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Association of body mass index, waist circumference, and metabolic syndrome with serum cystatin C in a Chinese population

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Abstract

Background: The aim of the study was to evaluate the association of body mass index (BMI), waist circumference (WC), and metabolic syndrome (MetS) with serum cystatin C (CysC) in a Chinese population.

Methods: The population was composed of 5866 subjects. MetS was diagnosed using the American Heart Association/National Heart, Lung, and Blood Institute 2005 (NCEP-R) criteria. Covariates were analyzed using logistic regression and Spearman partial correlation.

Results: In this population, triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), high sensitivity C-reactive protein (hs-CRP), BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), serum creatinine (Scr), and CysC were significantly higher, and HDL-C and the estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration) ($eGFR_{CKD\text{-}EPI}$) were significantly lower in the MetS than in the non-MetS group. TG, LDL-C, FPG, hs-CRP, BMI, WC, SBP, DBP, and Scr were significantly higher, and HDL-C and $eGFR_{CKD\text{-}EPI}$ were significantly lower in the 4th quartile than in the 1st quartile of CysC. Logistic regression analysis showed that sex, age, hs-CRP, and CysC were independently associated with the presence of MetS (OR = 3.732, 1.028, 1.051, and 3.334, respectively; $P < 0.05$). No significant association between the presence of MetS and either Scr or $eGFR_{CKD\text{-}EPI}$ was observed. After adjustment for age and sex, BMI, WC, hs-CRP, and Scr were all positively correlated, whereas $eGFR_{CKD\text{-}EPI}$ was negatively correlated with CysC ($r = 0.029$, 0.061, 0.189, 0.227, and −0.210, respectively; $P < 0.05$).

Conclusion: The present study revealed that the CysC was more closely associated with the presence of MetS, as compared Scr or $eGFR_{CKD\text{-}EPI}$. CysC was positively correlated with BMI, and more strongly, positively correlated with WC and inflammation.

Abbreviations: BMI = body mass index, CysC = cystatin C, DBP = diastolic blood pressure, $eGFR_{CKD\text{-}EPI}$ = estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration), hs-CRP = high sensitivity C-reactive protein, LDL-C = low-density lipoprotein cholesterol, MetS = metabolic syndrome, SBP = systolic blood pressure, Scr = serum creatinine, TG = triglyceride, WC = waist circumference.

Keywords: body mass index, cystatin C, metabolic syndrome, waist circumference

1. Introduction

Cystatin C (CysC) is an extracellular inhibitor of cysteine proteases and is produced in all nucleated cells. CysC is freely filtered at the level of the renal glomeruli, and almost all of it is reabsorbed and metabolized in the proximal tubule.[1,2] CysC can be used as a measure of kidney function. In recent years, multiple studies have shown that CysC may be used as a more accurate indicator of glomerular filtration rate (GFR) than creatinine.[3–7] CysC has also served as a predictive marker of cardiovascular disease.[8,9]

Metabolic syndrome (MetS) is highly prevalent worldwide[10–12] and is associated with an increased risk for cardiovascular disease and diabetes.[13–15] Many studies on the treatment of MetS have recently been conducted, including studies examining complementary and alternative medicine (CAM) treatments and the use of berry fruits.[16,17] Some researchers have found that low testosterone concentration and high serum ferritin level were risk factors for MetS.[18,19] Others have demonstrated that CysC is associated with MetS[20–23] and have reported a positive relationship between CysC, body mass index (BMI), and waist circumference (WC).[20,23] To the best of our knowledge, research on the association between MetS and CysC is limited. In the present study, we assessed the association of BMI, WC, and MetS with serum CysC in a large Chinese population.

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2. Methods

2.1. Study designs and population

A total of 6306 subjects visited our health care center for their regular checkup between January and December 2013. The medical history, including medications, of each subject was obtained. Subjects with thyroid dysfunction, pregnancy, malignant disease, cirrhosis, infectious disease, active liver disease, chronic kidney disease, missing a valid measurement for necessary indices, or less than 18 years old were excluded (n = 440). Of the total sample (N = 5866), none had a history of corticosteroid or cyclosporine use, hyperhomocysteinemia, or rheumatic diseases.

