Prevalence and Predictors of Renal Artery Stenosis in Patients Undergoing Cardiac Catheterization

Takehiro YAMASHITA *,**, Fumihiro ITO *, Naoki IWAKIRI *, Hirofumi MITSUYAMA *, Satoshi FUJII ***, and Akira KITABATAKE ***

Renal artery stenosis (RAS) is recognized as a major co-morbid condition for patients with cardiovascular disease. Although the prevalence of RAS in Western countries has been reported as 13.5–18% in patients with suspected coronary artery disease (CAD) undergoing coronary angiography, there is little information available about the prevalence of RAS in Asian populations, which are less susceptible to atherosclerosis. To evaluate the prevalence of RAS in Japanese patients suspected of cardiovascular disease and the relationships among RAS and vascular risk factors, especially hypertension, renal artery angiography was performed in a total of 289 consecutive patients receiving diagnostic cardiac catheterization. RAS with a stenosis diameter greater than 50% was considered significant. The prevalence of RAS was 21/289 (7%) including 18 (6%) cases of unilateral stenosis and 3 (1%) of bilateral stenosis. RAS accompanied 14/220 (6%) cases of CAD, 4/34 (12%) cases of valvular heart disease and 1/14 (7%) cases of cardiomyopathy. In the subgroups of CAD, the prevalence of RAS was 5%, 10%, 9%, and 19% in cases of 0, 1, 2 and 3-vessel disease, respectively. Hypertension was more frequent among patients with than among those without RAS (86% vs. 45%, \( p = 0.0003 \)). The prevalence of RAS was 13% in hypertensives and 2% in normotensives (\( p = 0.004 \)). Thus RAS was frequent in patients with established CAD, and particularly in those with 3-vessel disease. Together, the results showed that hypertension was closely associated with RAS, appearing as both a risk factor and a possible clinical manifestation of the disease. We conclude that more attention should be paid to RAS in Japanese patients with hypertension and cardiovascular disease. *(Hypertens Res 2002; 25: 553–557)*

**Key Words:** renal artery stenosis, atherosclerosis, cardiac catheterization, prevalence, Japanese

Introduction

Atherosclerotic renal artery stenosis (RAS) is often identified as one of the associated conditions in patients with cardiovascular disease (CVD). One, 2 and 3-vessel coronary artery disease (CAD) showed significant RAS in 10%, 20%, and 30% of cases in a study by Harding et al. *(1)*. In other studies, RAS was observed in 34% of congestive heart failure patients over age 70 (2) and in 28% of patients with peripheral vascular diseases such as aneurysm or arteriosclerosis obliterans *(3)*. RAS has deleterious effects on the prognosis of CVD. Some elderly patients with occult renovascular disease who are taking angiotensin converting enzyme inhibitors will be at risk of developing uremia (2), and the risk may be particularly high if such patients have bilateral RAS. In a study by Stack, the prognosis of CAD patients with RAS was dramatically poor, with a 4-year survival rate as low as 62% *(4)*. On the other hand, it was shown that the prognoses of patients with CVD and RAS could be improved by treating RAS *(4, 5)*. Among patients with congestive heart failure and RAS, 90% had no further episodes of decompensation after renal artery stenting *(4)*. Thus, RAS has recently been recognized as a serious co-morbid condition of
CVD in Western countries. In Japan, RAS has frequently been overlooked, and limited information on the disease is available (6). The purpose of this study was to evaluate the prevalence of RAS in high-risk patients undergoing cardiac catheterization and to clarify the relationships among RAS and vascular risk factors, especially hypertension.

Methods

Patients
A total of 289 consecutive patients who received routine cardiac catheterization for evaluation of suspected CVD at our institution from April to October 2000 were enrolled. The institutional ethical committee approved the study and all patients gave their written informed consent. Patients were recruited after admission to the cardiology division or attendance at the cardiology clinic of our hospital. Patients with a history of hypertension (systolic blood pressure $\geq 140$ mmHg, diastolic blood pressure $\geq 90$ mmHg measured before any treatment) that resulted in lifestyle modification and/or antihypertensive treatments were considered to have a positive history of hypertension. The possibility of overt secondary hypertension was excluded by clinical and laboratory tests. Exclusion criteria also included acute heart failure and acute coronary syndrome. A known history of smoking (current smokers included individuals who stopped smoking < 5 years before the enrollment) was recorded. Subjects with an elevated serum total cholesterol ($> 220$ mg/dl) or subjects with a history of elevated serum total cholesterol that resulted in cholesterol-lowering treatment were considered to have a positive history of hyperlipidemia. No subject had documented familial hyperlipidemia. Subjects with an elevated fasting plasma glucose ($> 126$ mg/dl) or subjects with a history of elevated fasting plasma glucose that resulted in anti-diabetes treatment were considered to have a positive history of diabetes mellitus.

