Capillary Pressure in Subjects With Type 2 Diabetes and Hypertension and the Effect of Antihypertensive Therapy

P. Gerard Fegan, John E. Tooke, Kim M. Gooding, Jayne M. Tullett, Kenneth M. MacLeod, Angela C. Shore

Abstract—Raised capillary pressure has been implicated in the formation of diabetic microangiopathy in type I diabetes, in which it is elevated in those with the earliest signs of diabetic kidney disease but remains normal in those without complications. In subjects with type 2 diabetes without complications, capillary pressure is normal, although alterations in the pressure waveforms suggested enhanced wave reflections. The nature of skin capillary pressure in subjects with type 2 diabetes and hypertension remains to be elucidated, as does the effect of blood pressure–lowering therapy on capillary pressure in these subjects. Three studies were performed in well-matched groups. First, capillary pressure was elevated in hypertensive subjects with type 2 diabetes compared with normotensive subjects with type 2 diabetes (20.2 [17.4 to 22.7] mm Hg versus 17.7 [16.1 to 18.9] mm Hg, respectively, P<0.03, Mann-Whitney U test). Second, no significant difference was detected between hypertensive subjects with type 2 diabetes and hypertensive subjects without type 2 diabetes (19.4 [15.8 to 21.3] mm Hg versus 17.2 [15.1 to 19.8] mm Hg, respectively, P=0.5, Mann-Whitney U test). Finally, patients with type 2 diabetes were recruited to a case-control study. Seven subjects received blood pressure–lowering therapy and 8 did not. Therapy reduced capillary pressure from 18.2 [15.8 to 20.1] mm Hg to 15.9 [15.4 to 17.0] mm Hg (P=0.024 ANOVA), in contrast to the lack of effect of time alone. Mean arterial pressure was reduced from 110 [102 to 115] mm Hg to 105 [101 to 111] mm Hg (P=0.006, ANOVA). These findings provide a plausible mechanism by which reducing arterial hypertension may reduce the risk of microangiopathy in type 2 diabetes. (Hypertension. 2003;41:1111-1117.)

Key Words: antihypertensive therapy ■ capillaries ■ diabetes mellitus ■ microcirculation ■ vasculature

Hemodynamic abnormalities are well established in type 1 diabetes and contribute to the expression of microvascular complications.1 In particular, skin capillary pressure is increased in subjects with incipient nephropathy.2 The presence of capillary hypertension in type 1 diabetes is not associated with systemic blood pressure but is thought to be an early functional event, perhaps secondary to precapillary vasodilation, which may promote microvascular sclerosis, consistent with the hemodynamic hypothesis proposed by Parving and colleagues.3 The prevalence of microvascular complications is different, however, in type 2 diabetes, suggesting the underlying pathophysiology of microangiopathy may also differ. In type 2 diabetes, a striking abnormality is the impaired maximum skin microvascular hyperemic response to local heating present at diagnosis.4 This would suggest that changes are occurring in the prediabetic stage, and decreased microvascular reactivity in the skin of individuals at risk of developing type 2 diabetes supports this.5,6

Despite the changes in capillary pressure in type 1 diabetes and the early microvascular abnormalities in type 2 diabetes, skin nailfold capillary pressure appears to be normal in normotensive subjects with type 2 diabetes.7 However, whereas in young healthy control subjects, a small increase in systemic blood pressure is not transmitted to the skin capillary bed, probably because of alterations in precapillary resistance,8,9 in normotensive subjects with type 2 diabetes there is an association between blood pressure and capillary pressure, which suggests that the autoregulatory processes involved in the control of capillary pressure may be failing. It is well recognized that type 2 diabetes often coexists with other adverse hemodynamic and metabolic factors, with arterial hypertension present in >50% of subjects with type 2 diabetes, and other than good glycemic control, antihypertensive therapy is the only other therapy shown to play a major role in retarding the progression of microangiopathy.10 Microcirculatory abnormalities are also present in essential hypertension,11-14 and increased skin capillary pressure has been demonstrated in subjects with hypertension,15 although the underlying mechanisms remain unclear. In contrast to diabetes, the maximum microvascular hyperemic response is not impaired, although the minimum vascular resistance is increased, suggesting a structural adaptation to increased systemic pressure.16

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The nature of skin capillary pressure in the patient with type 2 diabetes and hypertension remains to be elucidated, as does the effect of antihypertensive therapy on capillary pressure in these patients.

