Indian Journal of Basic and Applied Medical Research; June 2014: Vol.-3, Issue- 3, P. 391-399

Original article:

Relationship between coronary artery lesions distribution and renal artery stenosis in patients undergoing simultaneous coronary and renal angiography

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ABSTRACT:

Background: Atherosclerosis is by far the most common etiology of renal artery stenosis(RAS) in the elderly. RAS and coronary artery disease (CAD) originate from similar multiple risk factors for the development of atherosclerosis so that not surprisingly patients with RAS more commonly have CAD and vice versa.We aimed to find out if any association between distribution of coronary artery lesions and RAS exists. In parallel, we would evaluate the relationship between atherosclerotic risk factors and renal function, and RAS.

Material and Methods: From January 2013 to November 2013, data was collected and analyzed prospectively of 152 consecutive patients who underwent simultaneous renal angiography following coronary angiography in SMS hospital, Jaipur.

Results: Out of 152 patients, significant RAS was present in 14 patients (9.21%). It was unilateral in 13 patients (8.55%) and bilateral in 1 patient (0.6%).In 11 (7.23%) patients with unilateral disease, RAS was detected on left renal artery and in 2 patients (1.2%) right renal artery was involved. In 106(69.73%) patients, significant CAD was present. Significant RAS was more common in significant CAD group than with normal coronaries or insignificant CAD group but was statistically insignificant (78.57% vs 68.84%, p value=0.653). Significant RAS was more common in patients with three vessel CAD compared to those with single or two vessel CAD but was statistically insignificant. Relationships between involved locations of coronary arteries and RAS were also insignificant. Patients with significant RAS were older compared to those without significant disease (64.64 +_5.93years vs 56.8+_11.06years, p value=0.01).After log regression analysis, only increased pulse pressure and low eGFR was found to be significantly associated with significant RAS.

Conclusion: There is no significant association seen between distribution of coronary artery lesions and RAS. However, increased pulse pressure and reduced eGFR were found to be significantly associated with RAS.

Keywords: Atherosclerosis,renal artery stenosis, coronary artery disease

INTRODUCTION

Renal artery stenosis is a potential cause of secondary hypertension, ischemic nephropathy, and end-stage renal disease. Atherosclerosis is by far the most common etiology of renal artery stenosis in the elderly.[1,2]Although as the narrowing of the renal artery lumen progresses, renal perfusion declines and eventually renal function and structure are compromised.[3,4] Patients with atherosclerotic renal artery stenosis (RAS) are often asymptomatic with no characteristic laboratory findings, making its early diagnosis a major clinical problem.

Paradoxically, diagnosis of RAS at an early stage is of paramount importance because despite the uncertainty that exists about the benefit of revascularization over medical therapy for RAS,[5] it has been demonstrated that timely intervention using revascularization technique, surgery, or percutaneous transluminal angioplasty (PTA) may modify the natural history and outcomes.[6]

RAS and coronary artery disease (CAD) originate from similar multiple risk factors for the development of atherosclerosis so that not surprisingly patients with RAS more commonly

have CAD and vice versa.[7-10] Presence of RAS worsens the course of CAD, leading to increased risk of adverse coronary events, more frequent episodes of coronary revascularization, and higher mortality.[11-13]Because of the high coexistence of CAD and RAS in patients with angiographically documented CAD,[9,10] it has been proposed that renal angiography be performed consecutively in the same setting.[14]

However, operators are reluctant to perform renal angiography in combination with coronary angiography for several reasons: renal angiography is an invasive method; it can result in the dislodgment of the atheromatous debris; and it has severe complications, including contrast-associated nephropathy. Therefore, identifying patients at high risk for RAS in patients referred for coronary angiography is of great clinical importance and may influence treatment decisions in this population.

The prevalence of RAS has been reported to be in the range of 20–30 percent in high risk populations including patients with known atherosclerotic vascular disease elsewhere.[16-18] In these patients invasive screening for RAS is highly cost-effective especially when done at the time of another invasive diagnostic procedure like cardiac catheterization, and may affect treatment strategies.[19]The association between extent and severity of CAD and RAS has been well established in most previous studies,[20-22] but a few has addressed the relationship between the distribution of lesions in coronary tree and RAS.[12,23,24]

The main purpose of our study was to find out if any association between distribution of coronary artery lesions and RAS exists. In parallel, we would evaluate the relationship between atherosclerotic risk factors and renal function, and RAS.

