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ORIGINAL ARTICLE

Albumin to creatinine ratio as a predictor to the severity of coronary artery disease

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KEYWORDS

Coronary artery disease (CAD);
Microalbuminuria (MA);
Albumin–creatinine ratio

Abstract *Introduction:* Microalbuminuria (MA) is a well-known risk factor for coronary artery disease (CAD). It is associated with higher cardiovascular mortality, especially in diabetics. However, there are few data linking angiographic severity of CAD to MA.
Aim: The aim of the present study was to assess the albumin to creatinine ratio as a new predictor for CAD and to correlate with its severity apart from other traditional CAD risk factors.
Methods: Our study included 100 patients with documented CAD by coronary angiography in Alexandria main university hospital. The severity of CAD was scored on the basis of the number and the extent of lesions within the coronary arteries by using Syntax score. Urine albumin excretion was measured for all patients in morning spot urine samples by immune precipitation technique. We correlate between MA and severity of CAD.
Results: In a total of 100 patients (74 males and 26 females), (mean age 55.71 ± 8.99 *y*) MA was present in 34 patients only. Patients were divided into two groups; group I included those without MA and group II with MA. CAD occurred more frequently in males than in females and in smokers than in non-smokers. There were no significant differences in the prevalence of hypertension and hypercholesterolemia between the two groups. A direct relationship between MA and extension of atherosclerotic coronary lesions was noticed ($P = 0.009$).

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Conclusion: Patients with MA having more severe angiographic CAD were compared to those without MA. This relation is independent of other risk factors. MA could be utilized as an independent risk factor for CAD.

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1. Introduction

Coronary artery disease (CAD) is a major cause of death and disability in both developed & now in developing countries. Atherosclerosis is responsible for almost all cases of CAD. CAD is a multifactorial disorder with several different risk factors. Advancing age, male sex, hypertension, diabetes mellitus, cigarette smoking and dyslipidemia are the major and independent well known risk factors for CAD.[1]

However, they do not entirely explain the variation in cardiovascular disease incidence and mortality between individuals and among populations. Therefore, additional risk factors have been proposed to better identify patients potentially at risk of CAD. Many individual new biomarkers have been related to cardiovascular risk, including levels of CRP (C-reactive protein),[2] B-type natriuretic peptide (BNP),[3] fibrinogen,[4] D-dimer[5] and homocysteine.[6]

Among these new biomarkers is microalbuminuria (MA), which is gaining recognition as a marker of an atherogenesis, owing to its association with several atherosclerotic risk factors and early systemic vascular (endothelial) damage.[7]

An increasing number of studies in different patient populations have reported that MA is associated, independently of traditional risk factors, with all causes of cardiovascular morbidity and mortality in patients with diabetes,[8] hypertension[9] and in the general population.[10] Our aim in the present study is to assess the albumin to creatinine ratio as a new predictor for coronary artery disease & to correlate with its severity.

Although a 24 h urine collection is the gold standard for the detection of MA, several studies have found that a urinary albumin to creatinine ratio is equally sensitive, specific and can be easily utilized on a daily basis.[11]

The aim of the present study was to assess the albumin-to-creatinine ratio as a new predictor for CAD and to correlate with its severity apart from other traditional CAD risk factors.

2. Methods

This is a non-randomized prospective study, that included 100 patients with documented CAD by elective coronary angiography in cardiovascular department, Alexandria main university hospital with the following exclusion criteria: liver insufficiency, renal insufficiency or recent urinary tract infection in the last 3 months.

Patients included in this study were subjected to the following: Thorough history taking with stress on history of risk factors for CAD, complete clinical examination, laboratory investigations, including: CBC, blood glucose level, blood urea, serum creatinine, lipid profile and Urine sample for measurement of urinary albumin to creatinine ratio, echocardiography and standard 12-Lead ECG.

2.1. Measurement of urinary albumin to creatinine ratio (ACR)

We collected a morning random urine sample before coronary artery catheterization. Urinary albumin concentration was measured using the Turbidometric immunological technique, Turbiquick – Labmedica – Italy.[12] The ratio of urine albumin to creatinine was used to define microalbuminuria.

