High prevalence of carotid artery disease in patients with atheromatous renal artery stenosis

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Abstract

Background. Renovascular disease is the most frequently encountered secondary cause of hypertension and is one of the few potentially reversible causes of chronic renal failure. These patients are at increased risk of having cerebrovascular events following operative management for atheromatous renal-artery stenosis. We studied the prevalence of carotid-artery disease in patients with atheromatous renal-artery stenosis.

Methods. A cross-sectional study was carried out on 38 consecutive patients with atheromatous renal-artery stenosis who underwent renal-artery balloon angioplasty. Extracranial carotid atherosclerosis was assessed using a commercially available colour Doppler scanner, depending on the velocity of the peak systolic waveform in the internal carotid artery, and the internal carotid-artery/common carotid-artery ratio.

Results. Twenty-one patients (55.3%) had normal or mild carotid-artery disease, 10 (26.3%) had moderate, and 7 (18.4%) had severe carotid-artery disease. Nine patients had previously suffered a stroke (eight infarction, one haemorrhage) and one had multiple transient ischaemic attacks.

Conclusions. Our results suggest that, in patients with atheromatous renal-artery disease severe enough to require angioplasty, 4 out of 10 appear to have moderate to severe carotid-artery disease. This may explain the increased prevalence of atherothrombotic cerebrovascular events in these patients, and also previous observations that, following operative management for atheromatous renal-artery stenosis, some patients had developed an acute or late cerebrovascular event. We suggest therefore that such patients should always be regarded as having generalized vascular disease not confined to one system, and need to be assessed for carotid-artery disease prior to operative management for atheromatous renal-artery stenosis.

Key words: artery; atheromatous; carotid; disease; renal

Introduction

Renovascular disease is the most frequently encountered secondary cause of hypertension and is one of the few potentially reversible causes of chronic renal failure [1,2]. It is also an important and potentially reversible cause of recurrent pulmonary oedema and apparent congestive heart failure in patients without overt coronary or valvular heart disease [3–5]. Certain groups of patients, those with peripheral vascular disease, are particularly at risk of having renal-artery disease [6–8]. In these patients the prevalence of atheromatous renal-artery stenosis increases with increasing severity of peripheral vascular disease [6]. However, little is known of the prevalence and importance of coexistent carotid-artery disease in patients with atheromatous renal-artery stenosis.

We performed a cross-sectional study to investigate the prevalence, severity, and vascular risk factors of carotid-artery disease in patients undergoing elective renal percutaneous balloon angioplasty.

Subjects and methods

We studied 38 hypertensive subjects (mean age 65.5±7.9 years; 21 males) who were consecutively referred between January 1992 and January 1994 for percutaneous balloon renal angioplasty (PTA). Thirty-six were white and two Asian. Clinical indications for performing PTA included the following: (1) severe or uncontrolled hypertension, (2) worsening renal function, (3) apparent congestive heart failure in the absence of an obvious cause such as ischaemic or valvular heart disease.

Supine systolic and diastolic pressures were recorded three times, 2 min apart, using a semiautomatic ultrasound sphygmomanometer (Arteriosonde, Roche), 2–4 weeks prior to the renal PTA. Non-fasting venous blood samples were taken at the same time with the subject seated and without stasis for determination of serum electrolytes, creatinine, blood glucose and cholesterol. Subjects gave informed consent for

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the studies which were approved by the hospital ethical committee.

Renal digital subtraction angiography (DSA) was performed using a 4F pigtail catheter positioned below the origin of the superior mesenteric artery. The renal arteries were imaged in the right posterior oblique position at an angle of 25° [9]. The severity of renal-artery stenosis was assessed by an experienced vascular radiologist unaware of the risk factors measurements and of the results of the carotid duplex examinations. The severity of atherosclerotic renal-artery disease was assessed depending on the presence of either unilateral or bilateral stenosis; a grade 1 was assigned if there was unilateral disease (stenosis ≥ 75%); a grade 2 if bilateral renal-artery stenosis (at least one artery with a ≥ 75% and the other with ≥ 50% stenosis); and grade 3 if there was one occluded renal artery and a stenosis in a single functioning kidney (stenosis ≥ 75%).

