

Article

Frequency of renal artery stenosis in patients with recurrent pulmonary edema

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Abstract

Background: The prevalence of atherosclerotic renal artery stenosis in patients with hypertension, stroke, peripheral vascular disease and coronary artery disease is well defined in the literature but the prevalence of atherosclerotic renal artery stenosis in patients with recurrent pulmonary edema is unknown.

Objectives: This study discusses, in detail, the characteristics of patients with recurrent pulmonary edema at risk of renal artery stenosis (RAS).

Materials and methods: Patients presenting with recurrent pulmonary edema underwent selective coronary and renal angiography.

Results: Sixty consecutive patients were included in this study. A total of 29/60 (48.3%) patients had renal artery stenosis $\geq 50\%$ and 10/60 (16.7%) had severe stenosis ($\geq 70\%$) in at least one renal artery. Severe bilateral stenosis (70–99% in both renal arteries) was detected in 3/60 patients (5%) and total occlusion of the renal artery was detected in 1/60 (1.7%). Analysis of the results of renal function tests showed that of the 10 patients with severe renal artery stenosis, 5 (50%) had blood urea nitrogen (BUN) < 18 mg/dl and 4 (40%) had serum creatinine < 1.2 mg/dl.

Conclusions: Prevalence of atherosclerotic renal artery stenosis in this approach was 48.3% in patients with acute pulmonary edema which is obviously higher than that previously observed in hypertension, stroke, peripheral vascular disease and coronary artery disease.

Keywords: Atherosclerosis; heart failure; pulmonary edema; renal artery stenosis.

Introduction

Atherosclerosis is a common cause of heart failure^[1]. It can affect both coronary and renal arteries. It is possible that renal artery stenosis (RAS) caused by atherosclerosis plays a significant role in the pathophysiology and progression of heart failure in some patients. Atherosclerotic renovascular disease (ARVD) is often asymptomatic^[2]. Hypertension is the most common presentation of RAS; 1–5% of all patients with hypertension have RAS^[2]. Other clinical presentations include progressive renal

dysfunction, marked rise in serum creatinine with blockade of the renin–angiotensin–aldosterone system (RAAS), proteinuria, congestive heart failure (CHF) and flash pulmonary edema^[3]. Recurrent pulmonary edema, both in the absence and in the presence of systolic left ventricular dysfunction, is an important clinical manifestation of renal artery stenosis^[3]. Renal angiography remains the gold standard procedure for diagnosis, providing information about the site and severity of stenosis and guiding appropriate revascularization strategies.

The aim of this study was to evaluate the clinical profile of patients with recurrent pulmonary edema in whom scheduled cardiac catheterization afforded an opportunity to determine the presence of RAS.

Materials and methods

Between May 2005 and June 2006, patients with documented recurrent cardiogenic pulmonary edema (more than once a year) were invited to participate and asked to provide informed written consent. We excluded patients for any of the following reasons: pure valvular heart disease including rheumatic and congenital valve disorders, congenital heart disease, previous coronary angiogram in the last 2 years, kidney transplant, known or suspected acute renal failure, history of contrast nephropathy, hemodynamic instability, digoxin toxicity, physician preference, or refusal or inability to provide informed consent. Participating patients underwent selective coronary and renal angiography. Administration of peri-procedural intravenous fluids or *N*-acetyl cysteine was left to the discretion of the physician. Selective coronary angiography was performed with the left and right Judkins coronary catheter. If the patient had a history of coronary artery bypass graft (CABG), engagement of left internal mammary artery (LIMA) and saphenous vein graft was done by IMA catheter and right Judkins coronary catheter, respectively. Selective renal angiography was employed with a right Judkins coronary catheter with hand injection of 4–8 ml of contrast agent in each main and accessory renal artery. All images were recorded digitally at 30 frames/s. Digital subtraction was reserved for cases with poor visualization of the renal artery due to overlying gas or structures. Significant coronary artery lesion was defined as >50% stenosis in the left main coronary artery or >70% narrowing in other coronary arteries. Categorization of abnormal renal arteries was done according to visually estimated diameter of narrowing (<50%, mild; 50–70%, significant; >70–99%, severe; or 100%, totally occluded). The consensus of at least two experienced angiographers was required in cases where severity of stenosis was initially uncertain. When uncertainty remained and consensus could not be achieved, patients were excluded from the study. Descriptive statistics are presented as the mean value \pm 1SD or frequency (%). The clinical characteristics of patients were compared using analysis of variance for continuous variables and chi-square test for categorical variables. A value of $p < 0.05$ was considered as statistically significant.

Table 1 Patient demographic data

Number of patients	60
Male/female	20/40
Age (years)	60 \pm 10.6
Smoker (%)	8 (13.3)
Diabetes (%)	14 (23.3)
History of HTN (%)	19 (31.6)
History of CVA (%)	4 (6.6)
Previous CABG (%)	5 (8.3)
Systolic BP on admission (mmHg)	148.7 \pm 15.3
Diastolic BP on admission (mmHg)	91 \pm 6
Baseline BUN (mg/dl)	22 \pm 11
Baseline creatinine (mg/dl)	1.4 \pm 0.8
Ejection fraction (%)	34 \pm 11
No. of antihypertensive drugs for patients	2.1 \pm 0.65
Diuretics (<i>n</i>)	54
Beta-blockers (<i>n</i>)	11
Calcium channel blockers (<i>n</i>)	23
Angiotensin converting enzyme inhibitors (<i>n</i>)	22
Angiotensinogen receptor antagonists (<i>n</i>)	31
Clonidine (<i>n</i>)	5
Alpha receptor blockers (<i>n</i>)	2
Hydralazine (<i>n</i>)	1

HTN, hypertension; CVA, cerebrovascular accident; CABG, coronary artery bypass graft; BP, blood pressure; BUN, blood urea nitrogen.

