ORIGINAL PAPER

doi: 10.5455/medarch.2019.73.154-156
MED ARCH. 2019 JUN; 73(3): 154-156
RECEIVED: FEB 22, 2019 | ACCEPTED: APR 25, 2019

1Departments of Cardiology, Cardiovascular Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Mazandaran, Iran
2Departments Clinical Biochemistry, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Mazandaran, Iran

Corresponding author: Mehdi Rasouli, PhD, Department of Clinical Biochemistry and Immunogenetics Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Mazandaran, Iran. E-mail: mehdi.rasouli@yahoo.com. ORCID ID: http://orcid.org/0000-0002-5133-2481

Serum Creatinine and Occurrence and Severity of Coronary Artery Disease

Babak Bagheri1, Najme Radmard2, Atena Faghani-Makrani2, Mehdi Rasouli2*

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 anthropometrics 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
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 ± 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 erythrocyte 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 leucocytes 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 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).
Serum Creatinine and Occurrence and Severity of Coronary Artery Disease

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 reviewing it critically for important intellectual content, and each author gave final approval to be published.
- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

REFERENCES

1. Hall WD. Abnormalities of kidney function as a cause and a consequence of cardiovascular disease. Am J Med Sci. 1999; 317(3): 176-182.

2. Culleton BF, Larson MG, Wilson PW, et al. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int. 1999; 56(6): 2214-2219.

3. Hsieh MC, Hsiao YJ, Tien KJ, et al. Chronic kidney disease as a risk factor for coronary artery disease in Chinese with type 2 diabetes. Am J Nephrol. 2008; 28(2): 317-323. doi: 10.1159/000113188

4. Harita N, Hayashi T, Sato KK, et al. Lower serum creatinine is a new risk factor of type 2 diabetes: the Kansai healthcare study. Diabetes Care. 2009; 32(3): 424-426. doi: 10.2337/dc08-1265.

5. Lorenzo C, Nath SD, Hanley AJ, et al. Risk of type 2 diabetes among individuals with high and low glomerular filtration rates. Diabetologia. 2009; 52(7): 1290-1297. doi: 10.1007/s00125-009-1361-4.

6. Rasouli M, Okhovatian A, Enderami A. Serum proteins profile analysis as an indicator of malignancy: multivariate logistic regression and ROC analyses. Clin Chem Lab Med. 2005; 43(9): 913-918. doi:10.1515/CCLM.2005.156.

7. Hoseini VN, Rasouli M. Microalbuminuria correlates with the prevalence and severity of coronary artery disease in non-diabetic patients. Cardio J. 2009; 16(2): 142-145.

8. Onat A, Cak G, Ademoglu E, et al. Coronary disease risk curve of serum creatinine is linear in Turkish men, U-shaped in women. J Invest Med. 2013; 61(1): 27-33. doi:10.2310/JIM.0b013e318276de59.

9. Rye K-R, Barter P. Function and metabolism of pre-beta migrating, lipid-poor apolipoprotein A-I. Arterioscler Thromb Vasc Biol. 2004; 24(3): 421-428. doi:10.1161/01.ATV.0000104029.74961.f5.

10. Onat A, Yüksel H, Can G, et al. Serum creatinine is associated with coronary disease risk even in the absence of metabolic disorders. Scand J Clin Lab Invest. 2013; 73(7): 569-575. doi: 10.3109/00365513.2013.821712.

11. Rasouli M, Trischuk TC, Lehner R. Calmodulin antagonist W-7 inhibits de novo synthesis of cholesterol and suppresses secretion of de novo synthesized and preformed lipids from cultured hepatocytes. Biochim Biophys Acta. 2004(1-3); 1682: 92-101. doi:10.1016/j.bbalip.2004.02.002.

12. Lorenzo C, Nath SD, Hanley AJ, et al. Risk of type 2 diabetes among individuals with high and low glomerular filtration rates. Diabetologia. 2009; 52(7): 1290-1297.

13. Rasouli M, Kiasari AM. Interactions of lipoprotein(a) with diabetes mellitus, apolipoprotein B and cholesterol enhance the prognostic values for coronary artery disease. Clin Chem Lab Med. 2008; 46(5): 667-673. doi: 10.1515/CCLM.2008.137.

14. Rasouli M, Kiasari AM, Arab S. Indicators of dehydration and hae- mocencentration are associated with the prevalence and severity of coronary artery disease. Clin Exp Pharmacol Physiol. 2008; 35(8): 889-894. doi: 10.1111/j.1440-1681.2008.04932.x.

15. Bagheri B, Zargari M, Meshkini F, et al. Uric acid and coronary artery disease, two sides of a single coin: A determinant of antioxidative system or a factor in metabolic syndrome. J Clin Diagn Res. 2016; 10(2): OC27-31 doi: 10.7860/JCDR/2016/16355.7281.

16. Rasouli M, Nesarhosseini V, Kiasari AM, et al. The multiplicative interactions of leukocyte counts with some other risk factors enhance the prognostic value for coronary artery disease. Cardio J. 2011; 18(3): 246-253.