Hemodynamic Studies in Patients with Borderline Blood Pressure Elevation

By STEVO JULIUS, M.D., Sc.D., AND JAMES CONWAY, M.D., PH.D.

SUMMARY

Ninety-four patients with occasionally elevated (borderline) blood pressure, 61 patients with asymptomatic established hypertension, and 63 normal subjects have been studied at rest and during a progressive exercise test on a cycle ergometer. Subjects with borderline blood pressure had increased cardiac output in the resting recumbent position, but this was not maintained in the sitting position or during exercise. In the resting recumbent position there was overlap in the total peripheral resistance of normal subjects and patients with borderline blood pressure, but when analyzed in relation to the cardiac output, the total peripheral resistance of patients with borderline blood pressure was significantly elevated. In the sitting position the peripheral resistance of the patients with borderline blood pressure was elevated and remained elevated during light exercise, but fell into the normal range at higher loads. In this respect patients with borderline blood pressure differed from hypertensive patients who maintain a higher peripheral resistance than the normal subjects do at all levels of exercise. In conclusion, patients with occasional elevation of blood pressure have an abnormal peripheral resistance in relation to cardiac output both at rest and at low levels of exercise. This observation may indicate a prehypertensive state.

Additional Indexing Words:
Labile hypertension  Peripheral resistance  Exercise  Arterial blood pressure
Cardiac output  Oxygen consumption

An increase in cardiac output during rest in persons with labile hypertension, or "borderline blood pressure elevation" as we would prefer to call it, has been shown by several investigators.1-6 However, the magnitude of this elevation and the frequency of its occurrence in patients with borderline blood pressure elevation has been variable from one study to the next.

It is not generally known whether the elevation in the cardiac output during rest in these patients represents an abnormality in cardiac regulation or whether it is associated with a corresponding increase in oxygen consumption. The behavior of cardiac output and peripheral resistance as well as the blood pressure of patients with borderline blood pressure elevation on exercise is also of particular interest, since patients with essential hypertension have been shown to have a characteristic hemodynamic response to exercise.6-8 Thus, it may be possible to obtain evidence bearing upon the suggestion that transient hypertension is an early stage of essential hypertension.9

This report, therefore, examines the hemodynamic characteristics at rest and during exercise of a large group of subjects with borderline elevation of pressure. The data will be reported with particular emphasis on the influence of age and will be compared to data on normal subjects of comparable age. The findings on subjects with borderline blood pressure elevation will also be compared to results obtained on patients with

From the Clinical Physiology Laboratory, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan.

This investigation was supported by Grant CD-00081 from the U. S. Public Health Service.

282 Circulation, Volume XXXVIII, August 1968
BORDERLINE BLOOD PRESSURE ELEVATION

established hypertension studied in an identical manner in this laboratory.8

Methods

The subjects performed progressively intensive exercise on a bicycle ergometer up to their maximal voluntary level. Oxygen consumption, intraarterial blood pressure, cardiac output, and heart rate were measured at rest and during the exercise by methods described in detail elsewhere.9 As in the previous study the individual respiratory and hemodynamic data have been programmed for analysis by computer to give mean values for increasing exercise which was indicated by increments of oxygen consumption.

A patient was said to have a borderline pressure elevation if during recumbency at least one diastolic pressure reading taken in our outpatient clinic was above and one was below 90 mm Hg within the year preceding the test. Three readings were required for inclusion in the study, but 80% of the subjects have five or more readings prior to the test. Ninety-four such subjects have been studied and compared with 63 healthy, paid, normotensive volunteers of similar age and sex. The volunteers were solicited among hospital personnel and medical students. A previously described group of 61 hypertensive patients was also utilized for comparison.8

Since subjects were enrolled for testing at different stages of this study, not all of them had the complete test.

Fifty-seven normal subjects and 45 with borderline pressure elevation had all the studies at rest and during exercise. An additional six normal volunteers and 38 patients with borderline blood pressure did not have cardiac output measured, but respiratory data and the arterial blood pressure measured at rest and during the exercise were available. Finally, 11 subjects with border-line blood pressure had only resting cardiac output studies.

