Association of Atherosclerotic Renal Artery Stenosis with Coronary Artery Disease

Krishna Kanta Sen[1], Mahboob Ali [1], Amal Kumar Choudhury[1], Pradip Kumar Karmakar[1], Md. Khalequzzaman[1], Md. Akhtaruzzaman[2], Salahuddin Ulubbi[1], Md. Arifur Rahman[1], Md. Shaheeen Kabir[1], Md. Badiuzzaman[1], Sharafat Nurul Islam[1], Bithi Rani Roy[3]

[1]Dept. of Cardiology, NICVD, Dhaka, [2]Junior Consultant cardiology, UHC, Kahaloo, Bogra, [3]Department of Gynae & Obs, Sir Salimullah Medical College, Dhaka.

Key Words : *Renal artery stenosis, Coronary artery disease.*

Abstract:

Background: *The association between extent and severity of coronary artery disease (CAD) and renal artery stenosis (RAS) has been well established in many studies. The aim of this study was to assess the incidence and severity of RAS in patients with CAD.*

Methods: *Coronary angiogram (CAG) and renal angiogram was done in standard protocol. A total of 95 patients was included in the study and divided into two groups according to the presence of significant renal artery stenosis. In Group I 45 patients were having normal or insignificant renal artery stenosis. In Group II 50 patients were having significant renal artery stenosis. All data were recorded systematically in preformed data collection form.*

Results: *In Group I, most common CAG findings were single vessel disease (SVD) (91.1%), triple vessel disease (TVD) (2.2%) and double vessel disease (DVD) (6.7%). No patients in Group I had Left Main (LM) disease. In Group II, most common CAG findings were DVD (42.0%) followed by SVD 32.0%, TVD 26.0% and LM 8.0%. There is statistically significant difference in Vessels Score, Friesinger Score and Leaman Score between the groups ($p<0.05$).*

Conclusion: *The study revealed significant association between atherosclerotic renal artery stenosis (RAS) and severity of coronary artery disease (CAD). This indicates significant atherosclerotic renal artery stenosis (RAS) predict the severity of coronary artery disease.*

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Introduction:

The prevalence of renal arterial disease in the general population is poorly defined. Assessment of general population by renal duplex ultrasound in individuals older than 65 years has revealed a 6.8% prevalence of RAS.[1]The prevalence of RAS increases to 20-30% in high risk population (e.g.-patient with known atherosclerotic vascular disease.[2] 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%. Small series have also noted significant renal artery stenosis in 29% of patients with coronary artery disease.[3] This is unsurprising as the degree of atherosclerosis of the renal arteries is reflective of the atherosclerotic burden in other blood vessels.[4]Atherosclerotic RAS is a progressive kidney disease despite control of hypertension. Presence and severity of incidental RAS is an independent predictor of mortality in atherosclerotic patients despite of mode of treatment of underlying coronary artery disease.[3] Contrast angiography is a standard criterion for diagnosis of RAS; it is readily performed in combination with coronary angiography. A correlation between coronary disease burden and the prevalence of RAS has already been established, but associations between patient demographic characteristics, coronary disease burden, extracoronary atherosclerosis, putative manifestations of RAS, and the prevalence of RAS have not been prospectively and rigorously examined.[5] Patients with advanced age, evidence of diffuse atherosclerosis, hypertension, renal insufficiency, and the presence of coronary artery disease have increased association with atherosclerotic renal artery disease . 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

Address of correspondence: Dr. Krishna Kanta Sen, Department of Cardiology, NICVD, Dhaka, Bangladesh.

renal artery disease.[6] Cardiologists are frequently confronted with 'Cardio renal' problems and have the expertise necessary for stenting of renal artery lesions with equipments adapted from coronary artery interventions. [7] Needless to mention, that in Bangladeshi perspective, we don't have an exact data on the incidence, prevalence and survival outcome of patient with RAS associated with CAD and other co morbid renal condition.[8] The aim of this study was to see the association of ARAS with coronary artery disease (CAD) in Bangladeshi perspective.

Methods:

This is a cross sectional study was done in the department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka from January 2012 to December 2012. Considering inclusion and exclusion criteria, 95 patients was included in the study and divided into two groups according to the presence of significant renal artery stenosis. In Group I 45 patients were having insignificant renal artery stenosis. In Group II 50 patients were having significant renal artery stenosis. Patients of coronary artery diseases admitted in NICVD and undergone coronary angiogram and renal angiogram showing atherosclerotic renal artery stenosis and coronary artery involvement were included in the study. Patients with ischeamic heart disease associated with following condition excluded from the study congenital and valvular heart disease, cardiomyopathy obstructive pulmonary disease, severe systemic illness (Liver & Kidney disease), patient unwilling to be included in this study.