2.2. Coronary angiography

Coronary angiography was done according to standard techniques[13] for the assessment of severity of CAD according to: number of vessels affected, number of lesions and type of lesions. CAD was defined significant if there was $\geqslant 50\%$ diameter stenosis in $\geqslant 1$ more coronary artery. The severity of CAD was scored on the basis of Syntax score. The SYNTAX score is a unique tool to score complexity of coronary artery disease as follows: low [0–22], which is suitable for PCI, intermediate [23–32]; which is suitable for either PCI or CABG, and high ($\geqslant 33$) where CABG is the preferred method of treatment.[14]

2.3. Statistical methods

Statistical analysis was performed using SPSS software version 17.0) SPSS, Chicago, IL, USA).

Data were statistically described in terms of mean and standard deviation, while categorical variables were expressed as numbers and percentages when appropriate. Comparison of continuous variables among groups was made using Student's *t*-test.

Associations between two categorical variables were tested using the Likelihood ratio χ^2 test, as appropriate. Statistical correlation between continuous variables was tested using Pearson's product-moment coefficient of correlation (r). All tests of significance were two tailed and a p-value of 0.05 was considered statistically significant.

3. Results

The study included 100 patients with documented CAD by elective coronary angiography with no specific relation to medical history of hypertension or diabetes.

3.1. The patients were classified into two groups based on the levels of urinary ACR

- **Group I:** consisted of patients with ACR level < 30 mg/g (66 patients, 66%).
- **Group II:** consisted of patients with ACR level > 30 mg/g (34 patients, 34%).

Table 1 Demographic data of the studied patients.

	Group I	Group II	*p*-Value
	Normal urinary ACR < 30 mg/g "*n* = 66 (66%)"	Positive urinary ACR > 30 mg/g "*n* = 34 (34%)"	
Age			0.935
Range	31 – 81	39 – 74	
Mean	55.64	55.79	
S.D.	9.44	8.54	
Sex			0.560
Males	49 (74.2%)	25 (73.5%)	
Females	17 (25.8%)	9 (26.5%)	
Family history of CAD			0.300
No	54 (81.8%)	30 (88.2%)	
Yes	12 (18.2%)	4 (11.8%)	
Hypertension			0.106
Yes	40 (60.6%)	25 (73.5%)	
No	26 (39.4%)	9 (26.5%)	
Smoking			0.445
Non smoker	30 (45.5%)	20 (58.8%)	
Current smoker	16 (24.2%)	6 (17.6%)	
Ex smoker	20 (30.3%)	8 (23.5%)	
Diabetes mellitus			
No	37 (56.1%)	13 (38.2%)	0.114
Yes	29 (43.9%)	21 (61.8%)	
Dyslipidemia			0.492
No	43 (65.2%)	23 (67.6%)	
Yes	23 (34.8%)	11 (32.4%)	

P value $\leqslant$0.05 was considered significant.

3.2. Demographic data of the studied patients (Table 1)

The two groups matched as regards age and sex. The mean age in group I was 55.64 ± 9.44 years ranged from 31 to 81 years, and the mean age for group II was 55.79 ± 8.45 years ranged from 39 to 74 years. In group I, there were 49 males (74.2%) and 17 females (25.8%). In group II, there were 25 males (73.5%) and 9 females (26.5%).

In our study, diabetes was present in 50 patients, hypertension in 65 patients, dyslipidemia in 66, family history of CAD was present in 20 patients, 22 patients were smokers and 28 patients were ex-smokers.

3.3. Correlation between number of vessels affected and ACR (Table 2)

The percentage of patients with more than one vessel affected was higher in group II ($p = 0.012$).

In group I: 13 patients (19.7%) had only one vessel affected and 53 patients (80.3%) had two or three vessels affected. **In group II:** 5 patients (14.7%) had one vessel affected and 29 patients (85.3%) had two or three vessels affected.

3.4. Correlation between total number of lesions per patients and ACR (Table 3)

The percentage of patients with more than 3 lesions was higher in group II ($p = 0.020$).

In group I: 50 patients (75.8%) had up to 3 coronary lesions, and 16 patients (24.2%) had more than 3 lesions. **In group II:** 18 patients (52.9%) had up to 3 lesions and 16 patients (47.1%) had more than 3 lesions.

If we classify the patients into those who had up to 4 lesions and patients having more than 4 lesions, **in group I:** 62 patients (93.9%) had up to 4 coronary lesions, and 4 patients (6.1%) had more than 4 lesions. **In group II:** 14 patients (41.2%) had up to 4 lesions and 20 patients (58.8%) had more than 4 lesions. The percentage of patients with more than 4 lesions was higher in group II and the results were more significant ($p = 0.00029$).

