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The Prevalence and Associated Risk Factors of Renal Artery Stenosis in Patients Undergoing Cardiac Catheterization

Hyun Yong Song[1], Jae Ha Hwang[1], Hyunjin Noh[1], Sug Kyun Shin[1], Dong Hoon Choi[2], Won Hum Shim[2], Ho Yung Lee[1], Seung Yun Cho[2], Dae Suk Han[1], and Kyu Hun Choi[1]

Abstract

Renal artery stenosis may be a cause of hypertension and a potential contributor to progressive renal insufficiency. However, the prevalence of renal artery disease in a general population is poorly defined. The purposes of this study were to evaluate the prevalence of angiographically-determined renal artery narrowing in a patient population undergoing routine cardiac catheterization, and to identify the risk factors for renal artery stenosis. After left ventriculography, abdominal aortography was performed to screen for the presence of renal artery stenosis. A total of 427 patients (274 males, 153 females) were studied and the mean age was 59 years. Renal artery narrowing was identified in 10.5% of patients. Significant ($\geq$50% diameter narrowing) renal artery stenosis was found in 24 patients (5.6%) and insignificant stenosis was found in 21 patients (4.9%). Significant unilateral stenosis was present in 4.2% of patients and bilateral stenosis was present in 1.4%. The stem of the renal artery was a more common site of stenosis in 62.2% of patients than in the ostium (37.8%), but the severity of stenosis was not significantly different according to the site of stenosis. By univariate and multivariate logistic regression analysis, the association of clinical variables with renal artery stenosis was assessed. Multivariable predictors included age, hypertension and peripheral vascular disease ($p<0.05$). The variables such as sex, smoking history, hyperlipidemia, renal insufficiency, as well as the presence of obesity, severity of coronary heart disease and D.M., were not associated. In conclusion, the prevalence of angiographically-determined renal artery narrowing in a patient population undergoing cardiac catheterization is 10.5%. Old age, hypertension and evidence of peripheral vascular disease represent the predictors of renal artery stenosis.

Key Words: Renal artery stenosis, prevalence, risk factor, cardiac catheterization

INTRODUCTION

Renovascular disease as a cause of end-stage renal disease has been mostly overlooked until recently.[1] As the overall population ages, the number of individuals with atherosclerotic renovascular disease will increase, as will the number of patients with renovascular hypertension and end-stage renal disease. The anatomic presence of atherosclerotic renovascular disease as a threat to renal function has become a more pressing concern than that of hypertension secondary to renovascular disease.[2,3] A review of comorbid atherosclerotic disease in end-stage renal disease patients indicated that occlusive disease of the renal arteries may contribute to progressive renal failure.[1]

Stenosis of the renal arteries usually results from atheromatous lesions, and this prevalence then increases with age and with atherosclerosis at extrarenal sites.[4] Renal artery stenosis (RAS) is a potentially correctable problem because revascularization techniques including surgery and percutaneous renal artery angioplasty have been shown to be effective in treating RAS and in preserving renal function.[3,5] However, the prevalence and predictors of renal artery disease are poorly defined. The population of patients referred for cardiac catheterization exhibits many clinical features that could be associated with atherosclerotic renal artery disease. Thus, abdominal aortography at the time of cardiac catheterization provides a readily performed means of screening for the presence of RAS in a population likely to have renal artery disease.

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Departments of [1]Internal Medicine and [2]Cardiovascular Center, Institute of Kidney Disease, Yonsei University College of Medicine, Seoul, Korea.

Address reprint request to Dr. K. H. Choi, Department of Internal Medicine, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul 120-752, Korea. Tel: 82-2-361-5437, Fax: 82-2-393-6884, E-mail: khchoi6@yumc.yonsei.ac.kr

To evaluate the prevalence of angiographically-determined renal artery narrowing in a patient population undergoing routine cardiac catheterization and to identify the risk factors for RAS, we reviewed the medical records and angiographic findings in this population.

MATERIALS AND METHODS

Patient population

Four hundred and twenty seven consecutive patients undergoing cardiac catheterization were screened for the presence of renal artery disease between July 1998 and December 1998 through the use of abdominal aortography. Before the patients had cardiac catheterization, demographic data, medical history, physical findings, and blood chemistries were recorded. Peripheral vascular disease was defined as a history of claudication, previous vascular procedure, a history of stroke or transient ischemic attack, or physical evidence of carotid, femoral, or abdominal bruits. Congestive heart failure was diagnosed by echocardiography or ventriculography. Hypertension was defined as diastolic blood pressure >90 mmHg when subjects were measured as outpatients before catheterization, or while the patient was taking antihypertensive medications. Renal insufficiency defined as a creatinine level was above 1.5 mg/dL.

