Effects of Ouabain on the Left Ventricular Response to Exercise in Patients with Angina Pectoris


SUMMARY
The response of the left ventricle to a level of supine bicycle exercise that induced angina, and the effects of ouabain (0.01 mg/kg) on this response were evaluated in 14 patients with coronary arterial disease. Before administration of ouabain, exercise was associated with depressed pumping performance of the left ventricle in four patients: stroke work fell with exercise while left ventricular end-diastolic pressure (LVEDP) increased. In five patients left ventricular (LV) performance was not frankly depressed, but nevertheless was abnormal: stroke work increased, but was accompanied by an inordinately large rise in LVEDP. In the remaining five patients LV function was essentially normal. Ouabain improved LV performance at rest in only a minority of patients, but during the stress of exercise, LV hemodynamics were improved by ouabain in 12 of the 14 patients. Five patients, however, continued to show either depressed or abnormal function with exercise after they were given ouabain. As judged by the relationship of LVEDP to LV peak dp/dt, left ventricular contractility was increased by ouabain in most patients both at rest and during exercise. Despite its beneficial effects on left ventricular performance, ouabain did not consistently alter either exercise tolerance or the LV tension-time index and pressure-rate product at which angina occurred.

Additional Indexing Words:
Coronary arterial disease
Cardiac glycosides
Coronary arteriography
Left ventricular end-diastolic pressure
Ventricular function
Exercise capacity
Left ventricular stroke-work
Myocardial ischemia
Tension-time index

Previous investigations1-6 have demonstrated that most patients with ischemic heart disease respond to exercise with an abnormal increase in left ventricular end-diastolic pressure (LVEDP), and this has been interpreted as a manifestation of left ventricular (LV) failure.5,6 We undertook the present study to determine whether LV function invariably deteriorates when angina pectoris is induced by exercise in patients with coronary arterial disease, and whether LV hemodynamics and exercise tolerance can be favorably altered by the administration of a cardiac glycoside. In addition, we attempted to correlate the hemodynamic data with the cineangiographic appearances of the coronary arteries and left ventricle.

Methods
Thirteen men and one woman, aged 30 to 60 years (average, 46 years), were studied. All were limited by typical angina pectoris, and eight had a history of previous myocardial infarction. Three patients also had mild aortic stenosis with peak transvalvular gradients of 4, 10, and 12 mm Hg, respectively, and one of these three had mild aortic regurgitation as well. One patient was receiving methyldopa for systemic arterial hypertension and when studied was normotensive. Two patients were receiving digoxin when admitted to

