International Journal of Biomedical and Advance Research
ISSN: 2229-3809 (Online); 2455-0558 (Print)
Journal DOI: 10.7439/ijbar
CODEN: IJBABN

Original Research Article

Incidence and associates of renal artery stenosis in patients undergoing peripheral and coronary angiography

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Abstract

Objectives: Increasing prevalence of renal artery stenosis (RAS) in coronary artery disease (CAD) patients has been reported by many. We aimed to study the incidence and risk factors of renal artery disease in patients undergoing coronary angiography (CAG) and/or peripheral angiography (PAG).

Methods: Data of 2209 consecutive patients undergoing CAG and/or PAG followed by renal angiography was collected from January-June 2013. Pervasiveness of risk factors such as hypertension, diabetes, dyslipidemia, smoking, family history and incidence of CAD were studied. Significant difference in profiles of patients with or without compelling atherosclerotic renal artery stenosis (ARAS) was tested by chi-square and unpaired t-test.

Results and conclusion: Of 2209 patients, the prevalence of RAS in the study population was 6.11%. Mean age of the RAS patient group was 57.17 ± 10.82 years. Advancing age, hypertension, diabetes, smoking and dyslipidemia were found to be strongly associated with RAS. Patients with significant CAD had increased chances to develop ARAS. Ageing and presence of risk factors were closely associated with significant ARAS and hence they could be used in effectively predicting the presence of RAS in patients undergoing routine CAG and/or PAG.

Keywords: Coronary Artery Disease, Renal Artery Stenosis, Coronary Angiography, Peripheral Angiography

1. Introduction

Atherosclerotic renal artery stenosis (ARAS) is the most common cause of secondary hypertension in elderly. Renal artery stenosis (RAS) is often present without any clinical signs or symptoms and is one of the few reversible causes of hypertension and renal insufficiency. About 90% of RAS are atherosclerotic which involve the ostium of the renal artery [1]. Atherosclerotic renal artery stenosis is a progressive disease leading to renal atrophy over time and chronic kidney disease despite control of hypertension. Angioplasty with renal artery stenting for ARAS is an effective treatment strategy to restore and preserve renal function and to control blood pressure [2]. It is an independent predictor of death regardless of presence, severity or method of revascularization of coronary arteries [3].

Atherosclerosis is a diffuse process but affects certain regions of the vascular bed preferentially. The association between extent and severity of coronary artery disease (CAD) and RAS has been well established in most previous studies [3,4], but a definite relationship between the distribution of lesions in coronary tree, peripheral vascular disease and RAS has not been studied. [5] Some researchers have reported ARAS to be commonly associated with peripheral artery disease than with CAD. [6] The prevalence of ARAS has been reported to be in the range of 20–30% in high-risk populations.[7–9] Renal artery stenosis is a common cause of renal insufficiency and end-stage renal disease and is present in 5–22% of patients more than 50 years old. [9] In these patients simultaneous screening for ARAS is highly cost-

effective, especially when done at the time of another invasive diagnostic procedure like cardiac catheterization, and may affect treatment strategies.

2. Method

2.1 Study design and patient population

Data of 2209 consecutive patients undergoing coronary angiography (CAG) and/or peripheral angiography (PAG) followed by renal angiography was collected from January-June 2013 at a tertiary care Cardiology Centre, Ahmedabad. The study protocol was reviewed and accepted by the ethical committee of the institute. The patients with known renal artery disease were excluded from the study.

Demographic variables, biochemical tests and history of atherosclerotic risk factors were obtained from the patient's medical records. Patients were considered hypertensive, if they had a positive history of hypertension or were under lifestyle modification and/or medical treatment. Patients were considered diabetic as either currently taking anti-diabetic medications or having more than one fasting plasma glucose of (>126 mg/dl) on record. Dyslipidemia was considered present if the patient was under medical treatment for known dyslipidemia or any of the following laboratory criteria existed: Fasting low-density lipoprotein cholesterol (LDL-C) (>130 mg/dl), high-density lipoprotein cholesterol (HDL-C) (<40 mg/dl) in men and (<50 mg/dl) in women and triglycerides (>150 mg/dl). Smoking was defined according to the current status of the patient. A positive family history was defined as a known history of CAD in a first degree male (<45 years) and/or female (<55 years) relative. Glomerular filtration rate was estimated by the Cockcroft–Gault formula using plasma creatinine concentration.

