Effects of Propranolol on Left Ventricular Function in Normal Men

STEVEN PORT, M.D., FREDERICK R. COBB, M.D., AND ROBERT H. JONES, M.D.

SUMMARY In this study we assessed the effects of β-adrenergic blockade on cardiac function during exercise. First-pass radionuclide angiography was used to measure left ventricular ejection fraction (LVEF), cardiac output (CO), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and pulmonary transit time (PTT) in 12 normal young men. Studies were first performed at rest and during upright bicycle exercise after 2 days of oral administration of propranolol 320 mg/day. A minimum of 48 hours after cessation of propranolol, hemodynamic measurements were made at rest, during exercise at the same heart rate achieved on propranolol and during exercise at the same work load achieved on propranolol. Control studies showed a progressive increase in LVEF, SV and CO at increasing levels of exercise and a progressive decrease in ESV and PTT. After propranolol administration, heart rate, LVEF and CO were decreased at rest (p = 0.0001 for all values). During exercise, heart rate, systolic blood pressure, LVEF and CO were significantly lower (p = 0.0001 for all values), while ESV and PTT were significantly increased (p < 0.0001 and p = 0.002, respectively) compared with control exercise at the same work load. Compared with control exercise at comparable heart rates but different work loads, hemodynamic measurements were not significantly different on propranolol. These data suggest that the effects of propranolol on rest and exercise hemodynamics in healthy adults are primarily due to alterations in heart rate.

PROPRANOLOL is a β-adrenergic competitive antagonist commonly used in the management of patients with cardiovascular disease. Hemodynamic effects known to result from β-adrenergic blockade include decreases in heart rate, stroke volume (SV) and cardiac output (CO) at rest and during exercise, reduction of systolic arterial pressure during exercise and elevation of left ventricular end-diastolic pressure. The decrease in CO has been attributed to both the negative chronotropic and inotropic effects of the drug; however, the effects of β-adrenergic blockade on left ventricular volume and ejection fraction (LVEF) at rest and during upright exercise have not been adequately characterized.

The purpose of this study was to examine the effects of propranolol on rest and exercise measurements of left ventricular function in normal young men by radionuclide angiography (RNA), a safe, non-invasive, accurate method for measuring ejection fraction. In addition, ventricular volume, CO and pulmonary transit time (PTT) can be determined.

Methods

Twelve male volunteers, ages 21–29 years, were interviewed and examined to exclude the presence of any cardiovascular abnormalities. Trained athletes and persons who routinely performed more than moderate physical exercise were excluded. No subject took any drugs other than propranolol during the study period. The study protocol was reviewed and approved by the Human Experimentation Committee of the Duke University Medical Center. Written informed consent was obtained from all volunteers.

Indices of left ventricular function were initially measured by RNA at rest and during bicycle exercise while on propranolol. Control measurements were made after cessation of propranolol. This sequence was followed so that the maximum heart rate and work load achieved during exercise on propranolol could be duplicated during the control evaluation. Each subject took 80 mg of propranolol hydrochloride four times a day for 2 days. Approximately 2 hours after the last dose, the subjects reported to the laboratory for study. Blood pressure was recorded at rest and at 2-minute intervals during exercise using cuff manometric technique. Heart rate was monitored continuously with a telemetered, modified CM lead. Forty-eight hours or more after discontinuation of propranolol, measurements of left ventricular function were repeated at rest and at two levels of exercise; the first measurements were made at the maximum heart rate and the second measurements at the maximum work load achieved during exercise on propranolol. The times between the propranolol and control studies were 48 hours in one subject, 3 days in three subjects and 5–20 days in the rest (mean 6.3 ± 4.7 days).

In order to assess the degree of β blockade, the sensitivity to intravenous isoproterenol was determined on each study day by a modification of the technique described by Cleaveland et al. With the subject in the supine position, individual boluses of isoproterenol hydrochloride were administered intravenously through a running intravenous line and flushed through with 10 ml of normal saline. Doses of isoproterenol began at 1 μg when on propranolol and...
0.1 μg off propranolol. Step-wise increments in dosage were administered up to the dose necessary to increase the heart rate by 25 beats/min or (while on propranolol) to a maximum of 50 μg. Each bolus of isoproterenol was administered after heart rate and blood pressure returned to baseline. Heart rate was calculated 15 seconds to 2 minutes after the dose of isoproterenol by counting for 30 seconds. No adverse reactions to isoproterenol were encountered.

