Study of serum cystatin C as a reliable marker for metabolic syndrome

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Abstract

Background: Serum concentration of cystatin C, a marker of glomerular filtration, has been associated with cardiovascular disease (CVD). The aim of this study was to elucidate the association of serum C with metabolic syndrome as a constellation of cardiovascular risk factors.

Methods: The study population consisted of 56 subjects with metabolic syndrome and 22 subjects free of metabolic syndrome (control group). Cholesterol, HDL-C, LDL-C, blood urea, triglycerides, glucose, HbA1c, serum cystatin C and serum creatinine were measured in both groups. GFR was calculated in both groups using Cockroft-Gault equation.

Results: Metabolic syndrome group presented significantly higher cystatin C levels than the control group (1.38 ± 0.57 *vs.* 0.954 ± 0.40; P=0.006). The sensitivity and specificity of cystatin C were 78.57% and 77.67%, respectively. Subjects with metabolic syndrome exhibited significantly higher blood glucose, triglyceride, cholesterol and HbA1c levels.

Conclusion: Our results suggest that cystatin C may be a marker for metabolic syndrome and may identify a certain degree of renal dysfunction even when serum creatinine does not exceed normal level.

Keywords: Cystatin C, Creatinine, Metabolic syndrome, diabetes, Renal disease

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Introduction

Cystatin C is a low molecular weight protein that acts as a potent inhibitor of cystatin C proteases (1). It is produced in a stable rate by all nucleated cells and released into the blood stream .The protein is freely filtered by the renal glomeruli and subsequently metabolized in the proximal tubules. Given these features serum cystatin C concentration has emerged as a novel surrogate marker of GFR. Furthermore, based on its reported independence from the effects of age, gender and composition (1) it has been suggested that increased cystatin C levels may be a more sensitive indicator of renal dysfunction than conventional creatinine based measures. An interesting observation from the results of clinical studies shows association between cystatin C and cardiovascular diseases (2-9).

However, the pathophysiology underlying this association and whether renal dysfunction or other processes have possible roles remains unclear.

Metabolic syndrome, which is specifically diagnosed when three of the followings are present: abdominal obesity, hypertriglyceridemia, low HDL, high cholesterol elevated blood pressure and hyperglycemia (10, 11), is constellation of cardiovascular risk factors and its related components (12). Therefore it is considered as an important risk factor for cardiovascular diseases (13). In this study we sought to determine whether serum cystatin C can be used as a reliable marker for metabolic syndrome.

Methods

In this case-control study, a total of 56 subjects who were diagnosed with diabetes for at least one year prior to the study in Mehrad Hospital, Tehran, Iran with high blood pressure (≥130/85 mm Hg) and BMI >25 kg/m2 were recruited as metabolic syndrome group. Twenty two healthy subjects with normal blood pressure, BMI<20 kg/m2 and normal blood glucose levels were included in our control group. Age range in our study population was 35 to 65 years. Blood samples were drawn after 12-14 hours overnight fasting. Cholesterol, HDL-c, LDL-c, triglycerides, glucose and blood urea levels were measured using Technicon RA-1000 (USA). Serum cystatin C levels were measured using ELISA method. The reference interval for serum cystatin C concentration in adults with the ELISA method was 0.5 to 1 mg/L. HbA1c was measured by chromatography method. GFR was calculated by the Cochcroft-Gault equation.

Statistical Analysis

The statistical analysis were performed using SPSS (Statistical Package for the Social Sciences), version 14. Data were analyzed using independent T-test. All values are expressed as the Mean and standard deviation (SD). The p-value lesser 0.05 was considered as statistically significant.

Results

Fifty six patients and 22 controls were included in this study. Mean serum cystatin C concentrations were significantly higher in metabolic syndrome group compared with the control group (p= 0.006), whereas serum creatinine concentrations showed no significant difference between two groups (Table1).