Angiographic analysis

The cardiac catheterization was performed via the femoral artery approach known as Judkins' technique. The presence and severity of coronary atherosclerotic lesions were determined in a routine fashion. Coronary artery lesions graded as $>70\%$ narrowing of the luminal diameter were classified as significant. After left ventriculography, the pigtail catheter was withdrawn into the abdominal aorta and positioned a few centimeters superior to the renal arteries. Aortography was performed in the anterior-posterior projection with ioxaglate de sodium (Guerbet S.A., Paris, France) power-injected at a rate of 20 mL/s to a total volume of 30 mL. The injection was recorded on 35 mm cine film or compact disc at 30 frames per second.

Aortograms were reviewed by two cardiologists blinded to the clinical information. The adequacy of the study as well as the presence or absence of renal artery disease were noted. The percentage of RAS was classified as a minor irregularity ($<25\%$ narrowing) or as 25, 50, 75 and 100% luminal diameter narrowing. By convention, an angiographically-significant lesion was defined as a $\geq 50\%$ luminal diameter narrowing of a major renal artery. Selective arteriography with a 5 F renal catheter was done if the renal artery lesion was significantly narrowed. Accessory renal arteries with disease were felt to be significant if more than one-third of the renal mass was estimated to be supplied by the vessel. Lesion location was classified as ostial, main artery, or branch vessel. Ostial lesions were defined as stenotic if the segment of the renal artery lumen immediately contiguous to the aorta was compromised. Lesions of the main segment of the renal artery began at least 2 to 3 mm beyond the ostial segment. Branch lesions were defined as stenotic lesions originating beyond the first bifurcation of the renal artery.

Statistical analysis

Statistical analysis was performed using the Chi-square test, stepwise univariate and multivariable logistic regression in order to identify the clinical and angiographic variables predictive of RASis. The variables that were significant in the univariate model were then entered into a multivariate logistic regression model to identify the best set of independent predictors of RAS. Data were expressed as mean$\pm$S.D. Statistical significance was defined as $p<0.05$.

RESULTS

Patient characteristics

The demographic data from the study patients are summarized in Table 1. The mean age of the group was 59.2 ± 10.3 yr. About half of the patients had a history of smoking. Of 427 patients, 216 (51%) had hypertension, and 92 (22%) had diabetes. Peripheral vascular disease and congestive heart failure were observed in 75 (18%) and 74 (17%) patients, respectively. Angiographically-significant coronary artery

Table 1. Demographic Data

	N=427 (%)
Mean age, yr	59.2±10.3
Men : Women	284 : 143
Smoking	218 (51)
% ideal body weight	102.6±19.8
Hypertension	216 (51)
Diabetes Mellitus	92 (22)
Peripheral vascular disease	75 (18)
Congestive heart failure	74 (17)
Coronary artery disease	
1 Vessel	131 (31)
multi-vessel	171 (40)
Serum creatinine, mg/dL	
Mean (range)	1.19 (0.40−4.70)
≥1.5 mg/dL	36 (8.4)

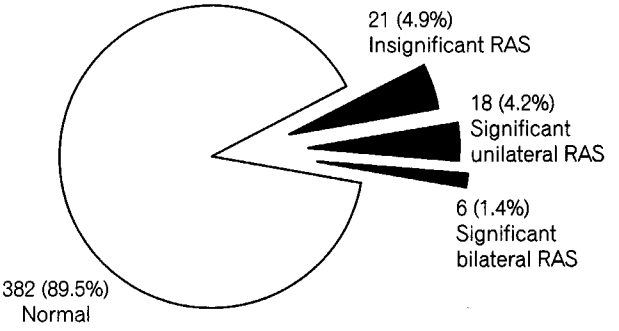

Fig. 1. The prevalence of renal artery stenosis (RAS) (N=427). Insignficant RAS is defined as <50% luminal narrowing, and significant RAS is defined as ≥50% luminal narrowing.

