Effects of Beta-Adrenergic Blockade
(Propranolol) on Left Ventricular
Hemodynamics and the Electrocardiogram
During Exercise-Induced Angina Pectoris

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J. WILLIAM COX, M.D., PH.D.

SUMMARY
The effects of intravenous propranolol were studied in nine patients with ischemic
heart disease during cardiac catheterization. Values were obtained at rest and during
exercise before and after propranolol. A work load known to produce angina and signifi-
cant ST depression was selected. Pressures were monitored during exercise and corre-
lated with electrocardiographic changes and appearance of angina. At rest and exercise,
propranolol caused a decrease in heart rate, cardiac output, mean systolic ejection rate,
stroke volume, left ventricular systolic pressure, first derivative, and work. Left ven-
tricular end-diastolic pressure did not significantly change. Angina, which developed
in all nine patients during control exercise, did not appear in four after propranolol,
while ECG abnormalities were less marked in all cases. Comparison of exercise re-
sponses following propranolol in angina-free patients (four) with those developing
angina (five) disclosed a more pronounced negative inotropism in the angina-free
group. It is concluded that propranolol is beneficial in angina. Improvement derives
primarily from suppression of positive chronotropic and inotropic responses, which
are major determinants of myocardial oxygen consumption.

Additional Indexing Words:
Beta blockade Propranolol Coronary artery disease

Angina pectoris Hemodynamics

With the development of pharmacologic agents capable of blocking beta-
adrenergic receptor sites, interest in the effects of the sympathetic nervous system on
myocardial and coronary dynamics has intensified. The negative chronotropic action
of these drugs was recognized to be of clinical value in a variety of cardiac arrhythmias.1

Reduction of cardiac sympathetic activity by bilateral cervicothoracic sympathectomy2 or
stellate ganglion block3 has produced beneficial effects in patients with angina. On the
basis of these observations, a beta blocking agent, such as propranolol, was thought likely
to be useful in controlling myocardial oxygen utilization. This consideration has led to a
number of clinical trials in patients with angina pectoris.4,5 Preliminary observations, in
general, have shown an increased exercise tolerance together with reduction in the fre-
quency and severity of angina.

The hemodynamic effects of beta-adrenergic blockade (propranolol) in patients with
 coronary heart disease complicated by angina pectoris constitute the subject of this in-
vestigation. Special emphasis is placed on the
manner in which propranolol alters left ventricular function at rest as well as during exercise.

**Methods**

The study was performed on nine male patients, whose ages ranged from 38 to 59. A typical history of recurrent angina pectoris was obtained from each patient. One patient had a history and electrocardiographic findings of a previous myocardial infarction. The resting electrocardiogram was normal in three but all demonstrated typical ischemic ST-segment changes in the postexercise electrocardiogram. Patients not included were those with evidence of ventricular aneurysm, congestive heart failure, or valvular disease (table 1).

All patients were brought to the laboratory on the day prior to the study. The procedures were explained, and each subject was exercised in the supine position on a bicycle ergometer. A work load was selected (table 1) that produced typical anginal pain and ischemic ST-segment depression within 3 to 5 minutes. Patients were instructed to grade angina as 1+ (mild), 2+ (moderate), 3+ (moderately severe), or 4+ (severe).

Controlled measurements were made at rest and exercise in a manner described in detail in the previous report. Propranolol* (10 mg) was given intravenously. An interval of 20 minutes was allowed to lapse. Observations were then repeated, in a similar fashion at both rest and during exercise. Work loads were maintained at the same level. Values chosen to represent changes induced by exercise were those obtained at the time of onset of

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**Table 1**

**Clinical Details of Patients**

<table>
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<tr>
<th>Patient</th>
<th>Age, sex</th>
<th>Resting ECG</th>
<th>Exercise ECG</th>
<th>Angina after propranolol</th>
<th>Heart size</th>
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<td>Minimal cardiomegaly</td>
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<td>Nonspecific T-wave changes</td>
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<td>Angina decubitus CA = diffuse disease involving three major arteries</td>
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<td>Within normal limits</td>
<td>610</td>
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<td>Normal</td>
<td>CA = severe obstruction of R coronary artery. Moderate obstruction of L coronary artery</td>
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<tr>
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<td>Within normal limits</td>
<td>610</td>
<td>Pos. Yes</td>
<td>Normal</td>
<td>CA = isolated severe obstruction in anterior descending artery</td>
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</table>

*Kg-m = kilogram meter.