2.2 Interventional procedure

All the patients underwent selective CAG and/or PAG followed by renal angiography. Only patients with peripheral artery disease underwent angiography by trans-radial route. Selective renal angiography was performed using a right Judkins' catheter and 0-20 straight left anterior oblique (LAO) projections with hand injection. In those patients for whom it was difficult to evaluate the degree of stenosis by selective angiography, aortography with digital subtraction angiography was performed with pigtail catheter and 10-20straight LAO projection with a pump injector at a rate of 15ml/sec. On an average, about 30-40ml additional contrast media was utilized with either Omnipaque (GE Healthcare, Ireland) or Visipaque-320 (GE Healthcare, Ireland). There were no procedural related complications with either method. Significant RAS was defined if luminal narrowing of ≥50% was present and the coronary artery lesions were considered significant if ≥70% stenosis was present [10]. The lesion severity was assessed independently by quantitative coronary angiography. All angiograms were digitally recorded at 15frames/sec speed and interpreted by two interventional cardiologists independently. The mean of the value interpreted by the both cardiologists and was compared to the value obtained by quantitative coronary angiography and again the mean of these two values obtained was used.

2.3 Statistical analysis

Data were expressed as mean±standard deviation or number (%) as applicable. Chi- Square test was used for categorical variables and unpaired t-test was used for continuous variables to find the risk factor distribution in patients with and without significant ARAS. A P-value of ≤0.05 was considered significant.

3. Results

Out of 2209 patients, 1712 (77.5%) were males and 497 (22.5%) were females. Demographic characteristics and risk factor profiles of the patient with and without significant ARAS are mentioned in Table I.A total of 2074 (93.9%) patients had no or insignificant RAS. The prevalence of significant RAS with a luminal narrowing of ≤50% which was 6.11%, consisted of 99 (73.3%) male and 36 (26.7%) female patients. Mean age of the patients with RAS (57.17 ± 10.82 years) was significantly higher than those without RAS (55.19 ± 10.44 years).Mean blood pressure (BP) and systolic BP were also found to be significantly higher in ARAS patients group. Among the risk factors studied, hypertension (P = 0.0002), diabetes (P = 0.0003), dyslipidemia (P = 0.002) and smoking (P = 0.046) were significantly associated in patients with RAS. Hypertension was the most predominant risk factor with 71.1% of prevalence. A positive family history and CAD incidence were not found statistical significant when linked to RAS.

The detailed angiographic characteristics and creatinine levels are outlined in Table II. The baseline serum creatinine was comparable (P = 0.0738) in patients with and without ARAS. Patients with and without RAS had significantly different creatinine clearance rate. Creatinine clearance of 30 - 59.9 mL/min/1.73 m^2 was more common in RAS patients as compared to patient without RAS (P = 0.008). Patients with Atherosclerotic Renal Artery Disease (ARAD) had increased numbers of obstructive CAD than those without ARAD (71.1% and 66.2% respectively); although this difference was not found significant (P =0.286). The prevalence of single vessel disease (SVD), double vessel disease

(DVD) and triple vessel disease (TVD) in both the groups were comparable. The incidence of left anterior descending(LAD) artery occlusion was the more in patients with RAS (8.1% vs 4.2%) while in those without RAS, left circumflex artery (LCx) occlusion (66.7% vs 40.0%) was higher. No significant (P = 0.529) association was observed between RAS and peripheral arterial disease.

Table III compares the characteristics of the patients with unilateral and bilateral RAS. Out of 135 patients, 28 (20.7%) patients had bilateral RAS and a majority of 107 (79.3%) had unilateral RAS. Values of serum creatinine was higher in bilateral RAS group with a significant (P = 0.019) difference from unilateral RAS group. Creatinine clearance showed statistical significance when the clearance was in between 30- 59.9 mL/min/1.73 m^2 (P =0.008). Complexity of coronary artery disease (SVD, DVD and TVD) was comparable in patients with unilateral and bilateral RAS.

