Renal Artery Stenosis: Prevalence and Associated Risk Factors in Patients Undergoing Routine Cardiac Catheterization


ABSTRACT

The purposes of this study were to determine the prevalence of angiographically significant renal artery stenosis in a patient population referred for diagnostic cardiac catheterization and to develop a model that predicts the highest-risk subset of patients who have significant renal artery narrowing. A prospective validation cohort study was undertaken in a referral-based university hospital. After left ventriculography, abdominal aortography was performed to screen for the presence of renal artery disease. A convenience sample of 1,302 of 1,651 consecutive patients undergoing diagnostic cardiac catheterization were enrolled in the study. Of the 1,302 abdominal aortograms performed, 1,235 (95%) were deemed of adequate quality for the evaluation of renal artery anatomy. Renal artery disease was identified in 30% of the patients. Insignificant renal artery stenosis was found in 187 (15%) and significant (≥50% diameter narrowing) stenosis was found in 188 (15%). Significant unilateral disease was present in 11%, and bilateral disease was present in 4%. By univariable and multivariable logistic regression analysis, the association of both clinically and catheterization-derived variables with renal artery disease was assessed. Multivariable predictors included age, severity of coronary artery disease, congestive heart failure, female gender, and peripheral vascular disease. Hypertension was not an associated variable. These data reveal the previously undetected high prevalence of renal artery disease in patients undergoing cardiac catheterization and provide clinical and angiographic features that assist in predicting its presence.

Key Words: Renal artery stenosis, cardiac catheterization, renovascular disease

Renal artery stenosis may be a cause of hypertension and may result in renal ischemia and loss of renal mass. Stenosis of the renal arteries usually results from atheromatous lesions that can lead to progressive arterial occlusion in many patients (1-3). Atherosclerotic renovascular disease is a frequently overlooked clinical entity and may be a common cause of progressive renal insufficiency (4,5). Renal artery stenosis is a potentially correctable problem because revascularization techniques including surgery and percutaneous renal artery angioplasty have been shown to be effective in treating renal artery stenosis and preserving renal function (6-11).

The prevalence of renal arterial disease in the general population is poorly defined. Necropsy studies suggest a frequency of "severe" stenosis to be 25% in subjects 40 yr of age or older (12). Renovascular hypertension is present in 5 to 10% of the total hypertensive population, but renal artery stenosis can be demonstrated in 35 to 43% of patients evaluated for renovascular hypertension (13,14). The occurrence of renal artery stenosis in patients with atherosclerosis elsewhere, especially in patients with abdominal aortic and aortoiliac disease, is as high as 39% (15). Small series have also noted significant renal artery stenosis in 29% of patients with coronary artery disease (16).

The population of patients referred for cardiac catheterization often exhibits many clinical features that one might anticipate would be associated with atherosclerotic renal artery disease, such as advanced age, evidence of diffuse atherosclerosis, hypertension, renal insufficiency, and the presence of coronary artery disease (12,15-18). Thus, abdominal aortography at the time of cardiac catheterization provides a low-risk, readily performed means of...
screening for the presence of renal artery stenosis in a population likely to have renal artery disease.

The purpose of this study is twofold. The first is to determine the prevalence of angiographically significant renal artery stenosis in a large, diverse population referred for cardiac catheterization. The second is to develop a model based on clinically and cardiac catheterization-derived parameters that predicts the highest-risk subset of patients who have significant renal artery narrowing, thus facilitating the screening procedure.

METHODS

Patient Population

During a 5-month period, 1,302 of 1,651 consecutive patients undergoing elective diagnostic cardiac catheterization at Duke University Medical Center were screened for the presence of renal artery disease through the use of abdominal aortography. Patients not screened were excluded at the discretion of the angiographers.

Before patients had cardiac catheterization, demographic data, medical history, physical findings, and blood chemistries were recorded and entered into a computerized medical information system (19). 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. Symptoms of congestive heart failure were recorded and classified in accordance with the New York Heart Association criteria (20). Hypercholesterolemia was defined as evidence of a cholesterol level elevated above 200 mg/dL. Hypertension was defined as diastolic blood pressure >90 mm Hg when subjects were measured as outpatients during the time before catheterization. Hypertension was also considered present if the patient was taking antihypertensive medications and if it could be confirmed that the indication for use was hypertension and not angina. Blood pressure was measured several times before and after catheterization but, because of the anxiety and discomfort surrounding the procedure, was not considered as basal blood pressure.

