A Single Factor Underlies the Metabolic Syndrome

A confirmatory factor analysis

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OBJECTIVE — Confirmatory factor analysis (CFA) was used to test the hypothesis that the components of the metabolic syndrome are manifestations of a single common factor.

RESEARCH DESIGN AND METHODS — Three different datasets were used to test and validate the model. The Spanish and Mauritian studies included 207 men and 203 women and 1,411 men and 1,650 women, respectively. A third analytical dataset including 847 men was obtained from a previously published CFA of a U.S. population. The one-factor model included the metabolic syndrome core components (central obesity, insulin resistance, blood pressure, and lipid measurements). We also tested an expanded one-factor model that included uric acid and leptin levels. Finally, we used CFA to compare the goodness of fit of one-factor models with the fit of two previously published four-factor models.

RESULTS — The simplest one-factor model showed the best goodness-of-fit indexes (comparative fit index 1, root mean-square error of approximation 0.00). Comparisons of one-factor with four-factor models in the three datasets favored the one-factor model structure. The selection of variables to represent the different metabolic syndrome components and model specification explained why previous exploratory and confirmatory factor analysis, respectively, failed to identify a single factor for the metabolic syndrome.

CONCLUSIONS — These analyses support the current clinical definition of the metabolic syndrome, as well as the existence of a single factor that links all of the core components.

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The metabolic syndrome refers to the clustering, within individuals, of several cardiovascular risk factors (1,2). The metabolic syndrome is highly prevalent (3) and is a risk factor for cardiovascular diseases (CVD), chronic kidney disease, and type 2 diabetes (4–6). Several definitions of the metabolic syndrome have been used, but all include insulin resistance or glucose intolerance, hypertension, dyslipidemia, and central obesity (7–9). Hyperuricemia and hyperleptinemia have also been proposed as components of the metabolic syndrome (1,10,11), and clinical, epidemiological, genetic, and physiologic studies have shown associations between these traits and both the metabolic syndrome components and CVD outcomes (10–22).

A central question in understanding the metabolic syndrome is why these traits cluster in individuals. For example, is there one or are there several factors, such as genetic or lifestyle characteristics, that influence the expression of metabolic syndrome traits in individuals? In an attempt to answer this question, many investigators have used exploratory factor analysis (EFA). This technique is used to analyze the interrelatedness of measured variables, so as to explain their observed correlations in terms of a smaller group of latent (i.e., unmeasured) variables, termed factors. For example, in the field of sociology, education level, income, and job status may all be related, and their relationship may best be explained by the presence of an unmeasurable factor called socioeconomic status. Similarly, EFAs of the metabolic syndrome identifying a single latent factor would suggest that the components of the metabolic syndrome are expressions of a common underlying factor. We have retrieved 30 published EFAs that have found between one and seven latent factors for the metabolic syndrome (online appendix [available at http://care.diabetesjournals.org]). Most EFAs have identified three or four factors and therefore concluded that a single underlying factor for the metabolic syndrome is unlikely. However, EFA cannot explicitly test whether a simpler, one-factor model would better explain the observed correlations among the metabolic syndrome components.

In contrast to EFA, confirmatory factor analysis (CFA) can explicitly test whether the proposed constellation of traits for a syndrome are best described by a single underlying factor (23–26). Re-

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Abbreviations: AIC, Akaike information criterion; CFA, confirmatory factor analysis; CVD, cardiovascular disease; EFA, exploratory factor analysis; HOMA-IR, homestasis model assessment of insulin resistance; MAP, mean arterial pressure.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

