Resting and Maximal Forearm Skin Blood Flows are Reduced in Hypertension

Peter A. Carberry, Alexander M.M. Shepherd, and John M. Johnson

To find whether the vasodilator capacity of nonacral skin is reduced in hypertension, we measured forearm blood flow by venous occlusion plethysmography in 10 seated normotensive (mean±SD mean arterial pressure, 94±5 mm Hg) and 10 hypertensive (112±9 mm Hg) men at rest for 39 minutes while the forearm was heated with water at 42°C, a maneuver known to selectively and maximally vasodilate skin. Blood pressure, measured every 5 minutes, did not change with heating. We found that in the normotensive group resting forearm blood flow was higher (3.64±1.12 versus 2.48±0.58 ml/100 ml tissue per minute, p<0.001; normotensive group versus hypertensive group) and resting forearm vascular resistance lower (30.17±10.99 versus 48.88±17.37 mm Hg · min · 100 ml tissue per minute, p<0.05; normotensive group versus hypertensive group), and maximal forearm blood flow with local heating was higher (29.32±11.99 versus 18.19±4.50 ml/100 ml tissue per minute, p<0.018; normotensive group versus hypertensive group) and vascular resistance lower (4.07±1.04 versus 6.54±1.17 mm Hg · min · 100 ml tissue per minute, p<0.005; normotensive group versus hypertensive group). To find whether this degree and duration of local warming maximally vasodilated the skin in hypertensive subjects (as it does in normotensive subjects), we measured forearm skin blood flow before and during local heating plus 10 minutes of ischemia using a laser Doppler flowmeter. Although six of 10 hypertensive subjects displayed a further increase in forearm skin blood flow when ischemia was added to local heating (mean, 65.3%; range, 53.5–81%), overall this was not a significant increase over that seen with heating alone (p>0.30).

We conclude: 1) the elevated minimal vascular resistance seen in some regional circulations in hypertensive subjects is also seen in nonacral skin, probably reflecting structural changes in skin blood vessels in hypertension; 2) skin is a useful site to study vascular changes in hypertension; and 3) these changes could contribute to impaired thermoregulatory mechanisms in hypertension. (Hypertension 1992;20:349–355)

Key Words • vasodilation • plethysmography • flowmeters • blood flow velocity

Increased resistance to blood flow in hypertensive individuals is an important component in the maintenance of high blood pressure. Current information indicates two general sources for this increased vascular resistance. One is increased vascular smooth muscle activity; the second results from structural changes in the vasculature. Several hemodynamic studies in humans have tried to differentiate tonically increased vascular smooth muscle activity from structural changes in the vasculature and thereby categorize the basis for the increased peripheral resistance seen in many hypertensive individuals. Structural changes have frequently been indexed by increases in minimum vascular resistance, although such increases could be due to either decreased lumen size secondary to an increase in medial thickness or a reduction in the number of vessels (rarefaction). Microscopic studies of vascular tissue have shown a definite increase in medial thickness at the arteriolar level in skin and kidney in hypertension, indicating structural changes. More recently, a mathematical model based on the hamster cheek pouch showed that anatomical arteriolar rarefaction occurs together with constriction of arterioles to cause an increase in vascular resistance and that rarefaction is a significant component of this increase. The debate continues as to which of the three components (increased vascular tone, vascular hypertrophy, and rarefaction) is the most significant.

The assessment, by hemodynamic methods, of structural vascular changes in human hypertension has for the most part relied on maximal vasodilator stimuli to the forearm or hand, from which estimates of minimal vascular resistance are made. Indeed, it has been uniformly found that minimal forearm vascular resistance (FVR) is elevated in a variety of hypertensive or prehypertensive groups. Similarly, minimal hand vascular resistance has been found to be elevated in hypertension. Several questions arise. First, the microvascular architecture and neural control of the skin of the hand differ substantially from those of the forearm. The characteristics of forearm skin are like those for most of the body surface (namely, the torso and limbs), whereas the architecture and neural control...
of the vasculature of hand skin are considered to be characteristic of acral regions, comprising in total only 10% of the total skin surface. Consequently, we believed it important to find whether the elevated minimal vascular resistance of the hand in hypertension is seen in the majority of body skin, as reflected in the forearm. Thus, the primary goal of this study was to find whether the forearm skin vasculature was affected by hypertension in a manner similar to that of hand skin.

