ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Phase angle and metabolic parameters in severely obese patients

Ángulo de fase y parámetros metabólicos en pacientes con obesidad severa

Karine Curvello-Silva[1], Lilian Ramos[1,2], Cláudia Sousa[3], and Carla Daltro[1,2,3,4]

[1]Escola de Nutrição. Universidade Federal da Bahia. Salvador, Bahia. Brazil. [2]Program in Food, Nutrition and Health. Escola de Nutrição. Universidade Federal da Bahia. Salvador, Bahia. Brazil. [3]Núcleo de Tratamento e Cirurgia da Obesidade. Salvador, Bahia. Brazil. [4]Program in Medicine and Health. Escola de Nutrição. Universidade Federal da Bahia. Salvador, Bahia. Brazil

Abstract

Introduction: obese patients present an inflammatory and metabolic profile that leads to oxidative stress and cellular damage. Phase angle is an indicator of cellular integrity and has been proposed as a prognostic parameter for changes in the metabolic profile.

Objective: to investigate the possible association between phase angle and metabolic parameters in obese patients.

Material and method: this was a cross-sectional study of adult obese patients who attended a specialized clinic between 2014 and 2016. All patients were ≥ 18 years of age, with a body mass index ≥ 35 kg/m^2. All data were obtained from medical records and made part of the clinical protocol. Patients were divided into two groups using a cutoff point for phase angle, and the groups were compared using the Kruskal-Wallis or Chi-squared test for quantitative and categorical variables, respectively. Correlations were identified by Spearman's and Pearson's correlation analyses. All between-group differences were considered statistically significant at $p \leq 0.05$.

Results: a low phase angle was present in 30.5 % of the 141 patients enrolled in the study. We found an association between low phase angle and presence of hyperuricemia ($p = 0.018$) when adjusted for waist circumference, dysglycemia, arterial hypertension, and hyperuricemia. There was no correlation between phase angle and the components of body composition.

Conclusions: there is an association of phase angle with uric acid levels, but not with other metabolic parameters.

Keywords:

Phase angle. Metabolic profile. Obesity. Bioimpedance. Cardiovascular risk. Uric acid.

Resumen

Introducción: los pacientes obesos presentan un perfil inflamatorio y metabólico que provoca estrés oxidativo y daño celular. El ángulo de fase es un indicador de integridad celular que se ha propuesto como parámetro pronóstico de los cambios del perfil metabólico.

Objetivo: investigar la posible asociación entre el ángulo de fase y los parámetros metabólicos en pacientes obesos.

Material y método: estudio transversal de pacientes obesos adultos que asistieron a una clínica especializada entre 2014 y 2016. Todos los pacientes tenían ≥ 18 años de edad y un índice de masa corporal ≥ 35 kg/m^2. Todos los datos se obtuvieron de los registros médicos y formaron parte del protocolo clínico. Los pacientes se dividieron en dos grupos usando un punto de corte para el ángulo de fase, y los grupos se compararon usando la prueba de Kruskal-Wallis o del chi cuadrado para las variables cuantitativas y categóricas, respectivamente. Las correlaciones se identificaron mediante el análisis de correlación de Spearman y el de Pearson. Todas las diferencias entre grupos se consideraron estadísticamente significativas si $p \leq 0.05$.

Resultados: se observó un ángulo de fase bajo en el 30,5 % de los 141 pacientes incluidos en el estudio. Encontramos una asociación entre el ángulo de fase bajo y la presencia de hiperuricemia ($p = 0.018$) cuando se ajustó para la circunferencia de la cintura, la disglucemia, la hipertensión arterial y la hiperuricemia. No hubo correlación entre el ángulo de fase y los componentes de la composición corporal.

Conclusiones: el ángulo de fase presenta asociación con los niveles plasmáticos de ácido úrico pero no con otros parámetros metabólicos.

Palabras clave:

Ángulo de fase. Perfil metabólico. Obesidad. Bioimpedancia. Riesgo cardiovascular. Ácido úrico.

Received: 04/06/2020 • Accepted: 25/07/2020

Conflicts of interest: the authors declare no conflicts of interest of any kind.