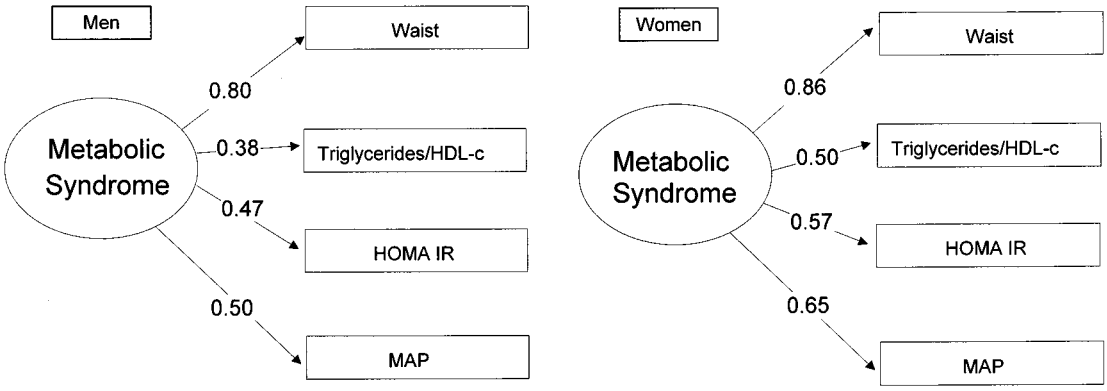

Figure 1—*CFA by sex. Standard one-factor metabolic syndrome model tested in the Spanish dataset with $\chi^2 = 4.7$ (df = 7, n = 410, P = 0.69), comparative fit index = 1, standardized root mean-square residual = 0.04, and root mean-square error approximation = 0.00. Standardized weights representing factor loadings are shown on paths. All weights are significant at P = 0.01 for the two-tailed test. To maintain presentation clarity, residual terms are not shown.*

cently, two studies (26,27) used CFA to test a four-factor model of the metabolic syndrome in which each factor was allowed to correlate with every other factor. Each factor included between two and four measured variables. For example, both systolic blood pressure and diastolic blood pressure were manifestations of the "blood pressure" factor. The four factors were blood pressure, obesity, insulin resistance, and lipids. Shen et al. (26) also tested a one-factor model but concluded that the four-factor model fit the data better. Both of these studies were restricted to male subjects.

In the present study, CFA was used to test the hypothesis that a single latent factor underlies the core components of the metabolic syndrome (central obesity, hypertension, insulin resistance, and dyslipidemia). We also explored whether this one-factor model could be expanded to include leptin and uric acid as additional components of the metabolic syndrome. Moreover, since CFA allows the researcher to specify and test both the number of factors and the relations among variables and factors (23), we were able to compare, in three different populations, previously published four-factor CFA models with simpler, one-factor models.

RESEARCH DESIGN AND METHODS

The study was performed using previously collected data from two cross-sectional studies, one from Spain (18) and the other from Mauritius (10). The Spanish and the Mauritian study populations included 410 (207 men and 203 women) and 3,061 (1,411 men and 1,650 women) individuals, respectively. The selection of these populations and the collection of data have been described in detail elsewhere (10,18). Briefly, both the Spanish and the Mauritian studies collected data, using similar methods, on fasting plasma glucose and glucose after a 2-h glucose tolerance test, homeostasis model assessment of insulin resistance index (HOMA-IR), leptin, total cholesterol, triglycerides, HDL cholesterol, and uric acid. Other measurements included blood pressure and anthropometric measurements such as weight, height, BMI, waist circumference, and waist-to-hip ratio. The Mauritian study also included 2-h post glucose challenge insulin. For comparison and validation purposes we also analyzed data from a third U.S. study population that included 847 men. The data required for CFA were obtained from the published tables displaying the covariance matrix and were also cross-sectional (26).

Rationale and definition of the models to be tested

We reviewed the literature on the metabolic syndrome, including the results of epidemiologic studies, prior factor analyses, and genetic studies. The metabolic syndrome is by definition a syndrome composed of several complex phenotypic traits. These traits are continuously distributed and are believed to result from a combination of polygenic and environmental influences. However, we hypothesized that an additional as yet unknown factor, genetic, environmental, or the interaction of both, accounts for the clustering of metabolic syndrome traits. There is both epidemiological (1) and genetic evidence (20) to support the one-factor model.

Previous factor analyses, both confirmatory (26,27) and exploratory (see online appendix), have not substantiated the single common factor hypothesis (24,25), and we considered possible reasons for this failure. It is possible that a single underlying factor does not, in fact, exist. In that case, the whole concept of a unified pathologic construct or syndrome might be called into question. This seems highly unlikely given the vast epidemiologic evidence, accumulating for over 20 years, of an association among the traits (1) and between the syndrome and CVD (4). Moreover, the previous EFAs are not consistent in their findings. Although most have identified separate factors for lipid and insulin resistance measurements, some have not. In the same way, some EFAs found blood pressure sharing the same factor with the rest of metabolic syndrome components (see online appendix).

The single most likely reason for the failure to show a single unifying factor is that most previous EFAs used two or more measures for the same trait, ensuring that these highly correlated measures will cluster together under a separate factor instead of loading on a common factor. We and others (24,28) have noted that, when both systolic blood pressure and diastolic blood pressure are included in the model, they usually load together to the exclusion of other postulated factors. The same can be said of HDL cholesterol and triglycerides or of fasting glucose and postprandial glucose (28). Therefore, we used only one measure for each of the four postulated metabolic syndrome components, namely HOMA-IR for insulin resistance, mean arterial pressure (MAP) for blood pressure, the ratio of triglycerides