2.2. Clinical indices and anthropometric measurements

Venous blood samples were drawn after a 10-hour fast for serum index measurements. Triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose (FPG), high-sensitivity C-reactive protein (hs-CRP), and serum creatinine (Scr) concentrations were measured using glycerol phosphate oxidase and peroxidase (GPO-POD), surfactant elution, selected inhibition, hexokinase, turbidimetric immunoassay, and sarcosine oxidase methods, respectively, using a Beckman Coulter AU 5400 machine. CysC concentrations were measured using the turbidimetric immunoassay method, specifically with a Beckman Coulter AU 5400 machine, at a reference range of less than 1.03 mg/L. Both the intra- and interassay coefficients of CysC were less than 10%. CysC levels were between 0.33 and 1.81 mg/L. Estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration) ($eGFR_{CKD\text{-}EPI}$) equation[24] was used. Blood pressure (BP) was measured after at least 5 minutes of rest. WC was measured on standing subjects with a measuring tape midway between the lowest rib and the iliac crest. Body weight was measured in kilograms (with light clothing), and height was measured in meters (without shoes). BMI was calculated by using the formula: Weight (kg)/[Height (m)]^2.

MetS was diagnosed according to the American Heart Association/National Heart, Lung, and Blood Institute 2005 (NCEP-R),[25] which requires at least 3 of the following criteria to be met: WC ≥90 cm in males and ≥80 cm in females; TG ≥1.7 mmol/L (150 mg/dL) or a specific treatment for TG; HDL-C < 1.03 mmol/L (40 mg/dL) in males and <1.29 mmol/L (50 mg/dL) in females or a specific treatment for reduced HDL-C; systolic blood pressure (SBP) ≥130 mm Hg, diastolic blood pressure (DBP) ≥85 mm Hg, or antihypertensive treatment; and FPG ≥5.6 mmol/L (100 mg/dL) or drug treatment for elevated glucose.

2.3. Ethical issues

The ethical committee of the Second Affiliated Hospital, School of Medicine, Zhejiang University approved the study. All subjects provided informed consent.

2.4. Statistical analyses

SPSS software (version 13.0; SPSS Inc., Chicago, IL) was used for statistical analysis. Normal distribution data were expressed as the mean ± standard deviation. Skewed distribution data were expressed as the median with 25th and 75th percentiles (P_{25}–P_{75}). The Mann–Whitney *U* test was used to compare relevant data between non-MetS and MetS groups. The non-MetS group was defined as those subjects without MetS (2 or less MetS criteria). The Mann–Whitney *U* test was used to compare the data between the 1st and 4th quartiles of CysC. Logistic regression was performed to identify independent factors of MetS, and estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for the factors. The following were considered covariates in the logistic regression analysis: age, sex, hs-CRP, Scr, $eGFR_{CKD\text{-}EPI}$, and CysC. SAS software (Version 9.2; SAS Institute Inc., Cay, NC) was used to perform a Spearman partial correlation analysis, adjusting for age and sex, to determine the association of BMI, WC, hs-CRP, Scr, and $eGFR_{CKD\text{-}EPI}$ with CysC. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical characteristics

The clinical data on this cohort are shown in Table 1. A total of 5866 subjects were included in the study (females: 2081, males: 3785; age range: 18–84 years). Compared to the non-MetS group, the MetS group exhibited significantly higher levels of TG, LDL-C, FPG, hs-CRP, BMI, WC, SBP, DBP, Scr, and CysC, and lower levels of HDL-C and $eGFR_{CKD\text{-}EPI}$.

3.2. CysC and other indices

The data were divided into 4 groups according to the quartiles of serum CysC concentration (Table 2). Comparisons between the indices in the 1st and 4th quartiles showed significantly higher values for TG, LDL-C, FPG, hs-CRP, BMI, WC, SBP, DBP, and Scr, whereas both HDL-C and $eGFR_{CKD\text{-}EPI}$ were significantly lower in the 4th quartile.

3.3. Logistic regression analysis

Logistic regression analysis revealed that sex, age, hs-CRP, and CysC were independently associated with the presence of MetS (OR = 3.732, 1.028, 1.051, and 3.334; 95% CI: 2.396–5.812, 1.004–1.053, 1.027–1.075, and 2.259–4.919; $P < 0.001$, 0.021, <0.001, and <0.001, respectively). No significant association was observed for presence of MetS and either Scr ($P = 0.089$) or $eGFR_{CKD\text{-}EPI}$ ($P = 0.253$) (Table 3).