Material and Methods:

Study Design: Hospital based observational descriptive study.

From January 2013 to November 2013, data was collected prospectively of 152 consecutive patients who underwent simultaneous renal angiography following coronary angiography in SMS hospital, Jaipur.

INCLUSION CRITERIA: All consecutive patients who underwent simultaneous coronary and renal angiography were included in our study.

EXCLUSION CRITERIA: Patients not willing for consent.

History of atherosclerotic risk factors and lab data was obtained from the patients' medical record. Risk factors of CAD were analysed which included age, male sex, cigarette smoking, hyperlipidemia, diabetes, hypertension, and family history of CAD.[15] A positive family history (FH) was established based on a known history of CAD in a first degree relative male or female less than 45 and 55 years respectively. Glomerular filtration rate (GFR) was estimated by the Cockcroft-Gault formula using plasma creatinine concentration, bodyweight, age, and gender.(Figure-1)

According to the catheterization laboratory routine practice, after coronary angiography, all of these patients underwent selective renal angiography using a right judkins catheter and 0–20 degrees straight LAO projections with hand injection. Significant RAS was defined if luminal-narrowing >50 percent was present. Patients having angiographic evidence of atherosclerosis (≥ 50% luminal stenosis in at least one coronary artery or major branch segment in their epicardial coronary tree) was considered to have CAD, and patients with no luminal stenosis or patients with < 50% luminal stenosis at coronary angiography was considered to have normal coronaries.Coronary artery disease was considered ostioproximal if it

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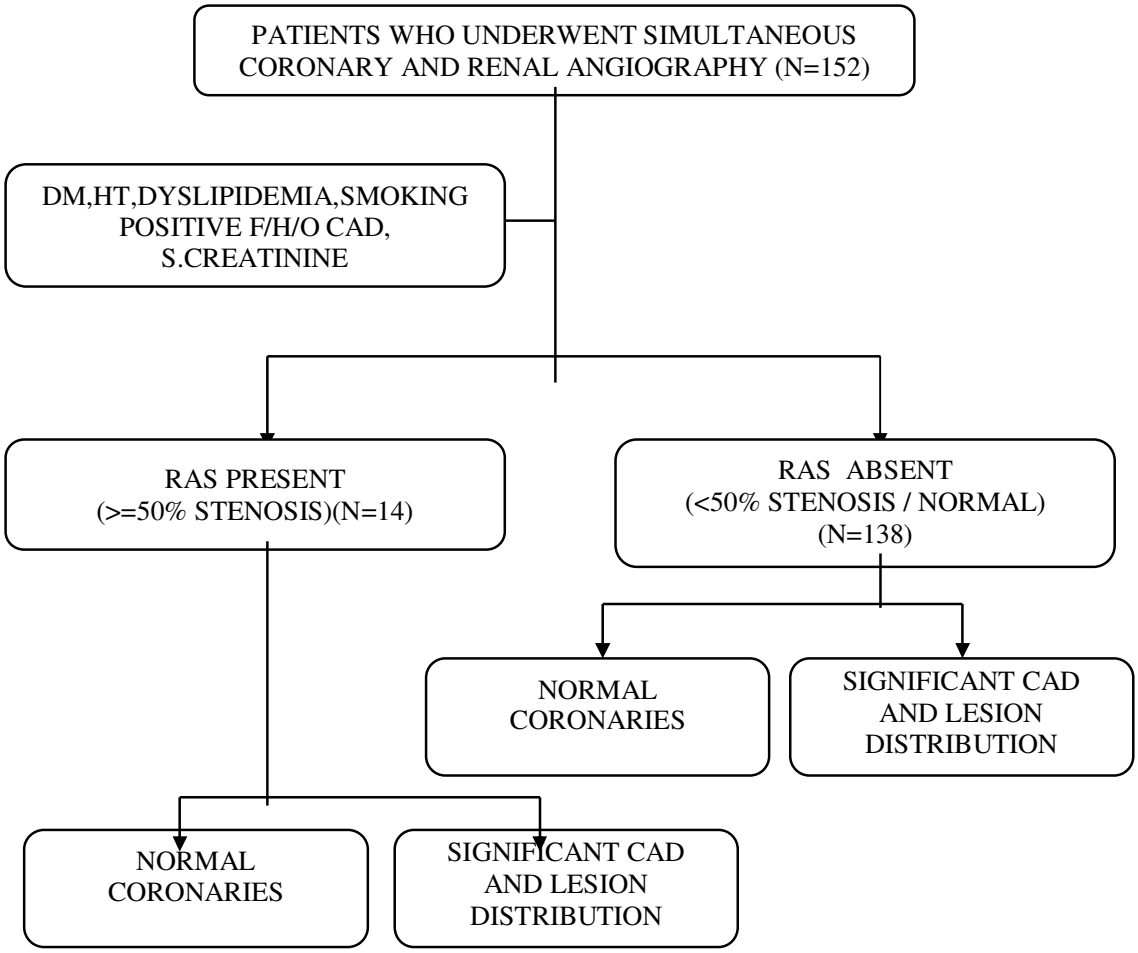
was observed before first diagonal or septal branch in LAD artery, before first sizable obtuse marginal (OM) branch in LCX artery and before the first bend of the vessel in RCA.

