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## Serum Creatinine and Occurrence and Severity of Coronary Artery Disease

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## ABSTRACT

**Introduction:** The risk for cardiovascular disease is increased in all stages of the impairment of renal function. It is proposed that serum creatinine is a marker of diabetes and coronary artery disease (CAD) as well as the kidney function. **Aim:** to study the association of serum creatinine with the likelihood and severity of CAD. The study population consisted of 262 males and 266 females who were classified as CAD cases and controls according to the results of coronary angiography. **Results:** Patients with CAD compared with the controls had increased levels of serum urea and creatinine. Serum creatinine showed significant positive correlation with male sex, hypertension and negative correlation with total- and HDL-cholesterol and apoAI. Serum urea, uric acid and potassium were the major determinants of creatinine. All hematological parameters were strong negative correlates of creatinine. None of markers of inflammation had significant correlation with creatinine. Creatinine was associated significantly with the prevalence [odds ratio of 1.79 (1.47-2.20),  $p < 0.001$ ] and severity of CAD [ $F(3,528) = 3.0$ ,  $p = 0.03$ ]. Serum creatinine was excluded from the regression equation after adjustment for major risk factors. **Conclusion:** Serum creatinine has significant association with CAD, but the correlation is not independent. Creatinine have significant association with markers of kidney function and body water status, but not with markers of inflammation and insulin function.

**Keywords:** Coronary artery, Creatinine, Kidney, Lipid.

## 1. INTRODUCTION

The impairment of kidney function is accompanied with the increased risk for cardiovascular disease (CVD) (1). The excess risk for CVD in renal disease is attributed partly to higher prevalence of older age, hypertension, diabetes, dyslipidemia and oxidative stress (2). Creatinine is anhydride form of creatine and serves as a marker of kidney function. Muscle as the major source of serum creatinine is also target tissue for insulin (3). So, it is assumed that creatinine will be an indicator of insulin, diabetes mellitus and coronary artery disease (CAD) (4, 5). Our preliminary data showed that creatinine in normal range had significant association with CAD (6, 7). It is reported that serum creatinine has significant correlation with pre-inflammatory markers such as Lp(a), apoAI and hsCRP (8, 9). Onat *et al* in a cohort study of 675 adult Turkish patients showed that creatinine within a normal range had a significant and independent relation with CAD even in the absence of metabolic syndrome (10). Serum creatinine as a marker of kidney function has a U-shaped correlation with CAD especially in men (11, 12). This means that both

hypo and hyper glomerular filtration rate associates with increased risk for diabetes and CAD (4, 5). The risks for CVD in patients with less recognizable renal disease is poorly described.

## 2. AIM

The objective of this study was to study the correlation of serum creatinine with the prevalence and intensity of CAD in the patients who underwent coronary angiography.

## 3. METHODS

The experimental design, angiographic assessment and anthropometric measurements were as described previously (13). In brief, the study population consisted of 528 subjects aged 35-76 years who had impaired sport test and underwent their first coronary angiography at Zahra hospital of university of Mazandaran. The subjects were excluded from the study who had a recent history of acute myocardial infarction, percutaneous transluminal coronary angioplasty, infectious or inflammatory disease, severe liver or renal disease, neoplasm and hematologic disorders. Subjects with one or more lesions that narrowed the

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lumen of any coronary artery significantly (70%) were considered to be CAD cases, whereas those without any narrowing (<10%) were taken as controls (13).

Blood samples collection, plasma preparations and the measurements of lipids are described in references 13 and 14. All measurements were done on fresh serum. Serum creatinine was assayed using the new homogeneous method, Pars-Azmon (Tehran, Inc). All other biochemical and hematological parameters were measured by routine laboratory methods.

#### Statistical analysis

The results are presented as the means  $\pm$  SD. The significance of any differences in the means and proportions were tested with student's t-test and Kruskal-Wallis analysis. All p-values are two-tailed and differences were considered significant if p-values were 0.05. Bivariate correlation analysis was performed to address the correlation of creatinine with other risk factors. The independence of the correlations with CAD was examined by using multivariate logistic regression analysis (SPSS version 21).

