Diabetes & Metabolic Syndrome: Clinical Research & Reviews xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Metabolic syndrome components and estimated glomerular filtration rate based on creatinine and/or cystatin C in young adults: A gender issue?

Thalia Medeiros[a,*], Natalia Fonseca do Rosário[a], Nycole Abreu Gama[a], Lyris Anunciata Demétrio Mérida[a], Amanda Sampaio Storch[a], Leda Ferraz[a], Patricia de Fátima Lopes[a,b], Andrea Alice da Silva[a,b], Jorge Reis Almeida[a,c]

[a] *Laboratório Multiusuário de Apoio à Pesquisa em Nefrologia e Ciências Médicas, Departamento de Medicina Clínica, Faculdade de Medicina, Universidade Federal Fluminense, Rio de Janeiro, Brazil*
[b] *Departamento de Patologia, Faculdade de Medicina, Universidade Federal Fluminense, Rio de Janeiro, Brazil*
[c] *Serviço de Nefrologia, Departamento de Medicina Clínica, Faculdade de Medicina, UFF, Rio de Janeiro, Brazil*

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Metabolic syndrome
Young adult
Chronic kidney disease
Glomerular filtration rate

ABSTRACT

Aims: This work aims to identify correlations between estimated glomerular filtration rate (eGFR) based on creatinine and/or cystatin C (Cr, CysC) with metabolic syndrome (MS) components in young adults, according to gender.
Material and methods: This is a cross sectional study, where young adults aged between 18 and 30 were matched by gender, age and body mass index. All subjects underwent clinical evaluation and blood sampling for laboratory measurements. MS was determined according to the JIS criteria. The eGFR was estimated using CKD-EPI equations ($eGFR_{Cr}$; $eGFR_{CysC}$; $eGFR_{Cr\text{-}CysC}$).
Results: We evaluated 78 subjects with a mean age of 24.5 years. 10.2% had MS, with higher incidence among males (15.4% ♂ vs. 5.1% ♀). Elevated waist circumference was the MS component most observed. Significant correlations (Pearson; $p < 0.05$) between eGFR and metabolic markers were observed only in males. In addition, we observed a significant association between the increase of MS components and the decay of $eGFR_{Cr}$ and $eGFR_{Cr\text{-}CysC}$ (zero vs. two or more components, ANOVA, $p < 0.05$) only among males.
Conclusion: eGFR decay associated with components of MS and insulin resistance in young male adults could represent a worrying specific risk and indicate that further studies are needed to better understand these findings.

1. Introduction

Metabolic syndrome (MS) is characterized by a set of cardiometabolic risk factors including obesity, hypertension, hyperglycemia, and dyslipidemia [1]. MS is closely associated with the development of cardiovascular diseases and possibly, also with an impairment of renal function. Studies have shown that the MS prevalence among females is crescent and mainly centered in post-menopausal period [2]. However, the presence of higher visceral fat deposits in male subjects favors the early development of insulin resistance, dyslipidemia and hypertension [4]. Moreover, the transition between adolescence to adulthood is associated with changes in lifestyle that could represent an increased risk for obesity-related comorbities [5].

Chronic kidney disease (CKD) is usually asymptomatic in the early stages. For renal function assessment, estimation of glomerular filtration rate (eGFR) has been performed by using

Abbreviations: BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; Cr, creatinine; CysC, cystatin C; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL-c, high density lipoprotein associated with cholesterol; HOMA-IR, homeostatic model for the assessment of insulin resistance; JIS, Joint Interim Statement; LDL-c, low density lipoprotein associated with cholesterol; MS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UA, uric acid; WC, waist circumference.

* Corresponding author at: Laboratório Multiusuário de Apoio à Pesquisa em Nefrologia e Ciências Médicas, Hospital Universitário Antônio Pedro – Marques de Paraná 303, Niterói, Rio de Janeiro, CEP 24033900, Brazil.
E-mail addresses: thaliamedeiros@id.uff.br (T. Medeiros), nataliarosario@id.uff.br (N.F. do Rosário), nycoleabreu@id.uff.br (N.A. Gama), lyrisdemetriomerida@gmail.com (L.A.D. Mérida), amandasstorch@gmail.com (A.S. Storch), ledaferraz@id.uff.br (L. Ferraz), patricialopes@id.uff.br (P. de Fátima Lopes), aasilva@id.uff.br (A.A. da Silva), jorgereis@id.uff.br (J.R. Almeida).

http://dx.doi.org/10.1016/j.dsx.2017.03.015
1871-4021/

formulas based on serum levels of creatinine (Cr) and/or cystatin C (CysC) [6]. Some authors recommended the use of formulas based on CysC due to the less influence of muscle mass [7]. However, recent studies reported that CysC levels could be influenced by age, gender [6,8] and obesity [9]. Considering all these findings, the combined formula ($eGFR_{Cr\text{-}CysC}$) could represent an advantage in promote the balance on the effect of these factors, including the population of young adults [6].

Despite the attention in the scientific literature about the relationship between MS and CKD, a few number of studies were conducted in order to identify risk factors associated with renal disease in young adults. Therefore, the present study aims to identify, according to gender, the correlation between kidney function, through the estimation of GFR using equations based on Cr and/or CysC, and the MS components in young adults.

2. Material and methods

2.1. Study design

This is an observational cross-sectional study, approved by the Research Ethics Committee of Universidade Federal Fluminense (HUAP/UFF) (CAAE: 0394.0.258.000-11). Young adults of both sexes aged between 18 and 30 years old were included. Exclusion criteria were: previous history of cancer, autoimmune and genetic diseases; recent infections; pregnancy and lactation; and chronic use of corticosteroids, beta blockers and diuretics. All volunteers were enrolled after a written informed consent was obtained.