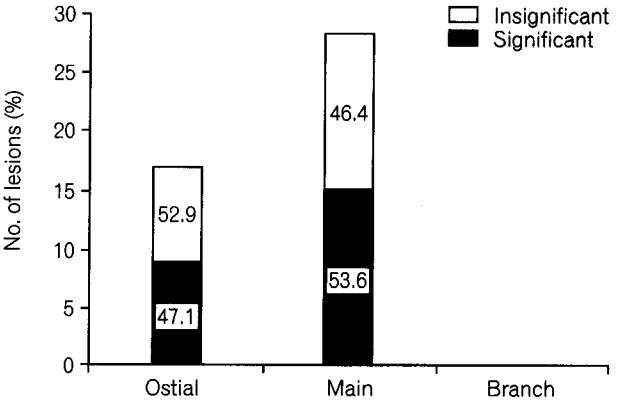

Fig. 2. Location and distribution of renal artery stenosis. The stem of renal artery was more common site of stenosis in 62.2% than the ostium in 37.8%. Definitions of insginificant and significant lesions were same as Fig. 1.

disease was noted in 302 (70.7%) patients.

Prevalence and location of RAS

The prevalence of RAS in this population is illustrated in Fig. 1. Bilaterally normal renal arteries were identified in 89.5% of patients screened. Insignificant RAS of at least one renal artery was seen in 21 (4.9%) patients. Significant unilateral RAS was identified in 18 (4.2%) patients, and 6 (1.4%) had significant bilateral RAS. Thus, 45 (10.5%) patients in the study group had angiographically RAS observed at the time of cardiac catheterization. All lesions were designated as being atherosclerotic. The majority of lesions were located in the ostium or the main segment of the renal artery (Fig. 2). The stem of the renal artery was a more common site of stenosis in 62.2% than the ostium in 37.8% ($p<0.05$), but the severity of stenosis was not significantly different according to the site of stenosis.

Predictors of RAS

By univariate logistic regression, the clinical and biochemical variables were analyzed to identify associations that were more common in patients with RAS. The predictive clinical variables (shown in descending order according to χ^2 values) are summarized in Table 2. The evidence of peripheral vascular disease was the most important predictor of RAS. Next in order of importance was age and then hypertension. The mean age of patients with RAS was 63.2±13.5 yr compared with 58.6±9.7 yr for patients with no RAS ($p<0.05$). The level of blood urea nitrogen was significantly higher in patients with RAS, compared to those with no RAS, though the creatinine level was not much different between the two groups. There was also no significant difference between the two groups in other variables including obesity, gender, smoking history, lipid levels and the presence of diabetes. The coronary artery disease tended to be more severe in patients with RAS, compared to those with no RAS (Table 3).

In univariate analysis for predictors of significant RAS, hypertension, peripheral vascular disease, and renal insufficiency defined as a serum creatinine level of 1.5 mg/dL were significantly more common in patients with significant RAS compared to those with

Table 4. Univariate Logistic Regression Analysis of Clinical and Biochemical Variables to Identify Predictors of Significant RAS

Variables	No RAS (N=402)	RAS (N=25)	χ^2	p value
Creatinine ≥1.5 mg/dL	29 (2.2%)	7 (29.2%)	20.20	0.0001
PVD	62 (15.4%)	13 (54.2%)	17.29	0.0001
Hypertension	198 (24.3%)	18 (75.0%)	5.95	0.0147
Lp (a), mg/dL	25.2±22.8	36.3±41.5	2.39	0.0665
Diabetes mellitus	88 (21.8%)	4 (16.0%)	1.57	0.2095
Coronary heart disease	283 (70.2%)	19 (79.2%)	1.34	0.2471
% IBW	102.9±20.1	97.4±10.2	1.29	0.2551
Smoking	204 (50.6%)	14 (58.3%)	0.32	0.5733
Female	137 (34.0%)	6 (25.0%)	0.22	0.6386
Mean age, yr	59.2±9.9	58.7±16.1	0.18*	0.6695
Triglyceride, mg/dL	151.9±127.4	129.9±95.8	0.05	0.8320
Total cholesterol, mg/dL	190.1±40.4	178.6±42.2	0.00	0.9622
Congestive heart failure	68 (16.9%)	6 (25.0%)	0.00	0.9869

PVD, peripheral vascular disease; Lp (a), lipoprotein (a); % IBW, percentile ideal body weight; RAS, renal artery stenosis. No RAS: no or insignificant RAS.
* Analyzed by 10-year increment.