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Table 1

Summary of Hemodynamic Findings in 14 Patients

<table>
<thead>
<tr>
<th></th>
<th>Rest (Legs elevated)</th>
<th>Exercise (At angina)</th>
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<tr>
<td></td>
<td>mean range</td>
<td>mean range</td>
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<tr>
<td>Left ventricular end-diastolic pressure (mm Hg)</td>
<td></td>
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<tr>
<td>Before ouabain</td>
<td>17.2 11-28</td>
<td>24.4 12-43</td>
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<tr>
<td>After ouabain</td>
<td>15.6 9-23</td>
<td>20.4 9-40</td>
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<tr>
<td>Cardiac index (liter/min/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>3.09 2.2-4.7</td>
<td>4.28 2.9-6.2</td>
</tr>
<tr>
<td>After ouabain</td>
<td>3.09 2.2-4.5</td>
<td>4.63 3.7-6.4</td>
</tr>
<tr>
<td>Stroke-volume index (ml/m²)</td>
<td></td>
<td></td>
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<tr>
<td>Before ouabain</td>
<td>43.3 30-55</td>
<td>41.4 25-53</td>
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<tr>
<td>After ouabain</td>
<td>45.7 33-59</td>
<td>46.9 34-58</td>
</tr>
<tr>
<td>Stroke-work index (g/m²)</td>
<td></td>
<td></td>
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<tr>
<td>Before ouabain</td>
<td>55.7 32-89</td>
<td>57.1 35-90</td>
</tr>
<tr>
<td>After ouabain</td>
<td>63.4 42-95</td>
<td>70.1 47-114</td>
</tr>
<tr>
<td>Mean systolic ejection rate index (ml/sec/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>140 97-181</td>
<td>155 96-212</td>
</tr>
<tr>
<td>After ouabain</td>
<td>154 121-222</td>
<td>177 124-243</td>
</tr>
<tr>
<td>Left ventricular peak dp/dt (mm Hg/sec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>1770 960-2660</td>
<td>2756 1590-6490</td>
</tr>
<tr>
<td>After ouabain</td>
<td>2146 1200-3730</td>
<td>2988 1830-6530</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>73 54-97</td>
<td>104 83-128</td>
</tr>
<tr>
<td>After ouabain</td>
<td>68 52-90</td>
<td>100 85-115</td>
</tr>
<tr>
<td>Systemic arterial mean pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>101 75-126</td>
<td>114 91-147</td>
</tr>
<tr>
<td>After ouabain</td>
<td>102 79-121</td>
<td>116 101-148</td>
</tr>
<tr>
<td>Tension-time index (mm Hg-sec/min)</td>
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<td></td>
</tr>
<tr>
<td>Before ouabain</td>
<td>2733 1740-4660</td>
<td>3800 2750-5430</td>
</tr>
<tr>
<td>After ouabain</td>
<td>2566 1780-3790</td>
<td>3791 2630-5300</td>
</tr>
<tr>
<td>Pressure-rate product (mm Hg/min × 10³)</td>
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</tr>
<tr>
<td>Before ouabain</td>
<td>9.89 6.40-16.80</td>
<td>15.88 12.00-23.30</td>
</tr>
<tr>
<td>After ouabain</td>
<td>9.73 6.50-15.40</td>
<td>15.66 11.50-22.40</td>
</tr>
</tbody>
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NS = P > 0.05.

the hospital; in each the drug was discontinued 2 weeks before catheterization. No patient had clinical evidence of cardiac failure at the time of study. The average cardiothoracic ratio, measured from standard posteroanterior chest roentgenograms, was 0.47 (range, 0.38–0.55); in two of the 14 patients this ratio exceeded 0.50. Mean pulmonary arterial pressure was normal (<21 mm Hg) in all patients and averaged 15 mm Hg; mean pulmonary arterial wedge pressure was also.
normal (<13 mm Hg) in the seven patients in whom it was measured, and averaged 9 mm Hg.

Before the study each patient exercised on the bicycle ergometer in the supine position one or more times in order to become acquainted with the procedure and to determine appropriate exercise workloads. Studies were performed with the patient fasting. Pentobarbital (100 mg) was given intramuscularly 1 hr before catheterization. Left ventricular pressure was obtained through a no. 7 Courand catheter, and brachial arterial pressure through a Courand needle. Pressures were measured with Statham strain-gauge transducers (P23Db series) set at midchest level, and were recorded with the patient resting in the supine position, after elevation of his feet onto the bicycle pedals, at the end of each minute of exercise, and when he experienced angina. During exercise, workload was increased at 3 to 5-min intervals. Initial workloads ranged from 180 to 660 ft-lb/min, and angina occurred at workloads of 180 to 1400 ft-lb/min. Cardiac output was measured by the dye-dilution technique with the patient at rest, with his feet elevated, at the end of each workload, and when angina occurred. Blood was withdrawn under sterile conditions and rein infused after each dye curve. After the control exercise, ouabain (0.01 mg/kg) was given intravenously over a 5-min period. Between 30 and 50 min later, the identical exercise protocol was repeated.

