Decreased Venous Distensibility in Borderline Hypertension

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SUMMARY There are abnormalities in venous structure and function in animal models of hypertension. In humans with borderline hypertension, there is a redistribution of blood from the periphery to the central circulation that may be produced in part by a decrease in peripheral venous distensibility. In this study we used a water-filled plethysmograph to determine forearm venous distensibility in nine young men with borderline hypertension and nine normotensive control subjects. The venous pressure-volume curve in men with borderline hypertension as compared to that in normotensive men was shifted toward the pressure axis (p < 0.05). This indicates that venous distensibility was significantly decreased in borderline hypertension. Phentolamine, 1 mg I.V. for 5 minutes, increased venous distensibility slightly but significantly (p < 0.05) in borderline hypertensive men, but not in normotensive men. Thus, decreased venous distensibility in borderline hypertensive subjects was due in part to α-adrenergic vasoconstriction. Venous distensibility after phentolamine was less in borderline hypertensive men than in normotensive men (p < 0.05). This finding suggests that most of the decrease in venous distensibility in borderline hypertension resulted from non-adrenergic mechanisms. Thus, there is a decrease in venous distensibility in young men with borderline hypertension that is related partly to adrenergic mechanisms, but also involves other factors, perhaps including structural changes in veins.

KEY WORDS • plethysmography • phentolamine • capacitance vessels • structural vascular changes

In experimental and spontaneous hypertension in animals there are abnormalities in veins as well as in arteries. Structural changes in arteries probably are produced in part by the increased intraluminal pressure, but veins are not exposed to increased blood pressure. Thus abnormalities in veins are presumably related to neurogenic or humoral influences or to primary vascular abnormalities.

In humans, venous distensibility has been examined in established essential hypertension. The results are somewhat conflicting, but recent studies have suggested a decrease in the venous distensibility in established hypertension. The observation that there is a redistribution of venous blood from peripheral to cardiopulmonary circulation in young men with borderline hypertension suggests that there might be abnormal venous function in borderline hypertension. However, there has been no study of venous distensibility in borderline hypertension.

The aims of this study were, first, to determine if young men with borderline hypertension have decreased venous distensibility and, second, to determine the role of α-adrenergic mechanisms in the venous distensibility in these young men.

Methods

Subjects

Nine young men with borderline hypertension (26 ± 1 years of age, mean ± se) and nine normotensive subjects (25 ± 2 years of age) were studied. Borderline hypertension was defined as blood pressure intermittently above 150 mm Hg systolic or 90 mm Hg diastolic. Blood pressure was measured with a cuff sphygmomanometer while the subjects were sitting. Blood pressure was measured after 15 minutes of rest at least four times on four different days.

Medical history and physical examination were normal, except for a history of borderline hypertension. There was no evidence of organic cardiovascular disease in any borderline hypertensive subject. Seven of nine borderline hypertensive patients had a family history of essential hypertension.
The study protocol was approved by the Human Study Committee of the University, and informed consent was obtained from all subjects participating in the study.

Determination of Venous Distensibility

Venous distensibility was determined by obtaining venous pressure-volume curves. A single-chamber water-filled plethysmograph was used for recording changes in volume of a segment of the left forearm. Subjects wore light clothing and felt comfortably warm at a room temperature of 72°F.

The details of the plethysmographic method that is used for determining venous distensibility have been described. The left forearm was enclosed in a plexiglass plethysmograph. Water was added to 23 cm above the upper aspect of the forearm. Under these conditions the external water pressure initially collapses the veins, but the arterial inflow drives the venous pressure to a level slightly greater than the external water pressure. The difference between the pressure within the veins and the external water pressure surrounding them is the distending or transmural pressure. Venous pressure was measured through a polyethylene tube (18.5 gauge) inserted in a superficial vein in the segment of forearm enclosed in the plethysmograph. Transmural venous pressure was measured by placing the reference level of the pressure transducer at the same level as the surface of the water in the plethysmograph. Transmural venous pressure at rest under those conditions was less than 1.5 mm Hg. The volume of blood in the vessels in the forearm at this low transmural venous pressure is approximately 1.3 ml/100 g of tissue and, under resting conditions, transmural venous pressure and volume are constant and reproducible in a given subject.