Extracranial carotid atherosclerosis was assessed using a commercially available colour Doppler scanner (Ultramark 9 ATL and Hitachi EUB 415 scanners; 4–7.5 MHz linear array probe), by an experienced ultrasound operator who had no prior knowledge of the results of renal angiography. The Doppler examinations were performed within 6 months of renal PTA. The severity of carotid-artery disease was assessed depending on the velocity of the peak systolic waveform in the internal carotid artery, and the internal carotid artery/common carotid artery (ICA/CCA) ratio: normal or mild disease if peak systolic velocity < 130 cm/s; moderate if peak systolic velocity > 130 cm/s (unilateral or bilateral) and ICA/CCA ratio > 1.8, and severe if peak systolic velocity > 250 cm/s (unilateral or bilateral), and ICA/CCA ratio > 3.5 [10]. Stenosis was considered haemodynamically significant if the peak systolic velocity was > 130 cm/s and ICA/CCA ratio > 1.8.

Patients were also clinically assessed for the presence of atherosclerosis in other major vessels. Coronary artery disease was diagnosed in those patients with a history of chronic stable angina and a positive exercise treadmill test and/or a well-documented history of acute myocardial infarction (including electrocardiographic and/or angiographic evidence). Peripheral vascular disease was diagnosed in those patients with effort-induced intermittent claudication and/or evidence of atheroma in aortoiliac and/or peripheral vessels on angiography. Smoking habits were also recorded.

Statistical analysis

Results are expressed as mean ± standard deviation, or as percentages where appropriate. Analysis of variance was used to assess differences between the means in multiple group comparisons. \( \chi^2 \) tests for trends were used to test for differences between the frequency data. A two-tailed \( P \) value of < 0.05 was considered to be statistically significant when comparing two groups, and 0.017 when comparing three groups.

Results

Clinical data

The clinical and demographic data of patients with atherosclerotic renal-artery stenosis are shown in Tables 1 and 2. Mean supine blood pressure of patients was 179/92 ± 22/13 mmHg, mean cholesterol 6.6 ± 1.35 mmol/l, and mean serum creatinine was 178 ± 92 μmol/l. All patients were on treatment with at least one drug for high blood pressure.

Nine of the above patients presented with signs and symptoms of 'apparent' heart failure [5] (in the absence of overt ischaemic or valvular heart disease) despite treatment with diuretics. In these nine patients renal angioplasty was followed by a large fall in blood pressure from 191/94 ± 7/3 mmHg to 150/75 ± 8/5 mmHg 2 days after intervention (\( P < 0.01 \)), and a fall in serum creatinine from 200 ± 37 μmol/l to 140 ± 11 μmol/l (\( P < 0.025 \)) in a week.

Atherosclerosis affecting renal and carotid vessels

Percutaneous balloon renal angioplasty was performed in 17 (44.7%) female and 21 (55.3%) male patients. Twelve (31.6%) had unilateral atheromatous renal-artery disease (grade 1), 11 (28.9%) had bilateral disease (grade 2), and 15 (39.5%) had one occluded vessel and stenosis to a single functioning kidney (grade 3).

Duplex carotid studies showed that 21 (55.3%) had normal or mild carotid-artery disease, 10 (26.3%) had moderate, and seven (18.4%) had severe carotid-artery disease. Nine patients had suffered a stroke and one a TIA (eight infarction, one haemorrhage) (Table 2). Of these, two patients had grade 1, three had grade 2, and five had grade 3 renal-artery disease.

Atherosclerosis affecting other vessels

Twenty-six patients (68.4%) had evidence of atheroma affecting other vessels (Table 2):

- Coronary artery disease: 14 patients had current or previous history of ischaemic heart disease (myocardial infarction and/or angina pectoris).
- Peripheral vascular disease: 19 patients had angiographic and/or clinical evidence of peripheral vascular disease.

However, subjects were not systematically investigated with angiography for vascular disease at other sites and it is likely that a much higher proportion of subjects would have been found, if this had been done.

Discussion

Our results demonstrate that in patients with atheromatous renal-artery stenosis who are electively referred for percutaneous renal balloon angioplasty there is a high prevalence of extracranial carotid-artery disease affecting four of 10 patients. This may explain the increased prevalence of atherothrombotic cerebrovascular events in these patients, and also previous observations that, following operative management for atheromatous renal-artery stenosis, some patients had developed an acute or late cerebrovascular event [11–13]. Our results are also consistent with previous post-mortem data showing a high prevalence of atheromatous renal-artery disease in patients who had died from cerebral infarction [14].