Stroke-volume index (ml/m²/s) was calculated by dividing cardiac index by heart rate, and left ventricular mean systolic ejection rate index (ml/sec/m²) by dividing stroke-volume index by systolic ejection time. Tension-time index (mm Hg-sec/min) was calculated as the product of heart rate, ejection time, and the mean left ventricular pressure during ejection (mean pressure was measured by planimetric integration), and the pressure-rate product (mm Hg/min) was calculated as the product of LV peak systolic pressure and heart rate. LV stroke-work index (LVSWI) was computed as follows:

\[
\text{LVSWI (g-m/m²)} = \frac{(\text{LVSP} - \text{LVEDP}) \times \text{SVI} \times 0.136}{S}
\]

where LVSP represents the mean LV pressure during ejection and SVI, the stroke-volume index. The maximal rate of rise of the left ventricular pressure pulse (LV peak dp/dt in mm Hg/sec) was measured directly from pressure tracings recorded at a paper speed of 200 mm/sec. Although dp/dt is measured most accurately with a catheter transducer, values obtained with a fluid-filled catheter and an external manometer show a high degree of correlation with those obtained with a catheter transducer. The statistical significance of differences was evaluated by Student's t-test, with the use of paired data where appropriate.

**Results**

The hemodynamic findings are summarized in table 1. Exercise values shown are those obtained at angina. Because angina occurred at different workloads after administration of ouabain in four patients, data obtained at the highest workload common to both the pre- and post-ouabain studies were also compared. The results were similar to the results found when data obtained at angina were analyzed.

**Left Ventricular End-Diastolic Pressure**

*Before Administration of Ouabain*

LVEDP averaged 12.7 mm Hg (range, 47

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*Figure 1*

Changes in LVEDP with exercise. In all patients LVEDP increased when legs were raised from the supine position (S) onto the pedals of the bicycle for control (C) measurements before exercise. In patient 13, as in most patients, LVEDP rose abruptly during the first minute of exercise and thereafter rose slowly until angina occurred (•). In patient 12 and in three others, LVEDP did not change, or increased by less than 3 mm Hg with exercise. Patient 6 was the only one who had a marked rise in LVEDP at the time of angina. In patient 5 LVEDP rose strikingly during the first minute of exercise and then fell as exercise was continued to the onset of angina.
5–22) when the patients were resting in the supine position, and was abnormally elevated (> 12 mm Hg) in eight of the 14 patients. LVEDP increased (average LVEDP, 17.2; range, 11–28 mm Hg) in each patient when his feet were raised onto the bicycle pedals. With exercise to the point of angina a further significant increase occurred (average LVEDP, 24.4; range, 12–43 mm Hg). In four of the 14 patients, however, LVEDP either remained the same during exercise or increased by less than 3 mm Hg. In 12 patients LVEDP was measured during exercise before angina developed. The average LVEDP was higher than at rest (22.1 vs. 17.7 mm Hg, \( P < 0.001 \)), but was not significantly different from the level present at angina (22.1 vs. 23.2 mm Hg). Thus, LVEDP was abnormally elevated in most patients at rest, and exertional angina was usually, but not always, accompanied by a further rise in LVEDP (fig. 1). When LVEDP did increase, the rise usually began with the onset of exercise and continued throughout the exercise period; an additional increase in LVEDP at the onset of angina was unusual. There was no correlation between the level of LVEDP at rest and the magnitude of its rise with exercise.

After Administration of Ouabain

LVEDP averaged 10.9 mm Hg (range, 5–19) when the patients were resting in the supine position, and was above 12 mm Hg in four of them. LVEDP again rose in every patient when the legs were elevated (average LVEDP, 15.6; range, 9–23 mm Hg). A further significant increase occurred with exercise (average LVEDP, 20.4; range, 9–40 mm Hg). In eight patients, however, LVEDP either remained the same during exercise or increased less than 3 mm Hg. In one additional patient LVEDP fell during exercise.

**Figure 2**

Effects of passive elevation of the legs on left ventricular hemodynamics before ouabain was given. Change in LVEDP is related to the changes that occurred in stroke-volume index (SVI), stroke-work index (SWI), and LV peak dp/dt when the patients' legs were raised onto the pedals of the bicycle ergometer. The same numbers are used to identify individual patients in the subsequent figures.

