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### RESEARCH ARTICLE

#### THE INCIDENCE AND PREDICTORS OF RENAL ARTERY STENOSIS IN MULTIVESSEL CORONARY ARTERY DISEASE PATIENTS

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#### Abstract

**Background:** Cardiovascular disease is the leading cause of death. Importantly, it remains the foremost cause of preventable death globally. Atherosclerotic renal artery stenosis (ARAS) is the most common primary disease of the renal arteries and it is associated with two major clinical syndromes; ischemic renal disease and hypertension.

**Objective:** To determine the incidence and predictors of renal artery stenosis in the multivessel coronary artery disease patients.

**Patients and Methods:** The study included 100 patients undergone coronary angiography at Matrouh Specialized Cardiac Surgery and Interventional Catheterization Center and proved to have multivessel coronary artery disease during the period from January 2014 to April 2016. They were 74 males and 26 females. Their age ranged between 50-70 years with a mean of  $57.28 \pm 6.74$  years.

**Results:** The study showed that 16 patients (16%) had renal artery stenosis. All patients with renal artery stenosis had unilateral RAS and no patients had bilateral RAS. Significant renal artery stenosis (> 50% diameter stenosis) was found in 10 patients (10%) and nonsignificant RAS was found in 6 patients (6%). The left renal artery was singly involved in 6 patients (6%) and the right renal artery was singly involved in 10 patients (10%). There was no significant relationship between the number of coronary arteries affected and incidence of significant renal artery stenosis. Also there was no significant relationship between the level of serum creatinine and incidence of significant renal artery stenosis.

**Conclusion:** Renal angiography was a reliable method to assess renal artery stenosis and may be more important in hypertensive patients with multivessel coronary artery disease.

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#### Introduction:-

Renal artery stenosis (RAS) usually refers to a disease of the large extra-renal arterial vessels and most frequently is caused by atherosclerotic obstructions. Atherosclerotic renal artery stenosis (RAS) causes cardiorenal problems. Thereby it is a matter of concern for both nephrologists and cardiologists. However, the kidney does not present organ-specific signs or symptoms of ischemia, unlike the heart, brain or lower limbs. Successful detection of RAS can thereby be very difficult in clinical practice.<sup>(1)</sup>

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Arterial hypertension (HTN), progressive renal failure, flash pulmonary edema, and multivessel coronary disease are clinical manifestations of RAS requiring intervention and treatment and may be resolved by revascularization therapy. In the past, RAS was underrecognized, underdiagnosed, and undertreated. With improved noninvasive imaging techniques such as magnetic resonance imaging angiography, computed tomography angiography, and high-resolution renal duplex sonography, the diagnosis is currently more frequently established.<sup>(2)</sup>

Several studies have emphasized the common association of renal artery stenosis with atherosclerotic diseases in other vascular beds. The incidence of renal artery stenosis in patients undergoing routine cardiac catheterization has been estimated to be in the range of 11-23%.<sup>(3)</sup> These studies show that there was a large discrepancy concerning the prevalence of atherosclerotic renal artery stenosis in patients undergoing coronary angiography.

The prevalence of RAS has yet not been evaluated completely; one of the reasons was the lack of noninvasive and valid screening procedures for this purpose. Despite the risks of contrast nephropathy and atheroembolic renal disease, arteriography has been considered to be the gold standard diagnostic test.<sup>(4)</sup>

Some trials found that the frequency of ARAS had increased in proportion with the number of stenotic coronary arteries; the incidence of ARAS was 10%, 15.8%, and 18.1% in patients with single-vessel, two-vessel, and three-vessel CAD, respectively. It infers that treatment of vascular risk factors would result in better management of the widespread atherosclerotic disease in this high-risk population.<sup>(4)</sup>

#### **Aim of the work:**

To determine the incidence and predictors of renal artery stenosis in the multivessel coronary artery disease patients.

#### **Patients and Methods:-**

In the current study we included 100 consecutive patients admitted to catheterization laboratory for diagnostic coronary angiography and proved to have multivessel coronary artery disease during the period from February 2014 to April 2016 at Matrouh Specialized Cardiac Surgery and Interventional Catheterization Center.

#### **Ethical approval and written informed consent:**

An approval of the study was obtained from Benha University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

#### **All patients included in the study were subjected to:**

##### **(1) Full medical History taking emphasizing on:**

Age, history of prior cardiac events & previous PCI or CABG, history of renal disease, history of hypertension, diabetes mellitus, smoking, dyslipidemia, history of cerebrovascular accidents and history of drug intake.