The aim of this study was therefore (1) to examine whether capillary pressure was elevated in hypertensive (HT) subjects with type 2 diabetes compared with normotensive (NT) subjects with type 2 diabetes (study 1), (2) to examine if capillary pressure was different in HT subjects with type 2 diabetes compared with those with essential hypertension without diabetes (study 2), and (3) to assess whether antihypertensive therapy could alter capillary pressure in HT subjects with type 2 diabetes (study 3).

Methods

Study Subjects and Study Design

Study 1

Two groups of patients with type 2 diabetes (defined as diagnosis at 33 years or older, with no ketones present at diagnosis and not requiring insulin therapy for at least 1 year from diagnosis) were recruited from the diabetes outpatient department. Thirteen patients were normotensive and 13 gender- and age-matched patients were hypertensive. The definition of hypertension was a blood pressure of >140/80 mm Hg, as defined by current British Hypertension Society guidelines for subjects with diabetes. 17 Both groups had capillary pressure measurements on one occasion (observational study).

Study 2

Nineteen patients with essential hypertension (without diabetes) were recruited from the general medical outpatient department, and 19 gender-matched patients with type 2 diabetes and hypertension were recruited from the diabetes outpatient department. Six patients in this group were also included in study 1. The definition of diabetes and hypertension remained as above. Both groups had capillary pressure measurements on one occasion (observational study). This study had 90% power to detect a 2.7-mm Hg difference in capillary pressure at the 5% level.

Study 3

Two groups of age- and gender-matched patients with type 2 diabetes and hypertension were recruited from the diabetes outpatient department to enter a case-control study. Seven subjects received blood pressure–lowering therapy and 8 did not. The choice of antihypertensive agent prescribed was at the general practitioner’s discretion. Both groups of patients had capillary pressure measurements at baseline and at 3 months. The investigator performing the measurements of capillary pressure was blinded to which group the subject was in. In this study, a 1.68-mm Hg change in capillary pressure could be detected with 90% power at the 5% level.

Because the patient with type 2 diabetes and hypertension will often have cardiovascular disease, it was necessary to keep the inclusion criteria broad. In all studies, subjects had to be stable on their current therapy for at least 6 months for inclusion and were excluded if there was evidence of significant renal impairment (serum creatinine >150 μmol/L), evidence of upper limb arterial insufficiency or cardiac failure, or if the subject was taking nitrate therapy.

All subjects were asked to refrain from smoking on the day of the study and to avoid caffeine-containing drinks for 2 hours before the study.

The local medical research ethics committee approved the studies, and written informed consent was obtained from all participants.

Experimental Protocol

Capillary pressure measurements were performed in the morning after a light breakfast. Before measurements, subjects acclimatized for 30 minutes in a temperature-controlled laboratory (22.0±0.5°C). During this period, brachial blood pressure was calculated as the mean of 3 measurements using an automated device (Dinamap XL, Critikon Inc, Johnson and Johnson). The subjects lay supine with the left arm and hand comfortably supported in the midaxillary position. The cuticle and upper layer of the stratum corneum were pared away with a scalpel blade, with care taken not to damage or inflame the underlying skin; the subject’s finger was molded in a plasticine holder to reduce fine movements. A thermocouple was secured to the finger to monitor skin temperature. Blood glucose concentrations were measured in the subjects with diabetes at the beginning and end of the studies by a Precision glucometer (Medisense). Capillary pressure measurements were not performed or accepted if the blood glucose level was out with the range of 3.5 to 17.5 mmol/L.

Urinary albumin (mg/mL) to urinary creatinine (mmol/L) ratios were calculated from spot urine samples. A ratio of >2.5 mg/mmol on 2 consecutive samples was used to define diabetic microalbuminuria. Retinal photography was used, when possible, to determine the presence of diabetic retinopathy, and vibration sensory threshold was measured on the great toes with the use of a biothesiometer to determine the presence of diabetic neuropathy.