Changes in forearm volume were recorded during stepwise increases in transmural venous pressure to 30 mm Hg by inflating a cuff on the arm proximal to the plethysmograph (fig. 1). Transmural venous pressure was increased slowly to minimize nonuniform filling of the veins and was held constant at each step until changes in forearm volume became stable (fig. 1). Changes in venous volume were reflected by the changes in forearm volume, which were measured by changes in the height of water. Increases in volume in response to congestion of the forearm take place primarily in vessels in which resting pressure is less than 10 mm Hg. Venous pressure-volume curves were constructed by plotting changes of forearm volume in ml/100 ml of forearm volume against corresponding levels of transmural venous pressure.

The resting forearm volume enclosed in the plethysmograph of subjects with borderline hypertension (603 ± 36 ml) did not differ from that of normotensive subjects (576 ± 39 ml).

To investigate the contribution of α-adrenergic mechanisms to venous distensibility, measurements of venous distensibility were obtained in five subjects with borderline hypertension and five normotensive subjects before and after I.V. administration of phentolamine at a rate of 1 mg/min for 5 minutes. To determine if the dose of phentolamine was sufficient to block α-adrenergically mediated venoconstriction, we measured the reflex venoconstrictor response to deep inspiration, using the occluded-vein technique, before and after infusion of phentolamine.

Heart rate and blood pressure were recorded at the time of study of venous distensibility.

Analysis of the Data

We performed statistical analysis of the data using one-way and two-way analyses of variance. We considered \( p \leq 0.05 \) as a statistically significant difference.

Results

Systolic and diastolic blood pressure under resting conditions were relatively reproducible on the same subject on different days. The maximal difference in systolic and diastolic pressure between four measurements on the same subjects averaged 13 ± 2 mm Hg (mean ± se) for systolic and 8 ± 2 mm Hg for diastolic pressure in subjects with borderline hypertension. These were similar to ranges noted in normotensive subjects, 13 ± 3 mm Hg for systolic and 6 ± 3 mm Hg for diastolic blood pressure.

Systolic and diastolic blood pressure at the time of measurements of venous distensibility of nine subjects with borderline hypertension (systolic 143 ± 4 mm Hg, diastolic 89 ± 4 mm Hg) were higher (\( p < 0.01 \) for both) than those in nine normotensive subjects (systolic 123 ± 4 mm Hg, diastolic 76 ± 2 mm Hg).

Systolic and diastolic blood pressure at the time of study were not different from the average value of four measurements both in subjects with borderline hypertension and in normotensive subjects.

Heart rate was not different between subjects with borderline hypertension (77 ± 4 beats/min) and normotensive subjects (71 ± 5 beats/min).

The venous pressure-volume curves in subjects with borderline hypertension and normotensive subjects are
shown in table 1 and figure 2. Before phentolamine, the venous pressure-volume curve in those with borderline hypertension was shifted toward the pressure axis \( p < 0.05 \) as compared to that in normotensive subjects. Thus, venous distensibility was decreased in subjects with borderline hypertension.

Phentolamine increased venous distensibility significantly \( p < 0.05 \) in subjects with borderline hypertension (fig. 2). In contrast, venous distensibility in normotensive subjects was not different before and after phentolamine. Phentolamine, at the dose used in this study, was sufficient to block reflex venoconstriction produced by a deep breath. A deep breath increased venous pressure in the occluded forearm by an average of 12 mm Hg before phentolamine, but did not increase venous pressure after phentolamine.

After phentolamine, venous distensibility in patients with borderline hypertension remained significantly \( p < 0.05 \) lower than that in normotensive subjects (fig. 2).

**Discussion**

The results of this study indicate that the distensibility of forearm veins of young men with borderline hypertension is considerably reduced as compared to the distensibility in normotensive subjects (table 1, fig. 2).

The validity of the equilibration technique for the measurement of venous distensibility in man has been extensively studied and discussed. A discussion of a few points are relevant to the present study.

In utilizing the equilibration technique for the measurement of venous distensibility, it is most important that venous pressure-volume curves are measured from the same reference point or baseline of venous volume and transmural venous pressure. In this regard, a water-filled plethysmograph has an important advantage compared to a strain gauge plethysmograph, since the external water pressure of 20 mm Hg reduces the transmural venous pressure to virtually zero and produces a large decrease in venous volume to the baseline level. It has been shown that baseline transmural venous pressure and venous volume under these conditions are constant and reproducible in a given subject. In this study, the baseline transmural venous pressure was less than 1.5 mm Hg and was not different in the two groups.