†CA = coronary arteriography.

*Circulation, Volume XXXVIII, August 1968*
### Table 2

**Hemodynamic Data in Patients (Group I) with Angina before and after Propranolol**

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<th>LVEDP</th>
<th>LV dp/dt</th>
<th>CI</th>
<th>SI</th>
<th>LVWI</th>
<th>SWI</th>
<th>S/D</th>
<th>BA</th>
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<th>S/D</th>
<th>PA</th>
<th>M</th>
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See table 3 for abbreviations.

*Angina delayed in appearance.
### Table 3

**Hemodynamic Data in Patients (Group II) with Angina before and No Angina after Propranolol**

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<th>LV dp/dt</th>
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**Abbreviations:** BSA = body surface area (m²), R = rest, E = exercise, Rp = rest after propranolol, Ep = exercise after propranolol, ECG = electrocardiogram, ST depr. = ST-segment depression (mm), angina = severity graded 1-4+, HR = heart rate (beats/min), LVEDP = left ventricular end-diastolic pressure (mm Hg), LVSP = left ventricular systolic pressure (mm Hg), LV dp/dt = left ventricular first derivative (mm Hg/sec), CI = cardiac index (L/min/m²), SI = stroke index (ml/min/m²), LWMI = left ventricular work index (g-m/beat/m²), SWI = stroke work index (g-m/beat/m²), BA = brachial artery pressure (mm Hg), PA = pulmonary artery pressure (mm Hg), S/D = systolic/diastolic, MSER = mean systolic ejection rate (ml/sec/m²).
angina. Following completion of these hemodynamic studies, coronary arteriography was performed by the Sones technique in six patients. All six had greater than 50% obstruction in at least one of the three major coronary arteries.

Results
The hemodynamic data at rest and during exercise, before and after propranolol are presented in tables 2 and 3. All nine patients developed angina during exercise prior to beta blockade. The patients were divided into two groups, depending on their pain response to exercise after propranolol. Group I, the angina group, were those patients in whom propranolol did not completely relieve angina. In these patients (five), exertional angina recurred but generally was delayed in appearance and less severe. Group II, the angina-free group were the remaining four patients in whom propranolol was totally effective in preventing exertional angina.

The differences between group I and group II were not statistically significant. However, both groups were small in number and an overlap of values may have resulted from the wide range of work loads imposed within each group. On the other hand, all observed changes following propranolol in the entire group were statistically significant ($P < 0.01$).

Electrocardiographic Changes
The electrocardiographic alterations were confined to ST-segment depressions, which were observed in all but two patients during the control exercise. A separate ergometry study prior to cardiac catheterization demonstrated ST-segment depression of 1.0 mm or greater in all subjects 2 minutes after exercise. After propranolol, both the exercise and postexercise electrocardiogram changes in the ST segment were less marked in all nine cases (fig. 1).

Systolic Pressure and Heart Rate
The response of heart rate and left ventricular systolic pressure to exercise prior to propranolol was quite variable, undoubtedly related to the wide range of work levels. The heart rate increased an average of 40 beats a minute (53%) and left ventricular systolic pressure rose from 141 to 172 mm Hg, a 22% increase.

