Eutrophic Remodeling of Small Arteries in Type 1 Diabetes Mellitus Is Enabled by Metabolic Control
A 10-Year Follow-Up Study

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Abstract—Type 2 diabetes mellitus profoundly changes small artery remodeling in response to hypertension. Abnormal increases of both wall thickness and lumen diameter are associated with an increased mortality. Changes to small artery structure in response to blood pressure (BP) in patients with type 1 diabetes mellitus have never been examined. In 1997, 17 patients with type 1 diabetes mellitus and 9 control subjects underwent in vitro assessment of gluteal-fat small arteries using pressure myography. Patients with BP <140/90 mm Hg (systolic BP: 119±3 mm Hg; n=12) had normal-resistance artery structure. However, patients with BP >140/90 mm Hg (systolic BP: 152±5 mm Hg; n=5) demonstrated vascular hypertrophic remodeling with a significant increase in the medial cross-sectional area and wall thickness. In 2008, 8 of the original 17 diabetic patients returned for a repeat assessment. All 8 of the patients had significantly improved cholesterol (2008: 154±9 mg/dL versus 1997: 191±9 mg/dL; P=0.01) and low-density lipoprotein cholesterol (2008: 79±8 mg/dL versus 1997: 122±9 mg/dL; P=0.003) but higher BPs (systolic BP: 2008: 136±3 mm Hg versus 1997: 119±6 mm Hg; P=0.03). Glycemia was improved (2008: 7.9±0.3% versus 1997: 8.9±0.6%; P=0.17), but not significantly so. In the small arteries studied, there were significant increases in medial wall thickness and wall:lumen ratio, but cross-sectional area was unchanged, indicating eutrophic remodeling. Collectively, these findings suggest that, with poor metabolic control, small arteries from patients with type 1 diabetes mellitus show hypertrophic growth in response to elevated BP, similar to that seen in type 2 diabetes mellitus. However, metabolic improvements enable eutrophic remodeling to occur in response to an increase in BP. This has only been observed previously in patients without diabetes mellitus. (Hypertension. 2009;54:134-141.)

Key Words: diabetes mellitus ■ hypertension ■ microalbuminuria ■ resistance artery ■ remodeling ■ complications

Hypertension and diabetes mellitus are 2 main determinants of small artery structure. In patients with essential hypertension, the wall of the small artery undergoes eutrophic inward remodeling, which results in a reduction in lumen diameter by increasing wall thickness.1,2 In patients with type 2 diabetes mellitus, hypertension causes a very different remodeling response. Outward growth increases wall thickness, and lumen diameter is preserved or increased.3,4 Recently, this difference in response to blood pressure (BP) has been suggested as an explanation for the propensity of patients to develop target organ damage in diabetes mellitus.5-6 It has been postulated that the inability of the small artery to reduce the lumen diameter in response to central hypertension may result in the transmission of elevated pressures downstream to susceptible organs, eg, the eye or the kidney.5-7 This appears to be supported by clinical observations, which have shown that the retinal vessel caliber is larger in patients with diabetes mellitus.8 Also, in patients with type 1 diabetes mellitus, a larger vessel caliber can predict progression to both nephropathy9 and retinopathy.10

To date, only 1 study has examined the structure of small arteries in type 1 diabetes mellitus, with no difference found between normoalbuminuric normotensive patients and control participants.11 In this study, we have had the opportunity to study subcutaneous small artery function and structure in patients with a long duration (23 years) of diabetes mellitus with varying degrees of microalbuminuria and hypertension. In addition, we have performed a 10-year follow-up study in a subgroup that remained normoalbuminuric despite an increase in BP.

Subjects and Methods
Patient Recruitment and Follow-Up
In 1997, patients with type 1 diabetes mellitus and healthy nondiabetic control subjects gave full written informed consent and took...
part in a study approved by the Manchester Local Research Ethics Committee. Study protocols were consistent with the principles of the Declaration of Helsinki, and procedures followed were in accordance with the institutional guidelines at Manchester Royal Infirmary. The presence of hypertension (diastolic pressure >90 mm Hg or systolic pressure >140 mm Hg on 2 consecutive occasions after being seated for 20 minutes) was accepted according to European Society of Hypertension guidelines, and type 1 diabetes mellitus was diagnosed using guidelines of the Expert Committee for the Diagnosis and Classification of Diabetes.13

On the day of the study, venous blood samples were drawn for assessment of renal function, random blood sugar, lipid profile, and glycylated hemoglobin. Microalbuminuria was quantified by analysis of overnight urinary albumin excretion rate on the day of the study. BP was measured with an appropriate cuff size while the patient was sitting, after 20 minutes of rest. A semiautomatic machine (Omron 705 CP, White Medical) was used for the study with the mean of 3 readings recorded.