Our findings are in agreement with a previous study...
Table 1. Association between degree of severity of renal-artery stenosis and carotid-artery disease, age, gender, and vascular risk factors. Results are mean ± SD

<table>
<thead>
<tr>
<th>Renal artery stenosis grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>12</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.9 ± 8.3</td>
<td>67.2 ± 7.3</td>
<td>66.3 ± 8.1</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>7/5</td>
<td>3/8</td>
<td>7/8</td>
</tr>
<tr>
<td>Carotid artery stenosis (n (%))</td>
<td>4 (33.3%)</td>
<td>5 (45.4%)</td>
<td>8 (53.3%)*</td>
</tr>
<tr>
<td>Supine BP (mmHg)</td>
<td>176/92 ± 21/16</td>
<td>183/94 ± 24/121</td>
<td>178/92± 20/11</td>
</tr>
<tr>
<td>Mean serum creatinine (μmol/l)</td>
<td>164 ± 115</td>
<td>142 ± 41</td>
<td>215 ± 92§</td>
</tr>
<tr>
<td>Mean cholesterol (mmol/l)</td>
<td>7.1 ± 1.1</td>
<td>6.2 ± 1.2</td>
<td>6.5 ± 1.6</td>
</tr>
</tbody>
</table>

*χ2 for trends = 0.69; P = NS. †No significant difference using analysis of variance. ¥Borderline statistical significance on multiple comparison test (P = 0.02, significance for multiple group comparisons P < 0.017 was required).

Table 2. Association between degree of severity of renal artery stenosis, vascular events, and smoking

<table>
<thead>
<tr>
<th>Renal artery stenosis grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular events (n (%))</td>
<td>2 (20%)</td>
<td>3 (30%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Peripheral vascular disease (n (%))</td>
<td>6 (31.5%)</td>
<td>4 (21.1%)</td>
<td>9 (47.4%)</td>
</tr>
<tr>
<td>Coronary artery disease (n (%))</td>
<td>4 (28.6%)</td>
<td>2 (14.3%)</td>
<td>8 (57.1%)</td>
</tr>
<tr>
<td>Current or ex-smoker (n (%))</td>
<td>11 (36.7%)</td>
<td>6 (20%)</td>
<td>13 (43.3%)</td>
</tr>
</tbody>
</table>

where Rossi found an increased number of haemodynamically significant carotid artery lesions (>75%) in 35 patients with renovascular disease (20 due to atheroma and 15 due to fibromuscular dysplasia) when compared to an age-matched group of hypertensive subjects with normal renal arteries (7 (20%) vs 2 (6%) carotid lesions in patients with and without renal-artery stenosis respectively [15]). However, none of their patients had clinical symptoms or signs of cerebrovascular disease. This is in contrast to our study, which demonstrated that in patients with atheromatous renal-artery stenosis severe enough to require angioplasty there was an increased prevalence not only of extracranial carotid atherosclerosis but also of cerebral infarction and/or TIA.

Prospective data from the Framingham Survey [16] as well as other clinical, pathological, and experimental studies have suggested that hypertension is the single most important aetiological factor in the development of cerebrovascular disease [17,18], the great majority of them due to cerebral ischaemia. [19] In our study no control group was available. However, Harrison and Wilson [20] demonstrated that the prevalence of extracranial carotid arterial disease in hypertensive subjects with cerebral tumours, who had been studied with an angiogram, was much smaller than the one we observed in patients with renovascular disease (only seven of 269 hypertensive patients had carotid stenosis). In addition, if patients with atherothrombotic stroke are considered, there is evidence for only a small increase in extracranial carotid-artery disease in the presence of essential hypertension [21,22].

A possible explanation of the above observation is that patients with atheromatous renovascular disease are more likely to have severe hypertension and additional risk factors for atherogenesis than patients with essential hypertension. This is supported by the finding that end-organ damage as assessed by left ventricular hypertrophy and vascular damage are indeed more frequent in renovascular hypertension than in essential hypertension [23,24]. Furthermore, the heart in patients with renovascular hypertension was reported to be more adversely affected than in those patients with essential hypertension, with depressed systolic function, increased left ventricular dilatation, and increased cardiac output secondary to salt and water retention.

In conclusion our results suggest that in patients with atheromatous renal-artery disease severe enough to require angioplasty, four of 10 appear to have moderate to severe carotid-artery disease. This may explain the increased prevalence of atherothrombotic cerebrovascular events in these patients, and also previous observations that, following operative management for atheromatous renal-artery stenosis, some patients had developed an acute or late cerebrovascular event. We suggest therefore that such patients should always be regarded as having generalized vascular disease not confined to one system, and need to be assessed for carotid-artery disease prior to operative management for atheromatous renal-artery stenosis.

References


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