##### **(2) Clinical examination:**

Systolic & diastolic BP measurements, general & cardiac examinations and abdominal examination emphasizing on renal bruit.

##### **(3) Laboratory investigations:**

Creatinine level measurement, fasting blood sugar & lipid profile.

All patients underwent selective left and right coronary arteriography using the standard technique. Selective renal arteriography was performed using a Judkins right catheter inserted consecutively in the ostium of both renal arteries in the left anterior oblique projection with 10 to 20-degree angulation.

A dose of 5 to 10 mL of iso-osmolar iodine containing contrast medium was injected into each renal artery. When the ostia of the renal arteries did not appear clearly, the angulation was modified to obtain better visualization.

Angiographic data were individually reviewed and the degree of stenosis was evaluated by visual estimation.

Patients were considered to have significant RAS if they had at least a 50% luminal obstruction of one or both of the main renal arteries or one of their major branches on the basis of visual estimation by two observers. The patients considered to have multivessel coronary artery disease were those having at least 70% or greater stenosis in at least

two major epicardial vessels (measuring >2.5 mm in diameter) seen in 2 different projections based on visual estimation by two observers. > 50% stenosis in the left main coronary artery (LMCA) was considered significant.<sup>(5)</sup> Vessel segments are: the proximal, middle, and distal right coronary artery, the proximal and middle left anterior descending artery, the first diagonal of left anterior descending artery, the proximal and distal left circumflex artery, and first and second obtuse marginals. We did not consider lesions in the posterior descending artery, second diagonal branch, or third obtuse marginal because of the relatively small amount of myocardium in jeopardy from these vessels<sup>(5)</sup>.

According to the presence and severity of RAS, we classified the population into patients with normal renal arteries (group 1), those with nonsignificant RAS (group 2), and those with significant RAS (group 3).

#### Statistical Analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean  $\pm$  standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing between two means. Chi-square ( $\chi^2$ ) test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following: P-value <0.05 was considered significant. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant.

#### Results:-

**Table 1:-** Baseline clinical variables of the studied patients.

Variable	N	%
<b>Sex distribution:</b>		
• Males	74	74
• Females	26	26
<b>Age (mean <math>\pm</math> SD)</b>	57.28 $\pm$ 6.74	
<b>Risk factors for CAD:</b>		
• Current smoker	48	48
• DM	68	68
• HTN	56	56
• Positive Family History of IHD	12	12
• Dyslipidemia	74	74
<b>Prior coronary revascularization:</b>		
• PCI	12	12
• CABG	4	4
<b>Prior acute coronary syndrome</b>	58	58
<b>Prior stroke</b>	2	2
<b>Medications</b>	N	%
• ACE inhibitors	86	86
• B. blockers	70	70
• Statins	58	58
• Aspirin	88	88

They were 74 males and 26 females. Their age ranged between 50 – 70 years with a mean of 57.28  $\pm$  6.74 years. Results of the current study regarding risk factors for CAD showed that 48 patients (48%) were current smokers, 68 patients (68%) had diabetes mellitus (DM), 56 patients (56%) were hypertensive, 12 patients (12%) had +ve family history of CAD and 74 patients (74%) had dyslipidemia. History of prior PCI was found in 12 patients (12%) and prior coronary artery bypass grafting (CABG) in 4 patients (4%). 58 patients (58%) had prior acute coronary syndrome and 2 patients (2%) had prior cerebrovascular stroke. The drug therapy of the studied patients showed that 86% of the patients were on ACE inhibitors, 70% were on B. Blockers, 58 % were on statins and 88% were on aspirin as shown in table (1).

**Table 2:-** Relationship between sex and age of the patients and significant RAS.

			Normal	Significant RAS	Non- significantRAS	X <sup>2</sup> / F	P-value
Sex	Male	N	66	2	6	18.176	0.001*
		%	89.2%	2.7%	8.1%		
	Female	N	18	8	0		
		%	69.2%	30.8%	.0%		
Age	Range		35 – 70	54 – 65	55 – 66	1.214	0.301
	Mean $\pm$ S. D		56.95 $\pm$ 6.98	57.60 $\pm$ 4.30	61.33 $\pm$ 5.09		

Table (2) shows the relationship between sex and age of the patients and significant RAS which revealed that the incidence of significant renal artery stenosis was higher in females than males as 8 females (30.8%) had significant renal artery stenosis in comparison to 2 males (2.7%) while the incidence of renal artery stenosis whether significant or nonsignificant was higher in females (30.8%) than in males (10.8%) ( $P < 0.05$ ). The age wasn't significantly higher among patients with renal artery stenosis than among those without renal artery stenosis ( $p < 0.05$ ).