Table 2 Results of renal angiography according to severity of renal artery stenosis

	Right renal artery	Left renal artery	Total
Normal	10	4	14
<50%	6	11	17
50–70%	5	14	19
70–99%	1	8	9
100%	0	1	1
Total	23	37	60

Results

During the screening period, 60 consecutive patients were included in this study. Table 1 shows the patients' demographic data.

Renal angiography

A total of 29/60 patients (48.3%) had stenosis \geq 50% and 10/60 (16.7%) had severe stenosis (\geq 70%) in at least one renal artery. Severe bilateral stenosis (70–99% in both renal arteries) was detected in 3/60 patients (5%) and total occlusion was detected in 1/60 (1.7%) (Table 2). Significantly, more abnormal renal arteries were observed on the left side ($p = 0.026$). A significant relationship was observed between renal artery stenosis and female gender ($p = 0.020$) and the presence of diabetes ($p = 0.030$).

Table 3 Severity of renal artery stenosis according to coronary angiography findings

Result of coronary angiography	Result of renal angiography				
	Normal (n)	<50% (n)	50–70% (n)	70–99% (n)	100% (n)
Normal (n=4)	0	0	4	0	0
Single vessel disease (n=19)	7	8	4	0	0
Two-vessel disease (n=16)	4	6	4	2	0
Three-vessel/left main disease (n=21)	3	3	7	7	1

Table 4 Results of renal function tests according to severity of renal artery stenosis

Result of renal angiography	BUN (mg/dl)		Creatinine (mg/dl)	
	<18 (n)	>18 (n)	<1.2 (n)	>1.2 (n)
Normal (n=14)	13	1	12	2
<50% (n=17)	16	1	15	2
50–70% (n=19)	14	5	13	6
70–99% (n=9)	5	4	4	5
100% (n=1)	0	1	0	1

Coronary angiography

Selective coronary angiography was done in 60 patients and revealed single vessel disease in 19 (31.6%), two vessel disease in 16 (26.6%), three vessel disease in 18 (30%) and left main disease in 3 (5%) patients. There was a significant relationship between severe renal artery stenosis (>70%) and three-vessel and left main disease ($p = 0.010$) (Table 3).

Renal function tests

Table 4 shows the results of renal function tests according to the severity of renal artery stenosis. Interestingly, from 10 patients with severe renal artery stenosis (>70%), 5 (50%) had blood urea nitrogen (BUN) <18 mg/dl and 4 (40%) had serum creatinine <1.2 mg/dl.

Discussion

This study outlines the frequency of atherosclerotic renovascular disease in patients with acute pulmonary edema, with a particular emphasis on coexisting heart failure. Prevalence of RAS in this approach is 48.3% in patients with acute pulmonary edema which is obviously higher than that previously observed in

hypertension (5%)^[2,4], stroke (10%)^[5], peripheral vascular disease (24%)^[6] and coronary artery disease (30%)^[7,8]. To our knowledge, the only published study reporting the prevalence of RAS in CHF showed that RAS >50% was present in 29/86 (34%) patients. Previous therapy with ACE-inhibitors and a serum creatinine level >300 $\mu\text{mol/l}$ (3.4 mg/dl) were exclusion criteria^[9]. However, a selection bias existed in that study because all patients were screened using captopril renography and only 53 patients underwent magnetic resonance angiography. Our study extends and quantifies the relationships between RAS and coronary artery atherosclerosis. In this study, coronary disease was found to have an important association with RAS. Patients with advanced three-vessel or left main coronary disease displayed a 71.4% prevalence of significant RAS. Renal artery stenosis remained strongly associated with atherosclerosis in coronary territories, in contrast to the previous study which revealed a lack of significant association between coronary disease and RAS^[10]. The association we observed between RAS and coronary disease simply reflects a relationship between RAS and generalized atherosclerosis. Interestingly, from 10 patients with severe renal artery stenosis (>70%), 5 (50%) had blood urea nitrogen (BUN) <18 mg/dl and 4 (40%) had serum creatinine <1.2 mg/dl. At a minimum, it appears that clinicians should consider that significant RAS may be present despite normal renal function tests. The strong association with female gender extends previous observations^[5]. Persistence of female gender after adjustment for age and other factors remains unexplained.

CHF and renovascular disease

Should intervention be offered to patients with CHF and atherosclerotic RAS?

The few randomized trials looking at cardiovascular outcomes in ARVD have used blood pressure and renal function as endpoints. They were underpowered to determine whether revascularization improved cardiovascular outcomes. Randomized controlled trials on the safety and efficacy of renal angioplasty for RAS in the presence of CHF and/or pulmonary edema are lacking. The majority of reports involved patients with significant bilateral RAS or unilateral RAS with a non-functioning contralateral kidney. Whether revascularization will improve the symptoms of heart failure in a patient with unilateral disease and two functioning kidneys is unclear.

Should clinicians screen routinely for RAS in patients with CHF/pulmonary edema?

Before adopting a screening test, it is important to know the approximate prevalence of the condition to ensure that screening is a proper use of resources and that detection will benefit patients by changing management. Neither of these conditions has been adequately fulfilled in patients with heart failure. This study reflects a relatively high prevalence of RAS in patients with recurrent pulmonary edema and thus promotes screening tests for RAS in patients with recurrent pulmonary edema and refractory CHF.

Conclusions

This study characterizes, in detail, patients with recurrent pulmonary edema at risk of RAS and found the overall prevalence of significant and severe RAS among patients with recurrent pulmonary edema and associations between RAS and clinical and laboratory variables. Long-term follow-up to determine the significance of RAS with particular emphasis on the presence of coexistent CHF is the focus of future research.

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