Rest and exercise RNA were performed with the subject in the erect position. After RNA at rest, exercise was performed on a bicycle ergometer (Fitron, Lumex, Inc.). Work load was measured in kilopond-meters per minute (kpm/min). When studied on propranolol, subjects began exercise at a work load of 300 kpm/min. After 1 minute at 300 kpm/min, the work load was progressively increased at 2-minute intervals to a final work load of 1000 kpm/min or until fatigue precluded further exercise. At peak exercise, the heart rate and work load for each subject were noted and RNA was repeated. On the day of the control study, a resting RNA was obtained and followed by the identical exercise protocol performed while on propranolol. Exercise RNA was performed twice, first at or as close as possible to the heart rate achieved at peak exercise while on propranolol (exercise 1) and second at the peak work load achieved on propranolol (exercise 2).

RNA was performed from an anterior projection using a Baird-Atomic System Seventy-seven multicrystal gamma camera equipped with a 1-inch, parallel-hole collimator. Ten millicuries of technetium-99m pertechnetate were used for each of the three control injections, and 15 mCi were used for each of the two injections on propranolol. Each subject received 30 mCi on each study day, a total of 60 mCi for the entire study. Details of the technique have been published. A 1-inch, 20-gauge Teflon cannula was introduced into an external jugular vein after anesthesia with 1% xylocaine. The radioisotope was dissolved in less than 1 ml of normal saline and flushed in as a bolus with 10–20 ml of saline. Precordial counts were recorded in binary form at 50-msec intervals for a 1-minute period.

**Data Collection and Analysis**

All RNA data were stored on magnetic disks and subsequently transferred to magnetic tape for permanent storage. Radionuclide data were processed using the computer and software of the Baird-Atomic System Seventy-seven after correction for background measured just before injection and for detector non-uniformity and electronic dead time count loss of the instrument. Details of data processing have been published. A curve representing count changes within the left ventricle was used to identify the times of end-systole and end-diastole of individual beats. Sequential addition of data from three to six beats starting at end-diastole produced an average or representative cardiac cycle. LVEF was calculated from the background-corrected representative cycle as ED counts – ES counts/ED counts × 100, where ED = end-diastole and ES = end-systole. A computer program outlined the end-diastolic and end-systolic perimeters at the 21% isocount contour of the end-diastolic image. Previous imaging of elliptical phantoms filled with 5 mCi of technetium-99m pertechnetate in water showed that the 21% count level corresponded most closely to the phantom border. The aortic valve plane was identified from dynamic images and by isolation of the zone demarcating alternate count increases and decreases during diastole and systole. The area of the end-diastolic image was obtained by planimetry and the length measured using a sonic digitizing device (Graph-Pen) coupled to a PDP-11/45 computer. The left ventricular end-diastolic volume (EDV) was calculated by the area-length method of Sandler and Dodge. Measurement of EDV and LVEF permitted calculation of left ventricular end-systolic volume (ESV), SV and CO.

A previously described computer program for analysis of time-activity curves in areas of interest was used to determine PTT, which was defined as the mean transit time of the curve recorded over the left atrium minus the mean transit time of the curve recorded over the pulmonary artery.

Regional left ventricular function was assessed by analysis of wall motion using both the cinematic display of the representative cycle and the static display of the superimposed end-diastolic and end-systolic perimeters. In addition, a regional ejection fraction image was generated by subtracting end-systolic counts from end-diastolic counts and dividing by the end-diastolic counts for each crystal in the left ventricular image. Differences in regional function were displayed using a 16-color coded image, each color representing approximately a 6% difference in regional ejection fraction.

**Validity Studies**

The radionuclide measurements made in this study have been validated by previous studies (unpublished data) in this laboratory. RNA determinations of CO and SV were compared with measurements made by simultaneous indocyanine green dye-dilution curves in 18 healthy young adults at rest and exercise. These data showed a close correlation (r = 0.94 for CO and 0.89 for SV) for COs of 4–17 l/min. RNA measurements of ejection fraction and EDV were compared with those made by contrast ventriculography and the correlation coefficient was 0.89 for both sets of measurements. A comparison of minor-axis dimensions at end-diastole in 20 dogs using implanted sonar crystals and RNA revealed a correlation coefficient of 0.82.