Blood samples were drawn from the antecubital vein without venous stasis. Samples were stored at -20°C. Laboratory for renal function, glucose, HbA1c, and urate by the Vitros 950 analyzer (Johnson and Johnson, Clinical Diagnostics, Amersham).

Measurements of Capillary Pressure

This technique has been described in detail elsewhere. 18 Briefly, after preparation of the nailfold, a ring of Granuflex is placed on the finger, which provides a reservoir to retain a pool of 0.9% saline in which atmospheric pressure was measured. Capillaries in the nailfold lie parallel to the surface of the skin and can be visualized by videomicroscopy. 19 The summit of the loop of the capillary was cannulated by a glass micropipette held by a micromanipulator (Leitz, Leica). A minimum of 4 cannulations were made in each subject. Capillary pressure was measured with a servonulled resistance system (IPM Model 4A). 18

For each subject, the mean capillary pressure was calculated as the mean of all capillaries cannulated. With the R wave of the ECG used as a timer to indicate the electrical start of the systolic beat, computer superimposition of several capillary pressure waveforms provided an averaged capillary waveform. From this, additional characteristics of the waveform were calculated. Although described further elsewhere,9 these included the capillary pulse pressure amplitude (CPPA), which is the difference between the diastolic trough to the systolic peak, and the systolic arrival time (SAT), which is the time from the peak of the ECG QRS complex to the start of the systolic increase in capillary pressure. Fast Fourier transformations were also calculated; these decompose the pressure waveform into its component frequencies and are represented by expressing the power of the second and third harmonics (H2 and H3) relative to the fundamental waveform.

Data Analysis

Data are presented as median value and 25th to 75th centiles. In study 1 and study 2, a comparison between groups was made by the Mann-Whitney U test. In study 3, two-way ANOVA of repeated measures was performed to assess the effect of blood pressure–lowering therapy compared with no additional therapy on capillary pressure and mean arterial pressure (MAP). Associations between variables were made by the Spearman rank correlation (Rs).

Results

Study 1: Normotensive Subjects With Type 2 Diabetes Compared With Hypertensive Subjects With Type 2 Diabetes

The 2 groups were well matched for age, gender, and skin temperature. They differed significantly in systolic blood pressure (SBP), diastolic blood pressure (DBP), and MAP,
per study design (Table 1). The median capillary pressure in the NT group was 17.7 (16.1 to 18.9) mm Hg as compared with 20.2 (17.4 to 22.7) mm Hg in the HT group ($P<0.029$) (Figure 1A). There was no difference in CPPA, SAT, or $H_2$ between the 2 groups (Table 2). Across both groups, there was a positive correlation between capillary pressure and SBP ($Rs=0.48$, $P<0.01$), DBP ($Rs=0.42$, $P<0.03$), and MAP ($Rs=0.51$, $P<0.008$) (Figure 1B). Five patients in the HT group were receiving antihypertensive therapy; there was no significant difference in the capillary pressure in this subgroup (HT subjects on BP therapy, 21.3 [18.6 to 22.7] mm Hg versus HT subjects not on therapy, 20.2 [15.0 to 22.9] mm Hg).

**Study 2: Hypertensive Subjects Without Diabetes Compared With Hypertensive Subjects With Type 2 Diabetes**

The 2 groups were matched for gender, skin temperature, and blood pressure. The groups differed in HbA1c as expected but also in those taking vasoactive therapy (9 in the diabetic group versus none in the nondiabetic group) (Table 3). Capillary pressure did not differ significantly in the 2 groups (17.1 [15.1 to 19.8] mm Hg HT without diabetes versus 19.4 [15.8 to 21.3] mm Hg HT with diabetes) (Figure 2). $H_3$ was higher in the nondiabetic group (22.1 [17.6 to 30.6] mm Hg) compared with the diabetic group (16.5 [10.4 to 33.3] mm Hg) ($P<0.02$). CPPA, SAT, and $H_2$ did not differ in the 2 groups (Table 4).