Acknowledgements: we must thank Dr. Erivaldo Alves, bariatric surgeon and director of the Center for the Treatment and Surgery of Obesity, for allowing us to access the patients' data, and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES-Brazil) for their support to Mrs. Thalane Souza.

Curvello-Silva K, Ramos L, Sousa C, Daltro C. Phase angle and metabolic parameters in severely obese patients. Nutr Hosp 2020;37(6):1130-1134

DOI: http://dx.doi.org/10.20960/nh.02928

Correspondence:

Karine Curvello-Silva. Escola de Nutrição. Rua Basílio da Gama, s/n. Sala C13. Canela, 40.110-907 Salvador, Bahia, Brasil
e-mail: karinelc@gmail.com

INTRODUCTION

Phase angle (PA) is an indicator determined by bioelectrical impedance analysis (BIA), and is associated with membrane integrity, body cell mass, and fluid balance (1). These parameters can help the health team to estimate a patient's clinical and surgical prognosis. Some studies have been conducted with postoperative, oncological, HIV, and dialytic patients, showing a reduction in cellularity under these critical conditions (2,3).

Obese patients frequently present a chronic inflammatory process characterized by increased proinflammatory and decreased anti-inflammatory cytokine levels, leading to poor glycemic control, dyslipidemia, hyperuricemia, and endothelial damage. All these conditions are associated with atherosclerosis, explaining the higher risk for a cardiovascular event, the main cause of death among obese patients (4,5). This subclinical inflammation status increases the production of reactive oxygen species (ROS) that oxidize lipids and proteins, including those in the cell membrane, which decreases cellularity (6) and interferes in their phase angle values.

Therefore, the aim of this study was to investigate the possible association between phase angle, as an indicator of cellular integrity, and metabolic parameters in severely obese patients.

MATERIALS AND METHODS

STUDY POPULATION AND SAMPLE

This cross-sectional study enrolled severely obese patients who consecutively attended a center specializing in the treatment of obesity from January 2014 to July 2016. A multidisciplinary team assessed and recorded the clinical, biochemical, anthropometric, and segmented electric bioimpedance parameters routinely used by the clinic.

The sample included individuals with BMI (body mass index) ≥ 35 kg/m^2; ≥ 18 years old; without cardiac, hepatic, pancreatic, renal or pulmonary insufficiency; who underwent a segmented electric bioimpedance assessment in the clinic.

VARIABLES

We analyzed the possible association between phase angle and fasting blood glucose, glycated hemoglobin (HbA1c), homeostatic model assessment for insulin resistance (HOMA-IR), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), total cholesterol, non-HDL cholesterol, and uric acid. The association between phase angle and some components of body composition was also evaluated. All these variables are related to higher cardiovascular risk, and are routinely evaluated in the preoperative workup of very obese patients.

HOMA-IR was calculated using the formula: HOMA-IR = [(glycemia (mg/dL)) x (insulinemia (µU/mL))] / 405 (7), and non-HDL cholesterol by the formula: total cholesterol – HDL-c (7). No diabetic patients were considered for HOMA-IR analysis.

Resistance (R) and capacitance (Xc) were obtained with direct segmental multifrequency bioelectrical impedance analysis (DSM-BIA) (INBODY 720®), and impedance (Z) was calculated by the software in the equipment. Phase angle (in degrees) was calculated as follows: arctan Xc/R. We considered phase angle values under 5° as low (3). Percentage skeletal muscle mass (SMM) was calculated as % SMM – (skeletal muscle mass x 100) / weight), and skeletal muscle mass was determined by DSM-BIA in kilograms.

Weight was obtained with the same equipment following the protocol indicated by the manufacturer (Biospace®). Height was measured using a stadiometer with a gradation of 1 mm. Body mass index was calculated and classified using the WHO recommendations (8). Waist circumference was measured by a trained team, and values higher than 90 cm (cutoff point for individuals from Central and South America) were considered elevated (9).

The criteria used for MetS diagnosis were proposed by the Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention (9). We considered to be dysglycemia any alterations of glucose metabolism such as elevated fasting plasma glucose (glycemia ≥ 100 mg/dL), glucose intolerance, or diabetes mellitus as defined by Alberti et al. (9). The dyslipidemia criteria used were those proposed by Faludi et al. (7).