The mean variability in ejection fraction was 4 ± 4% at rest and 3 ± 2% (SD) during exercise in 10 normal subjects studied on two different days. The variability of EDV was 10 ± 10 ml (SD) both at rest and during exercise.

In the present study, all data were analyzed by
paired t test, and differences with p values < 0.05 were considered significant.

Results

Isoproterenol Sensitivity

On the day of the control study, the mean maximum dose of isoproterenol administered was 3.0 ± 1.2 μg (SD), which resulted in a mean increase in heart rate of 25 ± 4.7 beats/min. While on propranolol, 11 of the 12 subjects received 50 μg of isoproterenol and had a mean increase in heart rate of 5.5 ± 4.8 beats/min. One subject received 20 μg and had an increase of 26 beats/min. In all subjects, the isoproterenol sensitivity was reduced at least 12-fold on propranolol.

The mean ± SD for all hemodynamic parameters at rest and exercise both on and off propranolol are shown in table 1.

Left Ventricular Function at Rest

The mean heart rate and systolic blood pressure are shown in figure 1. Propranolol administration decreased the resting heart rate from 64.8 ± 10.9 beats/min (range 48–90 beats/min) to 49.2 ± 6.8 beats/min (range 40–62 beats/min) (p < 0.0001). Systolic (mean 128.8 ± 12.1 mm Hg, range 114–152 mm Hg) and diastolic (mean 78.0 ± 6.1 mm Hg) blood pressures were unchanged from control (mean 123.6 ± 9.8 mm Hg, range 110–138 mm Hg and 79.0 ± 5.7 mm Hg, respectively). Figure 2 shows the individual values for LVEF, cardiac index, EDV and SV at rest. Eight of the 12 subjects had significant...

TABLE 1. Hemodynamic Parameters

<table>
<thead>
<tr>
<th></th>
<th>Heart rate (beats/min)</th>
<th>Systolic blood pressure (mm Hg)</th>
<th>LVEF (%)</th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
<th>SV (ml)</th>
<th>CO (l/min)</th>
<th>CI (l/min/m²)</th>
<th>PTT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Rest</td>
<td>64.8 ± 10.9</td>
<td>128.8 ± 12.1</td>
<td>65.3 ± 8.0</td>
<td>129.5 ± 20.9</td>
<td>45.1 ± 12.7</td>
<td>84.4 ± 15.6</td>
<td>5.5 ± 1.3</td>
<td>3.0 ± 0.8</td>
<td>7.2 ± 1.6</td>
</tr>
<tr>
<td>Exercise 1</td>
<td>118.9 ± 9.7</td>
<td>159.2 ± 17.2</td>
<td>76.3 ± 6.0</td>
<td>150.0 ± 25.5</td>
<td>35.7 ± 11.6</td>
<td>114.4 ± 21.4</td>
<td>13.6 ± 2.7</td>
<td>7.5 ± 1.5</td>
<td>3.4 ± 0.6</td>
</tr>
<tr>
<td>Exercise 2</td>
<td>166.0 ± 6.7</td>
<td>188.7 ± 11.6</td>
<td>86.3 ± 5.0</td>
<td>143.4 ± 20.1</td>
<td>19.2 ± 6.8</td>
<td>124.2 ± 20.7</td>
<td>20.7 ± 3.6</td>
<td>11.3 ± 2.5</td>
<td>2.5 ± 0.5</td>
</tr>
<tr>
<td>Propranolol Rest</td>
<td>49.2 ± 6.8</td>
<td>123.6 ± 9.8</td>
<td>57.3 ± 7.2</td>
<td>142.5 ± 22.0</td>
<td>58.8 ± 11.0</td>
<td>83.7 ± 19.4</td>
<td>4.0 ± 0.6</td>
<td>2.2 ± 0.3</td>
<td>8.2 ± 0.6</td>
</tr>
<tr>
<td>Exercise</td>
<td>119.2 ± 7.6</td>
<td>154.3 ± 13.7</td>
<td>74.8 ± 5.0</td>
<td>155.3 ± 20.0</td>
<td>38.4 ± 9.6</td>
<td>116.1 ± 16.0</td>
<td>13.8 ± 1.9</td>
<td>7.6 ± 1.1</td>
<td>3.3 ± 0.6</td>
</tr>
</tbody>
</table>

All values are means ± SD. Except where indicated, all changes from rest to exercise or from exercise 1 to exercise 2 are statistically significant (p < 0.05).
*p = NS from exercise 1 to exercise 2.
†p = NS from rest to exercise.
Abbreviations: LVEF = left ventricular ejection fraction; EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; CO = cardiac output; CI = cardiac index; PTT = pulmonary transit time.