A secondary goal was to develop a method by which minimal vascular resistance could be accurately and repeatedly assessed. In the determination of minimal FVR, the usual approach has been to occlude blood flow to the arm for 5–10 minutes, causing reactive hyperemia. Occasionally, exercise of forearm muscle has been added to this.2,4–17,20 Two problems arise with this approach. First, it does not yield a maximal relaxation of all the vessels in the forearm, as shown by the failure of forearm skin blood flow to reach maximal levels during reactive hyperemia of the normothermic forearm.21 Addition of exercise of forearm muscle ensures maximal dilation of muscle vessels but does not influence those in the skin.21–24

The second problem is related to the first. When reactive hyperemia is supplemented by forearm heating, maximal blood flow is achieved, but the level of blood flow is high, approaching or exceeding the limits of reliable measurement of blood flow by plethysmography.24–26 When all forearm vessels are maximally dilated, the blood flow into the forearm is so great that the forearm veins reach their distensibility limits in one or two heartbeats, making determination of the rate of filling very difficult. This is also true for measurement of maximal hand blood flow.

Taylor et al23 showed that local heating of the forearm skin to 42°C for 30–45 minutes in normotensive individuals removes all tone in cutaneous arteriolar smooth muscle, yielding maximal forearm skin blood flow. This vasodilation occurs only in the skin and occurs at levels of blood flow well within the capability of plethysmography. The conclusion that local heating caused maximal vasodilation of the forearm skin was confirmed by showing that reactive hyperemia during local heating did not provoke further vasodilation beyond that seen with local warming alone.21

In the present study we adopted the above approach and examined normotensive and hypertensive subjects to determine if forearm skin blood flow and FVR, measured by venous occlusion plethysmography, differed between groups at rest and at maximal vasodilation with local heating. If so, it would suggest that the cutaneous vasculature undergoes structural modification in hypertension and would permit minimal vascular resistance to be determined serially during therapeutic maneuvers aimed at the reversal of structural changes due to and in hypertension.

To confirm that local heating to 42°C did indeed produce a maximal cutaneous vasodilation in hypertensive individuals as it does in normotensive persons, we also used laser Doppler flowmetry to find whether addition of reactive hyperemia to local heating of the forearm induced a greater vasodilator response than heating alone.

**Subjects**

The study included 10 normotensive (NT) and 10 hypertensive (HT) men matched for age and weight. The age range was 30–47 years (36.9±1.5 [mean±SD] years NT, 38.9±1.68 years HT), and the weight range was 56.8–133.75 kg (93±25.9 kg NT, 86.4±13.6 kg HT). There were no significant differences between groups in these measures.

Inclusion criteria for the NT group were normal supine blood pressure (<130/90 mm Hg), no personal or family history of hypertension, and no recent history of the use of medications. Inclusion criteria for the HT group were essential hypertension diagnosed by exclusion of secondary hypertension through history, physical examination, electrocardiography, chest roentgenography, and blood chemistry; blood pressure >130/90 mm Hg; absence of other disease; and no antihypertensive medication for at least 4 weeks preceding the study. Written, witnessed, informed consent was obtained as approved by the Institutional Review Board of the University of Texas Health Science Center at San Antonio.

