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CLINICAL STUDY

Continuous metabolic syndrome score (siMS) enables quantification of severity of cardiometabolic affliction in individuals not presenting with metabolic syndrome

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ABSTRACT
BACKGROUND: Assessment of degree of cardiometabolic affliction in subjects not presenting with metabolic syndrome (MS) yet, would be helpful in the management of preventive health maintenance.
OBJECTIVES: To evaluate continuous metabolic syndrome score (siMS) in estimation of severity of cardiometabolic affliction in individuals not presenting with MS.
METHODS: We analyzed data from 3166 volunteers (56 % females) aged ≥ 16 years. siMS score was calculated as waist/height/0.5 + fasting plasma glucose (FPG)/5.6 + triacylglycerols (TAG)/1.7 + systolic blood pressure (SBP)/130 – high-density lipoprotein cholesterol (HDL-C)/1.02 (males) or 1.28 (females). In siMS quintiles, numbers of individuals presenting with 0-to-5 MS components were calculated. MS was considered as the presence of any 3 out of its 5 components.
RESULTS: 33 % of participants without MS scored ≥ 4th quintile; 13 % of those free from MS components; 49 % of participants presenting with 1, and 83 % of those displaying 2 MS components. 11 % of individuals presented with MS, all but 1 displayed siMS within the 2 upper quintiles.
CONCLUSIONS: Considerable proportion of individuals without MS presented with siMS in range displayed by individuals presenting with MS. SiMS might be useful in estimation of severity of cardiometabolic affliction prior to manifestation of MS, to identify individuals requiring early intervention to counteract developing pathological processes *(Tab. 1, Ref. 21)*. Text in PDF *www.elis.sk.*
KEY WORDS: continuous metabolic syndrome score, metabolic syndrome components.

Introduction

Metabolic syndrome (MS) is a cluster of abnormalities that, if occurring together, impose an increased risk of development of chronic degenerative diseases, such as type 2 diabetes and cardiovascular diseases, even in young individuals (1, 2). Current diagnosis of MS is based on dichotomous classification, requiring either presence of any three out of the five criteria (e.g., central obesity, elevated blood pressure, elevated triacylglycerols (TAG), low high density lipoprotein cholesterol (HDL-C), and elevated fasting plasma glucose (FPG) (3); or presence of central obesity and any 2 out of remaining above mentioned criteria (4).

Dichotomous classification enables a simple, and unequivocal diagnosis of MS, but it does not allow for assessment of continuously rising cardiometabolic affliction. To this point, different approaches to calculate continuous MS score have been proposed (5–7). Continuous MS scores are precise, provide a way of tracking the changes in severity of cardiometabolic burden over time, and to evaluate its severity in individuals not presenting with MS yet. However, these scores are sample (e.g. sex- ethnicity/race-, and age) specific, not allowing between-population comparison, and often are not easy to calculate (5–7). The recently proposed siMS score (8, 9) is easy to calculate and comparable across different studies and populations, since it normalizes the individual measures to the accepted international standards (3, 4, 10). Its utility in following-up individual patients has been documented (8). As the continuous MS score is particularly suitable for detecting an increased cardiometabolic risk prior to the manifestation of MS (5–8), we asked what proportion of individuals not presenting with MS will score within the range of siMS score generally displayed by patients with MS. We assumed that the prevalence of these subjects might be rather high, as Slovaks present the highest cardiovascular mortality among the European Union countries (11). To confirm our hypothesis, we retrospectively calculated the siMS score in individuals formerly participating as volunteers in cross-sectional clinical studies and expressed frequency of sub-

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jects manifesting zero to five MS components in each siMS score quintile.

Participants and methods

We analyzed data from individuals participating during the period 2009–2012 in studies focusing on the prevalence of MS and its components. All volunteers were White Caucasians of Central European descent, residing, working or studying in western Slovakia. They were recruited via advertisements, or information provided at work or at schools. Exclusion criteria were any acute or chronic disease, particularly treatment for hypertension, dyslipidemia, diabetes, and participation in weight reducing programs, in females also pregnancy and lactation. From the database of 3750 volunteers aged 12-to-81 years, we extracted data on individuals aged ≥ 16 years, in whom data on body weight, height, waist circumference, blood pressure, FPG, TAG and HDL-C concentrations were available. Limiting the age to ≥ 16 years enabled to employ the same MS classification criteria in the whole cohort. Full-aged participants signed a written consent to participate, those aged < 18 years gave a verbal asset, and a written consent from their caregivers was obtained. The studies were approved by local Ethics Boards and conducted in accordance with the Declaration of Helsinki.