In 2008, the diabetic patients from the 1997 cohort were contacted and asked to return for a repeat study visit. Full written informed consent was given, and the study was approved by the Manchester Local Research Ethics Committee. BP, blood tests, and microalbuminuria were assessed as outlined above.

Pressure Myography
A single subcutaneous gluteal fat biopsy was obtained from each subject using 3 to 5 mL of 1% lignocaine, allowing tissue (2.0×1.5×1.5 cm) to be harvested and placed immediately in ice-cold physiological saline solution (PSS).4 Small arteries, 150 to 300 μm, were dissected from the tissue and carefully cleaned under a dissecting microscope. Isolated vessels were then transferred to an arteriographic bath chamber (Living Systems Instruments)4 and cannulated as described previously2,14. The chamber was placed on the stage of an inverted microscope, superfused with PSS, and gassed with 5% CO2-95% air (pH 7.40 to 7.45) at a superfusion rate of 25 mL/min. PSS composition was (in mmol/L) 130.000 NaCl, 4.700 KCl, 1.170 KH2PO4, 1.170 MgSO4, 0.026 EDTA, 1.600 CaCl2, and 5.500 glucose. The artery was connected to a chart recorder. The temperature of the bath chamber was increased and kept at 37°C using a circulating water heater.

Calculations
The wall:lumen ratio was calculated as WT/Do×100, where WT is wall thickness and D is lumen diameter. Wall cross-sectional area (CSA) was calculated as follows: CSA = π(D2−WT2)/4. Stress (σ) = P×CSA/2WT, where P is pressure and 1 mm Hg =1334 dyn/cm². Strain (ε) = (D−Do)/Do, where Do is the lumen diameter at 3 mm Hg.

The remodeling index is defined as the percentage of the observed difference in the ID of hypertensive and normotensive vessels that could be accounted for by remodeling of the normotensive vessel. The remodeling index is calculated as follows: consider a “normotensive” vessel, with internal and external media diameters (D1h) and (D1e), respectively, and a “hypertensive” vessel with internal and external media diameters (D2h) and (D2e), respectively. The corresponding media cross-sectional areas are as follows: CSAh = [(π/4)×(Dh)²] and CSEA = [(π/4)×(De)²]−[(π/4)×(Dh)²], respectively. Remodeling of the normotensive vessel in which the cross-sectional area is kept equal to CSAh but its external diameter became (D1e) then would give an index (D1e)/remodel given by the following equation:

\[
(D1e/\text{remodel}) = \sqrt[4]{(Dh^2 - D_e^2)} / 2 \times (\text{CSA}_h / \pi).
\]

Thus, remodeling index equals the following: 100×(D1e−(D1e/\text{remodel}))/[(D1h−D1e)/D1h] If the remodeling index is not equal to 100, then there will have been growth, which is here defined as follows: growth index = (CSA−CSA)/(CSA).

This equation can also be used to quantify reverse remodeling, i.e., an increase in lumen without a change in media cross-sectional area. Here, a remodeling index <100% will be associated with a negative growth index, implying atrophy. By comparing vessel characteristics from diabetic groups with and without hypertension with vessels from control subjects, it is possible to determine whether remodeling, either eutrophic or hypertrophic, has occurred. Data from remodeling indices are calculated from mean values, so SE values are not provided. Stress=(P×D)/2WT, where pressure (P)=1334 dyn/cm²; strain=(D−Do)/Do, where Do is the diameter at 3 mm Hg.

Statistical Analysis
Statistical analysis was performed using SPSS for Windows. Data are expressed as the mean±SE. Statistical comparisons were made using the Student unpaired t test (comparison of clinical data and endothelial function: Tables 1 and 2) or, for multiple readings, a multiple ANOVA (comparison of pressure/diameter graphs: Figures 1 to 5). P<0.05 was considered significant.