Table I: Demographic characteristics and risk factor profile of patients with and without RAS

	Insignificant/No RAS	**Significant RAS**	**P value**
n	2074 (93.9%)	135 (6.1%)	<0.0001*
Variable	**(mean ± SD)**		
Age (yrs)	55.19 ± 10.44	57.17 ± 10.82	0.033*
Weight (in Kgs)	62.87 ± 11.04	62.61 ± 10.02	0.789
MBP (mmHg)	107.31 ± 19.18	111.79 ±17.76	0.008*
SBP (mmHg)	138.11 ± 26.47	147.65 ± 28.50	0.0001*
DBP (mmHg)	91.92 ± 18.50	93.85 ± 17.12	0.238
Variable	**n (%)**		
Male	1613 (77.8)	99 (73.3)	0.275
Female	461 (22.2)	36 (26.7)	0.275
Hypertension	1121 (54.1)	96 (71.1)	0.0002*
Diabetes	747 (36)	70 (51.9)	0.0003*
Smoking	726 (35.0)	52 (38.5)	0.0462*
Family History of CAD	359 (17.3)	32 (23.7)	0.076
Dyslipidemia	217 (10.5)	26 (19.3)	0.002*
CAD	1374 (66.2)	96 (71.1)	0.286

*- Significant with P ≤ 0.05;

[CAD- Coronary Artery Disease; DBP- Diastolic Blood Pressure; MBP- Mean Blood Pressure; RAS- Renal Artery Stenosis; SBP- Systolic Blood Pressure**]**

Table II Detailed characteristics of the study population

Variables	**Insignificant/ No RAS**	**Significant RAS**	**p-Value**
n	2074 (93.9%)	135 (6.1%)	
	mean ± SD		
Creatinine (mg/dl)	0.95 ± 0.38	1.01 ± 0.34	0.0738
	n (%)		
Cr Cl-c (mL/min/1.73 m^2)			
>90	783 (37.8)	38 (28.1)	0.031*
60- 89.99	831 (40.1)	56 (41.5)	0.814
30- 59.99	423 (20.4)	38 (28.1)	0.041*
15- 29.99	32 (1.5)	3 (2.2)	0.797
<15	5 (2)	0 (0)	0.716
Significant CAD	1374 (66.25)	96 (71.11)	0.286
Diseased vessels			
SVD	561 (40.8)	34 (35.4)	0.348
DVD	430 (31.3)	33 (34.4)	0.607
TVD	383 (27.9)	29 (30.2)	0.707
Lesion location			
LMCA	87 (4.2)	11 (8.1)	0.051
LAD	1061 (51.2)	75 (55.6)	0.367
LCx	1384 (66.7)	54 (40.0)	<0.0001*
RCA	754 (36.4)	55 (40.7)	0.351
Peripheral arterial occlusive/ obstructive disease	39 (1.9)	1 (0.7)	0.529

*- Significant with P ≤ 0.05

[CAD- Coronary Artery Disease; Cr Cl-c- Creatinine Clearance; SVD- Single vessel disease; DVD- Double vessel disease; TVD- Triple vessel disease; LMCA-Left main coronary artery; LAD- Left anterior descending; LCx- Left circumflex artery; RCA- Right coronary artery]

Table III: Laboratory and angiographic characteristics of the Significant Renal Artery Stenosis patients

	Unilateral RAS	Bilateral RAS	p-Value
Number of patients	107 (79.3%)	28 (20.7%)	<0.0001*
	Mean ± SD		
Creatinine (mg/dl)	0.97 ± 00.31	1.19 ± 0.39	0.019*
	n (%)		
Cr Cl-c (mL/min/1.73 m^2)			
>90	33 (30.8)	5 (17.9)	0.261
60 – 89.99	48 (44.9)	8 (28.6)	0.179
30 – 59.99	24 (22.4)	14 (50.0)	0.008*
15 – 29.99	2 (1.9)	1 (3.6)	0.860
<15	0	0	
Significant CAD	76 (71.0)	20 (71.4)	0.847
No. of diseased vessels			
SVD	27 (35.5)	7 (35.0)	0.826
DVD	26 (34.2)	7 (35.0)	0.864
TVD	23 (30.3)	6 (30.0)	0.802
Lesion location			
LMCA	8 (7.5)	3 (10.7)	0.865
LAD	58 (54.2)	17 (60.7)	0.686
LCx	43 (40.2)	11 (39.3)	0.896
RCA	45 (42.1)	10 (35.7)	0.695