**Study 3: Case-Control Study of Blood Pressure Lowering in Subjects With Type 2 Diabetes and Hypertension**

Both groups were well matched (Table 5). There were no significant differences in the groups at baseline. Eight patients served as time control subjects (controls) and 7 patients received blood pressure–lowering therapy (cases). Of these 7, 3 subjects were antihypertensive therapy naïve, 3 subjects received add-on agents to existing therapy, and 1 had intensification by increasing dose of current agent. Ramipril was used in 5 subjects, benfrofluazide in 1, and doxazosin in 1. Compared with the time controls, blood pressure–lowering therapy had a significant effect on reducing capillary pressure ($P=0.024$, ANOVA) (Figures 3A and 3B) and reducing MAP ($P=0.006$) (Figures 3C and 3D). SBP ($P=0.02$) and DBP ($P=0.02$) were also reduced. In the treatment group, mean capillary pressure was lowered from 18.2 [15.8 to 20.1] mm Hg to 15.9 [15.4 to 17.0] mm Hg and MAP from 110 [102 to 115] mm Hg to 105 [101 to 111] mm Hg. Blood pressure–lowering therapy did not have a significant difference on CPPA ($P=0.08$), SAT ($P=0.4$), $H_2$ ($P=0.6$), or $H_3$ ($P=0.9$) (all ANOVA).

**Discussion**

We have shown in this study that (1) skin capillary pressure is elevated in subjects with type 2 diabetes and concomitant hypertension, (2) skin capillary pressure was not significantly different between HT subjects with type 2 diabetes and HT subjects with type 2 diabetes, and (3) blood pressure–lowering therapy had a significant effect on reducing capillary pressure and reducing MAP.
TABLE 2. Study 1 Capillary Pressure Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normotensive Subjects With Type 2 Diabetes (n=13)</th>
<th>Hypertensive Subjects With Type 2 Diabetes (n=13)</th>
<th>Mann-Whitney U Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary pressure, mm Hg</td>
<td>17.7 (16.1–18.9)</td>
<td>20.2 (17.4–22.7)</td>
<td>P=0.03</td>
</tr>
<tr>
<td>CPPA, mm Hg</td>
<td>4.9 (4.4–7.8)</td>
<td>6.2 (3.0–8.2)</td>
<td>P=0.8</td>
</tr>
<tr>
<td>SAT, ms</td>
<td>184.5 (177–203)</td>
<td>187 (178–204)</td>
<td>P=0.7</td>
</tr>
<tr>
<td>Harmonic 2</td>
<td>24.4 (19.9–34.8)</td>
<td>21.9 (15.6–27.8)</td>
<td>P=0.2</td>
</tr>
<tr>
<td>Harmonic 3</td>
<td>8.1 (5.0–11.4)</td>
<td>5.6 (2.6–6.4)</td>
<td>P=0.2</td>
</tr>
</tbody>
</table>

Data are shown as median (25th–75th percentile). Harmonic 2 indicates power in 2nd harmonic as % of fundamental; Harmonic 3, power in 3rd harmonic as % of fundamental.

TABLE 3. Study 2 Subject Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypertensive Subjects Without Type 2 Diabetes (n=19)</th>
<th>Hypertensive Subjects With Type 2 Diabetes (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>67 (64–72)</td>
<td>63 (57–66)</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>9/10</td>
<td>9/10</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.9 (26.4–34.8)</td>
<td>30.0 (29.0–33.5)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Creatinine, µmol/L</td>
<td>93 (71–97)</td>
<td>80 (67–93)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>152 (150–164)</td>
<td>161 (150–171)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>85 (83–89)</td>
<td>86 (80–94)</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>109 (106–112)</td>
<td>112 (102–121)</td>
</tr>
<tr>
<td>Skin temperature, °C</td>
<td>27.5 (24.4–30.0)</td>
<td>28.5 (25.7–31.0)</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.0 (4.8–5.6)</td>
<td>7.4 (6.4–8.1)</td>
</tr>
<tr>
<td>Subjects on BP therapy*</td>
<td>0</td>
<td>9</td>
</tr>
</tbody>
</table>

Data are shown as median (25th–75th percentile).

Subjects without diabetes, and (3) skin capillary pressure is lowered in HT subjects with type 2 diabetes by conventional antihypertensive therapy.

