 0.07</td>
<td>403 ± 49</td>
</tr>
<tr>
<td><strong>P</strong></td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
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</tbody>
</table>

Abbreviations: HR = heart rate; MABP = mean arterial blood pressure; CI = cardiac index; CSBF = coronary sinus blood flow; LV CR = left ventricular coronary resistance; A pO₂ = arterial oxygen tension; CS pO₂ = coronary sinus oxygen tension; A O₂ cont = arterial oxygen content; CS O₂ cont = coronary sinus oxygen content; A-CS O₂ diff = coronary arteriovenous oxygen difference; LV O₂ cons = left ventricular oxygen consumption; A L = arterial lactate concentration; CS L = coronary sinus lactate concentration; Myoc lact ext = myocardial lactate extraction.

Hg, on the average, in both groups. The coronary sinus pO₂ increased in both groups. The coronary arteriovenous oxygen difference fell slightly in the coronary group. Left ventricular oxygen consumption decreased in both groups from 21.5 ± 2.1 to 18.2 ± 2.4 and from 19.9 ± 2.0 to 16.7 ± 1.7 ml/min, respectively. Myocardial lactate extraction (%)
increased in both groups. In four patients oxygen breathing reverted myocardial lactate production to lactate extraction.

Discussion

In dogs the coronary sinus drains 75-95% of the left coronary arterial inflow, and this proportion is reasonably constant under various hemodynamic conditions. Inflow-outflow studies in man are not available. However, Hood found in postmortem studies that 96% of left ventricular veins 1 mm in diameter drain into the coronary sinus with an approximately 15% admixture from the right ventricle near the ostium of the coronary sinus. It appears justifiable, therefore, to accept coronary sinus blood flow as representative of left ventricular perfusion.

A reduction in coronary blood flow and an increase in coronary resistance was also found in dogs breathing normo- or hyperbaric oxygen. These changes do not represent a simple autoregulatory adjustment of the coronary bed to the increase in arterial oxygen tension, since they are associated with a reduction in myocardial oxygen consumption. This reduction, found also in dogs breathing oxygen, is probably secondary to a reduction in heart rate and possibly other factors. Myocardial oxygen consumption did not fall in patients breathing oxygen when the heart rate was fixed by pacing. Similarly, myocardial oxygen was not reduced in dogs breathing oxygen when the heart rate and tension-time index were kept constant by bilateral vagotomy and blockage of adrenergic alpha- and beta-receptors.

Previous studies found either no change in myocardial lactate extraction during oxygen breathing in patients with coronary artery disease or normal coronary arteries or a reduction in patients with severe triple-vessel disease, whereas in the present study an increase in the extraction was found in both groups. The cause of the discrepancy is not known.

The reversal of myocardial lactate production to extraction in three patients with severe disease of all major coronary arteries and one patient with disease of two arteries and severe aortic stenosis indicates that oxygen breathing diminished the discrepancy between oxygen demand and oxygen supply in the left ventricle. This could be due to an increase in oxygen supply and/or to a reduction in oxygen demand.

Further studies are necessary before a more definite conclusion on the role of oxygen breathing in myocardial ischemia is possible.

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