All angiograms were digitally recorded at 15 frames/sec speed and were interpreted at a consensus of two interventional cardiologists

Figure 1: FLOW CHART



Statistical Analysis

All data collected were entered on Excel sheet. Quantitative data was summarized in form of Mean+_SD. The difference in means was analyzed using student t test. Qualititative data was summarized in form of proportion. The difference in proportion was analyzed using chi square test. The significance level for all statistical analysis was kept at 95%.

Results

Out of 152 patients, 116(76.32%) were male and 36 (23.68%) were female. Mean age was 57.53+_10.62 years. 113 patients (74.34%) had HTN, 71 patients (46.71%) were diabetics, 69 patients (45.39%) had DLP, 46 (30.26%) of them were smoker and 12 patients (7.89%) had a positive FH (Table 1).

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Table 1: Patient ‘s clinical characteristics

Variable)	TOTAL (n=152)	RAS (n=14)	RAS<50%/N (n=138)	p value
Age	57.53(+_10.62)	64.64(+_5.93)	56.8(+_11.06)	0.01
Female	36(23.68%)	3(21.42%)	33(23.91%)	0.903
Hypertension	113(74.34%)	11(78.57%)	102(73.91%)	0.953
Diabetes mellitus	71(46.71%)	7(50%)	64(46.37%)	0.982
Dyslipidemia	69(45.39%)	7(50%)	62(44.92%)	0.935
Smoking	46(30.26%)	5(35.71%)	41(29.71%)	0.872
Positive family history	12(7.89%)	1(7.14%)	11(7.97%)	0.681
Pulse Pressure	61.21(+_18.73)	76+_25.5	59.61+_17.95	0.0031
RBS(mg/dl)	131(+_37.98)	131.7(+_36.88)	129.8(+_37.7)	0.862
S.Creatinine(mg/dl)	1.21(+_0.41)	1.37(+_0.47)	1.19(+_0.41)	0.126
eGFR	70.45(+_13.30)	62.43+_14.09	71.26(+_13.23)	0.019
HDLc(mg/dl)	43.45(+_6.86)	41.64(+_6.89)	41(+_6.4)	0.335
RBS= Random Blood Sugar, eGFR= Estimated Glomerular Filtration Rate				

Significant RAS was present in 14 patients (9.21%). It was unilateral in 13 patients (8.55%) and bilateral in 1 patient (0.6%).In 11 (7.23%) patients with unilateral disease, RAS was detected on left renal artery and in 2 patients (1.2%) right renal artery was involved. In 106(69.73%) patients, significant CAD was present.(Table-2) Significant RAS was more common in this group than with normal coronaries or insignificant CAD group but was statistically insignificant (78.57% vs 68.84%, p value=0.653). Significant RAS was more common in patients with three vessel CAD compared to those with single or two vessel CAD but was statistically insignificant. Relationships between involved locations of coronary arteries and RAS were also insignificant.