Previous work has shown that mean skin capillary pressure in normotensive subjects with type 2 diabetes (median capillary pressure, 17.6 [13.1 to 21.2] mm Hg) did not differ significantly from healthy control subjects. Our normotensive subjects with diabetes (17.7 [16.1 to 18.9] mm Hg) have capillary pressure in the normal range, confirming these results. In contrast, capillary pressure is elevated early in type 1 diabetes, especially in those patients at risk of nephropathy (also unpublished observations, AC Shore and JE Tooke, 2000). The elevation of capillary pressure and resultant microvascular sclerosis in type 1 diabetes supports the hemodynamic hypothesis. However, the presence of hypertension and accelerated atherosclerosis, commonly found with type 2 diabetes, increases the complexity when applying the same concept of the development of microangiopathy to type 2 diabetes.

In the presence of systemic hypertension, we have shown that skin capillary pressure is elevated in type 2 diabetes, suggesting that protective mechanisms have failed to prevent transmission of the increased pressure to the capillary bed. This is consistent with the increased transcapillary permeability to albumin seen in these patients. Whether elevated capillary pressure occurs elsewhere than the nailfold is not known and cannot be measured directly in humans. Imanishi and colleagues assessed glomerular capillary pressure indirectly in subjects with type 2 diabetes and near normal blood pressure, demonstrating an association of increased glomerular pressure with degree of microalbuminuria but not systemic pressure.

We did not show a significant difference when comparing HT subjects with type 2 diabetes and HT subjects without diabetes, although there was a trend to higher pressures in the diabetic group. The possibility of a type 2 error should be considered in this regard. The study had 90% power to detect a difference of 2.7 mm Hg between groups at the 5% significance level. A few issues from this study (study 2) are worth discussing. With increasingly effective clinical therapies available, the study of “clean” patients becomes more difficult. The different number of subjects taking antihypertensive therapy in our groups (Table 3) may have masked a difference by lowering the capillary pressure in the diabetic group. However, the blood pressure and capillary pressure were not different between those on therapy and those not on therapy in the subjects with diabetes. Although there was no statistical difference between the HT diabetic group and the HT nondiabetic group, Figure 2 appears to show 4 nondiabetic subjects who lie separate from the main group. We were...
TABLE 4. Study 2 Capillary Pressure Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypertensive Subjects Without Type 2 Diabetes (n=19)</th>
<th>Hypertensive Subjects With Type 2 Diabetes (n=19)</th>
<th>Mann-Whitney U Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary pressure, mm Hg</td>
<td>17.2 (15.1–19.8)</td>
<td>19.4 (15.8–21.3)</td>
<td>P=0.5</td>
</tr>
<tr>
<td>CPPA, mm Hg</td>
<td>4.4 (2.6–7.9)</td>
<td>4.9 (2.3–7.0)</td>
<td>P=0.9</td>
</tr>
<tr>
<td>SAT, ms</td>
<td>196 (180–214)</td>
<td>197 (178–210)</td>
<td>P=0.6</td>
</tr>
<tr>
<td>Harmonic 2</td>
<td>22.1 (17.6–30.6)</td>
<td>16.5 (10.4–21.3)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Harmonic 3</td>
<td>5.8 (2.5–9.5)</td>
<td>2.9 (1.8–6.2)</td>
<td>P=0.07</td>
</tr>
</tbody>
</table>

Data are shown as median (25th–75th percentile). Harmonic 2 indicates power in 2nd harmonic as % of fundamental; Harmonic 3, power in 3rd harmonic as % of fundamental.

unable to find any difference in the subject variables (Table 3) that distinguish these subjects from the rest, and therefore the complete data set probably represents the spread of capillary pressure in this population. The median capillary pressure values in the HT subjects with diabetes from study 1 (20.2 [17.4 to 22.7] mm Hg) and study 2 (19.4 [15.8 to 21.3] mm Hg) do not differ significantly, the small difference being explained by the different skin temperatures (31.0°C versus 28.5°C, respectively). In study 2, we were unable to accurately match for age, although in this study age was not correlated with capillary pressure. Finally, the attenuation of harmonic 2 in the HT subjects with diabetes compared with HT subjects without diabetes (study 2) may have occurred as a chance finding or could represent subtle vascular changes specific to diabetic angiopathy.