Hyperuricemia was defined as an uric acid > 6 mg/dL and > 7 mg/dL in women and men, respectively (10). The medical team diagnosed diabetes and hypertension on the basis of cutoff points for blood pressure and fasting plasma glucose, also as described by Alberti et al. (9).

STATISTICAL ANALYSIS

The statistical package SPSS for Windows® v. 16.0 was used for the analysis. Quantitative variables are presented as mean and standard deviation (SD) or median and interquartile range. Categorical variables are shown as absolute and relative frequencies.

The subjects were divided into two groups using the cutoff point for phase angle, and classified into low phase angle "yes" or "no". The groups were compared using Student's *t*-test and the Mann-Whitney and Chi-squared tests. Correlations were calculated using Pearson's and Spearman's correlation tests. After the initial analysis, the variables that showed a p value < 0.20 between groups were adjusted in the logistic regression (waist circumference, dysglycemia, arterial hypertension, and hyperuricemia; the others were not included because of collinearity). P values < 0.05 were considered statistically significant.

ETHICS

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Human Research Ethics Committee at a local institution under the code number 1.534.548/2016. Patient records were received by the clinic in an Excel 2010 file, without names or any other patient identifiers.

RESULTS

The sample consisted of 141 subjects referred for bariatric surgery with an average (standard deviation) age of 37.9 (10.7) years, and the majority were women (80.1 %). Their BMI ranged from 35.0 to 64.0 kg/m^2 and their phase angle from 3.32 ° to 7.21 °. Other demographics and clinical data are presented in table I.

Table II describes subject characteristics according to phase angle. It was observed that those with a low phase angle had higher BMI, WC, and glycated hemoglobin values. Moreover, they presented more hyperuricemia, arterial hypertension, dysglycemia, and metabolic syndrome, although these differences did not reach statistical significance. However, the regression analysis showed an association between hyperuricemia and low phase angle.

The correlations between metabolic parameters, body composition variables, and phase angle are shown in table III. There was no statistically significant linear association between them.

Table I. Demographic and clinical characteristics of severely obese patients attended to in a center for the treatment of obesity between 2014 and 2016

Characteristics	n	Results
Age (years)*	140	37.9 (10.7)
Female	141	113 (80.1 %)
Physical activity	135	21 (15.6 %)
Diabetes mellitus	130	19 (14.6 %)
Arterial hypertension	130	60 (46.2 %)
Metabolic syndrome	141	72 (51.1 %)
Dyslipidemia	141	96 (68.1 %)
Dysglycemia	137	46 (33.6 %)
Hyperuricemia	122	34 (27.9 %)
BMI (kg/m^2)*	141	41.9 (5.4)
Waist circumference (cm)*	134	120.0 (13.2)
Glycemia (mg/dL)†	137	100.6 (23.7)
HOMA-IR†,‡	97	4.7 (3.0-6.5)
HbA1c (%)†	132	5.7 (5.4-6.1)
Total cholesterol (mg/dL)*	141	195.8 (37.6)
LDL-c (mg/dL)*	137	114.6 (35.0)
HDL-c (mg/dL)*	139	48.0 (41.0-58.0)
Triglycerides (mg/dL)†	139	136.0 (97.0-180.0)
Non-HDL cholesterol (mg/dL)*	139	145.2 (38.2)
% SMM*	141	24.9 (4.9)
Body fat (%)†	141	45.9 (36.1-51.0)
Phase angle (°)*	141	5.4 (0.73)

**Average (standard deviation); †Median (interquartile range); ‡Diabetic patients were excluded to calculate HOMA-IR. MetS: metabolic syndrome; BMI: body mass index; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; HbA1c: glycated hemoglobin; LDL-c: low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; VFA: visceral fat area; % SMM: (skeletal muscle mass x 100)/weight.*

DISCUSSION

Our findings showed that obese patients with low values of phase angle, an indicator of membrane integrity, presented a higher prevalence of hyperuricemia, even after adjustment for waist circumference, dysglycemia, and arterial hypertension.