Anthropometric measurements were performed by qualified and trained medical personnel, according to the same protocol. Briefly, height was measured using stadiometer, body weight using electronic scales, waist circumference using flexible tape. Body mass index (BMI) and waist-to-height ratio were calculated. Blood pressure was measured in a sitting position after 10 minutes rest using a sphygmomanometer. The mean of last 2 measurements out of 3 was recorded.

Blood was sampled after overnight fasting from antecubital vein. FPG, TAG, and HDL-C were analyzed using standard laboratory methods.

siMS score was calculated according to Soldatovic et al (8), as follows:

siMS score = Waist/Height/0.5 + FPG/5.6 + TAG/1.7 + SBP/130 – HDL-C/1.02 (males) or 1.28 (females)

Waist and height were measured in cm; FPG, TAG, and HDL in mmol/l, and SBP in mm Hg. Quintiles of siMS score were calculated.

MS components were classified as present, if SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg, if TAG ≥ 1.7 mmol/l), HDL-C; < 1.03 mmol/l in males and < 1.29 mmol/l in females, or FPG ≥ 5.6 mmol/l. Participants presenting waist-to-height ratio ≥ 0.5 were classified as centrally obese (10). In each siMS score quintile, we expressed the number and frequencies of individuals free from MS components, and those presenting with 1, 2, 3, 4 or 5 components.

Data were presented as the mean ± standard deviation, median and interquartile range (IQR), or as counts and percentages. Frequencies were compared using Chi-square test, $p < 0.05$ was considered significant. Data were analyzed using the SPSS v.16 for Windows software (SPSS, USA).

Results

The study group consisted of 3166 individuals (56 % women). The mean age was 22.8 ± 11.0 years, BMI averaged 23.6 ± 4.6 kg/m^2, waist-to-height ratio averaged 0.46 ± 0.07; SBP averaged 118 ± 15 mm Hg, DBP averaged 74 ± 9 mm Hg, FPG averaged 4.9 ± 0.5 mmol/l, TAG concentration averaged 1.03 ± 0.64 mmol/l, and that of HDL-C concentration 1.38 ± 0.33 mmol/l. 23 % of participants presented with central obesity, 25 % had elevated blood pressure, 8 % presented elevated FPG, 11 % showed elevated TAG, and 23 % low HDL-C concentrations. siMS score ranged between 0.65 to 7.08, with median of 2.09 and IQR 1.79–2.48.

Approximately 50 % of participants did not manifest any sign of MS, 28 % presented with one component, 11 % presented with two components, 6 % manifested three components, 4 % displayed four components, and in 1 % of participants all five components of MS were present (Tab. 1).

Among participants manifesting MS (n = 349), all but one presented with siMS score within the 4th and 5th quintile (Tab. 1). Thus, 11 % of our participants, who presented with MS accounted for 27 % of those with siMS in upper 2 quintiles. Remaining 73 % of participants with siMS score in upper 2 quintiles did not fulfil 3 MS criteria, and 16 % did not even present with a single MS component.

About 13 % of participants free from any MS component presented with siMS score within the 4th and 5th quintile (Tab. 1). Forty-nine percent of individuals manifesting one component of MS displayed siMS score in the range of the upper two quintiles

Tab. 1. Distribution of individuals presenting with zero to five components of metabolic syndrome according to siMS score quintile.