Angiography

Coronary angiography was performed via femoral artery approach by the Judkins technique (21). The presence and severity of coronary atherosclerotic lesions were determined in the 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 iohexol (Omnipaque 350; Winthrop, Bronx, NY) 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 at 30 frames per second.

Aortography Analysis

Aortograms were reviewed by a single observer blinded to the clinical information. The adequacy of the study and the presence or absence of renal artery disease were noted. Renal artery percent stenosis was classified as a minor irregularity (<25% narrowing) or 25, 50, 75, 95, or 100% luminal diameter narrowing. By convention, an angiographically significant lesion was defined as a ≥50% luminal diameter narrowing of a major renal artery (12,15,16,22–25). 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 with 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. The stenotic lesions were designated as atherosclerotic if they did not demonstrate a distinctive string-of-beads appearance characteristic of fibromuscular dysplasia (26). No complications related specifically to the aortogram were observed. Retroperitoneal bleeding (0.002%), laceration of the femoral artery (0.002%), contrast nephrotoxicity (increase in serum creatinine >0.5 mg%, 6%; >1 mg%, 1.4%), and cholesterol embolization (0.0015%) were not increased in the study group compared with retrospective controls who received cardiac catheterization only. Patients were followed-up at 24 h and as outpatients. It is reasonable to assume that the risk of renal arteriography is at least as low as combined coronary and renal arteriography.

Statistical Analysis

Stepwise univariate and multivariate logistic regression was performed in order to identify clinical and angiographic variables predictive of significant renal artery stenosis. A binary logistic model (27) was used to identify univariate predictors of significant renal artery stenosis. The variables that were significant in the univariate model were then entered into a stepwise logistic regression model to identify the best set of independent predictors of significant renal artery stenosis. From these data, a model was developed to predict the probability of significant renal
artery stenosis in patients undergoing cardiac catheterization.

RESULTS

Of the 1,302 studies performed, 67 (5%) were deemed technically inadequate because of either poor opacification of the renal vessels or the presence of overlying mesenteric vessels obscuring the renal anatomy. The remaining 1,235 studies were considered technically adequate for the evaluation of the renal artery anatomy and form the basis of this study. A representative cine angiographic visualization of renal artery obstruction is shown in Figure 1.

The demographic data from the study patients are summarized in Table 1. The mean age of the group was 60 ± 11 yr. Sixty percent were men, and 85% were white. Many had risk factors for atherosclerosis. About half of the patients had a history of hypertension. The serum creatinine ranged from 0.2 to 0.6 mg/dL with a mean of 0.10 mg/dL. Abnormal lipids were noted in 599 (49%) patients. Congestive heart failure was noted in 185 (15%) patients.

The prevalence of renal artery disease in this population is illustrated in Figure 2. Lesions were designated as being atherosclerotic 97% of the time. All lesions classified as fibromuscular dysplasia appeared angiographically insignificant. Bilaterally normal renal arteries were identified in 70% of the patients screened. Insignificant renal artery stenosis (<50% luminal narrowing) of at least one renal artery was seen in 187 (15%) patients. Significant unilateral renal artery stenosis (≥50% luminal narrowing) was identified in 36 (3%) patients, and 52 (4%) had significant bilateral renal artery stenosis. Thus, 188 patients or 15.2% of the study group had angiographically significant renal artery narrowing observed at the time of cardiac catheterization.

More severe stenosis (≥75% luminal diameter narrowing) was seen unilaterally in 76 (6%) patients and bilaterally in 17 (1.4%) patients. Eight patients had in essence one functional kidney either because of congenital absence, surgical removal, or total occlusion of one renal artery. Of these eight patients, one had significant disease in the renal artery supplying the solitary kidney.

The overwhelming majority of lesions were located in the ostium or the main segment of the renal artery, with even distribution between these two locations (Figure 3). Of the 253 significant lesions observed in the 188 patients, 48% were in the ostium, 49% were in the main segment of the renal artery, and only 3% were beyond the first bifurcation of the renal artery in a branch vessel.