2.2. Clinical and laboratory measurements

The anthropometric measurements were obtained: current weight (kg) and height (m) (Digital scale Charder® MOD MS 6121R/Wall Stadiometer Welmy®), for calculating the body mass index [BMI = weight/(height)^2, kg/m^2]; measurement of waist circumference (WC; cm) using inelastic tape, taken at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest; blood pressure (BP; mmHg) by using a digital arm BP monitor (model MA100 the Master Line, G-TECH®) in three steps in the left arm with a 5 min interval, after resting in a sitting position for at least 10 min. Finally, the subjects were matched by gender, coinciding one year age ranges; and according to the same body mass index (BMI) ranges.

Venous blood samples were obtained after an overnight 12 h fasting. Serum levels of total cholesterol (TC), cholesterol associated with high density lipoproteins ($HDL\text{-}_C$), cholesterol associated with low density lipoprotein ($LDL\text{-}_C$), triglycerides (TG), fasting glucose, insulin, glycated hemoglobin, Cr and uric acid (UA) were performed by automated methods using Siemens – Dimension RxL Max® equipment. The serum CysC were evaluated using commercial enzyme immunoassay kit (cat. RD191009100, Biovendor Research and Diagnostic Products®, Czech Republic). Insulin resistance was determined according to the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR): [fasting plasma glucose (mmol/L) × fasting insulin (mIU/mL)]/22 5].

2.3. MS classification

We adopted the Joint Interim Statement (JIS; 2009) criteria for MS classification, which considers the presence of at least three of the following parameters: WC, adjusted for the Latin American population, ≥90 cm for men and ≥80 cm for women; TG ≥ 150 mg/dL and/or use of statins; $HDL\text{-}_C$ < 40 mg/dL for men and HDL-C < 50 mg/dL for women; systolic BP (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg and/or use of antihypertensive drugs; and fasting glucose ≥100 mg/dL and/or use of insulin or hypoglycemic medications [1].

2.4. Estimation of GFR

Three different equations derived from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) study were used to estimate GFR on the basis of serum Cr and/or CysC ($eGFR_{Cr}$, $eGFR_{CysC}$ and $eGFR_{Cr\text{-}CysC}$) [10]. Besides the serum Cr and the CysC, we used only age and sex in the equations. We did not use any correction factor for ethnicity because of the grade of miscegenation present in the Brazilian population [11].

2.5. Statistical analysis

Results were expressed as mean ± SD. Differences between genders were evaluated with Student's *t*-test or Mann-Whitney

Table 1
Clinical and laboratory profile of young adult volunteers (n = 78).

Parameters	Total (n = 78)	Male (n = 39)	Female (n = 39)	p[a]
Age (y)	24.5 ± 2.8	24.9 ± 2.8	24.2 ± 2.7	NS
Fasting glucose (mg/dL)	85.7 ± 6.6	86.9 ± 6.9	84.5 ± 6.0	NS
HOMA-IR	1.27 ± 0.9	1.27 ± 1.03	1.25 ± 0.7	NS
Glycated hemoglobin (%)	5.4 ± 0.29	5.38 ± 0.29	5.46 ± 0.28	NS
Triglycerides (mg/dL)	93 ± 49.3	83.7 ± 46.9	102.3 ± 50.5	NS
Total cholesterol (mg/dL)	168.6 ± 30.7	158.5 ± 26.4	178.8 ± 31.7	0.005
LDL-c (mg/dL)	95 ± 25.9	93.1 ± 25.9	96.8 ± 26.1	NS
HDL-c (mg/dL)	55.3 ± 15.1	48.5 ± 13.7	61.3 ± 13.7	< 0.0001
Uric acid (mg/dL)	4.35 ± 1.33	5.17 ± 1.21	3.52 ± 0.84	< 0.0001
$eGFR_{Cr}$ (mL/min/1.73m^2)	94.9 ± 14.9	94.9 ± 14.9	95 ± 16.2	NS
$eGFR_{CysC}$ (mL/min/1.73m^2)	141.6 ± 7.5	141.6 ± 7.5	140.9 ± 7.6	NS
$eGFR_{Cr\text{-}CysC}$ (mL/min/1.73m^2)	121.6 ± 12.6	121.6 ± 12.6	120.8 ± 13.1	NS
BMI (kg/m^2)	25.7 ± 5.6	25.7 ± 5.4	25.7 ± 5.9	NS
WC (cm)	87.4 ± 13.4	88.5 ± 13.9	86.3 ± 13.0	NS
SBP (mmHg)	114.3 ± 11.6	120.6 ± 11.2	108.1 ± 8.2	<0.0001
DBP (mmHg)	71.3 ± 7.8	73.9 ± 7.4	68.7 ± 7.3	0.001

Values are expressed as mean ± SD.
HOMA-IR: homeostatic model assessment of insulin resistance; LDL-c: low density lipoprotein; HDL-c: high density lipoprotein; eGFR: estimated glomerular filtration rate; Cr: creatinine; CysC: cystatin C; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure.
[a] Student's *t*-test was performed to evaluate differences between genders.

Please cite this article in press as: T. Medeiros, et al., Metabolic syndrome components and estimated glomerular filtration rate based on creatinine and/or cystatin C in young adults: A gender issue?, Diab Met Syndr: Clin Res Rev (2017), http://dx.doi.org/10.1016/j.dsx.2017.03.015