No. of MS components	siMS score quintiles					All
	1Q (0.65–1.72) n=633	2Q (1.721–1.98) n=633	3Q (1.981–2.23) n=634	4Q (2.231–2.62) n=633	5Q (2.621–7.08) n=633	
0 (n; (% of subjects not presenting with MS components))	580 (36.4%)	469 (29.4%)	340 (21.3%)	189 (11.9%)	16 (1.0%)	1 594 (100%)
1 (n; (% of subjects presenting with 1 MS component))	47 (5.3%)	153 (17.3%)	253 (28.7%)	319 (36.1%)	111 (12.6%)	883 (100%)
2 (n; (% of subjects presenting with 2 MS components))	6 (1.7%)	11 (3.2%)	40 (11.8%)	108 (31.8%)	175 (51.5%)	340 (100%)
3 (n; (% of subjects presenting with 3 MS components))	0	0	1 (0.6%)	17 (9.4%)	162 (90.0%)	180 (100%)
4 (n; (% of subjects presenting with 4 MS components))	0	0	0	0	131 (100%)	131 (100%)
5 (n; (% of subjects presenting with 5 MS components))	0	0	0	0	38 (100%)	38 (100%)

Q – quintile; No. – number; MS – metabolic syndrome

(Tab. 1). Eighty-three percent (n = 730) of participants presenting with one component of MS were lean, 17 % (n = 153) presented with central obesity. Proportion of individuals displaying siMS score within the two upper quintiles was similar in lean participants presenting with one MS component, and individuals manifesting only central obesity (48 % and 51 %, respectively, $p_{chi} = 0.534$). Among individuals displaying two components of MS, 83 % had siMS score within the 4th and 5th quintile. Thirty-two percent (n = 109) of participants presenting with two MS components did not display central obesity, and among them 83 % (n = 90) displayed siMS score within two upper quintiles. Among centrally obese individuals presenting with an additional MS component (n = 231), 193 (84 %) showed siMS score ≥ 4th quintile (p_{ch} vs. centrally lean = 0.821).

Discussion

MS score describes the continuum of the processes underlying abnormalities in the components of MS. It reflects how individual components of MS cluster together, and the current severity of cardiometabolic affliction, even in subjects not presenting with MS. Similarly to our data calculated using siMS score, specific population-derived continuous MS score rises with the number of manifested components of MS (12, 13). Moreover, population-derived MS scores show a significant relationship with different markers of cardiometabolic risk, such as those of inflammation and fibrinolysis, adipokines, adhesion molecules (14) or subclinical atherosclerosis (12, 15). Unlike e.g. the Framingham Risk Equation (16) or the AUSDRISK score (17), continuous MS severity scores were not specifically formulated to be risk predictors. However, recent studies document that they are significantly associated with long-term risk of development of coronary heart disease (18), myocardial infarction (19), type 2 diabetes (19, 20), as well as of cardiovascular and overall mortality (19, 21).

The presence of MS according to dichotomous classification indicates an increased risk to develop cardiometabolic events. In our analysis, except for one individual, those presenting with MS displayed siMS scores in the range of 2 upper quintiles, indicating an above average cardiometabolic burden. Similarly scored about 33 out of 100 participants not presenting with MS, and even about 13 out of 100 not presenting with any component of MS. This prevalence is quite high, when we consider that we analyzed subjects participating as volunteers in clinical studies, e.g. individuals, who are likely to be interested in their health status. Thus, additional studies on a representative sample of the population are needed to clarify the real prevalence. To our knowledge, similar data from other populations are not available. Between-countries comparison employing siMS score would be of interest, as cardiovascular mortality in Slovaks is the highest in the European Union (11). Since we analyzed siMS scores retrospectively, we neither could follow-up potential changes in individual siMS scores over time, nor assess siMS score as an outcome predictor. However, simplicity of siMS calculation and its availability in Excel spreadsheet or Android application (8, 9) allows the physician for tracking of changes in severity of cardiometabolic affliction in individual patients over time.

In conclusion, in clinical practice, calculation of siMS might help to estimate the severity of cardiometabolic affliction in so called "low-risk" subjects, e.g. individuals, who do not present with MS components yet. Proportion of these individuals is not negligible, and they logically escape the attention of the physician, and thus the opportunity of being early motivated to implement changes in lifestyle, which could slow-down or even interrupt pathological processes. Availability of automated calculation of siMS score using the electronic health record could facilitate its wider use toward identification of patients with severe cardiometabolic affliction.

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