*- Significant with $P \leq 0.05$

[CAD = Coronary Artery Disease; Cr Cl-c = Creatinine Clearance; SVD- Single vessel disease; DVD- Double vessel disease; TVD- Triple vessel disease; LMCA-Left main coronary artery; LAD- Left anterior descending; LCx- Left circumflex artery; RCA- Right coronary artery]

4. Discussion

The overall prevalence of RAS in our study population undergoing CAG and/or PAG for suspected CAD was found to be 6.1%. Main risk factors associated with RAS were advancing age (P = 0.033), hypertension (P = 0.0002), diabetes (P = 0.0003), smoking (P = 0.046) and dyslipidemia (P = 0.002). Patients with CAD were higher in patients with RAS than those without, although the difference was not significant (P = 0.286). LMCA as the main lesion containing site, resultant as left main disease more prevalent in patient affected by RAS. As reported, in Europe and America the prevalence of RAS has been reported to be 13.5–18% among all patients undergoing routine cardiac catheterization; where as other studies in Asian population reported a lower incidence of RAS as low as 3.1% to 7%. [16,17] Researchers from different parts of the world reported major risk factors associated with RAS as hypertension, left main disease, TVD and smoking.[10,16-18] We found left main coronary artery (P = 0.041) and circumflex lesions (P < 0.0001) to be independent predictors of RAS parallel to the findings of Rokni N *et al.* and Harding MB and associates. [11,18] Although we found a statistically significant association of diabetes and dyslipidemia with RAS which in discordance to the results from other similar studies. [4,13,18]

Higher creatinine levels and peripheral vascular disease have also been associated with ARAS. [18-21]Contrariwise, we did not find any significant association of TVD or severity of CAD (P = 0.286) and peripheral vascular disease in patients with and without RAS. Though peripheral artery disease is a manifestation of atherosclerosis we did not found any significant association between peripheral vascular disease and ARAS. In patients with peripheral vascular disease, RAS has been reported as 35- 60% incidence. [6] Although some researchers have also concluded that peripheral vascular disease not to be associated with ARAS.[12] The major reason behind this could be due to the fact that atherosclerosis does not involve all the arterial beds in unison.

The presence of ARAS may also complicate the medical management of patients with hypertension and/or congestive heart failure. [22] Renal artery stenosis may be a cause of hypertension and may result in renal ischemia and loss of renal mass.[18] Patients with a creatinine clearance of 30 – 59.99 ml/min/1.73m^2 was found to be strong predictor of RAS in our study population. It has been reported that patients with GFR values low than 60 ml/min/1.73$m^2$are more inclined to cardiovascular diseases. Some researchers in their study have also mentioned that moderate to severe renal impairment is also associated with accelerated atherosclerosis. [11] So, early detection and treatment of RAS are important, because AS deteriorates the prognosis of cardiovascular diseases. [24-26]

Often due to delay in detection and due to compensatory contralateral renal hypertrophy, the

ischemic nephropathy may not be evidenced by altered renal function till ARAS is bilateral and renal function is largely affected. Researchers mentioned the importance of the prognoses of patients with cardiovascular diseases and RAS as it could be improved by treating RAS. [23,24] Many studies have shown that renal failure secondary to ARAS is preventable and reversible by percutaneous intervention as well as surgery. [1] In case of untreated ARAS, renal ischemia will result in progressive irreversible fibrosis. As mentioned earlier, kidney dimensions are decreased and even deteriorated in course of time as observed. Restoration of renal perfusion and correction of renal artery stenosis improves patients' clinical state in terms of further advancement of the disease and management of associated risk factors as hypertension. A 2-year follow-up study showed 11% of RAS patients progressed to complete occlusion over the follow-up time period. [27] Thus, intervention and correction of RAS may prevent progressive narrowing of the vessel and deterioration of renal function which has also been reported by Harden *et al.*, showing that stenting results in a 4-fold slowing of the progression of renal dysfunction.[28] Currently, trans-radial approach has been gaining increased acceptance for coronary angiography/ intervention due to reduced access site complication and increased patient compliance. However, there are high chances of nonselective renal angiography during trans-radial approach. Thus, clinicians are often reluctant to perform renal angiography during trans-radial coronary angiography/intervention, leading to under diagnosis of ARAS.