The patients were grouped by age: group I, included those 18 to 34 years of age; group II,

Table 1
Cardiopulmonary Data at the Voluntary Maximal Exercise Level in Eighty-three Subjects with Borderline Blood Pressure Elevation

<table>
<thead>
<tr>
<th>Age group</th>
<th>Oxygen consumption (ml/min STPD)</th>
<th>Cardiac output (L/min)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>2258 ± 82*</td>
<td>17.4 ± 0.7</td>
<td>179 ± 2.2†</td>
</tr>
<tr>
<td>II</td>
<td>1660 ± 89</td>
<td>14.1 ± 1.2</td>
<td>156 ± 4.6</td>
</tr>
<tr>
<td>III</td>
<td>1442 ± 166</td>
<td>11.1 ± 1.4</td>
<td>141 ± 5.9</td>
</tr>
</tbody>
</table>

*Mean ± standard error.
† = P < 0.05 above the normal subjects. Data for the normals are not given since they are essentially the same as those described in an earlier paper.10

Figure 1
Effect of exercise on heart rate. In figures 1, 2, 5, and 7 the levels of exercise have been indicated by the oxygen consumption. Mean values (± s.e) obtained in the resting recumbent position (RR) are followed by mean values obtained in the resting sitting position (RS). The curves have been constructed from the data for each subject with increasing oxygen consumption of 200 ml/min. As the exercise test was a progressive one, the number of subjects decreased toward the maximal level. All curves have been drawn to the point at which there were six subjects remaining. In this and the other figures significant differences from the normal are indicated by asterisks: * = P < 0.05; ** = P < 0.01; *** = P < 0.001.

Circulation, Volume XXXVIII, August 1968
35 to 49 years, and group III, 50 to 62 years. Subdivision by sex was not carried out since our data show insignificant differences in this respect, but as there were only male patients with borderline blood pressure in age group I, the controls for that group were also limited. In other groups the ratio of males to females was approximately 2:1.

Results

Findings at Maximally Achieved Levels of Exercise

The maximally achieved oxygen consumption and cardiac output in patients with borderline blood pressure declined with age in a manner similar to that of normal subjects (table 1). The same applied to heart rate except that at maximal effort in age group I the heart rate was significantly above the normal.

Observations According to Levels of Exercise

Heart Rate and Blood Pressure

The heart rate of patients with borderline blood pressure in group I was higher at maximal exercise and at rest and at all levels of exercise than that of the normal controls for age group I (fig. 1). For the age groups II and III, on the other hand, the heart rate was normal throughout. The resting mean blood pressure of patients with borderline elevation was, of course, significantly higher than normal. This difference was maintained during exercise and the rise of the mean blood pressure in patients with borderline
BORDERLINE BLOOD PRESSURE ELEVATION

blood pressure was the same as that in normals (fig. 2). This applied to all age groups and the same pattern was observed for systolic and diastolic pressures. Such a blood pressure pattern is, incidentally, different from the response generally seen in hypertensive subjects.6–8

Cardiac Output and Oxygen Consumption

The cardiac index in the resting recumbent position was significantly higher in the patients with borderline pressure elevation than in the normal subjects (P < 0.05), but the difference decreased with age and was not significant in the small group of patients over age 50 (fig. 3). The subjects having a higher cardiac index also tended to have higher heart rate (fig. 4). Upon assuming the sitting position, the cardiac output in subjects with borderline pressure elevation did not differ from that of normal subjects and thereafter remained the same throughout exercise (fig. 5).

Since the relationship of the cardiac output to oxygen consumption in patients with borderline blood pressure appeared normal during exercise, this relationship was also analyzed at rest in the sitting position. The subjects with borderline blood pressure elevation maintained significantly increased oxygen consumption at rest. For the normal controls the mean oxygen consumption (± SE) was 166 ± 7.4, 153 ± 6.7, 147 ± 6.2 ml/min/m², and for patients with borderline blood pressure, it was 189 ± 7.3, 184 ± 6.6, and 164 ± 8.3 for age groups I, II, and III, respectively. When the individual resting data were plotted (fig. 6), persons with a higher oxygen consumption also maintained a higher cardiac output. However, the general relationship of the cardiac output to the metabolic rate in patients with borderline blood pressure is the same as it is in normal persons. One regression line adequately describes both populations. When the regression lines are separately computed for each group, they are not different.

Total Peripheral Resistance

In contrast to the elevated peripheral resistance of hypertensive patients, the total peripheral resistance of subjects with borderline pressure elevation in the resting recumbent position was within the normal range (fig. 7). However, at rest in the sitting position and during mild exercise, subjects with borderline pressure elevation had a significant elevation of the total peripheral resistance. On higher exercise levels their peripheral resistance was not different from that of normal subjects. By contrast, the hypertensive subjects maintained an elevated resistance across all the levels of exercise. Al-

Figure 5
Effect of exercise on cardiac output. Data for age group III are not presented since the number of subjects with borderline pressure elevation is too small.
though there was a wide scatter of individual values for peripheral resistance at rest and the mean values were the same for the normal volunteers and the patients with borderline blood pressure, further analysis revealed an important difference between them. It was earlier noted that the total peripheral resistance of certain patients with established hypertension was within the normal range.11 These patients also had higher than normal levels of cardiac output. However, when the resistance level was related to the level of cardiac output, the peripheral resistance in hypertensives was always elevated. This relationship is illustrated in figure 8, where individual peripheral resistance is plotted against cardiac output in the resting recumbent position. The difference between the normal subjects and the hypertensive patients is seen. Patients with borderline blood pressure also have elevated total peripheral resistance for any given level of cardiac output and the regression line falls between the normal and the hypertensive subjects. The difference in peripheral resistance between patients with borderline blood pressure elevation and normal subjects was highly significant by analysis co-variance. As was observed with the exercising subjects this difference diminished at higher levels of cardiac output.