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When end-diastolic pressures before and after ouabain was administered were compared, no significant differences were found at rest. During exercise, however, LVEDP was significantly lower after ouabain was given (table 1).

**Cardiac Output, Stroke Volume, and Stroke Work**

Cardiac output increased with exercise both before and after ouabain was given (table 1). The increase in output was roughly proportional to the increase in heart rate, and thus stroke volume did not change significantly. LV stroke work did not change with exercise before ouabain was administered, but increased ($P < 0.05$) with exercise after the glycoside was given. Ouabain did not significantly alter cardiac output, stroke volume, or stroke work at rest, but during exercise each of these indices was significantly ($P < 0.01$) higher after the drug was given.

**Mean Systolic Ejection Rate**

Although stroke volume was essentially unchanged by exercise, systolic ejection period decreased, and, therefore, mean systolic ejection rate increased with exercise both before (average increase 11%; $P < 0.025$) and after (average increase 15%; $P < 0.01$) ouabain was given. Ouabain increased the average systolic ejection rate (table 1) both at rest (by 10%) and during exercise (by 14%), but only the latter change was significant ($P < 0.01$).

**LV Peak dp/dt**

$dp/dt$ increased ($P < 0.01$) with exercise in each patient both before and after administration of ouabain. Moreover, ouabain caused a significant ($P < 0.05$) increase in $dp/dt$ at rest and during exercise. Thus, exercise and ouabain each caused an increase in $dp/dt$, and the effects of the two interventions on $dp/dt$ were additive.

![Figure 3](http://circ.ahajournals.org/)

*Effects of exercise on left ventricular hemodynamics before ouabain was given. (A) Changes in LVEDP that occurred with exercise are related to changes in stroke-volume index. The shaded area includes those responses considered normal by Ross and associates.*

(C) A similar graph relating the changes in LVEDP and stroke-work index that occurred with exercise before ouabain was given.

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Effects of Exercise on the Relationship of LVEDP to Stroke Volume and Work

Before Administration of Ouabain

Pressures, cardiac output, and dp/dt were measured in ten patients in the supine position and again after their feet were raised onto the pedals of the bicycle ergometer, an intervention that would be expected to increase filling of the left ventricle without changing its contractile state. Raising the legs uniformly resulted in a rise in LVEDP, and in most patients this was accompanied by a rise in stroke volume, stroke work, and dp/dt (fig. 2). Although in an occasional patient the increase in LVEDP was accompanied by a fall in either stroke volume, stroke work, or dp/dt, in no patient did all three of these indices fall.

In all 14 patients measurements made at rest with the patients' feet on the bicycle pedals were compared with those made during exercise at the time of angina. In only two patients (1 and 5) did LVEDP and stroke volume respond to exercise in an unequivocally normal manner (shaded area, fig. 3A), as defined by Ross and associates;\(^9\) three others (patients 4, 11, and 12) had responses which were only slightly outside the limits of normal values. The remaining nine patients exhibited either depressed LV function (values falling within the right lower quadrant of the graph) or changes that, although not necessarily indicative of a depression in function, were nonetheless abnormal (values falling within the right upper quadrant of the graph). Similar results were obtained when LVEDP was related to LV stroke work (fig. 3B).

After Administration of Ouabain

LVEDP and stroke volume responded normally to exercise in the five patients with normal or near-normal responses before they were given ouabain. In addition, two of the nine patients with abnormal or depressed LV

![Figure 4](http://circ.ahajournals.org/)

**Figure 4**

Effects of exercise on left ventricular hemodynamics after ouabain was given. Changes in LVEDP that occurred with exercise are related to changes in stroke-volume index (A) and stroke-work index (B).
function before they received ouabain had normal responses to exercise after receiving the drug, and two others had nearly normal responses (fig. 4A). Neither before nor after administration of ouabain did any patient have what might be considered the optimal response to exercise: a fall in LVEDP, although in one patient LVEDP fell and stroke work increased with exercise after he received ouabain (fig. 4B).