Methods
Left and right coronary angiography and left ventriculography were performed before abdominal aortography. The aortic image was tracked during left ventriculography and the approximate positions of the renal arteries were recorded. A pigtail catheter was positioned at the level of those arteries and a total of 30 ml of contrast was injected at 17 ml/s. Abdominal aortography for evaluation of RAS took less than 3 min and was not associated with complications. In 20 cases for which it was difficult to evaluate the degree of RAS via aortography, selective renal arteriography using a Judkins catheter was also performed. Based on the previously published criteria (2, 7, 8), the degree of stenosis was considered significant when the diameter of stenosis was greater than 50%.

Statistical Analysis
Data are expressed as the mean $\pm$ SD. The relationships between RAS and potential risk factors were examined using univariate methods. The univariate analyses consisted of Student’s t-tests for RAS status for continuous factors and $\chi^2$ tests for RAS status for discontinuous factors. All statistical procedures were performed using StatView 5.0 software (SAS Institute, Inc., Cary, USA). Values of $p < 0.05$ were considered to indicate statistical significance.

Results

Patient Characteristics
The average age of the 289 patients was 65.8 $\pm$ 10.6 years. Among them, 125 patients (43%) were female. As for coronary risk factors, 138 patients (48%) had hypertension and 81 patients (28%) had diabetes mellitus, of which 6 patients (2%) were receiving insulin treatment. Among the 289 patients, 91 (32%) had hyperlipidemia and 90 (31%) were active smokers.

Pre-cardiac Catheterization Diagnosis
The clinical diagnosis before cardiac catheterization was CAD in the majority of cases (76%), followed by valvular heart disease (12%), cardiomyopathy (5%), extremity atherosclerosis obliterans (2%) and aortic aneurysm (2%). Another 2% of patients had been diagnosed with arrhythmia and were being investigated for underlying heart disease, 1% had been referred for arteriography for suspected renovascular hypertension, 1% had infectious endocarditis, and 2% had been diagnosed with other diseases.

Prevalence of RAS
Among the 289 patients, 21 (7%) had significant unilateral or bilateral RAS. In 18 (6%) of these patients the RAS was unilateral (on the left side in 11 patients and on the right in 7), and in the remaining 3 (1%) it was bilateral. The frequency of significant RAS differed according to the underlying disease: the frequency was 6% among patients with CAD, 12% among those with valvular heart disease and 7% among those with cardiomyopathy (Fig. 1). The frequency of significant RAS also differed according to the number of coronary arteries affected. Significant RAS was observed in 5% of patients who did not have any significant stenosis in the coronary arteries (Fig. 2). RAS was observed in 10% of patients with 1-vessel disease, 9% of those with 2-vessel disease and 19% of patients with 3-vessel disease. Thus, the presence of RAS tended to be increased with the severity of CAD, but this trend did not reach the level of statistical significance ($p = 0.07$). Hypertension was observed in 45% of patients with 0-vessel disease, 60% of those with 1-vessel disease,
52% of those with 2-vessel disease and 46% of patients with 3-vessel disease.

Comparison of Clinical Characteristics

A comparison of clinical characteristics was made between patients with and those without RAS (Table 1). There were no differences between the two groups in age or gender. The prevalence of diabetes mellitus, hyperlipidemia and active smoking was similar between the two groups. Hypertension was more prevalent in patients with than in those without RAS (86% vs. 45%, $p = 0.0003$) (Table 1). In a comparison between patients with unilateral and those with bilateral RAS, the prevalences of hypertension, diabetes mellitus, hyperlipidemia and active smoking were all similar (Table 2). In hypertensives and normotensives, the prevalence of RAS was 13% and 2%, respectively ($p = 0.004$) (Fig. 3). RAS in normotensives was moderate, with a diameter of stenosis equal to or less than 75%. As to the relationship between RAS and the number of risk factors studied, the prevalence of RAS was 14% in patients with hypertension alone; 11% in patients with hypertension and diabetes mellitus; 15% in patients with hypertension and hyperlipidemia; 17% in patients with hypertension and active smoking; 14% in patients with hypertension, diabetes mellitus and hyperlipidemia; 18% in patients with hypertension, diabetes mellitus and active smoking; and 18% in patients with hypertension, hyperlipidemia and active smoking. No patients with hyperten-

Table 1. Characteristics of Patients with or without RAS

<table>
<thead>
<tr>
<th></th>
<th>RAS (+)</th>
<th>RAS (-)</th>
<th>$p$-value</th>
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</thead>
<tbody>
<tr>
<td>$n$</td>
<td>21</td>
<td>268</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>68.9 ± 8.7</td>
<td>65.6 ± 10.8</td>
<td>0.1814</td>
</tr>
<tr>
<td>Female</td>
<td>48%</td>
<td>43%</td>
<td>0.6749</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86%</td>
<td>45%</td>
<td>0.0003</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24%</td>
<td>28%</td>
<td>0.6478</td>
</tr>
<tr>
<td>Insulin requirement</td>
<td>0%</td>
<td>2%</td>
<td>0.7505</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>38%</td>
<td>31%</td>
<td>0.5059</td>
</tr>
<tr>
<td>Smoking</td>
<td>38%</td>
<td>31%</td>
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</tr>
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</table>