3.4. Partial correlation analysis

Spearman partial correlation coefficients of BMI, WC, hs-CRP, Scr, and $eGFR_{CKD\text{-}EPI}$ with CysC are summarized in Table 4. After adjustment for age and sex, the results indicated that BMI, WC, hs-CRP, and Scr were positively correlated with CysC, whereas $eGFR_{CKD\text{-}EPI}$ was negatively correlated with CysC (r = 0.029, 0.061, 0.189, 0.227, and −0.210; $P = 0.0260$, <0.0001, <0.0001, <0.0001, and <0.0001, respectively).

4. Discussion

MetS is characterized by high fasting blood glucose, TG, BP levels, elevated WC, and low HDL-C levels. The worldwide prevalence of MetS has recently been acknowledged as an important public health challenge.[26] MetS was present in 26.1% of the current study subjects, identical to that found in the literature.[10–12,27–29] Furthermore, CysC concentrations were significantly higher in the MetS group than in the non-MetS group. Similar to our findings, Liu et al[30] demonstrated higher

Table 1

Relevant data according to the presence or the absence (non-MetS) of MetS.

	Non-MetS	MetS	P*
N (all:5866)	4334	1532	
Sex ratio (M/F), %	2538/1796 (58.6/41.4)	1247/285 (81.4/18.6)†	<0.001
Age, years	41 (34–48)	47 (40–53)	<0.001
TG, mmol/L	1.12 (0.80–1.57)	2.34 (1.83–3.30)	<0.001
LDL-C, mmol/L	2.70 (2.27–3.20)	3.12 (2.64–3.62)	<0.001
HDL-C, mmol/L	1.35 (1.16–1.57)	1.02 (0.90–1.20)	<0.001
FPG, mmol/L	4.78 (4.48–5.07)	5.25 (4.79–5.91)	<0.001
hsCRP, mg/L	0.4 (0.2–0.8)	0.8 (0.4–1.6)	<0.001
BMI, kg/m^2	22.77 (20.91–24.76)	26.62 ± 2.67	<0.001
WC, cm	81 (75–87)	93 (89–97)	<0.001
SBP, mm Hg	118 (108–129)	138 (130–149)	<0.001
DBP, mm Hg	71 (64–79)	84 (78–91)	<0.001
Scr, μmol/L	67 (56–77)	71 (63–80)	<0.001
$eGFR_{CKD-EPI}$, mL/min/1.73 m^2	109 (101–117)	105 998–111)	<0.001
CysC, mg/L	0.72 (0.61–0.86)	0.81 (0.69–0.96)	<0.001

The normal-distribution data were expressed as the mean ± SD. Skewed distribution data were expressed as the median with 25th and 75th percentiles (P_{25}–P_{75}). A total of 2086 subjects: BMI ≥25 kg/m^2; 718 females: WC ≥80 cm, 1639 males: WC ≥90 cm. BMI = body mass index, CysC = cystatin C, DBP = diastolic blood pressure, $eGFR_{CKD-EPI}$ = estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration), FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, hsCRP = high sensitivity C-reactive protein, LDL-C = low-density lipoprotein cholesterol, MetS = metabolic syndrome, SBP = systolic blood pressure, Scr = serum creatinine, SD = standard deviation, TG = triglyceride, WC = waist circumference.

* *P* values for the comparisons between the non-MetS and MetS group. Mann–Whitney *U* tests were used.

† Comparison of sex between the non-MetS and MetS group using Chi-square test.

serum CysC levels were positively and independently associated with the presence of MetS in a sample of Chinese premenopausal and postmenopausal women. Based on group-stratified CysC values, MetS significantly differed in the lowest CysC quartile compared to the highest quartile. Last, our data reflected a correlation between CysC and MetS.

The association between inflammation and MetS has been well documented.[31,32] A previous report suggested that chronic subclinical inflammation may be partly influenced by MetS.[33] Some studies have suggested a significant association between CysC and CRP,[34–36] and CysC may be considered as a potential inflammatory biomarker.[21] Our data showed that CysC and hs-CRP were independent covariates of MetS. Partial correlation analysis indicated a positive correlation between CysC and hs-CRP, after adjusting for age and sex. Therefore, our data suggest an association between CysC and inflammation.

