ibc Interdisciplinary Bio Central

IBC 2012;4:4, 1-4 • DOI: 10.4051/ibc.2012.4.2.0004

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RAPID REPORT

Validity of Serum Cystatin C for Prediecting Obesity Nephropathy

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Subject areas; Pharmaceutical bioscience and technology

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Editor; Yoshio Tateno, National Institute of Genetics, Japan

Received April 26, 2012
Revised May 14, 2012
Accepted May 27, 2012
Published May 28, 2012

Citation; Asefy, Z., et al. Validity of Serum Cystatin c for Prediecting Obesity Nephropaty. IBC 2012, 4:4, 1-4.
doi: 10.4051/ibc.2012.4.2.0004

Competing interest; All authors declare no financial or personal conflict that could inappropriately bias their experiments or writing.

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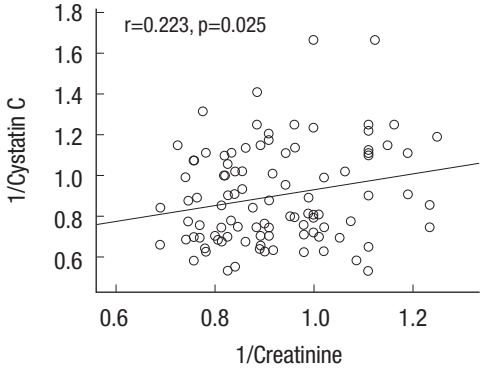
SYNOPSIS

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 evaluate cystatin C as a marker of obese patients without chronic kidney disease (CKD).

Materials and Methods: The study population consisted of 36 subjects with metabolic syndrome and 32 subjects free of metabolic syndrome (the control group). 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: Obese patients showed higher cystatin C levels than normal samples (1.28 ± 0.29, $P < 0.05$). In the binary logistic regression, obese patients were significantly associated with elevated cystatin C levels.

Conclusion: Our results suggest that cystatin C may be a marker for obese patients and may identify a certain degree of renal dysfunction even when serum creatinine does not exceed the normal level. In this study, we demonstrated that serum creatinineand GFR did not differ significantly between the diabetic and the control groups. Serum concentration of cystatin C was significantly higher in the diabetic group compared with the control group. The strengths of this study are the evaluation of reliability and sensivity in comparison with a 'routine test of GFR'. The methodology used allows an appropriate statistical comparison of reliability in contrast to most other previous evaluations of GFR.



Key Words: serum cystatin C; renal dysfunction; obesity; nephropathy; specifity

INTRODUCTION

Central obesity is one of the fundamental factors the metabolic syndrome, and for any given BMI, it is more common in men. It might be expected that prevalence of metabolic syndrome would be higher in men than in women. Among non-diabetic European men and women from eight different population sets, the prevalence of metabolic syndrome (defined using modified WHO criteria) was generally higher in men than in women[1]. The effect of generalized obesity is also extremely important (see below) such that, in any given population where obesity is more common in women than in men, the prevalence of metabolic syndrome will be higher in women than in men. This pattern can be observed in Indian, Iranian and Turkish populations[2-6]. Recent epidemiologic studies show that obesity is associated with chronic kidney disease (CKD) and ESRD[7]. And a higher BMI has been found to be a strong independent risk factor for ESRD even after adjustment for other major risk factors that are associated with ESRD including smoking, baseline hypertension, and diabetes. The adjusted relative risk for ESRD increased steadily from a lower to a higher BMI, and reached up to 7 for a BMI of 40 kg/m^2 [8]. Cystatin C is a low molecular weight protein that functions as an excellent inhibitor of cystatin C proteases[9]. It has been suggested that an increased level of cystatin C may be a more sensitive indicator of renal dysfunction than conventional creatinine based measures. An interesting observation drawn from these results and clinical studies shows a strong association between cystatin C and cardiovascular disease[10-13]. However, whether the pathophysiology underlying this association involves renal dysfunction or other processes remains unclear.

RESULTS AND DISCUSSION

Results

In this study, 36 obese and 32 control subjects were evaluated. The mean serum cystatin C concentration was significantly higher in the obese group compared with the control group ($p = 0.001$), whereas serum creatinine concentration showed no significant difference between the two groups (Figure 1 and Table 1).

Clinical characteristics of study population are given in Table 2 based on the results obtained. There was no significant age difference between the two groups. The group with metabolic syndrome showed significantly higher levels of HbA1C, glucose, and triglyceride, whereas the level of HDL-c was significantly lower in the group with metabolic syndrome. Glomerular filteration rate showed no significant difference between the two groups.

Discussion

Metabolic syndrome is a combination of several factors which may share a common etiology, and each of which is a risk factor for renal disease. Obesity has been shown to be an independent risk factor for CKD[14,15], and treating obesity might stabilize renal

Table 1. Mean cystatin C and creatinine concentration in control and obese patients

	Control	Obese patients	*P* value
Cystatin C	1.00 ± 0.26	1.28 ± 0.29	$P < 0.05$
Creatinine	1.04 ± 0.15	1.13 ± 0.19	NS

NS: not significant.