## 4. RESULTS

There were significant differences in the prevalence of male gender, smoking and diabetes between control and case groups (Table 1). Patients with CAD compared with the controls had increased levels of serum glucose, triglycerides, apoB100, Lp(a), BUN, creatinine, potassium and erythrocytes counts.

Serum creatinine showed significant positive correlation with male sex, hypertension and negative correlation with total- and HDL-cholesterol and apoAI (Table 2). Serum urea (BUN), uric acid and potassium were the major determinants of creatinine. All hematological parameters were negative strong correlates of creatinine. Neither of the markers of inflammation including leukocytes counts, ESR and hsCRP nor of serum glucose or diabetes showed significant correlation with creatinine.

Figure 1 shows that, serum creatinine had significant association with the severity of CAD [F(3,528)=3.0, p=0.03]. Serum BUN, uric acid, glucose and HDLc showed also significant association with the severity of CAD (results not shown). Both uni- and multi-variate logistic regression analyses were performed to test the independence of the correlations between risk factors and CAD (results not shown). In univariate analysis, serum creatinine correlated with CAD by the odds ratio (OR) of 1.79 (1.47-2.20), p<0.001. If major classical risk factors were included in the multivariate conditional forward analysis, creatinine would be excluded from the regression equation. Finally, male sex, age, diabetes, hypertension, total- and HDL- cholesterol were kept in the model significantly.

## 5. DISCUSSION

The results of the present study indicate that, serum creatinine is significantly associated with the prevalence and severity of CAD. But, the correlation was not independent and exerted via the classical risk factors. Serum creatinine was strongly correlated to other indicators of

	Without CAD (n≈198)	With CAD (n≈330)	P
Clinical parameters:			
Age, year	53.2 $\pm$ 10.8	57.8 $\pm$ 9.8	0.001
Gender, male%(n)	47.7 (95)	50.6 (167)	0.001
Physical activity, %(n)	52.8 (105)	56.7 (187)	0.458
Smoking, %(n)	46.2 (92)	48.5 (160)	0.016
Diabetes mellitus, %(n)	45.8 (91)	50.3 (165)	0.007
Hypertension, %(n)	58.8 (117)	63.9 (211)	0.067
Biochemicals:			
Glucose, mg/dL	108.6 $\pm$ 33.0	128.8 $\pm$ 62.9	0.001
Triglycerides, mg/d	178.2 $\pm$ 110	216.4 $\pm$ 163	0.002
Total cholesterol, mg/dL	192.1 $\pm$ 45.7	195.4 $\pm$ 56.9	0.476
HDLc, mg/dL	43.7 $\pm$ 11.8	39.5 $\pm$ 10.8	0.001
ApoAI, mg/dL	156.3 $\pm$ 30.4	150.3 $\pm$ 45.1	0.124
ApoB100, mg/dL	119.7 $\pm$ 29.9	127.9 $\pm$ 36.8	0.012
Lp(a), mg/dL	42.2 $\pm$ 30.9	68.8 $\pm$ 60.0	0.001
BUN, mg/dL	16.0 $\pm$ 5.0	18.3 $\pm$ 7.8	0.001
Creatinine, mg/dL	0.92 $\pm$ 0.19	1.13 $\pm$ 0.82	0.002
[Na <sup>+</sup> ], mEq/L	140.1 $\pm$ 2.9	139.6 $\pm$ 2.9	0.068
[K <sup>+</sup> ], mEq/L	4.4 $\pm$ 0.4	4.5 $\pm$ 0.4	0.048
Hematologic factors:			
Erythrocytes counts	4.7 $\pm$ 0.7	4.8 $\pm$ 0.7	0.036
Leukocyte counts	7.6 $\pm$ 1.9	8.0 $\pm$ 2.2	0.521
ESR, mm/h	16.1 $\pm$ 11.0	18.7 $\pm$ 14.5	0.033
hsCRP mg/dL	1.9 $\pm$ 1.3	2.3 $\pm$ 1.9	0.059