Hence, taking in account the current scenario researchers would like to suggest that identification of patients undergoing CAG and/or PAG for suspected CAD with risk factors as dyslipidemia, hypertension, diabetes and LMCA and circumflex as lesion site should be termed high risk and be screened for ARAS. Accordingly, these patients could be enhanced optimized treatment with better health outcome. Renin–angiotensin blockers modify the course of both ARAS and CAD and help significantly to reduce the progression of the disease.

5. Conclusion

The prevalence of ARAS among the patients undergoing routine cardiac catheterization was found to be 6.11%. Hypertension, diabetes mellitus, dyslipidemia, and altered renal functions were found to be strongly associated with significant ARAS. Hypertension was the most predominant risk factor among the study population with 71.1% prevalence. Left main coronary artery and circumflex artery lesions were also found to be significantly associated with RAS. These associated risk factors can be useful for predicting the incidence of RAS. There were no association found between peripheral artery disease and ARAS. Provided the progressive nature of ARAS there is a need for its early detection and intervention.

We would like to suggest considering, renal angiography along with coronary angiography particularly in high risk patients with above clinical conditions.

References

[1] Zeller T. Renal artery stenosis: epidemiology, clinical manifestation, and percutaneous endovascular therapy. *Journal of interventional cardiology* 2005; 18(6):497-506.

[2] Gonçalves JAA, Amorim JE, Soares Neto MM, Ribeiro AB, Lima VC. Clinical efficacy of percutaneous renal revascularization with stent placement in atherosclerotic renovascular disease. *Arquivos brasileiros de cardiologia* 2007; 88(1):85-90.

[3] Conlon PJ, Little MA, Pieper K, Mark DB. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. *Kidney international* 2001; 60(4):1490-97.

[4] Wang Y, Ho D, Chen W, Wang Y, Lam W, Shen Z, *et al*. Prevalence and predictors of renal artery stenosis in Chinese patients with coronary artery disease. *Internal medicine journal* 2003; 33(7):280-85.

[5] Weber-Mzell D, Kotanko P, Schumacher M, Klein W, Skrabal F. Coronary anatomy predicts presence or absence of renal artery stenosis. *Eur Heart J* 2002; 23:1684-91.

[6] Leertouwer TC, Pattynama PM, Van Den Berg-Huysmans A. Incidental renal artery stenosis in peripheral vascular disease: a case for treatment?. *Kidney international* 2001; 59(4):1480-83.

[7] Ollivier R, Boulmier D, Veillard D, Leurent G, Mock S, Bedossa M, *et al*. Frequency and predictors of renal artery stenosis in patients with coronary artery disease. *Cardiovascular Revascularization Medicine* 2009; 10(1):23-29.

[8] Buller CE, Nogareda JG, Ramanathan K, Ricci DR, Djurdjev O, Tinckam KJ, *et al*. The profile of cardiac patients with renal artery stenosis. *Journal of the American College of Cardiology* 2004; 43(9):1606-13.

[9] Rihal CS, Textor SC, Breen JF, McKusick MA, Grill DE, Hallett JW, *et al*. Incidental renal artery stenosis among a prospective cohort of hypertensive patients undergoing coronary

angiography. *Mayo Clinic Proceedings* 2002; Elsevier.

[10] Bageacu S, Cerisier A, Isaaz K, Nourissat A, Barral X, Favre JP. Incidental visceral and renal artery stenosis in patients undergoing coronary angiography. *European Journal of Vascular and Endovascular Surgery* 2011; 41(3):385-90.