**Effects of Ouabain on the Relationship of LVEDP to Stroke Volume and Work**

In the majority of patients ouabain did not improve the performance of the left ventricle as a pump during resting conditions (fig. 5). In contrast, the pumping characteristics of the left ventricle were improved by ouabain in 12 of 14 patients when the heart was stressed by exercise (fig. 6): stroke volume and stroke work increased, while LVEDP remained the same or decreased.

Patients 2 and 14 had the largest increases in LVEDP with exercise before they were given ouabain (fig. 3), and in these two patients ouabain improved ventricular performance at rest (fig. 5) and during exercise (fig. 6). Despite this improvement, ventricular performance still deteriorated during exercise in both of them (fig. 4). These results contrast with those obtained in patient 7, who also

![Figure 5](http://circ.ahajournals.org/)

**Figure 5**

Effects of ouabain on left ventricular hemodynamics at rest. Changes in LVEDP that occurred after the administration of ouabain are related to changes in stroke-volume index (A) and stroke-work index (B). In patients 2 and 14, LV performance at rest was improved appreciably by ouabain. In most patients, however, LVEDP and stroke volume (or work) changed in the same direction so that LV performance cannot be said to have improved or worsened. No patient had a rise in LVEDP accompanied by a fall in stroke volume or work.
showed a markedly depressed ventricular response to exercise before ouabain was given (fig. 3). In this patient ouabain caused a striking hemodynamic improvement during exercise (fig. 6), such that the response of the left ventricle to exercise became normal (fig. 4).

Effect of Ouabain on the Relationship of LVEDP to LV Peak dp/dt

Because systemic arterial pressure and heart rate were not significantly altered by the administration of ouabain (table 1), the relationship of LVEDP to dp/dt before and after administration of the drug could be used to assess ouabain's effect on the contractile state of the left ventricle. Both at rest and during exercise ouabain increased LV contractility in the majority of patients (fig. 7).

Exercise Capacity Before and After Administration of Ouabain

Four of the 14 patients were able to exercise longer after digitalization: two of the four

Effects of ouabain on left ventricular hemodynamics during exercise. Changes in LVEDP that occurred after the administration of ouabain are related to changes in stroke-volume index (A) and stroke-work index (B).

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achieved a more intense level of exercise before angina occurred, and two were able to exercise longer at the same level. Two patients experienced angina at a less intense level of exercise, and in the remaining eight patients angina occurred at an identical intensity and similar duration of exercise.

**Tension-Time Index and Pressure-Rate Product**

Ouabain did not significantly alter the heart rate, systemic arterial pressure, tension-time index, or pressure-rate product either at rest or at the onset of angina (table I). This was true both in patients who experienced angina at the same duration of exercise and in those whose exercise capacity changed after they were given ouabain.

**Correlation of Hemodynamic Data with Cineangiographic Findings**

Thirteen patients underwent selective cinecoronary arteriography and left ventriculography after the hemodynamic studies. In six of these (patients 3, 4, 8, 9, 11, and 12), the left ventricle had a normal angiographic appearance. In six others (patients 1, 2, 5, 6, 7, and 10), the left ventricle had one or more large, focal areas of akinesis or hypokinesis. The left ventricle of patient 14 showed no focal abnormalities, but it did not contract with normal vigor. In eight patients (1, 2, 5, 6, 7, 10, 12, and 14) the lumens of all three major coronary arterial branches were narrowed by 50% or more. In the other five patients, each of whom had a normal left ventriculogram, two major branches were narrowed by 50% or

*Figure 7*

Effects of ouabain on left ventricular contractility. Both at rest (A) and during exercise (B) ouabain increased the contractility of the left ventricle in most patients: LV peak dp/dt increased while LVEDP decreased or remained the same.
more. Thus, all patients had severe coronary arterial disease, but in general it was more extensive in those with abnormal left ventriculograms.