Table 5. Multivariate Logistic Regression Analysis of Clinical and Biochemical Values to Identify Predictors of RAS

Variables	β	p value	Odds ratio
Age*	0.0762	0.0069	1.08
Hypertension	0.2739	0.0324	1.03
Peripheral vascular disease	0.5862	0.0499	1.01

RAS, renal artery stenosis.
* Analyzed by 10-year increment.

disease where roughly 60% of atherosclerotic lesions and 40% of fibromuscular dysplasia were found in patients investigated for renovascular hypertension.[8] This discrepancy is likely because of the vastly different populations being studied. Renovascular hypertension was not suspected in this population referred for evaluation of cardiac disease. Olin et al.[9] and Vetrovec et al.[10] confirmed the overwhelming preponderance of atherosclerotic rather than fibrodyplastic renovascular disease in similar subsets of patients with advanced age and evidence of multiorgan atherosclerosis, respectively.

Both univariate and multivariate analyses of the clinical and biochemical variables showed that old age, hypertension, and the presence of peripheral vascular disease are the most important markers for increased risk of coexistent angiographic RAS. It is not surprising that advancing age is the strongest predictor because it is commonly accepted that atherosclerosis in general, as well as atherosclerotic renovascular disease, most often occurs later in life.[11,12] Schwartz and White[13] found severe stenosis (>50% renal artery diameter reduction) in only 5% of autopsy material from patients younger than 64 years. By contrast, 18% of autopsy material from patients 65 to 74 years and 42% from patients over 75 years demonstrated severe RAS.

Almost half of the patient population studied had a history of hypertension, and of the 216 hypertensive patients, 16.2% had RAS, while significant RAS was identified in 8.3%. This finding is similar to another finding of 15.3% incidence of RAS in hypertensive patients who underwent cardiac catheterization.[6] Renovascular hypertension was not suspected in this population referred for the evaluation of cardiac disease, but based on these findings, it appears that about 15% of hypertensive patients may have atherosclerotic RAS.

The presence of peripheral vascular disease, known as a marker for renal artery disease, was also a good predictor of RAS. In our study, 28% of patients with evidence of peripheral vascular disease had RAS and 54.2% of significant RAS patients had peripheral vascular disease. Patients with atherosclerosis elsewhere, especially with abdominal aortic aneurysms, aorto-occlusive disease, or lower-extremity occlusive

disease, have previously been shown to have a high prevalence of significant RAS.[9,14,15] This finding supports the belief that atherosclerotic renovascular disease is often a manifestation of generalized atherosclerosis involving the abdominal aorta. Therefore, physical evidence of carotid, femoral, or abdominal bruits seems to raise suspicion of RAS.

Angiotensin-converting enzyme inhibitors have recently been proposed as the treatment of choice in patients with hypertension and peripheral vascular disease since they are free of many of the side effects of other antihypertensive agents. They can, however, induce acute renal failure in patients with RAS.[16] Evidence of RAS probably indicates that those patients are at high risk of renal complications during treatment with angiotensin-converting enzyme inhibitors. We believe that in patients with evidence of peripheral vascular disease, angiotensin-converting enzyme inhibitors should be used with caution. Consideration should be given to the possibility of underlying RAS.

Considering the diffuse nature of atherosclerotic disease, patients with coronary artery disease would also be more likely to have RAS. It has been previously shown that 58% of patients with unsuspected RAS had clinically overt coronary artery disease.[17] Harding et al.[4] reported that the greater the number of coronary arteries involved, the greater was the likelihood of significant RAS. Our data revealed that 71.1% of patients with RAS had coronary artery disease. However, there was no significant correlation between the severity or the number of coronary artery disease and the presence of RAS. This finding suggests that coronary artery disease is not a strong predictor of unsuspected RAS. Other cardiovascular risk factors such as obesity, diabetes, hyperlipidemia, and congestive heart failure were not correlated with RAS.

By univariate analysis, an elevated creatinine concentration was found to be more common in patients with significant RAS, though it was not a significant predictor of significant RAS by multivariate analysis. The incidence of 29.2% in our study is less than that of Hansen et al.,[18] who found 65% of renal insufficiency (creatinine $\geq$1.3 mg/dL) in patients on surgical management of renovascular disease. Renal function seems to be significantly influenced by the site, type and severity of lesion. In addition, progressive deterioration of renal function in patients with atherosclerotic RAS is common and occurs even in the presence of blood pressure control.[19] It could be argued that the changes of renal function are evaluated regularly in patients with an elevated creatinine concentration and angiographic evidence of RAS.

In conclusion, the prevalence of angiographically renal artery narrowing, primarily due to atherosclerotic disease, in a population undergoing cardiac catheterization is 10.5%. Old age, hypertension and evidence of peripheral artery occlusive disease represent the important predictors of RAS. Abdominal aortography at the time of cardiac catheterization offers a safe and effective means for evaluating the renal vasculature in this potentially high-risk group.

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