![Figure 1. Change in mean heart rate (HR) and mean systolic blood pressure (BP) at rest and exercise before and after oral propranolol. HR and BP increase progressively during control exercise. After propranolol, HR is lower at rest (p < 0.0001), while at exercise to the same work load, both HR (p = 0.0001) and BP (p = 0.0001) are lower. Values are mean ± SD.](http://circ.ahajournals.org/)
decreases in LVEF on propranolol ranging from 8–21%. Three subjects had insignificant changes, two with decreases of 3% and 4% and one with a 1% increase, while the remaining subject had no change. The mean resting LVEF of 57.3 ± 8.2% on propranolol was 8% lower than control (p = 0.0001). Cardiac index decreased from 3.0 ± 0.8 l/min/m² to 2.2 ± 0.3 l/min/m² on propranolol (p = 0.002). One subject had a much higher control resting cardiac index than the rest of the group; propranolol decreased his cardiac index markedly, suggesting a high basal sympathetic tone. The decrease in cardiac index on propranolol remains significant (p = 0.0002) when that subject is excluded.

The EDV and ESV increased on propranolol (p = 0.02 and 0.0003, respectively), but the SV was unchanged. The PTT was prolonged on propranolol from 7.2 ± 1.6 seconds to 8.2 ± 2.0 seconds (p = 0.05), which further reflects the decrease in CO.

Left Ventricular Function During Exercise: Same Work Load

All but one subject reached the same peak work load on propranolol as reached during control exercise. One subject reached 900 kpm/min on and 1000 kpm/min off propranolol. There was no significant difference in the duration of exercise on and off propranolol. Figure 1 is a summary of changes in mean heart rate and mean systolic blood pressure with exercise. The mean maximum heart rate was 166 ± 6.7 beats/min off and 119.2 ± 7.6 beats/min on propranolol (p = 0.0001). The mean systolic blood pressure was also markedly decreased after β blockade, from 154.3 ± 13.7 mm Hg to 118.7 ± 11.6 mm Hg (p = 0.0001).

The mean LVEF during exercise to maximum work load on propranolol was 74.8 ± 5.0%, 11% lower than the mean LVEF during control exercise at the same work load (p = 0.0001). The changes in LVEF with exercise are shown in figure 3. During the control study, the LVEF at peak exercise in all subjects was 11–31% higher than at rest, and the mean increase was 21.0 ± 6.0% (p = 0.001). As during control exercise, all subjects had a significantly increased ejection fraction during exercise on propranolol, and the mean increase was 17.0 ± 4%, only slightly less than the control increase (p = 0.03). However, after propranolol, 11 of the 12 subjects had a significantly lower LVEF and one had a 3% lower LVEF (fig. 4).

The cardiac index on propranolol was lower in 11 of the 12 subjects and unchanged in one. The latter subject markedly increased his EDV and SV during exer-
Responses of left ventricular ejection fraction (LVEF) to exercise. During control exercise, all subjects but one show an increase in LVEF from rest to the first level of exercise. All but two show subsequent additional increases in LVEF at the second level of exercise. After propranolol, LVEF increases with exercise in all subjects ($p < 0.001$) despite β blockade.

Figure 3.

Hemodynamic parameters during exercise at the same work load before and after propranolol. Left ventricular ejection fraction (LVEF) and cardiac index (CI) are reduced after propranolol. Although individually variable, mean end-diastolic volume (EDV) and stroke volume (SV) are unchanged.

Figure 4.
However, after β blockade, the ESV was significantly larger both at rest and exercise. The PTT was prolonged by propranolol (p = 0.002), but the normal decrease in PTT with exercise was unchanged (−4.7 seconds off, −4.9 seconds on propranolol).