[11] Yamashita Takehiro, Ito Fumihiro, Iwakiri Naoki, Mitsuyama Hirofumi, Fujii Satoshi, Kitababatake Akira. Prevalence and predictors of renal artery stenosis in patients undergoing cardiac catheterization. *Hypertension Research* 2002; 25:553–57.

[12] Akram A. Saleh and Basem B. Bustami. Prevalence of renal artery stenosis in patients undergoing routine cardiac catheterization. *Saudi Med Journal* 2004; 25(1):52-54.

[13] Harding MB, L.R. Smith, SI. Himmelstein, K. Harrison, H.P. Phillips. S.J. Schwab, J.B. Hermiller. C.J. Davidson, J.M. Bashore, Duke University Medical Center, Durham, NC. Renal Artery Stenosis: Prevalence and Associated Risk Factors in Patients Undergoing Routine Cardiac catherization. *Journal of American society of Nephrology* 1992; 2:1608-16.

[14] Rokni N, Salarifar M, Kazazi EH, Goodarzynejad H. Frequency and predictors of renal artery stenosis in patients undergoing simultaneous coronary and renal catheterization. *The journal of Tehran Heart Center* 2012; 7(2):58.

[15] Jean WJ, Al-Bitar I, Zwicke DL, Port SC, Schmidt DH, Bajwa TK. High incidence of renal artery stenosis in patients with coronary artery disease. *Catheterization and cardiovascular diagnosis* 1994; 32(1):8-10.

[16] Ghaffari S, Sohrabi B, Siahdasht RB, Pourafkari L. Prevalence and predictors of renal artery stenosis in hypertensive patients undergoing coronary angiography. *Hypertension Research* 2009; 32(11):1009-14.

[17] Crowley JJ, Santos RM, Peter RH, Puma JA, Schwab SJ, Phillips HR, Stack RS, Conlon PJ. Progression of renal artery stenosis in patients undergoing cardiac catheterization. *American Heart Journal* 1998; 136(5):913-18.

[18] Cohen MG, Pascua JA, Garcia-Ben M, Rojas-Matas CA, Gabay JM, Berrocal DH, Tan WA, Stouffer GA, Montoya M, Fernandez AD, Halac ME, Grinfeld LR. A simple prediction rule for significant renal artery stenosis in patients undergoing cardiac catheterization. *American Heart Journal* 2005; 150(6):1204-11.

[19] Olechnowicz-Tietz S, Gluba A, Paradowska A, Banach M, Rysz J. The risk of atherosclerosis in patients with chronic kidney disease. *International urology and nephrology* 2013; 45(6):1605-12.

[20] Hricik DE, Browning PJ, Kopelman R, Goorno WE, Madias NE, Dzau VJ. Captopril-induced functional renal insufficiency in patients with bilateral renal-artery stenosis or renal-artery stenosis in a soliatry kidney. *New England Journal of Medicine* 1983; 308:373-76.

[21] Gross CM, Kraemer J, Waigand J, *et al*. Ostial renal artery stent placement for atherosclerotic renal artery stenosis in patients with coronary artery disease. *Cathet Cardiovasc Diagn* 1998; 45:1–8.

[22] MacDowall P, Kalra PA, O'Donoghue DJ, Waldek S, Mamtora H, Brown K. Risk of morbidity from renovascular disease in elderly patients with congestive heart failure. *Lancet* 1998; 352:13–16.

[23] Valentine RJ, Clagett GP, Miller GL, Myers SI, Martin JD, Chervu A. The coronary risk of unsuspected renal artery stenosis. *J Vasc Surg* 1993; 18:433–40.

[24] Stack R: Renal artery stenosis-under-diagnosed and undertreated in the cardiac patient? *J Invasive Cardiol* 1999; 11: 103–6.

[25] Zierler RE, Bergelin RO, Isaacson JA, et al: Natural history of atherosclerotic renal artery stenosis: A prospective study with duplex ultrasonography. *J Vasc Surg* 1994; 19:250–58.

[26] Harden PN, MacLeod MJ, Rodger RSC, *et al*. Effect of renal-artery stenting on progression of renovascular renal failure. *Lancet* 1997; 349: 1133–36.