Archives of Gerontology and Geriatrics 48 (2009) 146–150

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

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

Metabolic syndrome in older subjects: Coincidence or clustering?

Mario Bo *, Alessandro Sona, Marco Astengo, Umberto Fiandra, Eleonora Quagliotti, Alessia Brescianini, Gianfranco Fonte

Section of Geriatrics, Department of Medical and Surgical Disciplines, University of Turin, Azienda Ospedaliera San Giovanni Battista, Molinette, Corso Bramante 88, I-10126 Torino, Italy

ARTICLE INFO

Article history:
Received 6 August 2007
Received in revised form 1 December 2007
Accepted 5 December 2007
Available online 19 February 2008

Keywords:
Metabolic syndrome
Elderly
Structural equation modeling

ABSTRACT

The prevalence of the metabolic syndrome (MS) increases with advancing age. However, aging per se is associated with increased prevalence of most of the abnormalities contributing to the MS. Whether MS in older people consistently identifies a true pathophysiological entity or a casual aggregation of aging-associated metabolic abnormalities, remains to be fully elucidated. In the present study, we aimed to evaluate whether in older subjects the aggregation of metabolic components of the MS, as defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), is consistent with a single latent variable. Age, waist circumference, systolic and diastolic blood pressure, metabolic variables were determined in 152 older (>70 years), non-diabetic, healthy men. Cronbach alpha was used to assess the internal consistency of the components contributing to the MS. Structural equation modeling, using the Normed Fit Index (NFI), the Root Mean Square Error of Approximation (RMSEA), the Comparative Fit Index (CFI), and the Tucker-Lewis Index (TLI) was used to assess the fit to a model with a single latent variable. The Cronbach alpha test showed low internal consistency among the metabolic variables ($\alpha = 0.31$). The calculated χ^2 values were 28.31 and 32.52 for model entering hypertension as dichotomous variable and for model entering blood pressure values, respectively, both expressing low fit to a model with a single latent variable. In both models, CFI (0.41 and 0.55), NFI (0.59 and 0.55), RMSEA (0.25 and 0.22) and TLI (−0.31 and −0.12) scores showed a low fit of the metabolic alterations to a single latent variable. These findings suggest caution in making diagnosis of MS at older ages, since metabolic and cardiovascular abnormalities being per se extremely common in elderly people, do not appear to cluster together under a single common factor.

1. Introduction

The term MS denotes a condition recognized by the co-occurrence of multiple metabolic abnormalities, including central obesity, abnormal fasting glucose, dyslipidemia and hypertension (Reaven, 1988; WHO, 1999). The MS has been associated with the development of diabetes and increased risk of cardiovascular morbidity and mortality, even in older subjects (Lempiainen et al., 1999; Lakka et al., 2002; Wannamethee et al., 2005a; McNeill et al., 2006), but several studies demonstrated that MS does not provide incremental risk information above and beyond its individual components (Yarnell et al., 1998; Lawlor et al., 2004a; Iribarren et al., 2006; Sundstrom et al., 2006a). Moreover, there remains a fundamental issue concerning the clinical nature of the syndrome, that is, whether MS is a true pathophysiological condition or merely a variegated cluster of risk factors produced by expert groups (Kahn et al., 2005; Reaven, 2005; Grundy, 2006a). The prevalence of MS is reported to rise dramatically with increasing age (Ford et al., 2002; Cameron et al., 2004). However, aging per se is associated with increased incidence and prevalence of most of the abnormalities contributing to the MS, including reduced lean/fat mass ratio, hypertension, alterations in glucose homeostasis and decreased high density lipoprotein (HDL) concentration. While it appears plausible that at young-adult age a single pathophysiological alteration (increased visceral adipose tissue and/or insulin-resistance) might drive the early and unusual clustering of metabolic abnormalities (dyslipidemia, hypertension, abnormal glucose tolerance and inflammation) (Shen et al., 2003; Bo et al., 2004; Kahn et al., 2005; Reaven, 2005; Pladevall et al., 2006), it seems much more hazardous to cluster in a syndrome risk factors which are extremely common in older subjects. Therefore, whether MS in older people consistently identifies a true pathophysiological entity or a casual aggregation of aging-associated metabolic abnormalities remains to be fully elucidated.

* Corresponding author. Tel.: +39 011 6335 006; fax: +39 011 6961 045.
E-mail address: mario.bo@unito.it (M. Bo).

0167-4943/$ – see front matter © 2008 Published by Elsevier Ireland Ltd.
doi:10.1016/j.archger.2007.12.003

On this background, we aimed to evaluate whether in older non-diabetic subjects the aggregation of metabolic components contributing to the MS is consistent with a common single syndromic variable. Therefore, several statistical procedures were used to assess whether a model with a single latent variable may account for the variables contributing to MS in older subjects.

2. Subjects and methods

An invitation to participate to the study was sent to five general practitioners working in different districts of the metropolitan area in Turin. A detailed description of the study, including design, aims and inclusion/exclusion criteria, was provided. A descriptive letter of the study was attached for eligible patients, in order to obtain an informed consent to participation. Men aged 70 years or older were eligible to the study. Further inclusion criteria were independence in daily living, i.e., score <1 on the index of activities of daily living (ADL) (Katz et al., 1963) and absence of cognitive impairment, i.e., score <4, on the short portable mental status questionnaire (SPMSQ) (Pfeiffer, 1975). Exclusion criteria were: known diabetes, hepatic or renal failure, conditions or disorders affecting metabolism, use of lipid-lowering drugs in the previous month, neoplasm or other severe diseases. Eligible subjects were enrolled in the period September–October 2006.