Results
1997: Baseline Patient Details
Seventeen patients with type 1 diabetes mellitus and 9 control subjects were studied. Patients with diabetes mellitus had a significantly higher HbA1c (9.0±0.3% versus 5.3±0.2%; P<0.001) than control subjects. There were no significant differences in systolic pressure (patients: 129±4 mm Hg versus controls: 138±4 mm Hg; P=0.136), diastolic pressure (patients: 78±3 mm Hg versus controls: 83±5 mm Hg; P=0.394), cholesterol (patients: 205±11 mg/dL versus controls: 190±9 mg/dL; P=0.291), or age (patients: 46±3 years versus controls: 47±4 years; P=0.943).

Diabetic patients were stratified according to their BP. Thus, 5 patients with BP >140/90 mm Hg were compared with 12 patients with BP <140/90 mm Hg. Patients with high BP tended to be older (high BP: 57±6 years versus low BP: 42±3 years; P=0.07) and with longer durations of diabetes mellitus (high BP: 29±6 years versus low BP: 21±3 years; P=0.228), although these differences were not significant. The remainder of the clinical details is shown in Table 1. Of the 5 patients with BP >140/90 mm Hg, 2 were on angiotensin-converting enzyme (ACE) inhibitor monotherapy, 1 patient was taking an ACE inhibitor and a thiazide diuretic, and 1 patient was taking an ACE inhibitor, a thiazide diuretic, and moxonidine. Of the 12 patients with BP <140/90 mm Hg, 5 were on monotherapy for hypertension with ACE inhibitors.
Table 1. 1997 Baseline Characteristics of Control Subjects (n=9) and Patients With Type 1 Diabetes Mellitus (n=17)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=9)</th>
<th>Type 1 Diabetes Mellitus (n=17)</th>
<th>Type 1 Diabetes Mellitus With BP &gt;140/90 mm Hg (n=5)</th>
<th>Type 1 Diabetes Mellitus With BP &lt;140/90 mm Hg (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>47±4</td>
<td>46±3</td>
<td>57±6</td>
<td>42±3</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>138±4</td>
<td>129±4</td>
<td>152±5</td>
<td>119±3*</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>83±5</td>
<td>78±3</td>
<td>86±6</td>
<td>75±3</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>190±9</td>
<td>205±11</td>
<td>224±26</td>
<td>197±12</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>67±6</td>
<td>65±4</td>
<td>62±3</td>
<td>66±5</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>98±16</td>
<td>133±25</td>
<td>188±77</td>
<td>110±15</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>108±8</td>
<td>129±9</td>
<td>146±21</td>
<td>122±10</td>
</tr>
<tr>
<td>Duration of diabetes mellitus, y</td>
<td>23±3</td>
<td>29±6</td>
<td>21±3</td>
<td></td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.3±0.2</td>
<td>9.0±3</td>
<td>8.8±0.5</td>
<td>8.9±0.4</td>
</tr>
<tr>
<td>UAER, µg/min</td>
<td>10.8±2.9</td>
<td>14.9±5.3</td>
<td>9.2±3.5</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors, n/N</td>
<td>9/17</td>
<td>4/5</td>
<td>5/12</td>
<td></td>
</tr>
</tbody>
</table>

Diabetic patients are also further stratified into those with BP >140/90 mm Hg (n=5) and those with BP <140/90 mm Hg. HDL indicates high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; UAER, urinary albumin excretion rate. Numbers shown are average value±SE unless otherwise described.

*Data show the significant differences between patient groups stratified by BP.

2008: Follow-Up Patient Details

Of the original cohort, at 10 years, 1 patient had died and another was incapacitated after a major stroke. Only 1 of the patients in this group was from the group with BP >140/90 mm Hg at baseline (Figure 1, pale blue line). Both their demographic and small artery details were compared directly across the 10-year follow-up period (ie, 8 patients in 1997 versus the same 8 patients in 2008). In 2008, the follow-up group was older (2008: 54±5 years versus 1997: 44±5 years; P=0.16) but also had significantly higher systolic BP (2008: 136±3 mm Hg versus 1997: 119±2 mm Hg; P=0.03). Total cholesterol (2008: 154±9 mg/dL versus 1997: 191±9 mg/dL; P=0.01) and low-density lipoprotein cholesterol (2008: 79±8 mg/dL versus 1997: 122±9 mg/dL; P=0.003) were significantly lower, most likely as a result of almost universal treatment with statin drugs (follow-up: 6 of 8 patients; baseline: 0 of 8 patients). At baseline, 5 of the 8 patients were taking ACE inhibitors, and 1 was taking an additional thiazide diuretic (Figure 1, pale blue line; this was the patient who was in the baseline group with BP >140/90 mm Hg). At follow-up, 4 of 8 patients were taking ACE inhibitors, whereas 1 was taking an angiotensin II receptor I blocker. The medication of the patient who was in the group with BP >140/90 mm Hg at baseline was unchanged over the 10-year follow-up period. Triglycerides, HbA1c, and urinary albumin excretion rate were lower at follow-up, but these differences were not significant (Table 2).