Table 1. Mean cystatin C and creatinine concentration in control and metabolic syndrome group

	Control	Metabolic syndrome	P-value
Cystatin C	0.954 ± 0.40	1.38 ± 0.57	0.006
Creatinine	1.09 ± 0.211	1.13 ± 0.87	NS

The sensitivity and specificity for cystatin C and creatinine are given in Table 2.

Table 2. Sensitivity and specificity of cystatin C and creatinine

	Sensitivity	Specificity
Cystatin C	78.57	77.27
Creatinine	16.07	86.36

Clinical characteristics of study population are given in Table 3. Based on results, there was no significant age difference between two groups. Metabolic syndrome group showed significantly higher HbA1C, glucose, triglyceride and cholesterol levels; whereas, HDL-c level was significantly lower in metabolic syndrome group. Glomerular filtration rate showed no significant difference between two groups. The mean value and standard deviation of waist measure in control and metabolic syndrome group were 86.06±9.89 Cm (95% CI: 82.49–89.63) and 96.89±11.77 Cm (95% CI: 94.06–99.72), respectively.

Table 3. Clinical characteristics of study population

Parameters	Subjects (n=56)	Controls (n=22)	P-Value
Age (years)	50.55 ± 8.91	47.72 ± 7.70	NS
HbA1C (%)	7.47 ± 1.11	5.50 ± 0.61	0.001
Glucose (mg/dl)	129.20 ± 64.84	88.45 ± 9.21	0.002
Blood urea (mg/dl)	35.98 ± 10.96	35.54 ± 6.48	NS
GFR	92.97 ± 12.98	99.21 ± 13.59	NS
LDL (mg/dl)	110.33 ± 25.24	115.27 ± 18.50	NS
Cholesterol (mg/dl)	162.85 ± 57.77	140.0 ± 32.31	NS
Triglyceride (mg/dl)	219.23 ± 35.54	130.90 ± 22.50	<0.001
HDL (mg/dl)	40.16 ± 9.25	52.13 ± 4.01	<0.001

Results are expressed as Mean ± standard deviation; NS: not significant

Discussion

The metabolic syndrome is combination of several factors which may carry a common underlying etiology and each of them is a risk factor for renal disease. For example, obesity has been shown to be an independent risk factor for chronic kidney disease (CKD) (14, 15); and treating obesity might stabilize renal function (16) or reverse early hemodynamic abnormalities and glomerular dysfunction (17). Obesity can affect renal dysfunction in several ways: excess excretory load, renal sodium retention, hyperinsulinemia, insulin resistance, or renal lipotoxicity (18). Obesity has been contributed to one type of focal segmental glomerulosclerosis called obesity-related glomerulopathy (19) and could facilitate developing of glomerulosclerosis. Insulin resistance also may have a direct role in the pathogenesis of renal injury, as a consequence of stimulating the sympathetic nervous system and the rennin-angiotensin-aldosterone system. Microalbuminuria has a direct pathophysiological link to insulin resistance; its relation to the syndrome by sheer associations with other metabolic abnormalities is largely unknown.

Microalbuminuria is also considered as a predictor of cardiovascular morbidity and mortality in diabetes (20).
In this study we demonstrated that although serum creatinine and GFR did not differ significantly between metabolic syndrome and control group, serum concentration of cystatin C was significantly higher in metabolic syndrome group compared with control group. Indeed, serum cystatin C behave parallel with other metabolic syndrome components and correlates with cardiovascular risk factors. These data suggests that increased cystatin C concentration is an early event in people who are at high risk for future developing cardiovascular disease (2-5). Many studies have shown that cystatin C can predict CVD, heart failure and leading mortalities better than serum creatinine and GFR (2-9). The pathophysiology linking cystatin C with cardiovascular diseases is not yet clearly explained. However, it has been suggested that this association may be due to mild degrees of renal dysfunction which can be detected with cystatin C much sooner than other renal markers as creatinine and GFR.

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