A detailed medical history was collected and the following variables were considered: age, smoking habits, alcohol consumption, and cardiovascular history. In each patient the following measures were obtained: weight (kg), height (m), body mass index (BMI), calculated according to the formula weight (kg)/height (m^2), waist and hip circumferences (cm) measured according to current guidelines (WHO, 1995), systolic and diastolic blood pressure (SBP and DBP, respectively) (mean value of 3 measures obtained with an appropriately sized cuff and standard mercury sphygmomanometer at the non-dominant upper arm after a 5-min rest in the supine position).

Blood samples were collected from an antecubital vein into vacutainer tubes containing EDTA after a 12-h overnight fast for routine blood chemistry, measurement of plasma lipid and lipoprotein levels, coagulative and inflammatory variables. Total cholesterol (TC) and triglycerides (TG) were measured using standard commercial enzymatic kits (CHOD-PAP and GPO-PAP methods, Roche Diagnostics, Mannheim, Germany). HDL-cholesterol (HDL-C) levels were measured through enzymatic colorimetric assay by a direct method (ADVIA 1650/2400, Bayer, Milano, Italy) after separation of cholesterol from non-HDL particles. LDL-cholesterol (LDL-C) concentration was calculated according to the formula of Friedewald et al. (1972). Plasma fibrinogen was quantified automatically through a functional coagulative assay according to the Clauss method (STA-Fibrinogen, Roche). Pentameric C-reactive protein (pCRP) levels were measured with a highly sensitive immunoassay that used a monoclonal antibody coated with polistirene particles; the assay was performed using a Behring BN-100 nephelometer (DADE Behring, Marburg, Germany), according to the method described by the manufacturer (Ledue et al., 1998; Roberts et al., 2001). Glucose was enzymatically determined by the hexokinase method. Serum insulin was determined by monoclonal antibody method (Insulin IRMA CT, RADIM, Pomezia, Italy). Insulin-resistance was calculated through the homeostasis model assessment (HOMA) according to the formula: fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/l)/22.5 (Galvin et al., 1992; Bonora et al., 2000).

Diagnosis of MS was made according to the NCEP-ATP III guidelines (Expert Panel, 2001). Participants taking anti-hypertensive medications were counted as meeting the blood pressure criterion (He et al., 2006). Patients with a new finding of diabetes were not included in the study.

The study protocol agreed with the recommendations of the World Medical Association for biomedical research involving human subjects.

2.1. Statistical analysis

The sample size was defined according to the structural equation modeling. In the absence of a definite rule, we adopted one of the several arbitrary "rules of thumb" proposed: at least 10 cases for item according to Bryant and Yarnold (1995) and at least 100 cases overall according to Hatcher et al. (1995).

Data were analyzed using SPSS for Windows 12 and Tetrad 4.0. Frequencies, mean and standard deviation (SD), skewness and kurtosis were calculated. Non-normally distributed variables were normalized according to Blom (1959). The Cronbach alpha test (score range 0–1: a score of 1 defines the maximal internal consistency) was used to assess the internal consistency of the components contributing to MS. The structural equation modeling methodology was used to assess the fit to a model with a single latent variable. This was assessed using the NFI, the RMSEA, the CFI, and the TLI. These fit indexes were appropriately used to minimize the effect of the sample size on the χ^2 values. The score range for NFI, CFI and TLI is 0–1: a score of 1 identifies the optimal fit, and score ≥0.9 are usually considered expression of a good fit. For the TLI negative values are considered equal to 0. For the RMSEA, negative values are conventionally considered equal to 0; values <0.05 suggest a good fit.

3. Results

A total of 156 subjects were selected for the study. Three of them received a new diagnosis of diabetes and were excluded from the study; one subject refused to participate. Analysis was conducted on 152 subjects.

Characteristics of the sample investigated are shown in Table 1. Mean age was 73.1 ± 4.7 years. SBP values ≥130 mmHg and DBP values ≥85 mmHg were found in 128 (84.2%) and 98 (64.5%) subjects, respectively; 94 subjects (61.8%) had elevated SBP and DBP. Seventy subjects (46%) were on anti-hypertensive medication. Mean waist circumference was 96.0 ± 12.5 cm and 92 subjects (60.5%) had central obesity according to the NCEP-ATP III criteria. Mean fasting

Table 1
Characteristics of the sample at baseline

Parameters	Values
Age (years)	73.1 ± 4.7
SBP (mmHg)	142 ± 17
DBP (mmHg)	87 ± 8
Median BP (mmHg)	106 ± 10
BMI (kg/m^2)	25.4 ±3.5
Waist circumference (cm)	96 ± 12.5
Fasting glucose (mg/dl)	90.9 ± 13.3
Fasting insulin (mU/l)[a]	16.5 (13.2–19.8)
HOMA-IR[a]	3.73 (2.7–5.0)
TC (mg/dl)[a]	217.5 (187.0–240.2)
HDL-C (mg/dl)	64.3 ± 15.2
LDL-C (mg/dl)[a]	128.2 (106.5–150.3)
TG (mg/dl)[a]	107.5 (83.5–134.2)
Apo-B (mg/dl)[a]	108 (95.2–132.8)
CRP (mg/l)[a]	1.85 (0.8–3.8)
Fibrinogen (mg/dl)	386 ± 70
Erythrocyte sedimentation rate (mm/h)	16.7 ±11.6
Creatinine (mg/dl)[a]	0.81 (0.75–0.95)

Mean ± S.D., unless otherwise indicated.
[a] Median and interquartile range.