Discussion

It has been suggested that subjects with borderline or "labile" hypertension are vascular hyperreactors to different stimuli.12,13 However, as others have already indicated,6,14 they are not "hyperreactors" to the stimulus of exercise. In this respect subjects with borderline pressure elevation behave differently from middle-aged and old patients with established hypertension who have a greater blood pressure rise during exercise.8 However, the steep rise in pressure seen in hypertension is probably not a sign of vascular hyperreactivity but may be related to increased rigidity of blood vessels produced by the disease. It is therefore unlikely that evidence of large vessel rigidity will be found in subjects with borderline pressure elevation.

Figure 6

Relationship of the cardiac output and oxygen consumption of normal volunteers and of subjects with borderline blood pressure elevation in the resting sitting position. There was no difference between the regresional lines for the two groups and therefore one line is inscribed accounting for the normals and borderlines. The coefficient of correlation for the total population is 0.60.
Effect of exercise on the total peripheral resistance. Data for the age group III are not presented since the number of subjects with borderline pressure elevation is too small for construction of curves.

The presence of an increased cardiac output in patients with borderline pressure elevation is still somewhat controversial. Although the majority of investigators have found that values are elevated in the resting recumbent position, others have not observed this. Similarly, increased cardiac output has been reported in patients with mild established hypertension, although we have not observed it. These differences probably represent variability in the selection of subjects. The prevalence of high cardiac output among patients with borderline blood pressure elevation, however, varies in different series from 70 to 80% to 40% and in our studies 18% had cardiac indices exceeding a normal value of 5 L/min/m². Likewise, the cardiac indices in our data showing a mean of 4.01 L/min/m² are less obvious than those of others who found mean values of 5 to 6 L/min/m², but our values are more in line with those of Bello and co-workers and of Sannerstedt.

Interestingly, the increase in cardiac output in cases of borderline pressure was demonstrated only in the resting recumbent position. In our study the statistical difference between normal subjects and patients with borderline blood pressure disappeared when the patients assumed the sitting position, and the cardiac output was also not high during exercise. A similar response to exercise was previously reported by Sannerstedt and Levy and associates. Furthermore, in the resting position the cardiac output of subjects with borderline blood pressure elevation appeared to be regulated by the oxygen consumption, and such an adjustment of the cardiac output to the metabolic demands at rest is characteristic of normal subjects. During exercise, again,
the cardiac output in patients with borderline blood pressure was normally related to the metabolic rate. It follows, therefore, that subjects with borderline pressure elevation do not have an abnormality of the regulation of the cardiac output, but in the recumbent position, under some unknown stimulus, they react with an increased output. The increased cardiac output in the resting recumbent position in these patients in our study was associated with a higher heart rate; therefore, increased cardiac sympathetic tone might be implicated.

It is not clear whether patients with borderline pressure elevation and increased cardiac output are potential hypertensives. Based on the dissimilarity of this pattern and the one seen in essential hypertension, Eich and associates\(^5\) regarded the high output state as a benign condition, but later, from follow-up studies, they were ready to regard it as a stage in the development of hypertension.\(^5\)

A supposedly normal peripheral resistance among subjects with borderline blood pressure has been found by numerous investigators.\(^1\)-\(^3\) However, when resistance is related to the prevailing cardiac output, our data show that the total peripheral resistance of such patients lies between that of normal and that of hypertensive subjects. Furthermore, in the resting sitting position when cardiac output returns to normal, patients with borderline pressure have elevated total peripheral resistance, and they maintain the increased resistance on mild exercise loads. With higher exercise loads their resistance falls into the normal range. Thus, subjects with borderline pressure elevation apparently have an underlying elevation of peripheral resistance which can be overcome by the stimulus of severe exercise.

In summary, therefore, we found that subjects with borderline blood pressure elevation have increased cardiac output at rest and the peripheral resistance when it is related to the level of cardiac output is abnormal. This observation may well indicate that borderline elevation of blood pressure is a prehypertensive state.

References

Hemodynamic Studies in Patients with Borderline Blood Pressure Elevation
STEVO JULIUS and JAMES CONWAY

_Circulation_. 1968;38:282-288
doi: 10.1161/01.CIR.38.2.282

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/38/2/282

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/