**Table 3:-** Relation between significant renal artery stenosis and risk factors for coronary artery disease.

			Normal renal arteries	Significant renal artery stenosis	Non-significant renal artery stenosis	X <sup>2</sup>	P-value
Smoking	Current smoker	N	44	2	2	4.302	0.117
		%	91.7%	4.2%	4.2%		
	non smoker	N	40	8	4		
		%	76.9%	15.4%	7.7%		
D. M	Yes	N	54	10	4	5.243	0.073
		%	79.4%	14.7%	5.9%		
	No	N	30	0	2		
		%	93.8%	.0%	6.3%		
HTN	Yes	N	42	8	6	8.279	0.016*
		%	75.0%	14.3%	10.7%		
	No	N	42	2	0		
		%	95.5%	4.5%	.0%		
Dyslipidemia	Yes	N	62	8	4	0.356	0.837
		%	83.8%	10.8%	5.4%		
	No	N	22	2	2		
		%	84.6%	7.7%	7.7%		
Positive Family History of IHD	Yes	N	6	4	2	11.887	0.003*
		%	50.0%	33.3%	16.7%		
	No	N	78	6	4		
		%	88.6%	6.8%	4.5%		

The incidence of significant renal artery stenosis was not significantly higher among smokers (2 patients, 4.2%) vs. non-smokers (8 patients, 15.4%) ( $P > 0.05$ ). There was no significant difference between diabetic patients with fasting blood sugar  $> 126$  mg/dl (American Diabetes Association definition of D.M.) (10 patients, 14.7%) and non-diabetics (0 patients, .0%) regarding the incidence of significant RAS ( $P > 0.05$ ). The incidence of significant renal artery stenosis was significantly higher among hypertensive patients (8 patients, 14.3%) vs. non hypertensive patients (2 patients, 4.5%) ( $P < 0.05$ ). The incidence of significant renal artery stenosis was not significantly higher among patients with dyslipidemia (8 patients, 10.2%) vs. non dyslipidemic patients (2 patients, 7.7%) ( $P > 0.05$ ). The incidence of significant renal artery stenosis was significantly higher among patients with +ve family history of CAD (4 patients, 33.3%) vs (6 patient, 6.8%) without +ve family history of CAD ( $P < 0.05$ ) as shown in table (3).

**Table 4:-** Relationship between the number of coronary vessels affected and significant renal artery stenosis.

Number of vessels affected		Normal	Significant RAS	Non-significant RAS	Total
2	N	30	4	0	34
	%	88.2%	11.8%	.0%	100.0%
3	N	30	2	2	34
	%	88.2%	5.9%	5.9%	100.0%
4	N	18	2	4	24
	%	75.0%	8.3%	16.7%	100.0%
5	N	6	2	0	8
	%	75.0%	25.0%	.0%	100.0%
Total	N	84	10	6	100
	%	84.0%	10.0%	6.0%	100.0%
Chi-square	X <sup>2</sup>	10.075			
	P-value	0.122			

Table (4) shows the relationship between the number of coronary vessels affected and significant renal artery stenosis which revealed that there was no significant relationship between the number of vessels affected in coronary artery disease patients and significant renal artery stenosis.

**Table 5:-** Comparison of creatinine level between patients with and without significant RAS.

		Range			Mean	±	S. D	F. test	p. value		
Creatinine	Normal	0.50	–	1.4	1.02	±	0.22	2.048	0.134		
	Significant RAS	0.9	–	1.3	1.01	±	0.16				
	Non-significant RAS	1.09	–	1.3	1.19	±	0.09				

Table (5) shows comparison of creatinine level between patients with and without RAS which revealed that there is no significant difference between creatinine level in patients with significant renal artery stenosis and those with normal renal arteries.

**Case presentation:**

59 years old female patient, diabetic, not hypertensive, not smoker, not dyslipidemic and have no family history of ischemic heart disease. The patient have history of previous myocardial infarction. There was no history of previous cerebrovascular strokes or coronary revascularization whether percutaneous intervention or coronary artery bypass grafting. Serum creatinine of the patient was 1 mg /dl. Coronary angiography revealed that the patient is having multivessel coronary artery disease.

**LAD:**

Shows mid-segment subtotal occlusion.

**D1:**

Shows ostial to proximal 90% stenosis.