Predictors of Renal Artery Stenosis

By univariate logistic regression, 14 variables were analyzed to identify associations that were more common in patients with significant renal artery disease. The predictive clinical variables (shown in descending order according to χ² values) are shown in Table 2. Older age was the most important predictor of significant renal artery stenosis. The mean age of the patients with significant renal artery stenosis was 66 ± 10 yr compared with 58 ± 11 yr for patients with insignificant or no renal artery disease. Next in order of importance were the evidence of peripheral vascular disease and then congestive heart failure. A creatinine of >106 μmol/L (1.2 mg/dL). cigarette

Table 1. Demographic data of the 1,235 patients with adequate abdominal aortograms

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Number (%)</th>
</tr>
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<tbody>
<tr>
<td>Mean age (yr)</td>
<td>60 ± 11</td>
</tr>
<tr>
<td>White: Nonwhite</td>
<td>1054: 181</td>
</tr>
<tr>
<td>Men: Women</td>
<td>736: 499</td>
</tr>
<tr>
<td>Hypertension</td>
<td>581 (49%)</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>185 (15%)</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>210 (17%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>764 (62%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>226 (18%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>599 (49%)</td>
</tr>
<tr>
<td>Serum Creatinine (μmol/L) Mean (range)</td>
<td>93.7 (17.7–937.0)</td>
</tr>
<tr>
<td>&gt;106</td>
<td>208 (17%)</td>
</tr>
<tr>
<td>Significant CADb</td>
<td></td>
</tr>
<tr>
<td>One Vessel</td>
<td>299 (24%)</td>
</tr>
<tr>
<td>Two Vessel</td>
<td>211 (17%)</td>
</tr>
<tr>
<td>Three Vessel</td>
<td>266 (22%)</td>
</tr>
<tr>
<td>Left Main</td>
<td>41 (3.3%)</td>
</tr>
</tbody>
</table>

a See text for definition.
b CAD, coronary artery disease; see text for definition.

Figure 1. Severe bilateral renal artery stenosis.
The prevalence of renal artery stenosis as determined by cine abdominal aortography at the time of cardiac catheterization (N = 1,235). Insignificant renal artery stenosis is defined as <50% luminal narrowing. Significant renal artery stenosis is defined as ≥50% luminal narrowing.

Figure 2. The prevalence of renal artery stenosis as determined by cine abdominal aortography at the time of cardiac catheterization (N = 1,235). Insignificant renal artery stenosis is defined as <50% luminal narrowing. Significant renal artery stenosis is defined as ≥50% luminal narrowing.

Figure 3. Location and distribution of renal artery lesions.

The prevalence of renal artery disease in the general population is unknown (17). In most cases, the diagnosis of renovascular disease is established during the course of evaluation for systemic hypertension. More recently, the effect of ischemic renal disease and the role of revascularization in preserving renal function have been debated (5,7). Obstructive renal artery lesions are potentially treatable by surgical or angioplastic techniques (6–11). The presence of renal arterial disease may also complicate the medical management of patients with hypertension and/or congestive heart failure (28). Because atherosclerosis is the primary cause of renal arterial obstruction and considering the diffuse nature of atherosclerotic disease, patients with coronary artery disease would logically seem to be at an increased risk for renal artery disease (7), which was confirmed in this study. 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. These data suggest that screening for this process can be improved by the use of certain predictors of disease.
Our finding of a 15% prevalence of significant renal artery narrowing in a cardiac catheterization population is consistent with findings from previous smaller studies, which have demonstrated a prevalence between 5 and 29% (16, 24). However, the discovery of the angiographic presence of renal artery stenosis does not necessarily imply functional significance.

The lesion type was presumed to be atherosclerotic 97% of the time on the basis of angiographic appearance. This is in contrast to findings from other reports of renovascular disease where roughly 60% atherosclerotic lesions and 40% fibromuscular dysplasia were found in patients investigated for renovascular hypertension (18). This discrepancy is likely because of the vastly different patient populations being studied. Renovascular hypertension was not suspected in this population referred for the evaluation of cardiac disease. Other studies have confirmed the overwhelming preponderance of atherosclerotic rather than fibrodysplastic renovascular disease in similar subsets of patients with advanced age and evidence of multigorgan atherosclerosis (15,16).