**Left Ventricular Function at Exercise: Same Heart Rate**

The mean heart rate during exercise on propranolol was 119.2 ± 7.6 beats/min (range 104–132 beats/min), and the mean heart rate at the first level of control exercise was 118.9 ± 9.7 beats/min (range 100–132 beats/min) (p = NS). The average work load that produced that heart rate was 616.7 ± 83.5 kpm/min during control and 983.3 ± 38.9 kpm/min on propranolol (p < 0.0001). The mean systolic blood pressure during control (159.2 ± 17.2 mm Hg, range 136–190 mm Hg) was the same on propranolol at the same heart rate (154.3 ± 13.7 mm Hg, range 130–174 mm Hg) (fig. 1). All but one subject increased the control ejection fraction from rest to the first level of exercise (fig. 3). One subject showed a significant decrease in control LVEF, from a resting value of 77% to 72% at a heart rate of 116 beats/min, but subsequently increased his LVEF to 94% at peak exercise. On propranolol, the mean LVEF was 76.3 ± 6% compared with 74.8 ± 5% off propranolol (p = NS) during exercise to a similar heart rate (fig. 6). The mean cardiac index was 7.6 ± 1.1 l/min/m² on propranolol compared with a control cardiac index of 7.5 ± 1.1 l/min/m² (p = NS) during exercise to the same heart rate (fig. 5). Similarly, EDV, SV, ESV and PTT were unchanged during exercise to the same heart rate after β blockade.

**Regional Left Ventricular Function**

During the control studies, regional left ventricular function was normal in all subjects. After propranolol administration no abnormalities of wall motion or regional ejection fraction were noted.

**Discussion**

Propranolol is widely used for the management of cardiovascular illness. Many of its hemodynamic effects have been documented. However, the lack of accurate methods for noninvasive assessment of left ventricular function has precluded adequate characterization of the hemodynamic effects of propranolol during exercise, especially in the upright position.

In the present study, ventricular function at rest and during upright bicycle exercise was evaluated using RNA. Indices of ventricular function that can be measured with this technique include LVEF, EDV, ESV, CO and interchamber transit times. Studies in this laboratory have established the accuracy (Scholz PM: unpublished data) and reproducibility (Upton MT: unpublished data) of these measurements. Accuracy of LVEF measurements by this technique has been reported by others. Measurement of CO and left ventricular volume have been reported using gated radionuclide imaging. Furthermore, the measurements of CO and SV at rest and exercise as measured by RNA in this study were comparable to those reported from other laboratories using Fick, dye dilution and contrast angiographic techniques.

At rest, propranolol administration produced significant reductions in heart rate, LVEF and cardiac index, while ESV and PTT increased. Because SV was unchanged, the reduction in cardiac index was
primarily caused by the reduction in heart rate. During the control exercise, heart rate, systolic blood pressure, LVEF, SV and CO increased progressively. PTT and ESV decreased with exercise. The pattern of these hemodynamic responses to exercise was unchanged during β-adrenergic blockade with propranolol. Compared with control exercise at the same work load, however, heart rate, systolic blood pressure, LVEF and cardiac index were all significantly lower, while ESV and PTT were increased on propranolol. As at rest, the reduction in cardiac index was due to a reduction in heart rate, as SV was unchanged. When compared with control exercise at comparable heart rates, systolic blood pressure, LVEF, SV, CO, cardiac index, ESV and PTT were not different on propranolol.

The mean LVEF on propranolol was 8% lower at rest and 11% lower compared with control exercise to the same work load (fig. 7). The reduction in LVEF at rest ranged from 8–22% in 10 of the 12 subjects, while two showed no change. The reduction in LVEF compared with control exercise to the same work load ranged from 3–20%. In a recent report of normal subjects given intravenous propranolol, Erhardt et al., using gated RNA, reported a 4% decrease in resting LVEF and a 12% decrease in exercise LVEF at the same work load. With intravenous propranolol and equilibrium RNA in patients with coronary artery disease, Borer et al. reported small but significant declines in resting and exercise ejection fractions.

Marshall et al. did not report a significant change in resting LVEF administering oral propranolol in doses of 80–240 mg/day in patients with coronary artery disease. The differences among these studies may result from both the differences in populations and the varying degrees of β blockade that are achieved with different doses and routes of administration. The degree of blockade was not assessed in the above studies, which makes direct comparison of results difficult.