Logistic regression analysis showed that the CysC was more closely associated with the presence of MetS, as compared Scr or $eGFR_{CKD-EPI}$. Previous studies demonstrated that CysC was considered as a "preclinical" state of renal disease, which was not detected with Scr or eGFR.[37] Thus, CysC is considered to be an accurate glomerular marker for early renal insufficiency.[38]

After adjusting for age and sex, the results indicated that, besides hs-CRP, BMI and WC were also positively correlated with CysC. Although both *r*-values were low, CysC was more strongly correlated with WC than with BMI. Previous studies have shown associations between BMI, WC, and CysC.[20,23] CysC is an endogenous inhibitor of cathepsin proteases. A recent report has shown that CysC affects adipose tissue and vascular homeostasis through the inhibition of cathepsins.[39] This particular study indicated that WC is more closely related to CysC than BMI. Magnusson et al[20] showed that abdominal obesity is the only component of MetS that is significantly associated with increased baseline levels of CysC. Another study illustrated a stronger correlation between CysC and WC compared to BMI.[40] These data indicate that the close association between CysC and MetS may be mediated by visceral fat.

A limitation of our study is that it only included subjects who visited our center for a checkup. The analysis was also limited by the cross-sectional design.

In conclusion, we found the CysC was more closely associated with the presence of MetS, as compared Scr or $eGFR_{CKD-EPI}$. CysC was positively correlated with BMI, and more strongly, positively correlated with WC and inflammation.

Table 2

Comparison of data among the different quartiles of CysC.

CysC, mg/L (quartiles)					
	Q1 (0.33–0.63)	Q2 (0.64–0.75)	Q3 (0.76–0.89)	Q4 (0.90–1.81)	P*
n (all: 5866)	1543	1491	1404	1428	
Sex ratio (M/F), %	600/943 (38.9/61.1)	981/510 (65.8/34.2)	994/410 (70.8/29.2)	1210/218 (84.7/15.3)†	<0.001
Age, years	39 (33–45)	42 (34–49)	43 (36–51)	47 (39–54)	<0.001
TG, mmol/L	1.09 (0.74–1.70)	1.36 (0.90–2.14)	1.44 (0.93–2.22)	1.59 (1.09–2.29)	<0.001
LDL-C, mmol/L	2.60 (2.21–3.11)	2.80 (2.33–3.32)	2.87 (2.40–3.39)	2.98 (2.52–3.53)	<0.001
HDL-C, mmol/L	1.44 (1.23–1.68)	1.28 (1.10–1.50)	1.22 (1.04–1.44)	1.11 (0.95–1.31)	<0.001
FPG, mmol/L	4.86 (4.54–5.16)	4.84 (4.53–5.20)	4.85 (4.52–5.21)	4.92 (4.58–5.35)	<0.001
hsCRP, mg/L	0.4 (0.2–0.7)	0.5 (0.2–0.9)	0.5 (0.3–1.1)	0.7 (0.4–1.5)	<0.001
BMI, kg/m^2	22.68 (20.82–24.88)	23.78 ± 3.24	24.01 ± 3.27	24.72 ± 3.16	<0.001
WC, cm	80 (73–86)	84 (76–90)	86 (78–92)	88 (82–94)	<0.001
SBP, mm Hg	117 (106–129)	122 (111–133)	125 (113–137)	130 (118–143)	<0.001
DBP, mm Hg	70 (62–79)	74 (66–82)	75 (67–84)	80 ± 12	<0.001
Scr, μmol/L	58 (51–69)	69 (58–77)	70 ± 15	75 (68–83)	<0.001
$eGFR_{CKD-EPI}$, mL/min/1.73 m^2	114 (107–120)	108 (101–116)	106 ± 12	102 (93–110)	<0.001

The normal-distribution data were expressed as the mean ± SD. Skewed distribution data were expressed as the median with 25th and 75th percentiles (P_{25}–P_{75}). BMI = body mass index, CysC = cystatin C, DBP = diastolic blood pressure, $eGFR_{CKD-EPI}$ = estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration), FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, hsCRP = high sensitivity C-reactive protein, LDL-C = low-density lipoprotein cholesterol, SBP = systolic blood pressure, SD = standard deviation, TG = triglyceride, WC = waist circumference.

* *P* values for the comparisons between the 1st and 4th quartile of CysC. Mann–Whitney *U* tests were used.

† Comparison of sex between the 1st and 4th quartile of CysC using Chi-square test.