Resistance Vessel Structure

1997: Type 1 Diabetes Mellitus Versus Control Subjects

Across the range of intraluminal pressures used, we found no significant differences in cross-sectional area (P=0.182), wall thickness (P=0.166), wall:lumen ratio (P=0.502), or lumen diameter (P=0.132) between patients with type 1 diabetes mellitus and control subjects.

1997: Type 1 Diabetic Patients Stratified by BP

Patients with BP <140/90 mm Hg (n=12) showed no difference in vessel structure compared with control participants (n=9; Figure 2). Conversely, diabetic patients with BP >140/90 mm Hg (n=5) had a significantly larger medial cross-sectional area (P=0.006 versus control and P=0.02 versus normotensive patients; multiple ANOVA), wall thickness (P=0.009 versus control and P=0.03 versus normotensive patients; multiple ANOVA), and lumen diameter (P<0.001 versus control and P=0.03 versus normotensive patients; multiple ANOVA) compared with both diabetic patients with BP <140/90 mm Hg and control participants. There was no significant difference in the wall:lumen ratio seen in this group. Compared with control participants, patients with a BP >140/90 mm Hg showed remodeling (index: 136%) and growth of the arterial wall (index: 64%) indicative of hypertrophic remodeling of the arterial wall.
betic patients with BP <140/90 mm Hg showed remodeling (152%) but, importantly, no growth (index: 10%). Treatment for hypertension with ACE inhibitors was greater in the group with high BP (4 of 5) compared with those with low BP (5 of 12).

Patients Without Microalbuminuria 2008 Versus the Same Patients in 1997
A direct comparison was made between structural characteristics of the arteries from the patients biopsied in 2008 (n = 8) and arteries from the same patients in 1997 (n = 8; Figure 3). Of the patients followed up, 1 was from the high-BP group at baseline, whereas the remaining 7 were from the group with normal BP. Over time, arteries showed a process of eutrophic remodeling with significant increases in the wall:lumen ratio ($P=0.004$; multiple ANOVA) and wall thickness ($P=0.05$; multiple ANOVA). There was a reduction in lumen diameter that did not attain significance ($P=0.08$; multiple ANOVA; Figure 3). Compared with 1997 structural characteristics, arteries from 2008 showed a remodeling index of 68% and a growth index of −13%, confirming eutrophic remodeling.

Small Artery Distensibility
At baseline (1997 group), resistance arteries from diabetic patients, irrespective of BP, tended to have a reduction in

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Figure 1. The change in the vascular data (BP and wall:lumen ratio) over the 10-year period is presented as individual line graphs for each patient at the 2 time points studied. To facilitate interpretation, each patient is allocated a different color. Wall:lumen ratio against time is shown in A. Systolic BP against time is shown in B.

Figure 2. Patients with type 1 diabetes mellitus and BP <149/90 mm Hg have no significant structural differences when compared with control subjects. Diabetic patients with blood pressure $>$140/90 mm Hg have significantly greater lumen diameter (A), cross-sectional area (B), and wall thickness (C) when compared with the normotensive patients and control participants. There is no difference in the wall:lumen ratio (D). *$P<0.05$ (comparison of diabetic patients with and without high BP) and **$P<0.05$ (comparison of diabetic patients with BP $>$140/90 mm Hg vs control participants) using multiple ANOVA.
distensibility when compared with control participants, but this did not achieve significance (Figure 4C). Over the 10-year follow-up period, the arteries from diabetic patients showed a significant increase in their distensibility \((P=0.004; \text{multiple ANOVA; Figure 5C})\), approximating the phenotype of the nondiabetic controls in 1997 (comparative data not shown).

**Figure 3.** Comparison of arteries taken from patients in 2008 \((n=8)\) with those taken from the same patients in 1997 \((n=8)\). At follow-up, arteries taken in 2008 show evidence of eutrophic remodeling. There is a nonsignificant reduction in lumen diameter \((A; P=0.08)\) and significant increases in wall thickness \((C)\) and in the wall:lumen ratio \((D)\). There are no significant differences in cross-sectional area \((B)\). \(^*P<0.05\) (comparison of 2008 arteries with 1997 arteries).