Table 2. Clinical characteristics of study population

Parameters	Overweight (n = 36)	Controls (n = 32)
Age (years)	48.72 ± 9.68	45.62 ± 7.67
HbA1C (%)	5.97 ± .23	5.47 ± 0.79
Glucose (mg/dL)	120.63 ± 10.4	90.84 ± 15.67
Blood urea (mg/dL)	32.83 ± 10.72	31.62 ± 8.24
GFR	89.95 ± 10.86	95.01 ± 11.31
LDL (mg/dL)	108.58 ± 35.20	108.41 ± 22.01
BMI	28.1 ± 4.05	23.93 ± 1.67
Triglyceride (mg/dL)	225.89 ± 48.83	141.00 ± 27.24
HDL (mg/dL)	41.05 ± 8.90	52.65 ± 5.78
Diastolic pressure	91.50 ± 6.84	79.78 ± 7.78
Systolic pressure	147.94 ± 30.83	113.59 ± 19.79

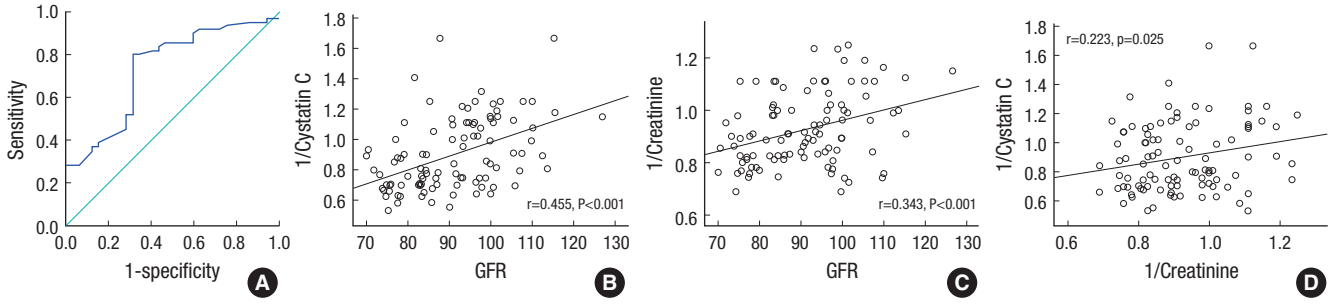


Figure 1. To obtein sensivity and specificity of cystatin C (We used the rock chart). (A) Attention to charts cystatin C cotpoin 0.98 with sensivity of 0.80 and spesivity of 65.6 was calculated. The correlation between cystatin C and GFR, and creatinine and GFR were calculated with Pearson's Correlation Coefficient (B,C and D). (B) and (C), correlations between 1/cystatin C and measured glomerular filtration rate (GFR) (B) and 1/serum creatinine (C).

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 with a type of focal segmental glomerulosclerosis called obesity-related glomerulopathy[19] which could facilitate the development of glomerulosclerosis. Insulin resistance may also have a direct role in the pathogenesis of renal injury, as a consequence of stimulating the sympathetic nervous system and the reninsangiotensin- 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 a predictor of cardiovascular morbidity and mortality in diabetes[18-20]. In this study, we demonstrated that although serum creatinine and GFR did not differ significantly between the obese and the control groups, serum concentration of cystatin C was significantly higher in the obese group compared with that of control group.

CONCLUSION AND PROSPECTS

CVD is the primary clinical outcome of metabolic syndrome which is a risk factor for type 2 diabetes, and diabetes is a major risk factor for CVD. Additionally, chronic kidney disease is now recognized as a risk factor for CVD. Several studies have shown an independent and graded relationship between the degree of kidney dysfunction and the risk for CVD. Data from the general population suggest that cystatin C level has a stronger association with CVD outcomes than does creatinine concentration or estimated GFR, especially in elderly population. The cystatin C level also had a stronger risk relationship with mortality than did creatinine concentration and creatinine clearance, as estimated by using the Cockcroft-Gault equation. We conclude that serum CysC has greater sensitivity in detecting reduced GFR in CKD than serum creatinine. However, further studies are necessary to compare CysC concentrations and CysC-based equations and to clarify which one can better detect small reductions in kidney function within the normal range. The determination of plasma CysC levels is more expensive than that of routine plasma creatinine and the absence of very significant advantages could explain its limited use in daily clinical practice.

MATERIALS AND METHODS

The group with metabolic syndrome consisted of a total of 36 subjects who were diagnosed with diabetes for at least a period of one year prior to our study at Mehrad Hospital with high blood pressure (≥ 130/85 mmHg) and BMI > 25 kg/m^2.

Our control group consisted of 32 healthy subjects with normal blood pressure, BMI < 25 kg/m^2 and normal blood glucose levels. The subjects were between the ages of 35 and 65 years. Blood samples were collected from the subjects after 12-14 hours over night fasting. Cholesterol, HDL-c, LDL-c, triglycerides, glucose and blood urea were measured using Technicon RA-1000 USA. Serum cystatin C was measured using ELISA method in consistency with WHO criteria for biochemical factors. The reference interval for creatinine was 0.5-1 mg/dL and HbA1c was measured using chromatography. GFR was calculated by the cochcroft-gault equation.

Statistical analysis

Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences), version 16. Data were analyzed using statistical software programs such as One-Way Analysis of Variance, DuncanOne-Sample Kolmogorov-Smirnov Test Pearson's Correlation Coefficient. All values were expressed as the mean and standard deviation (SD). The p value under 0.05 is significant.

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