**OM1:**

Shows ostial to proximal 90% stenosis.

**RCA:**

Shows mid-segment subtotal occlusion followed by distal 80 % stenosis.

**Renal angiography revealed:****Left renal artery:**

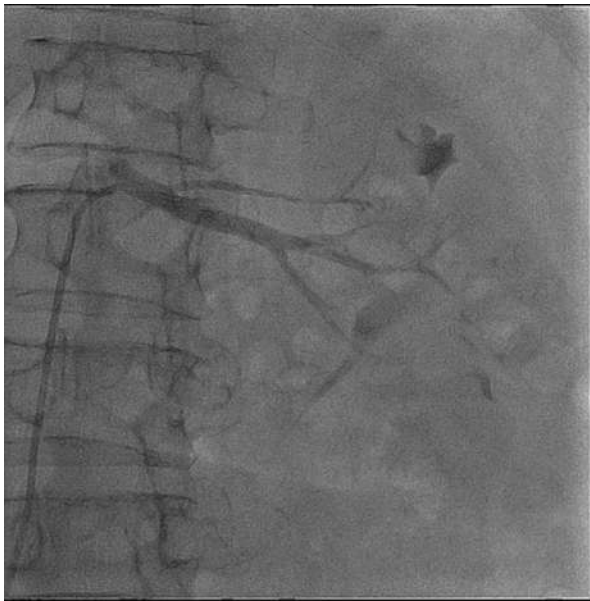
Normal vessel with normal caliber and flow. Right renal artery: Shows ostial 70 % stenotic lesion.



**Fig. (1):-** Left coronary system angiography of patient  
RAO 41.0: CAU 21.0.



**Fig. (2):-** Right coronary system angiography of patient  
LAO 30.0: CRA 0.0.



Normal left renal artery  
LAO 26.0: CRA 0.0



Significant right renal artery stenosis  
LAO 26.0: CRA 0.0

**Fig 3:-** Renal angiography of the patient.

### Discussion:-

#### The principle findings of our study were:

16 patients (16%) had renal artery stenosis. Significant renal artery stenosis (> 50% diameter stenosis) was found in 10 patients (10%) and nonsignificant RAS was found in 6 patients (6%). There was no significant relationship between the number of coronary arteries affected and renal artery stenosis whether significant or nonsignificant. Female gender was associated with higher incidence of significant renal artery stenosis. There was no significant relationship between the incidence of significant renal artery stenosis and the age of the patients. The incidence of significant renal artery stenosis was significantly higher among hypertensive patients and patients with positive family history for coronary artery disease. There was no significant relationship between the level of serum creatinine and the incidence of significant renal artery stenosis.

In our study there was no significant relationship between the number of coronary arteries affected and renal artery stenosis whether significant or nonsignificant.

These results are in agreement with Aqel et al.<sup>(6)</sup> that showed that peripheral vascular disease (but not CAD) was a predictive factor for RAS also Khatami et al.<sup>(1)</sup> found that there is no significant correlation between the number of the involved coronary arteries and RAS.

In contrary to our study, a recent study by Santanu et al.<sup>(7)</sup> showed that there was significant relationship between the number of involved coronary arteries in coronary artery disease and atherosclerotic renal artery stenosis (ARAS). Among total 304 CAD patients in this study, no significant RAS were found in single vessel coronary artery disease patients. Only three vessel disease, left main coronary artery disease (TVD/LMCA) disease and double vessel coronary artery disease (DVD) patients had significant renal artery stenosis.

Results of our study showed that the incidence of significant renal artery stenosis in the multivessel coronary artery disease patients was 10 % which is somewhat less than what was recorded in most of the studies. This discrepancy may be a result from differences in the study population including age, risk factors and social or environmental determinants. Other contributing factors may be involved.

The results of our study showed that female gender was associated with higher incidence of significant renal artery stenosis. The results are in agreement with the studies of Khatami et al.<sup>(1)</sup>, Buller et al.<sup>(8)</sup> and Cohen et al.<sup>(9)</sup>.

In contrary to our study and in contrary to many other studies Ollivier et al.<sup>(10)</sup> showed that male gender was associated with higher prevalence of renal artery stenosis. Also Alhaddad et al.<sup>(11)</sup> study showed that there was no significant relationship between the sex of the patient and the incidence of atherosclerotic renal artery stenosis.

The results of our study also showed that there was no significant relationship between the age of the patients and the incidence of renal artery stenosis which was in agreement with Santanu et al.<sup>(7)</sup> which showed that there was no significant relationship between the age of the patients and prevalence of RAS.