In healthy young men, Litter and Wood demonstrated that adding external water pressure of 10–15 mm Hg to collapse capacitance vessels decreases the "vascular volume" of the extremity from 3.9 to 1.5 ml per 100 ml. Raising the external water pressure an additional 45 to 50 mm Hg produced only a small additional decrease in vascular volume of 0.5 ml per 100 ml. These findings suggest that low-pressure capacitance vessels contribute predominantly to the venous volume of the extremity. Wiedeman suggested that post-capillary venules, which have higher venous pressure, comprise less than 5% of the total capacity.

However, Wiedeman suggested that small veins comprise significant venous volume. Although the measured venous pressure in a large vein was not different in the two groups, we considered the possibility that the venous pressure in small veins might be higher in young men with borderline hypertension. If this were the case, small veins might not have been collapsed by the external water pressure under resting conditions. If the small veins were not collapsed, the shift of the venous pressure-volume curve toward the pressure axis in borderline hypertension might have resulted from a higher baseline venous volume. Accordingly, to determine if the veins were collapsed by the external pressure of 20 mm Hg under resting conditions in subjects with borderline hypertension as well as in normotensive subjects, we measured the forearm volume in three subjects with borderline hypertension as the external water pressure was increased stepwise from 7 to 25 mm Hg (fig. 3). If venous pressure and volume in smaller veins were higher in subjects with borderline hypertension, then a stepwise increase in the external water pressure above...
10-15 mm Hg should have produced a progressive decrease in the baseline vascular volume. This did not occur. As shown in figure 3, increasing the external water pressure above 10 mm Hg did not produce an appreciable decrease in the baseline forearm volume.

Previous studies have suggested that adrenergic effects are increased in young subjects with borderline hypertension. Accordingly, we examined the possibility that the decreased venous distensibility in young men with borderline hypertension was produced by adrenergic venoconstriction. Phenolamine, in a dose sufficient to block reflex venoconstriction produced by a deep breath, increased the venous distensibility slightly in young men with borderline hypertension (fig. 2) but not in normotensive subjects. This suggests that part of the decreased venous distensibility in borderline hypertension is related to adrenergic venoconstriction, either by increased α-adrenergic activity or by increased responsiveness of the veins to adrenergic stimulation.

However, more importantly, the venous distensibility after phenolamine remained significantly less in young men with borderline hypertension than in normotensive subjects (fig. 2). Thus approximately 80% of the decrease in venous distensibility in borderline hypertension was related to non-adrenergic mechanisms. It is unlikely that angiotensin or vasopressin are responsible for the decrease in venous distensibility since they do not produce vеноconstriction. Although serotonin constricts veins, serotonin is not implicated in borderline hypertension. It is possible that humoral factors which act on membrane Na⁺-K⁺ ATPase might be involved. Such humoral factors might decrease venous distensibility directly by increasing venous tone or indirectly by increasing intracellular sodium and water contents.

The decrease in venous distensibility may be related to structural abnormalities of the veins. Although this study cannot directly define structural changes in the veins in borderline hypertension, studies in hypertensive animals have demonstrated various changes that could contribute to the decrease in venous distensibility. Such structural changes include changes in venous wall, such as increased water, sodium and potassium content of veins; increased ion-binding cellular and paracellular matrix; venous smooth muscle hypertrophy; or changes in interstitial space such as decreased compliance. A decrease in the number or size of veins also might account for the decreased venous distensibility in men with borderline hypertension.

The functional significance of the decreased venous distensibility in young men with borderline hypertension remains to be investigated. The decreased venous distensibility might contribute to redistribution of venous blood from peripheral to cardiopulmonary circulation, which is reportedly present in young men with borderline hypertension.

In summary, this study demonstrated that there is a decrease in venous distensibility in young men with borderline hypertension. The decrease in venous distensibility is produced primarily by non-adrenergic
mechanisms. These findings suggest that there is an abnormality in veins as well as in arteries in borderline hypertension.

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