Obesity is characterized by subclinical inflammation with important changes in the metabolic profile that contribute to a high cardiovascular risk. This profile frequently consists of dysglycemia and/or insulin resistance, elevation of triglycerides, and/or reduction of HDL-c, and in many cases hyperuricemia (4,5). This inflammatory condition is highlighted by an increase in markers of inflammation such as interleukin 6 (IL-6), C-reactive protein (CPR), PAI-1 (plasminogen activator inhibitor 1), leptin, and others (1,4).

This metabolic profile observed in very obese patients is associated with changes in body fluid distribution and reduced cellular integrity that can be estimated by phase angle (PA) measurement (10). This indicator is calculated based on impedance, which is determined by tetrapolar bioimpedance equipment. This analysis is a simple, fast, noninvasive, and safe technique for measuring human electrical tissue conductivity (2). The opposition of tissues to an alternating electric current presents two components: resistance (*R*) and reactance or capacitance (*Xc*). The first one is the capacity of tissues to restrict the flow of the current through the body, and is directly related to the amount of water present in the tissue. Capacitance is the resistive effect produced by the tissue and cell membranes that store part of the electric current, acting as a capacitor and creating a phase shift that is geometrically determined as PA (11).

Phase angle has been used as a good prognostic factor for postoperative complications, for different types of surgery, even after adjusting for individual confounders (3). It has also been proposed as a prognostic indicator for weight loss in patients undergoing bariatric surgery. Studies observed that lower values of baseline PA in those patients are associated with insufficient weight loss (2,12), suggesting that inflammation status in the preoperative period can be a determinant of surgery success. In our sample, approximately one third of patients presented with low PA, which indicates low cell integrity, and led us to hypothesize the presence of inflammation.

Although some studies indicate that low PA is also associated with some body composition components such as muscle mass and total body water (2,13), no statistically significant correlation was found between PA and percentage of skeletal muscle mass (% SMM) or other components evaluated in our study. We used the cutoff point of 5.0 ° proposed by Norman et al. (2012) (3) for the determination of low PA, as there is no reference value for our population, to our knowledge.

In our results, low PA was associated with hyperuricemia, even after adjustment for waist circumference, dysglycemia, arterial hypertension, and hyperuricemia. There was no separate association between PA and these other conditions. Hyperuricemia is a condition very often found in the obese population, including in our sample, and also associated with inflammation and higher cardiovascular risk (14,15).

Table II. Classification according to phase angle of 141 obese patients attended to at a specialized obesity treatment clinic between 2014 and 2016

Variables	Low phase angle		p	p adjusted§
	Yes	No		
	43 (30.5 %)	98 (69.5 %)		
Female gender	32 (74.4 %)	81 (82.7 %)	0.259	-
Age (years) *	38.8 (11.1)	37.6 (10.5)	0.523	-
BMI (kg/m²)†	42.0 (38.0-46.0)	40.0 (37.8-44.0)	0.099	-
WC (cm)*	123.3 (14.5)	118.6 (12.4)	0.062	0.754
HOMA-IR‡	4.6 (2.8-6.5)	4.7 (3.1-6.6)	0.684	-
HbA1c (%)†	6.0 (5.4-6.5)	5.6 (5.4-6.0)	0.089	-
TGL (mg/dL) †	144.0 (94.0-228.9)	132.0 (97.5-175.2)	0.316	-
LDL-c (mg/dL) *	111.0 (31.5)	116.3 (36.6)	0.414	-
HDL-c (mg/dL) †	47.0 (40.0-53.7)	49.0 (41.1-58.8)	0.230	-
Non HDL-c (mg/dL)*	143.3 (33.1)	146.0 (40.4)	0.699	-
% SMM†	28.1 (25.2-35.7)	27.6 (24.3-30.4)	0.202	-
% Body fat†	47.9 (36.4-51.4)	45.7 (34.6-50.9)	0.346	-
Dyslipidemia	31 (72.1 %)	65 (66.3 %)	0.499	-
Dysglycemia	18 (42.9 %)	28 (29.5 %)	0.126	0.108
Arterial hypertension	23 (56.1 %)	37 (41.6 %)	0.123	0.160
MetS	26 (60.5 %)	46 (46.9 %)	0.139	-
Hyperuricemia	15 (39.5 %)	19 (22.6 %)	0.054	*0.018*