**Small Artery Endothelium-Dependent Function**

At baseline, there were no significant differences in log-EC\(_{50}\) concentrations or maximum response to acetylcholine (control: log EC\(_{50}\): 7.10±0.13, maximum response: 81.0±10.5%; type 1 diabetes mellitus with BP: >140/90 mm Hg: log EC\(_{50}\): 6.80±0.12, M maximum response: 98.8±1.2%; type 1 diabetes mellitus with BP <140/90 mm Hg: log EC\(_{50}\):...
6.60±0.30, maximum response: 87.2±4.2%). Similarly, at follow-up there were no significant differences in log-EC_{50} concentrations or maximum response to acetylcholine compared with baseline measurements (type 1 diabetes mellitus in 2008: log EC_{50}: 6.9±0.13; maximum response: 80.0±7.4%).

**Discussion**

The main observation from this study is that, in patients with type 1 diabetes mellitus, changes to metabolic control are able to influence subcutaneous small artery wall remodeling in response to BP. In our baseline cohort, suboptimal lipid and glycemic controls were associated with hypertrophic remodeling of the small artery wall in response to elevated BP. After 10 years of follow-up, patients returning for a repeat biopsy had a 17-mm Hg increase in BP, but lipid and, to a lesser extent, glycemic, profiles were improved. In response to the rise in BP, small arteries from these patients did not show a hypertrophic growth response thought to be pathogenic of diabetes mellitus. Instead, there was eutrophic remodeling, with an increase in wall thickness and wall:lumen ratio and a reduction in lumen diameter. This process has not been observed previously in diabetes and, in our cohort, was associated with protection from the development of microalbuminuria despite an increase in BP.

The 2 main determinants of small artery diameter and wall structure are hypertension and diabetes mellitus. Essential hypertension causes eutrophic remodeling: inward growth of the wall results in a reduction in lumen diameter and an increase in wall thickness and wall:lumen ratio. In patients, this has been observed in both omental and subcutaneous arteries, but in experimental animals, eutrophic remodeling has been seen in arteries from the heart, brain, bowel, and kidney. Recently, it has been suggested that the ability to reduce the lumen diameter of small arteries in hypertension serves to limit downstream transmission of elevated central pressures, which may damage susceptible organs. This has particular significance for patients with type 2 diabetes mellitus who are overly at risk for hypertensive-related target organ damage. In type 2 diabetes mellitus and hypertension, growth of the arterial wall occurs in an outward fashion: there is an increase in wall thickness and preservation of the lumen diameter. Although in vitro this has only been seen in arteries from the subcutaneous fat, corroborative evidence has come from retinal screening studies. These have also demonstrated a larger vessel caliber in patients with diabetes mellitus compared with control participants. In addition, in patients with type 1 diabetes mellitus, a larger arterial caliber predicts progression of both retinopathy and nephropathy.

Small artery structure has only once previously been directly studied in patients with type 1 diabetes mellitus, with no differences found in the structure between normotensive normoalbuminuric patients and control participants. Similarly, in our baseline cohort, normotensive patients had normal wall structure and lumen diameter. However, in patients with BP >140/90 mm Hg, an abnormal hypertrophic growth response was seen, even with almost universal ACE inhibitor treatment. Our findings suggest that, without a growth stimulus (stretch of the arterial wall by hypertension), resistance arteries from patients with type 1 diabetes mellitus do not undergo structural change. However, when exposed to hypertension, the arteries grow outward (hypertrophic remodeling), which is associated with an increase in lumen diameter.

At follow-up, however, a different structural response to hypertension was seen. Eight patients of the original cohort of 17 consented to a repeat biopsy, and their arterial structure and function in 2008 were compared with those observed in 1997. Over the 10-year period of the study, small arteries underwent eutrophic remodeling in response to a 17-mm Hg increase in BP. Thus, compared with baseline, there were significant increases in wall thickness and wall:lumen ratio and a reduction in lumen diameter, which approached significance. Remodeling indices confirmed eutrophic change. These changes are more in keeping with essential hypertension than diabetes mellitus, and there are a number of possible explanations. The remodeling may be age related; changes to human small artery structure have never been studied over a...
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dysfunction. In vivo techniques, which are able to be used to investigate this.