Following propranolol, the resting heart rate and systolic pressure changed little in either group. Comparison of average values reached during exercise demonstrated a smaller increase in both heart rate and left ventricular systolic pressure in all patients studied. Propranolol modified the peak values reached to a slightly greater extent in the angina-free group (II) than in the angina group (I). The average peak heart rate and left ventricular systolic pressure reached by group II was 99 beats per minute and 158 mm Hg, respectively, whereas in group I, heart rate achieved was 107 beats per minute and left ventricular systolic pressure rose to 163 mm Hg (fig. 2).

**Figure 1**
Postexercise electrocardiograms following exercise-induced angina are demonstrated. ECGs on the left show typical ischemic ST-segment depression in all. After propranolol and exercise at the same work load and time interval, ST-segment depression is absent or less pronounced.

Circulation, Volume XXXVIII, August 1968
EFFECTS OF BETA-ADRENERGIC BLOCKADE

Propranolol produced small but significant reductions in left ventricular systolic pressure and heart rate.

Left Ventricular First Derivative (LV dp/dt)

Left ventricular first-derivative mean value at rest was 1,580 mm Hg per second and rose to 2,620 mm Hg per second with exercise. This represents a change of 60%. Propranolol resulted in a marked decline in LV dp/dt in both groups at rest and during exercise (fig. 3). Again, the postpropranolol exercise data demonstrated a distinct difference between groups I and II. When angina appeared, an overall increase of 55% in LV dp/dt was observed, although the absolute peak value reached was considerably less than control exercise levels. In those patients in whom angina was prevented, the average peak LV dp/dt attained during exercise was equal to control resting values. Moreover, the change in LV dp/dt induced by exercise in this group was minimal (+14%).

Left Ventricular End-Diastolic Pressure (LVEDP)

Resting values were normal in five patients and mildly elevated in the remaining four subjects. Prior to beta blockade, a precipitous marked increase of the LVEDP from 12 to 28 mm Hg was seen during exercise. Administration of propranolol had little effect on the mean levels of LVEDP at rest or during exercise, nor was a consistent pattern demonstrable. Within both groups the direction and

Figure 2

Propranolol produced small but significant reductions in left ventricular systolic pressure and heart rate.

Figure 3

With the administration of propranolol, a decrease in the left ventricular first derivative occurred at rest and during exercise. The reduction of the exercise derivative was more evident in the angina-free group.
The left ventricular end-diastolic pressure at rest was slightly elevated. Exercise produced a marked rise in end-diastolic pressure. Only minor changes resulted from beta blockade with propranolol.

magnitude of the individual response were quite variable (fig. 4).

Indices of Cardiac Output, Stroke Volume, Left Ventricular Work, and Stroke Work

The cardiac index mean value of 2.7 L/min/m² for nine patients in the resting state was within normal limits. However, of the nine patients, five were below normal levels. During exercise, an average increase in cardiac index to 4.2 L/min/m² was observed. In only one patient (O.T.), who had a previous myocardial infarction, did the cardiac index fail to rise. The stroke index was likewise normal (35 ml/m²) and rose slightly during exercise (37 ml/m²). Left ventricular work increased from 3,440 to 5,940 g-m/min/m², and stroke work increased from 46 to 53 g-m/beat/m². Propranolol resulted in a fall in all values, both at rest and during exercise. The most prominent changes appeared again in the angina-free group (II) exercise values, where a 30 to 40% reduction from control exercise values was observed. By comparison, the angina group (I) demonstrated only a 10 to 20% decline following propranolol (fig. 5).

Mean Systolic Ejection Rate (MSER)

Prior to propranolol, the MSER increased during exercise from an average value of 116
EFFECTS OF BETA-ADRENERGIC BLOCKADE

![Figure 6](http://circ.ahajournals.org)

During control exercise, mean systolic ejection rate increased normally. After propranolol, a fall in mean systolic ejection rate was observed at rest and during exercise. The greatest reduction was found in the angina-free group.