**Average (standard deviation); †Median (interquartile range); ‡Diabetic patients were excluded to calculate HOMA-IR; §Variables included in the regression model: waist circumference, dysglycemia, arterial hypertension and hyperuricemia. MetS: metabolic syndrome; BMI: body mass index; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; HbA1c: glycated hemoglobin; LDL-c: low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; VFA: visceral fat area; % SMM: (skeletal muscle mass x 100)/weight; TGL: triglycerides.*

Table III. Correlation between metabolic parameters, body composition variables, and phase angle in 141 obese patients cared for at a specialized clinic for the treatment of obesity between 2014 and 2016

Correlations	r	p
Phase angle X metabolic parameters		
HOMA-IR†,‡	0.015	0.887
HbA1c†	- 0.167	0.056
Glycemia†	- 0.107	0.213
Triglycerides*	0.047	0.586
Non-HDL cholesterol*	0.103	0.226
Phase angle X body composition variables		
Waist circumference*	- 0.127	0.144
Body mass index*	- 0.138	0.101
% SMM*	- 0.036	0.673

**Pearson correlation; †Ro of Spearman; ‡Diabetic patients were excluded to calculate the correlation between HOMA-IR and phase angle. BMI: body mass index; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; HbA1c: glycated hemoglobin; % SMM: (skeletal muscle mass x 100)/weight.*

The results of Kennan et al. (2012) suggest that the increased cardiovascular risk associated with hyperuricemia precedes obesity or metabolic syndrome, and that higher levels of uric acid increase the risk for a cardiovascular outcome by a factor of 2-3 (14). It seems that uric acid contributes to oxidative stress, decreases the release of anti-inflammatory adipokines, and increases that of pro-inflammatory ones (16), but its contribution to cardiovascular events, as an independent factor, has not been settled (17,18). Considering the recognized contribution of uric acid to cardiovascular risk, our results led us to believe that a low PA in severe obese individuals could be used to evaluate cardiovascular risk in this population.

We found no significant correlation between PA and fasting glycemia or between PA and HbA1c, a long-term marker of glycemic control; however, for the latter, a tendency toward significance was found. This might indicate that exposure to high glycemic levels can affect cellular integrity (19).

The small number of patients enrolled in the study due to missing BIA results and some metabolic information could be a limitation of our study; nevertheless, only a few studies have investigated PA in very obese patients. This group, mainly when undergoing bariatric surgery, needs effective indicators to evaluate possible complications.

Our study shows the association between low phase angle and uric acid, and a tendency for them to be correlated with HbA1c in the presence of severe obesity. This association suggests that PA can indicate an unfavorable metabolic profile in those patients. Studies with higher numbers of participants should be conducted to further investigate the use of PA as an indicator of the metabolic profile.