Table 3

Association of CysC, hsCRP and the presence of MetS in logistic regression models.

						95.0% CI for OR	
n = 5866	B	S.E.	Wald	*P*	OR	Lower	Upper
Sex	1.317	0.226	33.934	<0.001	3.732	2.396	5.812
Age, years	0.028	0.012	5.319	0.021	1.028	1.004	1.053
hsCRP, mg/L	0.050	0.012	18.244	<0.001	1.051	1.027	1.075
CysC, mg/L	1.204	0.198	36.803	<0.001	3.334	2.259	4.919
Scr, μmol/L	−0.024	0.014	2.895	0.089	0.976	0.949	1.004
$eGFR_{CKD-EPI}$, mL/min/1.73 m^2	−0.018	0.016	1.306	0.253	0.982	0.952	1.013

Variable (s) entered on step 1: sex, age, hsCRP, CysC, Scr, and eGFR. 95%CI = 95% confidence interval, CysC = cystatin C, $eGFR_{CKD-EPI}$ = estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration), hsCRP = high sensitivity C-reactive protein, MetS = metabolic syndrome, OR = odds ratio, Scr = serum creatinine.

Table 4

Further partial correlation analysis between BMI, WC, hsCRP, Scr, and eGFR with CysC.

(n = 5866)	*r*	*P*
BMI, kg/m^2	0.029	0.0260
WC, cm	0.061	<0.0001
hsCRP, mg/L	0.189	<0.0001
Scr, μmol/L	0.227	<0.0001
$eGFR_{CKD-EPI}$, mL/min/1.73 m^2	−0.210	<0.0001

r: Spearman partial correlation coefficient after adjustment for age and sex. BMI = body mass index, CysC = cystatin C, $eGFR_{CKD-EPI}$ = estimated glomerular filtration rate (Chronic Kidney Disease Epidemiology Collaboration), hsCRP = high sensitivity C-reactive protein, Scr = serum creatinine, WC = waist circumference.