To 155 ml/sec/m². This represents a 34% increase, which is within the normal range. During the resting state, a fall in MSER followed propranolol in group I from 123 to 105 ml/sec/m² and in group II from 108 to 97 ml/sec/m². The response to exercise was also altered. After propranolol, a subnormal increase was observed in the angina patients (I) where MSER rose only 19%. An even more abnormal exercise response was noted in the angina-free patients (II). In those patients, the MSER fell from 97 to 93 ml/sec/m² (fig. 6).

Discussion

The circulatory effects of propranolol in normal subjects and in patients with mild left ventricular disease, at rest and during exercise, have been reported by several investigators. Propranolol administration was usually followed by reductions in cardiac output and left ventricular work of about 20% and a 10 to 15% fall in pulse rate and systolic pressure, during both resting and exercise states. Wolfson and associates observed the effects of propranolol in resting normal subjects as well as in patients with coronary artery disease. Similar hemodynamic alterations were found. In addition, they noted a reduced myocardial oxygen consumption, which they attributed to a reduction in heart rate and ventricular systolic force.

The present investigation showed comparable decreases in resting left ventricular systolic pressure, cardiac output, and left ventricular work while heart rate fell but slightly. In addition, propranolol caused a reduction in left ventricular first derivative (25%), but failed to alter appreciably left ventricular end-diastolic pressure or pulmonary artery pressure.

During exercise in normal subjects, Epstein and associates demonstrated that beta-adrenergic blockade produced a decline in heart rate (-21%), cardiac output (-16%), mean arterial pressure (-7%), and left ventricular work (-21%). In our group of patients with ischemic heart disease, propranolol altered the exercise response by reducing the left ventricular first derivative (-33%), cardiac output (-21%), left ventricular work (-30%), left ventricular systolic pressure (-7%), and heart rate (-11%), while increasing pulmonary artery pressure (+10%); a marked elevation in left ventricular end-diastolic pressure was noted both before and after propranolol. In short, propranolol did not alter the rise in the left ventricular end-diastolic pressure, which occurred during the control exercise state (fig. 7).

Angina, which developed in all nine patients during control exercise, did not appear in four after propranolol, although the exercise workload was identical. In the remaining five patients, angina was generally less intense, delayed in onset, and of shorter duration. The postexercise electrocardiogram demonstrated less ischemic ST depression in all nine cases after propranolol, regardless of the appearance of angina.

Following beta-adrenergic blockade, the response to exercise in the four angina-free patients was compared with five patients with angina and disclosed some differences. Angina corresponded with an increase in left
ventricular dp/dt and heart rate of 55% and 40%, respectively. The angina-free group had a diminished response to exercise, that is, left ventricular dp/dt increased 14% and heart rate 32%. Comparable differences were noted in mean systolic ejection rate and left ventricular work, but little change was observed in systolic pressure.

Recent evidence indicates that increased quantities of endogenous catecholamines are mobilized during acute myocardial ischemia. Moreover, Raab and Gigee and later Gazes and associates compared plasma catecholamine levels during exercise in normal subjects and in patients having coronary heart disease and found increased amounts in the latter group. Propranolol has been shown to block beta sympathetic activity by competitive inhibition. It is possible that the hemodynamic differences, between those of our patients who developed exertional angina and those who did not, are based on a degree of myocardial ischemia, which increases catecholamine levels beyond effective sympathetic blockade.

Although conclusive evidence is not yet at hand, numerous studies have indicated the value of propranolol and other beta blockers in the management of angina pectoris. Robin and associates compared the action of nitroglycerin and propranolol in a group of patients with coronary heart disease and observed significant differences. Nitroglycerin caused a reduction in left ventricular end-diastolic pressure and accelerated heart rate; propranolol evoked an increase in left ventricular end-diastolic pressure and slowed the heart rate. Cardiac output, left ventricular work, left ventricular first derivative, mean systolic ejection rate, and tension-time index declined following nitroglycerin as well as after propranolol.