Although epidemiologic data suggest that hyperglycemia and hypertension are synergistic promoters of microangiopathy, there is relatively little direct evidence about the simultaneous effect of type 2 diabetes and hypertension on the microvasculature in humans. The impairment of maximum microvascular hyperemia is similar in normotensive and hypertensive patients with type 2 diabetes; the HT subjects, however, have a higher resistance to flow, suggesting structural (adaptive) changes. Rizzoni and colleagues demonstrated that whereas in hypertension eutrophic remodeling usually accounts for the increased media-to-lumen ratio, in type 2 diabetes hypertrophic remodeling is responsible, thus suggesting different pathogenetic mechanisms or cellular tissue responses. The coexistence of hypertension, however, did not worsen the already impaired endothelium vasodilation to acetylcholine and bradykinin in subcutaneous small arteries of patients with type 2 diabetes. Whatever processes are involved in the structural changes of the small resistance vessels, this supports our findings that the effect of diabetes and hypertension did not appear additive on skin capillary pressure.

The elevated skin capillary pressure in HT subjects with type 2 diabetes from study 1 supports the modified hemodynamic hypothesis proposed by Jaap and Tooke. Such that in contrast to type 1 diabetes, in which hyperglycemia results in precapillary dilation and increased capillary pressure, in type 2 diabetes changes occurring in “prediabetes,” for example, increased arteriolar resistance, are able to protect the capillary bed in the face of hyperglycemia until, in the presence of arterial hypertension, breakthrough capillary hypertension occurs. Abnormalities in the autoregulation of capillary pressure caused by failure of local or extrinsic mechanisms may also be involved.

TABLE 5. Study 3 Subject Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n=8)</th>
<th>Cases (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 (54–68)</td>
<td>63 (53–69)</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>5/3</td>
<td>6/1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.4 (28.0–33.5)</td>
<td>29.5 (25.0–31.8)</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>8.0 (6.9–9.2)</td>
<td>7.4 (6.3–8.0)</td>
</tr>
<tr>
<td>Subjects on BP therapy</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Retinopathy present</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>72 (64.3–99.3)</td>
<td>82 (55.0–91.0)</td>
</tr>
<tr>
<td>ACR, mg/mmol</td>
<td>2.15 (1.5–6.7)</td>
<td>1.6 (1.3–6.3)</td>
</tr>
<tr>
<td>Skin temperature, °C</td>
<td>31.7 (28.9–34.5)</td>
<td>31.6 (31.0–32.5)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>143 (131–174)</td>
<td>160 (142–174)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>80 (75–84)</td>
<td>88 (81–91)</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>102 (96–115)</td>
<td>107 (103–117)</td>
</tr>
<tr>
<td>Smokers</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes duration, y</td>
<td>9 (4–18)</td>
<td>5 (2–7)</td>
</tr>
</tbody>
</table>

Data are shown as median (25th–75th percentile). No significant difference between groups.
potentiation of bradykinin, is known to affect the ratio of precapillary to postcapillary resistance ratio, particularly in the glomerulus.\textsuperscript{21} We acknowledge that a weakness of study 3 is that it was not a randomized trial; the patients were selected for treatment by using blood pressure guidelines\textsuperscript{17} and compared with time control subjects who did not fulfill treatment requirements. However, we believe this study provides useful insights into the microvascular effects of commonly used therapies. Although intuitively it would seem likely that the reduction in skin capillary pressure was as a result of lower systemic pressure, the correlation between blood pressure and capillary pressure reduction failed to reach significance ($P=0.09$). This finding may be due to our sample size or could be due to more complex control mechanisms closer to the capillary bed.

In conclusion, in an extension of the work demonstrating abnormal skin capillary pressure dynamics in NT subjects with type 2 diabetes,\textsuperscript{7} these data show for the first time that capillary pressure is elevated in type 2 diabetes in the presence of hypertension and that conventional blood pressure–lowering therapy can influence this. This provides a plausible mechanism by which reducing arterial hypertension may reduce the risk of microangiopathy in patients with type 2 diabetes. Further research is required to focus on the reasons for the damaging effects of capillary hypertension and on specific therapeutic strategies that normalize not only systemic but also microvascular pressure.

Acknowledgments

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References

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