REFERENCES

1. de Luis DA, Aller R, Romero E, Dueñas A, Perez Castrillon JL. Relation of phase angle tertiles with blood adipocytokines levels, insulin resistance and cardiovascular risk factors in obese women patients. Eur Rev Med Pharmacol Sci 2010;14(6):521-6.
2. Nicoletti CF, Camelo JS, dos Santos JE, Marchini JS, Salgado W, Nonino CB. Bioelectrical impedance vector analysis in obese women before and after bariatric surgery: changes in body composition. Nutrition 2014;30(5):569-74. DOI: 10.1016/j.nut.2013.10.013
3. Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis--clinical relevance and applicability of impedance parameters. Clin Nutr 2012;31(6):854-61. DOI: 10.1016/j.clnu.2012.05.008
4. Jung UJ, Choi M-S. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. Int J Mol Sci 2014;15(4):6184-223. DOI: 10.3390/ijms15046184
5. Han G-M, Gonzalez S, DeVries D. Combined effect of hyperuricemia and overweight/obesity on the prevalence of hypertension among US adults: result from the National Health and Nutrition Examination Survey. J Hum Hypertens 2014;28(10):579-86. DOI: 10.1038/jhh.2014.31
6. Griendling KK, Touyz RM, Zweier JL, Dikalov S, Chilian W, Chen Y-R, et al. Measurement of Reactive Oxygen Species, Reactive Nitrogen Species, and Redox-Dependent Signaling in the Cardiovascular System: A Scientific Statement From the American Heart Association. Circ Res 2016;119(5):e39-75. DOI: 10.1161/RES.0000000000000110
7. Faludi AA, Izar MCO, Saraiva JFK, Chacra APM, Bianco HT, Afiune Neto A, et al. Atualização Da Diretriz Brasileira De Dislipidemias E Prevenção Da Aterosclerose – 2017 [Internet]. Vol. 109, Arquivos brasileiros de cardiologia. Arq Bras Cardiol; 2017 [cited 2020 Mar 31]. Available from: https://pubmed.ncbi.nlm.nih.gov/28813069/ ?from_term=Atualiza%C3%A7%C3%A3o+da+Diretriz+ Brasileira+de+Dislipidemias+e+ Preven%C3%A7%C3%A3o+da+Aterosclerose+
8. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894(i-xii):1-253.
9. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120(16):1640-5. DOI: 10.1161/CIRCULATIONAHA.109.192644
10. Bosy-Westphal A, Danielzik S, Dörhöfer R-P, Later W, Wiese S, Müller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. JPEN J Parenter Enteral Nutr 2006;30(4):309-16. DOI: 10.1177/0148607106030004309
11. Gupta D, Lammersfeld CA, Burrows JL, Dahlk SL, Vashi PG, Grutsch JF, et al. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in advanced colorectal cancer. Am J Clin Nutr 2004;80(6):1634-8. DOI: 10.1093/ajcn/80.6.1634
12. Vassilev G, Hasenberg T, Krammer J, Kienle P, Ronellenfitsch U, Otto M. The Phase Angle of the Bioelectrical Impedance Analysis as Predictor of Post-Bariatric Weight Loss Outcome. Obes Surg 2017;27(3):665-9. DOI: 10.1007/s11695-016-2315-9
13. Barbosa-Silva MCG, Barros AJD. Bioelectric impedance and individual characteristics as prognostic factors for post-operative complications. Clin Nutr 2005;24(5):830-8. DOI: 10.1016/j.clnu.2005.05.005
14. Keenan T, Blaha MJ, Nasir K, Silverman MG, Tota-Maharaj R, Carvalho JAM, et al. Relation of uric acid to serum levels of high-sensitivity C-reactive protein, triglycerides, and high-density lipoprotein cholesterol and to hepatic steatosis. Am J Cardiol 2012;110(12):1787-92. DOI: 10.1016/j.amjcard.2012.08.012
15. Ferreira T da S, Fernandes JFR, Araújo L da S, Nogueira L de P, Leal PM, Antunes VP, et al. Serum Uric Acid Levels are Associated with Cardiometabolic Risk Factors in Healthy Young and Middle-Aged Adults. Arq Bras Cardiol 2018;111(6):833-40. DOI: 10.5935/abc.20180197
16. Lima WG, Martins-Santos MES, Chaves VE. Uric acid as a modulator of glucose and lipid metabolism. Biochimie 2015;116:17-23. DOI: 10.1016/j.biochi.2015.06.025
17. Zhao G, Huang L, Song M, Song Y. Baseline serum uric acid level as a predictor of cardiovascular disease related mortality and all-cause mortality: a meta-analysis of prospective studies. Atherosclerosis 2013;231(1):61-8. DOI: 10.1016/j.atherosclerosis.2013.08.023
18. Ford ES, Li C, Cook S, Choi HK. Serum concentrations of uric acid and the metabolic syndrome among US children and adolescents. Circulation 2007;115(19):2526-32. DOI: 10.1161/CIRCULATIONAHA.106.657627
19. Wu T, Dorn JP, Donahue RP, Sempos CT, Trevisan M. Associations of serum C-reactive protein with fasting insulin, glucose, and glycosylated hemoglobin: the Third National Health and Nutrition Examination Survey, 1988-1994. Am J Epidemiol 2002;155(1):65-71. DOI: 10.1093/aje/155.1.65