Both at rest and during exercise the average LVEDP tended to be lower in the six patients with normal left ventriculograms than in the six with focal areas of hypokinesis or akinesis, but the only values which were significantly different were those obtained with the patients at rest before ouabain was given (15.2 vs. 20.5 mm Hg, \(P<0.05\)). Neither at rest nor during exercise were cardiac index, stroke volume, stroke work, systolic ejection rate, peak \(dp/dt\), tension-time index, or pressure-rate product significantly different between the two groups; this was true both before and after ouabain was given. In addition, there was no difference in the duration of exercise that induced angina. In each of the two groups, the left ventricular response to exercise was normal in some patients but abnormal in others (fig. 3), and the effects of ouabain were striking in some but negligible in others (figs. 4–7). There was, therefore, little correlation between the angiographic appearance of the left ventricle and its response to exercise or to ouabain.

Discussion

In this as in most other hemodynamic studies of patients with coronary arterial disease,\(^1\)-\(^6\) LVEDP was found to increase abnormally with exercise in the majority of patients. However, frank depression in the performance of the left ventricle as a pump (i.e., a rise in LVEDP accompanied by a fall in stroke volume and stroke work) occurred in only a minority of patients. In others, the abnormal rise in LVEDP with exercise was accompanied by an increase in LV stroke volume and/or work. Although this latter combination of changes cannot be interpreted as indicating an unequivocal depression of ventricular function, the response is not a normal one.\(^9\)

Several mechanisms could contribute to the impaired ventricular response to exercise manifest by these patients. If permanent myocardial damage caused by prior episodes of ischemia was extensive, the left ventricle might chronically be operating on the flat portion of a depressed function curve, and with exercise any increase in left ventricular end-diastolic volume would be accompanied by only a small rise, no change, or even a fall in stroke volume. Alternatively, the transient myocardial ischemia that occurs during angina, if sufficiently widespread, might depress ventricular function acutely even in the absence of permanent myocardial disease, or might exaggerate any chronic impairment of ventricular function.

Both of the above explanations are based on the assumption that the abnormal increase in LVEDP observed during exercise reflects an abnormal increase in left ventricular end-diastolic volume. It is possible, however, that the rise in LVEDP is due instead, or at least in part, to diminished ventricular compliance. If compliance were chronically decreased, a small increase in LV end-diastolic volume, which might be appropriate for the increase in stroke volume, would be accompanied by an abnormally large increase in LVEDP. A chronic change in compliance, however, can not in itself account for those situations in which a rise in LVEDP is associated with a fall in stroke volume and work. To evoke a decrease in compliance as the mechanism responsible for such a combination of changes, one would have to postulate that ischemia causes an acute reduction in left ventricular compliance so that LVEDP rises despite a lack of change, or even a reduction, in end-diastolic volume.\(^10\)

As has been found in other studies,\(^8\),\(^11\) a few patients developed exertional angina in the absence of an abnormal increase in LVEDP, or of any other indication of a deterioration in LV performance. This finding is not unexpected since pain presumably can arise from an ischemic segment of myocardium sufficiently small so as to produce no detectable abnormality in the function of the ventricle as a whole. When LVEDP does increase with exercise, it usually begins to rise during the first minute of exertion and before angina appears. Other investigators also have
found that LVEDP increases during the first minute or two of exercise in patients with coronary disease, and that some patients do not develop angina despite abnormal rises in LVEDP. Thus, although exertional angina and elevation of LVEDP are often found together, either may occur in the absence of the other.