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Table 2: Catheterization characteristics

Variable	Total(n=152)	RAS (n=14)	No RAS (n=138)	p value
Significant CAD	106(69.73%)	11(78.57%)	95(68.84%)	0.653
Extent of CAD				
1VD	19(12.5%)	2(14.28%)	17(12.31%)	0.832
2VD	34(22.36%)	2(14.28%)	32(23.18%)	0.671
3VD	53(34.86%)	7(50%)	46(33.33%)	0.391
LAD	99(65.13%)	10(71.42%)	89(64.49%)	0.822
LCx	77(50.65%)	8(57.14%)	69(50%)	0.819
RCA	70(46.05%)	9(64.28%)	61(44.20%)	0.248
Ostio-proximal LAD	38(25%)	4(28.57%)	34(24.63%)	1.00
Ostio proximal LCx	31(20.39%)	2(14.28%)	29(21.01%)	0.805
Ostio proximal RCA	31(20.39%)	2(14.28%)	29(21.01%)	0.805
Left main disease	6(3.94%)	0	6(4.34%)	0.948

1VD= Single Vessel Disease, 2VD= Double Vessel Disease, 3VD= Triple Vessel Disease, LAD= Left Anterior Descending Artery, LCx= Left Circumflex Artery, RCA= Right Coronary Artery

Patients with significant RAS were older compared to those without significant disease (64.64 ±5.93years vs 56.8±11.06years, p value=0.01).Neither sex nor other atherosclerotic risk factors showed any association with significant RAS. Significant relationship was observed between significant RAS, increased pulse pressure and eGFR levels.A logistic regression analysis was conducted to predict RAS for 152 suspected CAD patients using age, sex ,presence of hypertension, DM, eGFR, Systolic BP, Pulse Pressure, significant CAD, 1 Vessel Disease(VD), 2VD, 3VD, LAD, LCx, RCA as predictors. A test of the full model was statistically significant, indicating that the predictors as a set reliably distinguished between compliant and non compliant (chi square = 28.397, $p < .005$ with df=12).

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Table 3: Logistic Regression Analysis

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1a	Age	.072	.043	2.792	1	.095	1.075	.988	1.170
	Sex (1)	-.293	.864	.115	1	.735	.746	.137	4.058
	HT(1)	.503	1.209	.173	1	.678	1.653	.155	17.691
	DM(1)	.412	.829	.248	1	.619	1.510	.298	7.665
	eGFR	-.060	.027	4.794	1	.029	.942	.893	.994
	SBP	-.011	.024	.216	1	.642	.989	.942	1.037
	PP	.068	.028	5.958	1	.015	1.070	1.014	1.131
	CAD(1)	50.871	2.306E4	.000	1	.998	1.239E22	.000	.
	1 VD	-17.052	9.319E3	.000	1	.999	.000	.000	.
	2 VD	.813	1.189	.468	1	.494	2.256	.220	23.179
	LAD(1)	-33.32	1.647E4	.000	1	.998	.000	.000	.
	LCx(1)	-18.40	9.319E3	.000	1	.998	.000	.000	.
	Constant	11.092	9.319E3	.000	1	.999	6.568E4		

HT=hypertension,DM=diabetes mellitus,SBP= systolic blood pressure,PP= Pulse Pressure, 1VD= One Vessel Disease, 2VD= Two Vessel Disease

Also Hosmerand Lemeshow Test shows a good fit by high p value and low chi square value. NagelkerkeR2 of 0.371 indicated a moderate relationship between predictions and grouping. Prediction success overall was 94.1%. The Wald criterion demonstrated that only eGFR (with p value=.029) and Pulse Pressure (with p value=.015) made a significant contribution to prediction. Other predictors were not significant predictors. For eGFR: -EXP (B) value indicates that when eGFR is raised by one unit the odds ratio is 0.94 times as large and therefore patients are 0.94 more times likely to be having RAS. For PP:-EXP(B) value indicates that when pulse pressure is raised by one unit odds ratio is 1.070 times as large and therefore patients are 1.070 more times likely to suffer from RAS. (Table-3)