Meticulous history and detailed clinical examination were carried out and were recorded . Informed written consent was taken from each patient before enrollment. Demographic data: Age, sex, BMI were recorded. Risk factors profile such as Smoking, Hypertension, Diabetes mellitus, Dyslipidemia and Family history of coronary artery disease (CAD) were recorded. Pulse and BP was record and medications were recorded. Baseline investigations like random blood sugar, serum creatinine, serum lipid profile, screening blood tests for angiogram were done for each of the patients. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10mm standardization. Coronary angiogram was done in standard protocol. Stenosed vessels, number and degree of stenosis (expressed as percentage of occlusion, 0-100%). More than 70% narrowing of luminal diameter of epicardial coronary artery and more than 50% narrowing of luminal diameter of left main coronary artery was considered as significant. Renal angiogram was done during each coronary angiogram. Angiographic severity of coronary artery disease was assessed by Vessel score, Friesinger score, Leaman score. An angiographically significant renal artery stenosis (RAS) is defined by narrowing of the lumen more than 50% and high grade as more than 70% narrowing. The stenotic lesion was designed atherosclerotic if they do not demonstrate a distinctive string-of-beads appearance characteristic of fibromuscular dysplasia .All data were recorded systematically in preformed data collection form.

Results:

Demographic profiles of both groups were shown in the tables (I, II,) and Fig (1) which revealed there was no significant difference in term of age, sex and occupation.

Table I

Distribution of sex of patients by groups.

Sex	Groups		p value**
	Group I <50% Stenosis	Group II 50% Stenosis	
Male	36 (80.0)	35 (70.0)	0.263
Female	09 (20.0)	15 (30.0)	
Total	45 (100.0)	50 (100.0)	

**Chi-square test was done to measure the level of significance.

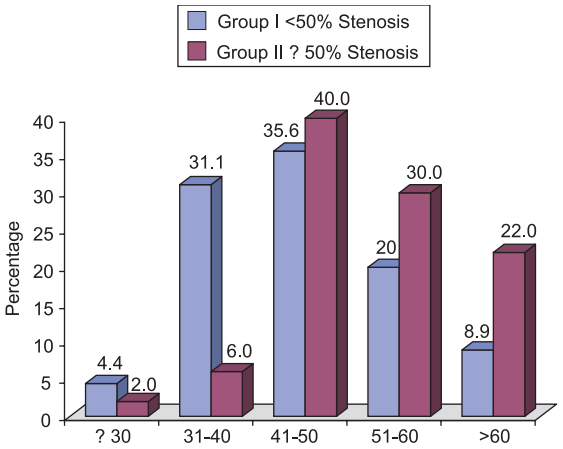

Fig.-1 : *Bar diagram of age of the patients by groups (Figure within parentheses indicates in percentage).*

Table-II
Distribution of associated co morbidity by groups.

Associated co-morbidity	Groups		p value**
	Group I <50% Stenosis	Group II 50% Stenosis	
DM	14 (31.1)	29 (58.0)	0.009
HTN	22 (44.0)	13 (28.9)	0.127
Smoking	24 (48.0)	29 (64.4)	0.107
Dyslipidaemia	01 (02.2)	33 (66.0)	0.001

**Chi-square test was done to measure the level of significance.

Table-III
Distribution of patients according to diagnosis by groups.

Diagnosis	Groups		p value**
	Group I <50% Stenosis	Group II 50% Stenosis	
AMI	06 (13.3)	08 (16.0)	0.001
NSTEMI	03 (06.7)	06 (12.0)	
OMI	04 (08.9)	19 (38.0)	
Chronic stable angina	26 (57.7)	17 (34.0)	
Unstable angina	06 (13.3)	0 (0.0)	
Total	45 (100%)	50 (100%)	

**Chi-square test was done to measure the level of significance.

Table III shows the distribution of patients according to diagnosis by groups. Most common diagnosis among the patients of Group I was chronic stable angina (57.7%) followed by both acute myocardial infarction (AMI) and unstable angina (13.3%). Three (6.7%) were presented with Non ST elevation myocardial infarction (NSTEMI) and 4 (8.9%) were presented with old myocardial infarction (MI). Most common diagnosis among the patients of Group II was chronic stable angina (57.7%) followed by both AMI and unstable angina (13.3%). Three (6.7%) were presented with NSTEMI and 4 (8.9%) were presented with OMI. There is statistically significant difference in diagnosis between the groups ($p<0.05$).