Table 2 Correlation between numbers of vessels affected per patient and ACR.

Total number of vessel per patients	Group I (*n* = 66)		Group II (*n* = 34)	
	No	%	No	%
One vessel	13	19.7	5	14.7
Two or more vessels	53	80.3	29	85.3
Total	66		34	
χ^2	8.65			
P	0.012[a]			

[a] *P* value $\leqslant$0.05 was considered significant.

Table 3 Relation between total number of lesions per patients and ACR.

Total number of lesions per patients	Up to 3 lesions		More than 3 lesions	
	No	%	No	%
Group I (n = 66)	50	73.5	16	50
Group II (n = 34)	18	26.5	16	50
Total	68		32	
χ^2	5.37			
P	0.020[a]			
	Up to 4 lesions		More than 4 lesions	
	No	%	No	%
Group I (n = 66)	62	72.1	4	33.3
Group II (n = 34)	14	27.9	20	66.7
Total	76		24	
χ^2	13.10			
P	0.00029[a]			

[a] P value $\leqslant$0.05 was considered significant.

Table 4 Relation between syntax score and ACR.

Urinary ACR	Syntax $\leqslant$22		Syntax $>$22		Total
	No	%	No	%	
Group A	52	78.8	14	21.2	66
Group B	13	38.2	21	61.8	34
Total	65		35		100
χ^2	14.487				
P	0.0001[a]				

[a] P value $\leqslant$0.05 was considered significant.

3.5. Correlation between SYNTAX score and ACR (Table 4)

In each group the severity of CAD by syntax score was evaluated as low score $\leqslant$22 and intermediate or high score $>$22. **In group I**, 52 patients (78.8%) had a low syntax score $\leqslant$22 and 14 patients (21.2%) had an intermediate or high score $>$22. **In group II**, 13 patients (38.2%) had a low syntax score $\leqslant$22 and 21 patients (61.8%) had an intermediate or high score $>$22. There was a strong relationship between the presence of MA and the extent and complexity of CAD (p = 0.012).

3.6. Correlation between numbers of vessels affected per patient and diabetes (Table 5)

When we compared the numbers of vessels affected per patients and diabetes, we found that there was no effect of presence or absence of microalbuminuria on the increased severity of CAD in both diabetic and non-diabetic patients in both groups.

4. Discussion

The detection of subclinical CAD before development of life-threatening cardiac complications has a great potential clinical relevance. However currently available non invasive techniques such as exercise treadmill testing and myocardial single photon emission computed tomography can identify only patients with advanced CAD who manifest myocardial ischemia.[15,16]

The risk of CAD is predicted by traditional risk factors including age, sex, smoking, diabetes mellitus, hypertension and dyslipidemia. However, these factors do not entirely explain the variation of CAD incidence and mortality in individuals and populations. This fact has led to studies on non-traditional cardiovascular risk factors and reside concentration of urinary albumin is one of these factors. Microalbuminuria is predictive, independent of classical risk factors of cardiovascular diseases and is associated with all-cause mortality and cardiovascular morbidity and mortality in patients with Diabetes, hypertension and in the general population.

As the association between microalbuminuria and cardiovascular events is well described, the purpose of this study is to investigate whether urinary albumin to creatinine ratio is a sign of atherosclerotic involvement of coronary artery in the general population.

Few studies have reported the correlation of angiographic severity of CAD with MA. The current study showed that patients with microalbuminuria have a greater atherosclerotic burden and a more severe coronary artery disease in the form of total number of vessels affected and total number of lesions per patient than those without microalbuminuria.

These results are supported by many studies such as Hoseini et al.[17] who performed a study in 2009 consisting of 153 non diabetic patients who underwent coronary angiography in Iran. This study was to assess the correlation of microalbuminuria with the severity of CAD in the general population. The study involved 79 men and 74 women aged 45–70 years, who

Table 5 Relation between number of vessels affected per patient and diabetes.