As such, the relative contribution of each factor to the increase in distensibility and the change in remodeling profile is unknown. Additional studies, which are likely to be in animal models of type 1 diabetes mellitus, are now indicated to investigate this.

Another important consideration is that, in 1997, the group with hypertension and hypertrophic remodeling had higher BP (mean systolic BP: 152 mm Hg) than that of the hypertensive patients with eutrophic remodeling in 2008 (mean systolic BP: 136 mm Hg). It is possible that, in patients with type 1 diabetes mellitus, there is a level of BP above which hypertrophic growth supervenes over inward eutrophic remodeling, irrespective of glycemic control or cholesterol, and this occurred in the group studied in 1997.

We did not find any significant differences in endothelial function in our patients. There have only been 3 previous studies of small artery endothelial function in patients with type 1 diabetes mellitus. In 2, endothelial function was preserved, whereas in the third there was endothelial dysfunction. In vivo techniques, which are able to be used on a larger scale, suggest that endothelial function is damaged in patients with type 1 diabetes mellitus only in the presence of microvascular complications or poor metabolic control. Clearly, however, these studies represent a different circulatory bed versus that studied here.

From a clinical perspective, both reviews and studies have emphasized the potential benefits of a reduction in small artery diameter in the context of hypertension and diabetes mellitus, and it is interesting to note that, at follow-up, all of the patients who were biopsied were free from microalbuminuria despite an increase in BP and >30 years of exposure to diabetes mellitus. There is, however, no evidence that renal arteries undergo similar remodeling processes to those from subcutaneous gluteal fat, and, as such, these findings may have been incidental. In addition, at baseline, patients with hypertension and associated hypertrophic growth of the artery wall did not show an increased urinary albumin excretion compared with normotensive patients who had normal arterial structure.

In conclusion, we have shown that remodeling of subcutaneous small arteries in response to hypertension in patients with type 1 diabetes mellitus is likely to be influenced by metabolic control. When lipids and glycemia are poorly controlled, there is a classical diabetic hypertrophic growth response with the preservation of lumen diameter. With good metabolic control, however, eutrophic remodeling supervenes, with a subsequent reduction in lumen diameter. Our findings are associative, because cause and effect cannot be established, and, furthermore, given the small size of the cohort, may be unique to the patients studied. However, the data are consistent with current thought, which holds that a reduction in vessel caliber is protective against the transmission of central pressures to vulnerable downstream tissues. If changes observed in the subcutaneous arteries are similar to those in similar-sized renal arteries, our findings may explain why, at follow-up, diabetic patients with an increase in BP were protected from the development of microalbuminuria.

Perspectives

The structural responses of small resistance arteries to high BP have been studied for >20 years. In every circulatory bed examined, the elevated intraluminal pressure (ie, hypertension) initiates inward remodeling of the arterial wall. Thus, there is an increase in wall thickness, a decrease in lumen diameter, and, so, an increase in the wall:lumen ratio. In type 2 diabetes mellitus, however, hypertension causes outward growth of the arterial wall, and, as a result, there is preservation or even an increase in lumen diameter. Recently, the inability of small arteries from patients with diabetes mellitus to undergo eutrophic remodeling in response to hypertension has been suggested as a contributory factor in the development of distal target-organ damage. It is thought that the unchanged lumen diameter allows downstream transmission of elevated central pressures. This process has also been referred to as a “passive pressure microcirculation.”

The response of small arteries to high BP in patients with type 1 diabetes mellitus has not been examined previously. We show that, in the presence of poor metabolic control, high BP is associated with outward growth of the arterial wall. However, in a subset of patients followed up over 10 years, improvements to metabolic control were associated with eutrophic remodeling of the artery in response to a 17-mm Hg increase in BP. The capacity of arteries to remodel in this fashion has never been observed in patients with diabetes mellitus. Additional studies are indicated to determine whether this is associated with protection from organ damage.

Acknowledgments

We thank all of the volunteers who participated in this study and staff of the Manchester Wellcome Trust Clinical Research Facility.

Sources of Funding

This study was funded by the European Society for Hypertension and the Wellcome Trust. A.M.H. has received speaking honoraria from Pfizer, Bayer, and Daiichi Sankyo. R.A.M. has received speaking honoraria from Pfizer, Astra-Zeneca, and Lilly. A.D.S. is a European Society for Hypertension Research Fellow.
Disclosures

None.

References

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Hypertension. 2009;54:134-141; originally published online May 26, 2009;
doi: 10.1161/HYPERTENSIONAHA.109.129718

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