Table IV
Coronary Angiographic findings of patients by groups.

CAG findings	Groups		p value**
	Group I <50% Stenosis	Group II 50% Stenosis	
Left Main (LM)	0 (0.0)#	04 (08.0)	
Triple Vessel TVD Disease	01 (02.2)	13 (26.0)	0.001**
Double Vessel Disease (DVD)	03 (06.7)	21 (42.0)	
Single Vessel Disease (SVD)	41 (91.1)	16 (32.0)	

**Chi-square test was done to measure the level of significance. #Figure within parentheses indicates in percentage.

Table IV shows the distribution of coronary angiographic findings of patients by groups. Among the 45 patients in Group I, most common CAG findings were Single Vessel Disease (91.1%). Other CAG findings in Group I Triple Vessel Disease (TVD) and Double Vessel Disease (DVD) were 02.2% and 6.7% respectively. No patients in Group I had Left Main (LM) disease. Among the 50 patients in Group II, most common CAG findings were Double Vessel Disease (42.0%) followed by Single Vessel Disease (32.0%). Other CAG findings TVD and LM in Group II were 26.0% and 8.0% respectively. There is statistically significant difference in CAG findings between the groups ($p<0.05$).

Table-V
Distribution of coronary artery severity score by groups.

Score (Mean ± SD)	Groups		p value**
	Group I <50% Stenosis	Group II 50% Stenosis	
Vessels Score	1.1± 0.4	2.1 ± 0.7	0.001
Friesinger Score	2.1 ± 0.8	7.8 ± 2.9	0.001
Leaman Score	1.9 ± 1.1	8.8 ± 5.1	0.001

*t test was done to measure the level of significance.

Table V shows the distribution of coronary artery severity score by groups. Mean±SD of Vessels Score among Group I and Group II were 1.1±0.4 and 2.1±0.7 respectively. Mean±SD of Friesinger Score among Group I and Group II were 2.1±0.8 and 7.8±2.9 respectively. Mean±SD of Leaman Score among Group I and Group II were 1.9±1.1 and 8.8±5.1 respectively. There is statistically significant difference in Vessels Score, Friesinger Score and Leaman Score between the groups ($p<0.05$).

Table-VI

Risk factor analysis for renal artery stenosis (multiple logistic regression models).

Variables	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% CI for EXP(B)	
							Lower	Upper
Male sex	-1.327	1.212	01.199	1	0.273	0.265	0.025	2.851
DM	1.624	0.786	04.268	1	0.039	5.075	1.087	23.694
HTN	2.586	0.809	10.222	1	0.001	13.275	2.720	64.787
Smoker	2.459	1.172	04.407	1	0.036	11.699	1.177	116.246
Dyslipidaemia	6.053	1.428	17.962	1	0.001	425.357	25.887	6.989E3
Constant	2.199	0.736	08.924	1	0.003	9.020		

Table VI shows the risk factor analysis for renal artery stenosis (multiple logistic regression models). A male compared to a female is 1.199 times more likely to have renal artery stenosis more than >50.0% [p >0.05; CI at 95.0% 0.025 to 2.851]. For diabetes mellitus, the reference group is non diabetic patients. A diabetic patient compared to a non-diabetic patient is 4.268 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 1.087 to 23.694]. For hypertension, the reference group is non hypertensive people. A hypertensive patient compared to a non-hypertensive one is 10.222 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 2.720 to 64.787]. For Smoker, the reference group is the non-smoker. A smoker compared to a non-smoker is 4.407 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 1.177 to 116.246]. A dyslipidaemic compared to a non-dyslipidaemic is 17.962 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 25.887 to 6.989E3].

Discussion:

Group I, 36 (80.0%) were male and 9 (20.0%) were female and in Group II, 35 (70.0%) were male and 15 (30.0%) were female. There is no statistically significant difference in sex between the groups (p>0.05).In the present study highest number of patients of Group I was in the age group of 41 to 50 years (35.6%) and in Group II was in the age group of 41 to 50 years (40.0%). Mean ± SD of age among the patients in Group I and Group II were 46.84±10.47 and 53.58±10.33 respectively. There is statistically significant difference in age between the groups (p<0.05). Ollivier R et al. found mean ±SD of age was 67±10 years and 80% were men. Islam AHMW et al. in their study reported 64.0% were male and 36.0% were female and the mean age of male was 62 yrs and that of female was 58 yrs.[10] In Group I, 14 (31.1%) were diabetic, 22 (44.0%) were hypertensive, 24 (48.0%) were smoker and one (2.2%) dyslipidaemia. In Group II, 29 (58.0%) were diabetic, 13 (28.9%) were hypertensive, 29 (64.4%) were smoker and 33 (66.0%) were dyslipidaemic. There is statistically significant difference in the incidence of DM and dyslipidaemia between the two groups (p<0.05). Islam AHMW et al. in their study found 79 (79%) were hypertensive; 57 (57%) were Dyslipidemic, 54 (54%) patients were Diabetic, 27 (27%) were smoker (all male) and 18(18%) were having positive FH for CAD.[10]