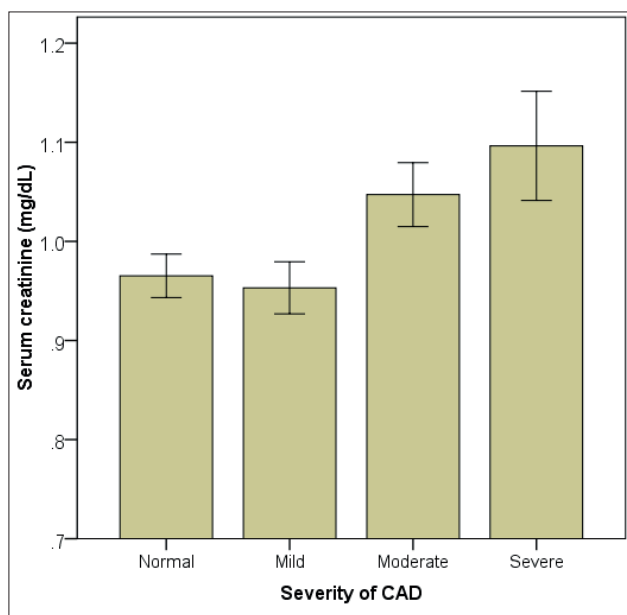
**Table 1. Demographic and clinical parameters in CAD controls and patients. The number in each group has shown in parentheses. The results are presented as the means  $\pm$  SD.**

Clinical characteristics:	r	P
Age	0.070	0.233
Sex	0.175	0.010
Diabetes mellitus	0.080	0.190
Hypertension	0.115	0.051
Glucose	0.029	0.627
Triglycerides	-0.070	0.232
Total cholesterol	-0.134	0.023
HDLc	-0.145	0.015
AopAI	-0.156	0.016
ApoB100	0.032	0.623
Lp(a)	0.082	0.209
BUN	0.694	0.001
Uric acid	0.255	0.001
Sodium	0.099	0.060
Potassium	0.235	0.001
Leukocytes counts	0.032	0.471
ESR	0.063	0.174
hsCRP	0.044	0.992
Hemoglobin	-0.263	0.001
Erythrocytes counts	-0.231	0.001
Hematocrit	-0.247	0.001

**Table 2. The correlation coefficients (r) of creatinine with other risk factors. The values of coefficients (r) was determined by using bivariate correlation analysis.**

kidney function and to the indices of body water status. Creatinine also did not exhibit any association with the markers of inflammation or diabetes mellitus.

Several mechanisms are involved in the relationship of serum creatinine with the increased risk for CAD (1). The



**Figure 1. Relationship of serum creatinine with the severity of CAD.** The intensity of CAD was accessed on the bases of the number and the extent of lesions in coronary arteries. \* indicates  $p < 0.03$ .

muscle is the major source for serum creatinine and also is target organ for insulin (2, 3). So, it is proposed that the level of serum creatinine may be a convenient indicator for diabetes and CAD. Nevertheless, creatinine did not exhibit such correlations with any of serum glucose or the existence of diabetes (Table 2). Some researchers reported that creatinine correlates with the markers of inflammation (9, 11). On the basis of the current data, creatinine had not any association with ESR, hsCRP and leukocyte counts. Creatinine showed a significant and negative correlation with apo AI and HDLc. The coordinate correlation of apo AI and HDL-cholesterol is due to participating in HDL particles. This phenomenon is not correlated to dysfunctional apo AI, as it is supposed by some researchers (9, 11). The present results showed that, urea and uric acid were the major determinants of serum creatinine (Table 2) (15). Hemoglobin, hematocrit and erythrocytes counts as the markers of body water status were associated negatively and strongly with serum creatinine. These data shows clearly that, creatinine is just a marker for kidney function and an index for body water (14), but not an indicator for inflammation or insulin action (16).

## 6. CONCLUSION

The results suggest that serum creatinine in normal range has significant association with the prevalence and intensity of CAD, but the correlation is not independent.

- **Author's contribution:** B.B. and M.R. gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data. B.B, N.R, A.F. and M.R. had a part in article preparing for drafting or revising it critically for important intellectual content, and each author gave final approval to be published.
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