Table 2. Characteristics of Patients with Unilateral or Bilateral RAS

<table>
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<tr>
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<th>Bilateral</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>18</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>70.1 ± 6.4</td>
<td>61.3 ± 17.7</td>
<td>0.1082</td>
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<tr>
<td>Female</td>
<td>44%</td>
<td>67%</td>
<td>0.4755</td>
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<tr>
<td>Hypertension</td>
<td>83%</td>
<td>100%</td>
<td>0.4450</td>
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<tr>
<td>Diabetes mellitus</td>
<td>22%</td>
<td>33%</td>
<td>0.6754</td>
</tr>
<tr>
<td>Insulin requirement</td>
<td>0%</td>
<td>0%</td>
<td>0.7859</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>39%</td>
<td>33%</td>
<td>0.8544</td>
</tr>
<tr>
<td>Smoking</td>
<td>39%</td>
<td>33%</td>
<td>0.8544</td>
</tr>
</tbody>
</table>

52% of those with 2-vessel disease and 46% of patients with 3-vessel disease.

**Comparison of Clinical Characteristics**

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Discussion

The overall prevalence of RAS was 7% in the present cohort of patients receiving routine cardiac catheterization. The prevalence of RAS was higher in patients with established CAD: 10%, 9%, and 19% in patients with 1, 2, and 3-vessel disease, respectively. RAS was also found frequently in non-CAD patients, such as patients with valvular heart disease (12%) and cardiomyopathy (7%). In Europe and America the prevalence of RAS has been reported to be 13.5–18% among all patients undergoing routine cardiac catheterization, and 10%, 20%, and 30% among those with 1, 2, and 3-vessel coronary artery disease, respectively (1, 9–11). Although the prevalence in Japanese in this study was lower, our results strongly suggest that there are a significant number of Japanese CVD patients with RAS.

This study suggested that hypertension may be closely associated with RAS in Japanese. Hypertension was shown to be a risk factor, as well as a possible clinical manifestation, of RAS. As the number of risk factors increased, the prevalence of RAS increased. Among the risk factors studied, hypertension appeared to play a particularly significant role in RAS. In normotensives, RAS was moderate and thus would not have contributed to a significant elevation of blood pressure.

Early detection and treatment of RAS are important, because RAS deteriorates the prognosis of CVD (2–4). RAS may progress regardless of whether or not the hypertension can be medically controlled (12–17). In a study by Zierler et al., 42% of patients with RAS showed progression of RAS over the 2-year follow-up period, and 11% of RAS eventually progressed to occlusion (16). Therefore, timely intervention and correction of RAS may prevent progressive narrowing of the vessel and deterioration of renal function. In a study by Harden et al., renal artery stenting resulted in a 4-fold slowing of the progression of renal dysfunction (18). And Dorros et al. reported a four-year survival rate of 80% among patients whose serum creatinine level was 1.5 mg/dl or less at the time of renal artery stenting (19). However, the rate was about 20% in those with a creatinine level of more than 2.0 mg/dl. In Europe and America, patients with RAS and uncontrolled hypertension and/or renal failure are considered appropriate candidates for renal artery revascularization (20–22). Patients with RAS and refractory congestive heart failure or unstable angina may also be candidates for stenting (23). These results indicate that early diagnosis and adequate revascularization before the onset of renal dysfunction could prevent deterioration of renal function and improve patient survival, underscoring the importance of recognizing all potential candidates for renal artery revascularization. Our study shows for the first time that there are considerable numbers of CVD patients who have RAS in Japan, although the prevalence is lower than that in Europe and America. It is necessary to recognize the importance of early detection of RAS. Although angiography is the gold standard, it has small risks for complications. Other less invasive diagnostic measures are expected to become useful for the practical screening of renal arteriosclerosis and RAS (23, 24).

Hypertension prevalent in the Japanese population is a significant predictor of renal disease (25), and some antihypertensive medications are reported to exert favorable effects on renal function (26, 27). In addition to medical therapies, cardiology can play an important role in renal artery revascularization treatment (28) because CAD is often associated with RAS, the skills necessary to perform coronary intervention are transferable to the peripheral vasculature (29), and the revascularization of renal arteries may improve hypertension and reduce volume overload. There are compelling reasons for cardiologists to undertake a more global approach to treatment of patients with atherosclerotic CVD and to pay more attention to the recognition, diagnosis, and management of RAS. Furthermore, the indications and outcome of renal artery stenting for Japanese patients should be widely investigated in the future.

In conclusion, the incidence of RAS in routine cardiac catheterization was 7% in the present series. Although this percentage is lower than those in Europe and America, RAS was still considerably frequent among patients with CVD. Hypertension was closely associated with RAS. Together, the results of this study showed that hypertension was closely associated with RAS, appearing as both a risk factor and a possible clinical manifestation of the disease. Additional effort is required for the appropriate detection and treatment of this important but often overlooked disease.

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References