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References

[1] Fliser D, Ritz E. Serum cystatin C concentration as a marker of renal dysfunction in the elderly. Am J Kidney Dis 2001;37:79–83.
[2] Filler G, Bökenkamp A, Hofmann W, et al. Cystatin C as a marker of GFR – history, indications, and future research. Clin Biochem 2005;38: 1–8.
[3] Pavkov ME, Knowler WC, Hanson RL, et al. Comparison of serum cystatin C, serum creatinine, measured GFR, and estimated GFR to assess the risk of kidney failure in American Indians with diabetic nephropathy. Am J Kidney Dis 2013;62:33–41.
[4] Mussap M, Dalla Vestra M, Fioretto P, et al. Cystatin C is a more sensitive marker than creatinine for the estimation of GFR in type 2 diabetic patients. Kidney Int 2002;61:1453–61.
[5] Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis 2002;40:221–6.
[6] Ito R, Yamakage H, Kotani K, et al. Comparison of cystatin C-and creatinine-based estimated glomerular filtration rate to predict coronary heart disease risk in Japanese patients with obesity and diabetes. Endocr J 2015;62:201–7.
[7] Shlipak MG, Matsushita K, Ärnlöv J, et al. Cystatin C versus creatinine in determining risk based on kidney function. N Engl J Med 2013;369:932–43.
[8] Shlipak MG, Katz R, Fried LF, et al. Cystatin-C and mortality in elderly persons with heart failure. J Am Coll Cardiol 2005;45:268–71.
[9] Shlipak MG, Sarnak MJ, Katz R, et al. Cystatin C and the risk of death and cardiovascular events among elderly persons. N Engl J Med 2005;352: 2049–60.
[10] Sánchez-Chaparro MA, Calvo-Bonacho E, González-Quintela A, et al. Occupation-related differences in the prevalence of metabolic syndrome. Diabetes Care 2008;31:1884–5.
[11] Guize L, Thomas F, Pannier B, et al. All-cause mortality associated with specific combinations of the metabolic syndrome according to recent definitions. Diabetes Care 2007;30:2381–7.
[12] Yu S, Guo X, Yang H, et al. An update on the prevalence of metabolic syndrome and its associated factors in rural northeast China. BMC Public Health 2014;14:877.
[13] Grundy SM. Metabolic syndrome: connecting and reconciling cardio-vascular and diabetes worlds. J Am Coll Cardiol 2006;47:1093–100.
[14] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415–28.
[15] Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001;24:683–9.
[16] Akilen R, Pimlott Z, Tsiami A, et al. The use of complementary and alternative medicine by individuals with features of metabolic syndrome. J Integr Med 2014;12:171–4.
[17] Kowalska K, Olejnik A. Current evidence on the health-beneficial effects of berry fruits in the prevention and treatment of metabolic syndrome. Curr Opin Clin Nutr Metab Care 2016;19:446–52.
[18] Tsujimura A, Miyagawa Y, Takezawa K, et al. Is low testosterone concentration a risk factor for metabolic syndrome in healthy middle-aged men? Urology 2013;82:814–9.
[19] Tang Q, Liu Z, Tang Y, et al. High serum ferritin level is an independent risk factor for metabolic syndrome in a Chinese male cohort population. Diabetol Metab Syndr 2015;7:11.
[20] Magnusson M, Hedblad B, Engström G, et al. High levels of cystatin C predict the metabolic syndrome: the prospective Malmö Diet and Cancer Study. J Intern Med 2013;274:192–9.
[21] Vigil L, Lopez M, Condés E, et al. Cystatin C is associated with the metabolic syndrome and other cardiovascular risk factors in a hypertensive population. J Am Soc Hypertens 2009;3:201–9.
[22] Servais A, Giral P, Bernard M, et al. Is serum cystatin-C a reliable marker for metabolic syndrome? Am J Med 2008;121:426–32.
[23] Muntner P, Winston J, Uribarri J, et al. Overweight, obesity, and elevated serum cystatin C levels in adults in the United States. Am J Med 2008;121:341–8.
[24] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.
[25] Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735–52.
[26] Khunti K, Davies M. Metabolic syndrome. BMJ 2005;331:1153–4.
[27] Hu G, Qiao Q, Tuomilehto J, et al. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. Arch Intern Med 2004;164: 1066–76.
[28] Riediger ND, Clara I. Prevalence of metabolic syndrome in the Canadian adult population. CMAJ 2011;183:E1127–34.
[29] Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287:356–9.
[30] Liu P, Ma F, Lou H, et al. Relationship between cystatin C and metabolic syndrome among Chinese premenopausal and postmenopausal women without recognized chronic kidney disease. Menopause 2015;22: 217–23.
[31] Lee SH, Park SA, Ko SH, et al. Insulin resistance and inflammation may have an additional role in the link between cystatin C and cardiovascular disease in type 2 diabetes mellitus patients. Metabolism 2010;59:241–6.
[32] Bagry HS, Raghavendran S, Carli F. Metabolic syndrome and insulin resistance: perioperative considerations. Anesthesiology 2008;108: 506–23.
[33] Festa A, D'Agostino RJr, Howard G, et al. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). Circulation 2000;102:42–7.
[34] Koenig W, Twardella D, Brenner H, et al. Plasma concentrations of cystatin C in patients with coronary heart disease and risk for secondary cardiovascular events: more than simply a marker of glomerular filtration rate. Clin Chem 2005;51:321–7.

[35] Okura T, Jotoku M, Irita J, et al. Association between cystatin C and inflammation in patients with essential hypertension. Clin Exp Nephrol 2010;14:584–8.
[36] Lee SH, Park SA, Ko SH, et al. Insulin resistance and inflammation may have an additional role in the link between cystatin C and cardiovascular disease in type 2 diabetes mellitus patients. Metabolism 2010;59:241–6.
[37] Shlipak MG, Katz R, Sarnak MJ, et al. Cystatin and prognosis for cardiovascular and kidney outcomes in elderly persons without chronic kidney disease. Ann Intern Med 2006;145:237–46.
[38] Coll E, Botey A, Alvarez L, et al. Serum cystatin C as a new marker for noninvasive estimation of glomerular filtration rate and as a marker for early renal impairment. Am J Kidney Dis 2000;36:29–34.
[39] Naour N, Fellahi S, Renucci JF, et al. Potential contribution of adipose tissue to elevated serum cystatin C in human obesity. Obesity (Silver Spring) 2009;17:2121–6.
[40] Panaich SS, Veeranna V, Bavishi C, et al. Association of cystatin C with measures of obesity and its impact on cardiovascular events among healthy US adults. Metab Syndr Relat Disord 2014;12:472–6.