The location of the renal artery narrowing has important clinical implications in regard to the approach toward potential revascularization. Ostial lesions are generally the result of atherosclerotic aortic plaques that overhang the orifice of the renal artery,
producing inflow obstruction. These are difficult to treat effectively by current percutaneous transluminal angioplasty techniques (29,30). Almost one half of the patients who had significant renal artery stenosis in this study had ostial lesions. Renal artery disease was clearly more likely to be present in those with coronary and peripheral vascular disease. These findings confirm other observations that atherosclerotic renovascular disease is often a manifestation of generalized atherosclerosis involving the abdominal aorta and the coronary, cerebral, and lower-extremity arteries (12,15,16).

Both multivariate and univariate analyses of clinically and cardiac catheterization-derived variables showed that older age, multivessel coronary artery disease, and the presence of congestive heart failure symptoms are the most important markers for an increased risk of coexistent angiographically significant renal artery stenosis. 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 late in life (4,8,26,29,31). It follows that patients with coronary artery disease would also be more likely to have renal artery stenosis. Moreover, the data reveal that the greater the number of coronary arteries involved, the greater the likelihood of significant renal artery stenosis. Vetrovec et al. have previously shown that significant coronary artery disease correlates with the presence of renal artery stenosis, but these authors did not relate this finding to the number of coronary artery vessels involved (16). Smaller series have not demonstrated a relationship between the number of coronary arteries and renal artery stenosis (24).

Patients with heart failure symptoms were significantly older, had a higher incidence of multivessel coronary artery disease and significant renal artery stenosis, and were more likely to have a history of hypertension compared with patients without symptoms of congestive heart failure (Table 5). There may be pathologic significance to the association between multivessel coronary artery disease and/or symptoms of congestive heart failure and significant renal artery stenosis. The presence of peripheral vascular disease was a predictor of significant renal artery stenosis and is a known marker for renal artery disease. Patients with atherosclerosis elsewhere, especially with abdominal aortic aneurysms (22 to 28%), aorto-occlusive disease (33%), or lower-extremity occlusive disease (18 to 39%), have previously been shown to have a high prevalence of significant renal artery stenosis, even in the absence of the other clinical clues to suspect renal artery stenosis (15,22,32). In this study, only 29 of the 188 patients with significant renal artery stenosis had no evidence of significant coronary artery disease or peripheral vascular disease.

Female gender as a predictor of significant renal artery stenosis is of interest because women are commonly not felt to have a high association with atherosclerotic disease. In other series, male gender, along with advanced age, have been cited as predictors of atherosclerotic renal artery lesions (3,18,26,33). It is well established, though, that women have a higher incidence of fibromuscular disease than do men (2,26). Furthermore, atheromatous lesions can develop in patients with hypertension and fibromuscular dysplasia within the proximal segment of the renal artery (14). It is speculative that fibromuscular renovascular disease could have accelerated coexistent atherosclerotic disease as the women became more elderly.

The Role of Renal Artery Disease in Clinical Syndromes

Although an elevated creatinine was not found to be an important predictor of significant renal artery stenosis, it deserves special attention. This issue is important in light of arguments promoting renal revascularization for the preservation of renal function rather than for the control of hypertension. Up to 14% of patients on dialysis have renal failure secondary to ischemic renal disease (4,7). Unilateral renal artery stenosis should not result in an elevated creatinine if the contralateral kidney functions properly. Instead, an elevated creatinine should be a marker for renal artery disease only if the stenosis is functionally significant in a solitary kidney or causes bilateral hemodynamic compromise of both kidneys (5). In this study, we found no significant difference in the mean serum creatinine between these patients with significant unilateral or bilateral renal artery stenosis (88.4 and 95.5 μmol/L, respectively).

A history of hypertension also did not predict the presence of renal artery stenosis. However, it is known that all renal artery obstructions do not cause hypertension and both hypertensive and normoten-

| TABLE 5. Comparison of patients with and without congestive heart failure symptoms |
|---------------------------------|---------|----------------|---------|
|                                | CHF (N = 185) | No CHF (N = 1,050) | P Value |
| Mean age (yr)                  | 62 ± 12  | 59 ± 11         | 0.02    |
| Hypertension                   | 101 (55%) | 480 (46%)       | 0.03    |
| Significant RAS                 | 47 (25%) | 141 (13%)       | 0.001   |
| Multivessel CAD                 | 81 (44%) | 398 (38%)       | 0.05    |

a CHF, congestive heart failure.
b RAS, renal artery stenosis.
c ≥ Two-vessel or left main CAD (coronary artery disease).
sive patients may exhibit renal artery stenosis (22,23,31,34). Almost half of the patient population studied had a history of hypertension, and of the 581 hypertensive patients, 100 (17%) had significant renal artery stenosis. This is similar to other findings of about an 18% incidence of renal artery stenosis in hypertensive patients who undergo cardiac catheterization (16).