	Non diabetics (n = 50)				Diabetics (n = 50)			
	Group I		Group II		Group I		Group II	
	No	%	No	%	No	%	No	%
One vessel	10	27	1	7.7	3	10.3	4	19
Two or more	27	73	12	92.3	26	89.7	17	81
Total	37		13		29		21	
χ^2	1.89				0.77			
P	0.223				0.38			

P value $\leqslant$0.05 was considered significant.

were classified as CAD-negative and CAD-positive according to the results of coronary angiography. Microalbuminuria was more prevalent in CAD-positive patients than in controls (62.9% vs. 8.8%; $p = 0.001$). Patients with microalbuminuria compared with controls had increased prevalence of one (15.3% vs. 7.4%, $p \leqslant 0.001$), two (50% vs. 22.2%, $p \leqslant 0.001$), and three vessel disease (29.2% vs. 19.8%, $p \leqslant 0.001$). Microalbuminuria exhibited a significant correlation with the severity of CAD ($r = 0.40$; $p \leqslant 0.001$). In addition, the patients with microalbuminuria had a much greater atherosclerotic burden in the form of multi-vessel disease than those without microalbuminuria.

Similar results were presented by Sukhija et al.[18] who examined coronary angiograms for the extent of severe CAD in patients with type 2 diabetes mellitus (DM) and MA (DM+ MA+, $n = 101$), patients with DM and without MA (DM+ MA−, $n = 101$), patients without DM and with MA (DM− MA+, $n = 64$), and patients without DM and MA (DM− MA−, $n = 64$). The purpose of this study was also to document the association between MA and severe CAD. The study was conducted on 330 patients who underwent coronary angiography at the University of Arkansas for Medical Sciences Hospitals between January 2001 and December 2005. The presence of 2- or 3-vessel CAD showed a linear increase from group DM− MA− to group DM+ MA+ ($p < 0.001$). Thus, patients with MA have more severe angiographic CAD than those without MA. This relation is independent of other risk factors and is particularly evident in patients with DM.

El Sherif et al.[19] in his study "Association Of Glycosylated Hemoglobin Level And Microalbuminuria With The Severity Of Coronary Artery Disease" between January 2011 and July 2011, enrolled 100 patients previously diagnosed as having type 2 diabetes mellitus (58 male and 42 female) and admitted to the Critical Care Department Cairo University for elective coronary angiography. A morning spot urine specimen was collected. Albumin and creatinine levels were measured in a single rapid assay format using the colorimetric method using Spectrum Diagnostic kits. Assessment of the severity of coronary artery disease was done by using Gensini score. There was a statistically significant difference between patients with versus those without microalbuminuria regarding their Gensini scores. Patients with microalbuminuria had higher Gensini scores compared to those without microalbuminuria, (73.1 ± 40 versus 43.6 ± 30.6, P value < 0.001).

In another study performed by Parvizi et al.[20] 228 patients with angiographically confirmed coronary atherosclerotic lesions, according to the number of diseased vessels, were divided into two groups: 114 patients with two diseased vessels and 114 patients with three diseased vessels. The level of albumin in all the studied patients was < 300 mg/24 h. The results showed that the urinary albumin/creatinine ratio in both groups of patients was higher than that of the control ($P = 0$). The ratio in the control group was markedly lower than that in the patient groups. Results of this study indicate the existence of a significant correlation between the extension of atherosclerotic lesions and the ratio of albumin/creatinine in urine.

Hashim et al.[21] in his study "MICROALBUMINURIA: ASSOCIATION WITH ISCHAEMIC HEART DISEASE IN NON-DIABETICS"' studied one hundred consecutive non diabetic patients with CAD (73 males, 27 females). Urinary albumin in the first morning sample was estimated by the immune-turbidimetry method. Albumin to creatinine ratio (ACR) was calculated as mg/g. The diagnosis of CAD was based on the finding of electrocardiographic changes, cardiac enzyme elevation, positive coronary arteriogram or hospital discharge diagnosis of CAD. Out of 100 selected non diabetic patients with CAD, a significant difference was observed in mean MA levels among different age groups. The frequency of MA (ACR > 30 mg/g) was 37% in patients. The mean ACR was 131.8 ± 66.2 mg/g. In this study it was found that the frequency of microalbuminuria was elevated in the study population (37%) which is significantly higher as compared to the general population which ranges from 2.2% to 10.2% in various studies. This study also highlights that MA is more frequent in non diabetic patients with CAD than the general population and thus may be an important emerging risk marker for CAD.

5. Conclusion

Patients with MA have more extensive and complex angiographic CAD compared to those without MA; this relation is independent of other risk factors. MA could be utilized as a simple, inexpensive and practical independent risk marker for CAD.

6. Study limitations

The major limitations of our study are that it is an observational non randomized study; also, it is a single center study, with a small number of patient subgroups.

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