Studies of the effect of intravenous propranolol on other indices of contractility have shown significant reductions in left ventricular dp/dt², and a downward shift of the force-velocity relationship and support the findings in this study. In the present study, the reduction in LVEF at rest could be caused either by a depression of intrinsic contractility or by the reduction in heart rate. Without a control study at the resting heart rate produced by propranolol, that question cannot be resolved. However, during exercise, the depression of LVEF by propranolol appears to be due to the depression of heart rate rather than to an independent effect on contractility. LVEF during exercise on propranolol was identical to LVEF during control exercise to the same heart rate (fig. 6). In addition, the increases in LVEF and SV with exercise on propranolol were identical to those off propranolol. Furthermore, at the same heart rate, SV, ESV, CO and PTT were also the same both on and off propranolol.

These findings contrast with those of Erhardt et al., who examined the effects of intravenous propranolol on left ventricular function in nine normal subjects at rest and during supine exercise and found that at the same heart rate LVEF was significantly lower on propranolol. The explanation for these contrasting results is not known, although the method of propranolol administration, position during exercise and technique of RNA were different.

In contrast to the results reported by Helfant et al., no abnormalities of regional left ventricular function were detected after propranolol administration either at rest or during exercise.

It is interesting to speculate on the mechanism by which CO and ejection fraction increase during exercise despite sympathetic blockade. Heart rate increased by 145% with exercise after β blockade, presumably due to withdrawal of parasympathetic tone, accounting for part of the increase in CO. LVEF and SV also increased with exercise, and the magnitude of these increases was the same as that during control exercise. Hence, the increase in CO on propranolol is accounted for by a vagolytic increase in heart rate and a presumably nonsympathetically mediated increase in LVEF. How LVEF increases with exercise despite sympathetic blockade has not been explained. Because heart rate still increases, its intrinsic effect on left ventricular contractility may be partially responsible. Sonnenblick et al., in an attempt to resolve this question, studied four subjects during exercise while on propranolol and while the

![Figure 7](http://circ.ahajournals.org/)

**Figure 7.** Response of mean left ventricular ejection fraction (LVEF) to exercise plotted against work load. Note that at rest and with exercise to the same work load, the LVEF is significantly lower after propranolol.
heart rate was maintained at control levels by atrial pacing. They noted that the increase in contractility measured by a shift in the force-velocity relationship was blocked to the same degree as without pacing, so they dismissed heart rate as an important contributor to the increase in contractility. They speculated that the Frank-Starling mechanism was probably more important. In support of that hypothesis, Horwitz et al. in exercising dogs and Crawford et al. in normal subjects, showed that left ventricular end-diastolic dimensions were larger during exercise on propranolol. In the present study, EDV was significantly larger at rest on propranolol, while during exercise, six of the 12 subjects had significantly higher EDVs on propranolol; however, neither the mean EDV during exercise nor the change in EDV from rest to exercise was significantly larger after propranolol administration. These findings are similar to those of Sorensen et al. who, using gated RNA and a count-proportional volume estimation, did not demonstrate a significant change in EDV during supine exercise at 400–1000 kpm/min after intravenous propranolol. However, both these RNA methods of measuring EDV may be too variable to detect small changes in EDV in a small study group. The changes demonstrated by Horwitz et al. and by Crawford et al. were very small, although significant.

An alternate hypothesis that may explain the ability of LVEF to increase despite marked suppression of heart rate is that the inotropic and chronotropic receptor respond differently to propranolol. Robinson et al. and Boudoulas et al. have suggested that the inotropic effect of propranolol persists for a much shorter time than the chronotropic effect when inotropic is measured by systolic time intervals. That hypothesis would not explain the findings in this study, however, because subjects exercised no later than 2 hours after propranolol cessation, a time when both inotropic and chronotropic inhibition were maximal in both Robinson’s and Boudoulas’ studies. Because propranolol is a competitive antagonist, the inotropic inhibition may be overcome during the sympathetic discharge of vigorous exercise. However, that would presuppose a differential sensitivity of chronotropic and inotropic receptors to propranolol, because the heart rate response to isoproterenol suggested maximum or near-maximum chronotropic inhibition. A differential sensitivity of the chronotropic and inotropic effects of propranolol has not been demonstrated.

In summary, propranolol has been shown to cause reductions in heart rate, LVEF and cardiac index and increases in EDV, ESV and PTT at rest. During exercise to comparable work loads, heart rate, systolic blood pressure, LVEF, and cardiac index are reduced by propranolol while ESV and PTT are increased. The reductions in cardiac index and LVEF appear to be dependent on the reduction in heart rate. The normal increases in LVEF and cardiac index are unchanged by propranolol. The mechanism by which LVEF increases despite sympathetic inhibition is unknown.

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