Possibly the most important aspect of our findings is the high incidence of renal atherosclerotic lesions observed. Although a prospective study on the natural history of renal artery stenosis has not been performed, retrospective studies suggest progression may occur in 36 to 63% of patients examined (1–3). Progressive deterioration of renal function has been observed to occur in 41% of medically treated patients with atherosclerotic renal artery stenosis and renovascular hypertension despite the presence of good blood pressure control (35).

When the decision is made to treat, there are currently three therapeutic options available for patients with renal artery disease: medical therapy, percutaneous transluminal angioplasty, and surgical therapy. Several factors must be weighed in determining whether medical or interventional management is appropriate for a given patient. These include the causal relationship of renovascular disease to hypertension, the adequacy of blood pressure control with medical therapy, the natural history of untreated renovascular disease, the medical condition of the patient, and the known results of surgical therapy and percutaneous transluminal angioplasty (36). To date no prospective trials have evaluated the outcome of patients randomized to surgical versus angioplasty treatments. Revascularization has been shown to be effective in treating renovascular hypertension and restoring renal function but not without considerable risk (6,9,13,37–40). Surgical mortality has been reported to be between 2 and 15%, with the predominant cause of death related to nonaortorenal disease, primarily myocardial infarction (5). The long-term technical success rate for percutaneous renal angioplasty is as high as 90% for lesions of the main segment of the renal artery, but ostial lesions fare much worse with a technical success rate of <25% (5). Major complications related to angioplasty occur in 3 to 14% of cases, and mortality as high as 2% has been reported (5,11,40).

Limitations

It should be emphasized that this study was designed to screen for renal artery disease in a simple and convenient manner in order to maximize the number and percentage of patients studied who underwent routine cardiac catheterization. The study was limited because of its dependency on the accuracy of cine abdominal aortography performed in a single view for determining the absence or presence of renal artery stenosis. Previous studies using the anterior-posterior projection have demonstrated that renal arteriography permits excellent visualization of the renal vascular anatomy but point out the difficulties in ruling out ostial lesions (12,30). Oblique views, however, may be necessary to completely evaluate the ostia and very proximal portions of the renal artery because these areas may be partially obscured by the aortic silhouette (16,18,29). In addition, distal branches of the renal artery may be less well seen. Five percent of the studies were deemed inadequate for visualizing both renal arteries. Selective renal arteriograms would likely have helped delineate disease in the main renal artery or its branches that were obscured by overlying mesenteric vessels. It is, therefore, probable that some renal artery lesions were missed, particularly in the ostium and distal branches of the renal arteries, and that the true prevalence of renal artery stenosis is somewhat greater than the 15% reported here.

A second shortcoming is the fact that 21% of the patients undergoing routine cardiac catheterization did not have abdominal aortography, and this could cause selection bias. Unfortunately, this was an inherent problem in a study of this magnitude, which involved up to 10 angiographers. A number of patients had only right heart studies, right heart biopsies, or "relook" coronary angiography after percutaneous transluminal coronary angioplasty, and these patients normally do not have ventriculography performed. In turn, the additional aortograms were not available. Although a few patients might have been excluded because of an elevated creatinine, these numbers were likely small because a previous, prospective study of 1,144 patients undergoing elective catheterization from our institution revealed only 6% had a creatinine >106 μmol/L (41).

CONCLUSION

The prevalence of angiographically significant renal artery narrowing, primary due to atherosclerotic disease, in a population going to cardiac catheterization is 15%. The yield of screening abdominal aortography at the time of cardiac catheterization can be increased if certain clinically and catheterization-derived variables including age, multivessel coronary artery disease, symptoms of congestive heart failure, female gender, and evidence of peripheral vascular disease are used to select those screened.

The high incidence of associated renovascular disease may contribute to clinical morbidity in this group of patients over time, and this should be remembered when unexplained renal dysfunction en-
issues in cardiac patients. Because renal vascular disease may result in the loss of renal mass and function, further prospective studies are needed to identify the natural history of atherosclerotic renal artery disease and to define the role of intervention and correction of these lesions in preventing the loss of renal function.

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