Ouabain did not significantly change stroke volume, stroke work, systolic ejection rate, or LVEDP at rest; but when the left ventricle was stressed by exercise, ouabain increased stroke volume, stroke work, and systolic ejection rate, and decreased LVEDP. When the relationship of stroke volume or stroke work to LVEDP was used for evaluation of the performance of the left ventricle as a pump, ouabain was found to improve LV performance in only a minority of patients at rest, but in almost all patients during exercise. In no patient was LV performance worse after ouabain was given. When the effects of ouabain on the performance of the heart as a muscle were considered, it was found that left ventricular peak dp/dt was significantly higher after ouabain was given, both at rest and during angina induced by exercise. Since systemic arterial pressure was unaltered by ouabain, and LVEDP was decreased or unchanged, these findings suggest that cardiac glycosides can improve myocardial contractility in patients with coronary arterial disease during the stress of physical exercise even when myocardial ischemia is present.

It should be emphasized that hemodynamic improvement after digitalization does not necessarily indicate LV failure, since cardiac glycosides previously have been found to improve various parameters of LV function in subjects without failure. In the present study, the improvement in LV performance after ouabain was given was generally of the same magnitude in patients who had a normal or nearly normal response to exercise before they received ouabain as in patients whose response to exercise before the drug was given was abnormal or depressed (figs. 3 and 6). In addition, five of the nine patients who displayed abnormal or depressed LV function during exercise before they received ouabain continued to do so after receiving the drug (figs. 3 and 4). Other investigators have obtained results that could be interpreted as showing similar effects of digitalis on LV function: during exercise left ventricular end-diastolic or pulmonary arterial wedge pressures were lower after ouabain was given, but in most patients the drug did not prevent abnormally large increases in these pressures with exercise.

Although LV performance improved after administration of ouabain in most patients, exercise capacity increased in only four subjects, decreased in two, and remained unchanged in eight. Malmborg reported improved exercise capacity in patients with coronary arterial disease after the administration of lanatoside C, but in two more recent studies, cardiac glycosides did not influence exercise tolerance. The failure of ouabain to delay significantly the onset of angina in our patients is not surprising since the frequency and magnitude of intraventricular pressure development, two important determinants of myocardial oxygen consumption, were not appreciably altered by the drug (table 1).

These are not, of course, the only determinants of myocardial oxygen consumption. Two others are left ventricular volume and the contractile state of the myocardium, and it is of interest that in each of the four patients who exercised longer after ouabain was given, LVEDP was lower while dp/dt was unchanged or diminished, whereas in both of the patients who experienced angina sooner after ouabain was given, dp/dt increased appreciably after administration of the glycoside while LVEDP did not change or increased slightly. Although these changes could explain the effects of ouabain on the exercise capacity of these patients, other patients whose exercise capacity was unchanged by ouabain had similar changes in LVEDP and dp/dt after receiving the drug. Thus, neither these nor any of the other hemodynamic parameters measured in this study could be used to
predict the effect of ouabain on exercise tolerance.

In this relatively small number of patients, we found little correlation between the angiographic appearance of the left ventricle and various hemodynamic parameters of its performance. Although other investigators also have noted abnormal LV function in patients whose ventricles had a normal appearance, in general they have found the hemodynamic abnormalities to be even more severe in patients with abnormal left ventriculograms. Rowe and associates could not correlate the severity of coronary arterial disease with hemodynamic measurements made with the patients at rest, and in the present study coronary arteriography was of no value in predicting either the patient's hemodynamic response to exercise or his exercise capacity. In addition, the response of the left ventricle to ouabain did not appear to be influenced by the extent of the coronary arterial disease or by the presence or absence of focal areas of ventricular akinesis.

In conclusion, it is clear that the hemodynamic effects of exercise and exercise-induced myocardial ischemia in patients with coronary arterial disease are not uniform; although most patients manifest an unequivocally abnormal response, other patients, under the circumstances of the present investigation, respond in a manner that is indistinguishable from that of normal subjects. In many patients with coronary arterial disease ouabain enhances left ventricular performance during exercise, but no firm conclusions can be drawn as to the relative roles of a depression in contractility and a decrease in compliance in producing the abnormal ventricular response so frequently observed during exercise. Finally, despite the beneficial hemodynamic effects produced by ouabain, the exercise capacity of patients with coronary arterial disease is not consistently improved by the administration of this drug.

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References


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