**Plethysmography**

Each subject sat upright in a comfortable chair with his right arm supported just above heart level. The forearm was enclosed in a Perspex cylindrical bath from which fine sprays of water at controlled temperature were directed onto the surface of the forearm.22 The rate of blood flow into the forearm was determined by venous occlusion plethysmography with a mercury-in-Silastic strain gauge situated 10 cm distal to the lateral condyle of the elbow. An adult-size blood pressure cuff was wrapped around the right upper arm and inflated to 40 mm Hg for 10 of each 20 seconds. The hand was isolated by a pediatric blood pressure cuff at the wrist inflated to 240 mm Hg during blood flow measurements. A thermocouple placed on the flexor aspect of the forearm 2 cm distal to the strain gauge was used to measure skin temperature. Forearm blood flow (FFB) was measured every 20 seconds for 4 minutes out of every 5-minute period. During the fifth minute of each period, the wrist cuff was deflated and blood pressure was measured in the opposite arm. Nine 5-minute sequences were performed. The first set of measurements was taken at the ambient forearm skin temperature of 32–34°C, and subsequent measures were made with warm water being sprayed onto the forearm to raise forearm skin temperature to 42°C.

**Laser Doppler Velocimetry**

In a separate session, forearm skin blood flow was monitored continuously by laser Doppler flowmetry (LASERFLO model BPM 403, TSI Inc., St. Paul, Minn.). This method provides a linear index of skin blood flow from an area of approximately 1 mm² and a depth of 1 mm. Local skin temperature was controlled with a 5-cm-diameter heater surrounding the flow probe. The analog signal was recorded with a wide-scale (25 mm span) recorder.

Subjects were seated upright in a comfortable chair throughout each procedure. Forearm skin blood flow was measured for 5 minutes at room temperature.
Occlusion of blood flow to the forearm by application of a blood pressure cuff at 250 mm Hg to the arm for 10 minutes followed. Upon release of the occlusion, forearm skin blood flow was measured for a further 10 minutes. Local skin temperature of the forearm was then raised to 42°C and held there for the remainder of the procedure. After local warming for 40 minutes, 10 minutes of occlusion was repeated. Blood pressure was monitored at 5-minute intervals on the opposite arm using a mercury sphygmomanometer.

Data Collection and Calculation

Plethysmography. FBF (milliliters per 100 milliliters forearm tissue · minute) and mean arterial pressure (MAP) were used to calculate FVR and forearm vascular conductance (FVC). Each 4-minute period produced 12 FBF values for each subject. The average of these was taken to represent FBF for that period. FVR was calculated as the ratio of the preceding blood pressure to the average FBF. FVC was calculated as the reciprocal of FVR.

Laser Doppler velocimetry. Average forearm skin blood flow, represented by millimeters of deflection on the analog printout corrected for changes in voltage and sensitivity, was obtained for each individual for each period of the procedure, namely, 1) after 5 minutes at a local skin temperature of about 32°C, 2) at peak reactive hyperemia at 32°C, 3) after 40 minutes of heating to a local skin temperature of 42°C, 4) after reactive hyperemia at 42°C, and 5) 3–5 minutes after reactive hyperemia at 42°C. We then derived individual and group absolute change in forearm skin blood flow normalized by using forearm skin blood flow at the beginning of the procedure as the control value.

Statistics

Group data are presented as mean±SD. Repeated-measures analysis of variance was used to compare FBF, FVR, FVC, and change in forearm skin blood flow between the two groups. Statistical significance was accepted when p<0.05.

Results

Plethysmography

Before local heating, FBF averaged 3.64±1.12 and 2.48±0.58 ml/100 ml · min for the NT and HT groups, respectively. The difference between these means was significant (p<0.001). In all subjects, FBF rose (Figure 1) and FVR fell with elevation of forearm temperature to 42°C. All subjects reached maximal FBF between 34 and 44 minutes of the protocol. In some subjects, FBF reached its peak before the end of the period of heating and began to subside somewhat during the next one or two 5-minute periods, in a pattern similar to the "die away" described by Barcroft and Edholm. For this reason, we compared the responses in two ways. The first comparison was of average FBF during the last 4 minutes of the study. At that time, average FBF was 29.32±11.99 ml/100
Group average MAP values are shown in Table 1. There was a significant difference between groups (p<0.0001) but no significant change over the course of the study within either group. Therefore, local heating of the right forearm did not significantly affect systemic blood pressure.