Most common diagnosis among the patients of Group I was chronic stable angina (57.7%) followed by AMI and unstable angina (13.3%). Three (6.7%) were presented with NSTEMI and 4 (8.9%) were presented with OMI. Most common diagnosis among the patients of Group II was chronic stable angina (57.7%) followed by AMI and unstable angina (13.3%). There is statistically significant difference in diagnosis between the groups (p<0.05).

In Group I, most common CAG findings were Single Vessel Disease (91.1%), followed by Triple Vessel Disease (2.2%) and Double Vessel Disease (6.7%) . No patients in Group I had Left Main (LM) disease. Among the 50 patients in Group II, most common CAG findings were Double Vessel Disease (42.0%) followed by Single Vessel Disease (32.0%), TVD (26.0%) and LM(8.0%) respectively. There is statistically significant difference in CAG findings between the groups (p<0.05). Islam et al. found the the angiographic association of atherosclerotic renal-artery stenosis (ARAS) with coronary artery disease, 52 (20.8%) patient had single vessel disease (SVD), 49 (19.6%) and 149 (59.6%) had double vessel disease (DVD) and triple vessel disease (TVD) respectively. In the present study the mean Vessels

Score (1.1±0.4 vs 2.1±0.7), Mean Friesinger Score(2.1±0.8 vs 7.8±2.9), Mean Leaman Score(1.9±1.1 vs 8.8±5.1) in Group I and Group II respectively. There is statistically significant difference in Vessels Score, Friesinger Score and Leaman Score between the groups (p<0.05).

In the present study the risk factor analysis for renal artery stenosis by multiple logistic regression models showed male compared to a female is 1.199 times more likely to have renal artery stenosis more than >50.0% [p >0.05; CI at 95.0% 0.025 to 2.851]. A diabetic patient compared to a non-diabetic patient is 4.268 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 1.087 to 23.694]. A hypertensive patient compared to a non-hypertensive one is 10.222 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 2.720 to 64.787]. A smoker compared to a non-smoker is 4.407 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 1.177 to 116.246]. A dyslipidaemic compared to a non-dyslipidaemic is 17.962 times more likely to have renal artery stenosis more than >50.0% [p <0.05; CI at 95.0% 25.887 to 6.989E3]. Buller CE et al. in their study reported that severe RAS was associated with age, female gender, reduced creatinine clearance, increased systolic blood pressure, and peripheral or carotid artery disease.[5] Cohen MG et al. in their study reported that independent predictors of significant RAS were older age, higher creatinine levels, peripheral vascular disease, number of cardiovascular drugs, hypertension, female sex, and 3-vessel coronary artery disease or previous coronary artery bypass graft.[11] Ollivier R et al. in their study reported that male sex (*P*<.05), presence and number of coronary artery lesions (*P*<.01), hypertension (*P*=.001), and renal insufficiency (*P*<.001) predicted the presence of RAS.[9] Islam MS et al. reported that ARAS is more common in female 44.3% vs 33.3%; p=0.02. ARAS prevalence increased with the number of stenosed coronary arteries (3.8% in 1-vessel, 26.5% in 2-vessel, 52.3%in 3-vessel CAD; p=.0001).[10]

Conclusion:

The study found the significant association between atherosclerotic renal artery stenosis (RAS) and severity of coronary artery disease (CAD). Therefore it can be concluded that significant atherosclerotic renal artery stenosis (RAS) predict the severity of coronary artery disease.

Study limitation:

Although the results of this study support the hypothesis, there are some fact which might affect the result. 1. Number of study population is small 2. It was a single centre study. 3. Angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of CAD and Renal artery stenosis.

Recommendation: 1. A multicentric study with large sample size should be undertaken to generalize the findings. 2. The study findings should be used with caution until validated by larger multicentric study.

Conflict of Interest - None.

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