Our observations differ somewhat in that propranolol failed to produce any significant change in left ventricular end-diastolic pressure at rest, and exercise induced an equivalent abnormal rise both before and after propranolol. Both drugs, nitroglycerin and propranolol, appear to produce their ameliorating effects on angina by decreasing left ventricular work, the rate of systolic pressure generation, and cardiac output. According to Ferrer and associates, the hemodynamic effects of nitroglycerin are primarily a consequence of diminished venous return, which results in a reduction of ventricular volume and end-diastolic pressure coincident with the development of tachycardia. Results reported by Najmi and associates differ from others. Patients with severe coronary heart disease, who developed marked elevations in pulmonary artery pressures during exercise, given nitroglycerin, demonstrated a significant increase in cardiac output and fall in pulmonary artery pressure. Their view is that nitroglycerin exerts its beneficial effects by shifting the left ventricular function curve to the left. On the other hand, Parker and associates studying the exercise effects after nitroglycerin in patients with coronary heart disease, showed no significant change in cardiac output, but a marked drop in left ventricular end-diastolic pressure. The authors attributed the beneficial effects of nitroglycerin to decreased myocardial oxygen needs through a reduction in ventricular volume.

In contrast to nitroglycerin, propranolol has been observed to increase heart volume. If left ventricular failure is significantly related to the development of angina pectoris, as suggested by some, it seems paradoxical.  

**Figure 7**

*Representative changes of heart rate, systolic pressure, and left ventricular first derivative during exercise following propranolol.*
that a drug which alters left ventricular function, in a manner comparable to that seen in typical heart failure, would afford any clinical benefit. The pharmacological basis for the observed improvement remains a matter of considerable speculation. Several investigators$^{25, 26}$ have proposed that sympathetic stimulation of catecholamines will increase the myocardial oxygen consumption out of proportion to the increment in left ventricular work, a so-called "oxygen wastage" effect. The salutary effect of propranolol may derive, not only from its reduction of left ventricular work, but, in addition, from inhibition of the "oxygen wastage."

Although myocardial oxygen consumption decreases following propranolol, other apparently less desirable effects on the coronary circulation have been demonstrated.$^{11, 27, 28}$ These include decreased coronary blood flow, widened A-V oxygen difference, and increased coronary vascular resistance. Recently Robin and associates$^{18}$ have studied myocardial metabolism in patients with coronary artery disease before and after propranolol. Their data indicate a negative reduction-oxidation potential or anaerobic metabolism in many of their patients at rest. After administration of propranolol, they found a decrease in the redox potential or further myocardial hypoxia. These findings are obviously inconsistent with the relief of chest pain and reduced electrocardiographic ischemia clinically observed after the drug. Further clarification of the metabolic changes produced by propranolol during angina would appear warranted.

Recent evidence points to the role of left ventricular first derivative, both as a reliable measure of myocardial contractility and as a major determinant of myocardial oxygen consumption.$^{29}$ Our findings indicate that the beneficial action of propranolol in angina derives predominantly from suppression of contractility (LV dp/dt) and, to a lesser extent, from its negative chronotropic action. Moreover, Moir and DeBra$^{30}$ have shown that the significant reduction in contractility achieved after propranolol administration results in decreased oxygen consumption, reduced systolic extravascular resistance to coronary flow, and a relative increase in endocardial perfusion. Studies conducted in this laboratory$^6$ have demonstrated the role of increased rate of pressure development in exercise-induced angina. When the rate of pressure development is depressed in the presence of coronary artery obstruction, a more satisfactory balance between nutrient requirements and myocardial work is obtained.

References

12. EPSTEIN, S. E., ROBINSON, B. F., KAMLER, R. L., AND BRAUNWALD, E.: Effects of beta adrenergic blockade on the cardiac response to max-
Effects of Beta-Adrenergic Blockade (Propranolol) on Left Ventricular Hemodynamics and the Electrocardiogram During Exercise-Induced Angina Pectoris

EDWARD M. DWYER, JR., LESLIE WIENER and J. WILLIAM COX

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