Table 2 is a summary of each HT patient's history of hypertension and medications used, together with FBF, FVR, and MAP values obtained during plethysmography. There was no correlation between duration of hypertension, presence or lack of treatment, type of medication, or duration on and off medications and baseline FBF, baseline FVR, FVR at 42°C, or MAP. There was a positive relation between MAP and FBF at 42°C (p=0.003) and a tendency toward lower minimal FVR values as MAP decreased at 42°C (p=0.056).

**Laser Doppler Velocimetry**

Figure 4 shows forearm skin blood flow as measured by the laser Doppler method in each group at different periods of the procedure. At room temperature, forearm skin blood flow was significantly higher (relative to maximal) in the NT group than in the HT group (9.58±4.26 versus 5.89±1.39 mm, p<0.025). Ten minutes of ischemia to the forearm at room temperature produced an increase in forearm skin blood flow in both groups; the increase was significantly greater in the NT group than in the HT group (19.5±18.47 versus 5.89±1.39 mm, p<0.001).
Forearm blood flow rose in both groups with the elevation of forearm skin temperature to 42°C. After heating for 40 minutes, both groups had reached a steady forearm skin blood flow, which was significantly higher in the NT group than in the HT group (108.18±39.76 versus 64.64±26.13 mm, p<0.05). The levels of forearm skin blood flow after ischemia at 42°C did not change significantly in either group when measured 3–5 minutes after release of occlusion of the forearm. However, application of ischemia at 42°C produced an initial increase in forearm skin blood flow within 1–2 minutes after release, over and above that seen with heating alone, in six of the 10 HT men. Overall, this increased flow was not significantly higher than the average forearm skin blood flow in these six patients seen before ischemia at 42°C (65.3±9.52 versus 53.1±26.13 mm) or 3–5 minutes after reactive hyperemia at 42°C (65.3±9.52 versus 61.7±11.2 mm). The other four HT men displayed a response similar to that of the NT men in that forearm skin blood flow after ischemia gradually increased during the next 3–5 minutes to preischemic levels at 42°C. Forearm skin blood flow at this time was not significantly different from preischemic levels in either HT subgroup but was significantly higher in the NT group than in the whole HT group (113.73±42.76 versus 59.9±29.26 mm, p<0.05). Figure 5 shows these different responses by the HT subgroups. Absolute change in forearm skin blood flow, derived as described above, is depicted. Once again, absolute change was higher in the NT group than in the HT group when ischemia was applied at 32°C (48.6±17.2 versus 26.4±11.2 mm, p<0.05), at 42°C (98.6±37.7 versus 49.7±26.9 mm, p<0.05), and after ischemia at 42°C (104.2±40.2 versus 53.7±29.9 mm, p<0.05). There was no significant difference between the two HT subgroups at any period.

Group MAP values taken during laser Doppler measurements of forearm skin blood flow are shown in Table 3. There was a significant difference between groups (p<0.0001) but no significant change within either group during the procedure. Because there were two patterns of response to ischemia at 42°C in the HT men, we wondered whether other characteristics differed. The only finding was that the six HT men with increased blood flow had a significantly higher average MAP than the other four (120.2±9.04 versus 108±7.14 mm Hg), but this did not correlate with any difference in forearm skin blood flow.

**Discussion**

The principal finding of this study is that the vasodilator capacity of forearm skin is reduced in hypertensive individuals. This is true whether the comparison is made on the basis of maximal blood flow or minimal vascular resistance. Therefore, in this instance, the vasculature of forearm skin and that of hand skin show similar alterations in hypertension. Together, these findings suggest that the elevation in minimal vascular resistance applies to skin in general and is not isolated to acral regions.