Discussion

Our study showed no difference in patients with significant RAS compared to those without, with respect to major atherosclerotic risk factors except for age. This may reflect that traditional risk factors have a limited potential for predicting RAS. Dzielińska et al[25] and Wang et al[20] had reported similar results, but considerable variability was seen in many other studies.In our study, age more than 64 years was significantly associated with RAS by bivariate analysis. But, logistic regression analysis failed to find any significant association between age and RAS. In a number of studies, this issue was addressed with different thresholds, in which it was more than 60 years at a minimum.[26,27] We also found significant association between reduced level of eGFR levels(less than 62ml/min/1.73m^2) and RAS. In most other studies also, reduced levels of eGFR(specifically less than 60 ml/min/1.73 m^2) was discovered to be an independent predictor of significant RAS. Bearing in mind that not all patients with even severe RAS have uncontrolled HTN, renal failure or other

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clinical clues[1,20] and the fact that well proven anti-atherothrombotic medications which block rennin-angiotensin system may act as a two edged sword in the presence of significant but clinically unsuspected bilateral RAS[28,29] underscores the need to step beyond traditional screening for RAS. Additionally hemodynamically significant RAS may have several deleterious systemic effects through activating this system, which may accelerate atherogenesis and contribute to cardiovascular events.[12,21]Our study showed a good relationship between pulse pressure and RAS, which is in agreement with study of Weber-Mzellet al[9] and Rihalet al.[4] In our study, pulse pressure in excess of 76 mmHg was found to be independent predictor of significant RAS. Wide pulse pressure may simply reflect more advanced arteriosclerosis and renal disease and in a recent published study of Dieter et al,[22] pulse pressure >100 mmHg was shown a powerful predictor of poor outcome following renal angioplasty and stenting.

We found no significant relationships between atherosclerotic involvement of LAD, LCX, RCA and LMCA and RAS, which remained insignificant in their ostio-proximal segments. This is in partial agreement with the study of Danesh et al[23] .There was no relationship seen between anatomical distribution of coronary artery lesions (proximal, mid or distal portions) and RAS in the study by Danesh et al,[23] but two and 3-vessel coronary disease were reported as an independent predictor of significant RAS. In our study,as for number of coronaries involved, patients with three vessels CAD showed statistically insignificant relationship with RAS. The predilections of certain sites in vascular system to develop atheroma are clear.[28]Atherosclerotic RAS predominantly affects the aorto-ostialsegment,[28] but relationship between distribution of coronary artery lesions and segments involved has not been addressed extensively.

In a study by Weber-Mzellet al,[9] LAD, LCX, and RCA stenosis were more frequent in patients with significant RAS but in multivariate analysis, having >2 significant coronary lesions was recognized as an independent predictor of RAS. In another study by Conlon et al,[12] LAD disease was more frequent in patients with RAS >75%.

In a study by Negar et al, age more than 62 years, SBP greater than 150 mmHg, PP in excess of 60 mmHg and RCA involvement were found to be independent predictors of significant RAS.

Although the therapeutic implications of incidentally detected RAS has remained controversial until now [5]it may be valuable to be aware of this condition given the progressive nature of the disease, the precautions in prescribing angiotensin antagonists and possibly the need to revascularization in appropriately selected cases.Given the considerable drawbacks of noninvasive imaging techniques [21,23,28] and safety of renal angiography,[16,17,21] recognizing potential candidates for screening of RAS based on readily available variables at the time of cardiac catheterization is important from a practical point of view.Patients with incidental RAS may deserve aggressive medical treatment and more close follow-up.

Conclusion: There was no significant association seen between distribution of coronary artery lesions and RAS. However, increased pulse pressure and reduced eGFR were found to be significantly associated with RAS.

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Date of submission: 04 April 2014 Date of Publication: 28 June 2014
Source of support: Nil Conflict of Interest: Nil
Website : www.ijbamr.com