In contrary to our study, most of the studies found that there was significant relationship between the age of the patients and the incidence of significant RAS as the incidence of significant RAS increased with increased age of the patients<sup>(4, 8)</sup>.

The results of our study showed that there was significant relationship between the incidence of significant RAS and hypertension.

This was in agreement with Carmelita et al.<sup>(12)</sup> study, which found significant relationship between hypertension and increased incidence of significant RAS (p value = 0.001) and Buller et al.<sup>(8)</sup> which found that hypertension was an important risk factor for patients with RAS. Also Liang et al.<sup>(4)</sup> had shown a trend of association between hypertension and increased incidence of RAS (p value = 0.056).

The results of our study showed that there was significant relationship between family history of coronary artery disease and significant RAS as there was increased incidence of significant renal artery stenosis in patients with family history of coronary artery disease. In contrary to our study El-Mawardy et al.<sup>(13)</sup> showed that there was no significant relationship between incidence of RAS and family history of coronary artery disease (p value = 0.74).

The results of our study showed that there was no significant relationship between smoking and incidence of significant renal artery stenosis. In agreement with our study Carmelita et al.<sup>(12)</sup> didn't find significant correlation between smoking and increased incidence of significant RAS (p value = 0.25) also El-Mawardy et al.<sup>(13)</sup> found that there was no significant increase in incidence of RAS with smoking (p value = 0.96). Unlike our study Santanu et al.<sup>(7)</sup> revealed that only smoking was the risk factor that have significant correlation with RAS (p value = 0.008).

The results of our study showed that diabetes mellitus had no significant relationship with renal artery stenosis which was in agreement with Khatami et al.<sup>(1)</sup>, Liang et al.<sup>(4)</sup>, Santanu et al.<sup>(7)</sup> and El-Mawardy et al.<sup>(13)</sup>. They did not find significant relationship between significant renal artery stenosis and DM (p value = 0.815, 0.624, 0.22 and 0.82

respectively). Unlike the current study Carmelita et al.<sup>(12)</sup> found that there was increased incidence of RAS with diabetic patients (p value = 0.04).

The results of our study didn't find significant relationship between significant RAS and dyslipidemia. In agreement with the current study Santanu et al.<sup>(7)</sup> didn't find significant relationship between dyslipidemia and significant RAS (p value = 0.360). Unlike the current study Carmelita et al.<sup>(12)</sup> found that there was significant relationship between dyslipidemia and significant RAS.

Our study showed that there was no significant increase in serum creatinine in patients with RAS which was not in agreement with most of the studies that showed that there was significant relationship between (increased serum creatinine and decreased glomerular filtration rate) and increased incidence of RAS.

Santanu et al.<sup>(7)</sup> showed that most of the subjects had depressed glomerular filtration rate. Khatami et al.<sup>(1)</sup> showed that there is significant increase in base serum creatinine in patients with RAS (p value = 0.18).

Ollivier et al.<sup>(10)</sup>, Carmelita et al.<sup>(12)</sup> and Ghaffari et al.<sup>(14)</sup> all showed results support that there is significant correlation between elevated serum creatinine and RAS. Harding et al.<sup>(15)</sup> showed that almost all ARAS patients had serum creatinine more than 1.2 mg/dl.

The difference between the result of our study and the other studies may be because most of the studies included patients with serum creatinine levels of > 1.5 mg/ dl but in our study, patients with serum creatinine of > 1.5 mg/dl were excluded for safety issues.

### Conclusions:-

Significant renal artery stenosis (> 50% diameter stenosis) was found in 10 patients (10%) and nonsignificant RAS was found in 6 patients (6%). There was no significant relationship between the number of coronary arteries affected and renal artery stenosis whether significant or nonsignificant. Female gender was associated with higher incidence of significant renal artery stenosis. There was no significant relationship between the incidence of significant renal artery stenosis and the age of the patients. The incidence of significant renal artery stenosis was significantly higher among hypertensive patients and patients with positive family history for coronary artery disease. There was no significant relationship between the level of serum creatinine and the incidence of significant renal artery stenosis.

Renal angiography was a reliable method to assess renal artery stenosis and may be more important in hypertensive patients with multivessel coronary artery disease.

### Recommendations:-

We recommend that the study could be done on a large scale of patients including patients with single vessel disease and on multicenter bases with long term follow up to assess the significance of renal artery stenosis on the outcome of patients with coronary artery disease.

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