The differences in maximal forearm skin blood flow and minimal FVR between the NT and HT groups...
whether this is because of increased neurogenic stimuli,
vascular tone is abolished by raising the skin tempera-
ture to 42°C abolishes the vascular tone but by a smaller absolute increase in FBF. Raising the
skin temperature to 42°C for 40 minutes. We also found that
hypertensive men responded to increasing skin temper-
ture at 42°C; 4, after reactive hyperemia at 42°C; SBP, systolic
Aukjaer C, Eikler H, Mulvany MJ, Jespersen B, Kjaer T,
Sorensen SS, Pedersen EB: Abnormal structure and function of isolated subcutaneous resistance vessels from essential hypertensive patients despite antihypertensive treatment. J Hypertens 1989;
7:305–310
Greese AS, Tonellato PJ, Lui J, Lombard JH, Cowley AW Jr: Microvascular rarefaction and tissue vascular resistance in hyperten-

TABLE 3. Distribution of Group Average Blood Pressure Mea-
sured by Laser Doppler Flowmetry

<table>
<thead>
<tr>
<th>Period</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensives</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>120</td>
<td>111</td>
<td>113</td>
<td>114</td>
</tr>
<tr>
<td>DBP</td>
<td>79</td>
<td>74</td>
<td>77</td>
<td>78</td>
</tr>
<tr>
<td>MAP*</td>
<td>92</td>
<td>87</td>
<td>89</td>
<td>90</td>
</tr>
<tr>
<td>Hypertensives</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>141</td>
<td>134</td>
<td>138</td>
<td>141</td>
</tr>
<tr>
<td>DBP</td>
<td>99</td>
<td>103</td>
<td>102</td>
<td>100</td>
</tr>
<tr>
<td>MAP*</td>
<td>113</td>
<td>116</td>
<td>114</td>
<td>114</td>
</tr>
</tbody>
</table>

1, baseline; 2, reactive hyperemia at 32°C; 3, maximal vasodilata-
tion at 42°C; 4, after reactive hyperemia at 42°C; SBP, systolic
blood pressure; DBP, diastolic blood pressure; MAP, mean arte-
rial pressure.
*p<0.0001 between normotensive and hypertensive groups for all
periods.

indicate a structural change in the skin vasculature in
hypertension caused by rarefaction, vascular hypertro-
phy, or both. However, it may be that part of the
difference in FVR at 42°C between the groups is due to
residual smooth muscle activity and increased intrinsic sensitivity to endogenous vasocon-
strictor stimuli, or decreased production of (or sensitiv-
ity to) vasodilatory humoral stimuli such as nitric oxide and prostaglandins or merely reflective of enhanced vascular resistance because of a greater wall-to-lumen ratio in hypertension.4

Maximal FBF differed greatly between the two
groups. The reduction in maximal FBF of almost 40% suggests that there is a potential for limited heat exchange in hypertension and, as a result, there may be impaired ability in hypertensive subjects to lose heat under conditions of increased heat production. Such a problem has been identified in hypertensive subjects exercising in the heat.31 The structural modification suggested by our study could contribute to this limited heat-lossing capability.

In conclusion, both venous occlusion plethysmogra-
phy and laser Doppler velocimetry give consistent and reproducible results in the study of maximal skin blood flow and vascular resistance. We used these methods to show that FVR in hypertensive men is significantly higher than in normotensive men, even after cutaneous vascular tone is abolished by raising the skin temperature to 42°C for 40 minutes. We also found that hypertensive men responded to increasing skin temperature in a pattern similar to that of normotensive men, but by a smaller absolute increase in FBF. Raising the skin temperature to 42°C abolishes the vascular tone due to cutaneous vascular smooth muscle activity and makes more apparent the differences between nor-

motensive and hypertensive individuals. Skin is a useful site to study these differences.

There are structural and, possibly, functional changes in skin blood vessels in hypertension. There may be impaired temperature regulation and heat exchange through the skin in hypertension.

Acknowledgment

We express our appreciation to W. Kosiba for his able technical assistance.

References

1. Daniel EE, Kwan CY, Lee RMKW, Smeda J: Structural changes in precapillary vessels in hypertension and their relationship to func-


Resting and maximal forearm skin blood flows are reduced in hypertension.
P A Carberry, A M Shepherd and J M Johnson

*Hypertension*. 1992;20:349-355
doi: 10.1161/01.HYP.20.3.349

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/20/3/349