Dataset (N)	Model (standardized weights)		Goodness of Fit Indices: χ^2 [df] (P value)	SRMR	RMSEA	RMSEA (90% CI)	AIC	CFI
Hypothetical (X)	One-factor model with perfect fit		0 [−] (1.00)	0	0	(0.00–0.05)	lowest	1.00
Spanish (16)	One-Factor (MetS) standard model*		4.7 [7] (0.69)	0.04	0.00	(0.00–0.05)	30.7	1.00
(N = 410)	Men	Women						
	Waist (0.80)	Waist (0.86)						
	Trigly/HDL-c (0.38)	Trigly/HDL-c (0.50)						
	HOMA IR (0.47)	HOMA IR (0.57)						
	MAP (0.50)	MAP (0.65)						
Spanish (16)	One-Factor (MetS) expanded model†		27.4 [18] (0.07)	0.05	0.04	(0.00–0.06)	75.4	0.99
(N = 410)	Men	Women						
	Waist (0.87)	Waist (0.89)						
	Leptin (0.73)	Leptin (0.80)						
	Uric Acid (0.56)	Uric Acid (0.48)						
	TGL/HDL-c (0.38)	TGL/HDL-c (0.48)						
	HOMA IR (0.45)	HOMA IR (0.57)						
	MAP (0.47)	MAP (0.60)						
Mauritian (9)	One-Factor (MetS) standard model*		40.9 [4] (<.001)	0.03	0.06	(0.04–0.07)	72.9	0.98
(N = 3061)	Men	Women						
	Waist (0.84)	Waist (0.83)						
	Trigly/HDL-c (0.56)	Trigly/HDL-c (0.46)						
	HOMA IR (0.71)	HOMA IR (0.62)						
	MAP (0.36)	MAP (0.37)						
Mauritian (9)	One-Factor (MetS) expanded model†		314.2 [18] (<.001)	0.05	0.07	(0.07–0.08)	362.2	0.94
(N = 3061)	Men	Women						
	Waist (0.88)	Waist (0.87)						
	Leptin (0.75)	Leptin (0.73)						
	Uric Acid (0.33)	Uric Acid (0.42)						
	Trigly/HDL-c (0.54)	Trigly/HDL-c (0.42)						
	HOMA IR (0.70)	HOMA IR (0.62)						
	MAP (0.36)	MAP (0.34)						

Figure 2—*Comparison of the standard and expanded one-factor CFA models of the metabolic syndrome (MetS) in study populations from Spain and Mauritius. *Trigylceride-to-HDL (Trigly/HDL-c) ratio and HOMA-IR were log transformed. All standardized weights are significant at P = 0.01 for the two-tailed test. †Leptin, trigylceride-to-HDL ratio, and HOMA-IR were log transformed. All standardized weights are significant at P = 0.01 for the two-tailed test. CFI, comparative fit index; SRMR, standardized root mean-square residual; RMSEA, root mean-square error of approximation.*

Study population (N)	Model tested (Men/Women or Men standardized weights)	Goodness of Fit Indices					
		χ^2 [df] (P value)	SRMR	RMSEA	RMSEA (90% CI)	AIC	CFI
Hypothetical (X)	One- or 4-factor hypothetical model with perfect fit	0[−] (1.00)	0	0	(0.00–0.05)	lowest	1.00
Spanish (410)	The original 4-factor Novak et al. Model (25) did not fit the data	—	—	—	—	—	—
Spanish (410)	Modified (one-factor) Novak et al. model including the same variables at the original 4-factor Novak et al. model* MetS factor BMI (0.67/0.85) Waist-hip ratio (0.27/0.47) Fasting insulin (0.47/0.48) Fasting glucose (0.41/0.48) Triglycerides (0.44/0.46) HDL-c (-0.19/-0.32) SBP (0.53/0.65) DBP (0.52/0.61)	60.3 [30] (<0.01)	0.05	0.05	(0.03–0.07)	144.3	0.96
Mauritian (3061)	Original 4-factor Novak et al. model† (25) Obesity factor BMI (0.87/0.80) Waist-hip ratio (0.67/0.65) IR factor Fasting insulin (0.92/0.66) Fasting glucose (0.23/0.33) Lipids factor Triglycerides (0.60/0.57) HDL-c (-0.47/-0.33) Hypertension factor SBP (0.74/0.88) DBP (0.99/0.83) Range of correlations between factors (0.22–0.73/0.35–0.91)	414.2 [26] (<0.001)	0.07	0.07	(0.06–0.08)	506.2	0.94
Mauritian (3061)	Modified (one-factor) Novak et al. model including the same variables as the original 4-factor Novak et al. model* MetS factor BMI (0.77/0.76) Waist-hip ratio (0.57/0.62) Fasting insulin (0.73/0.62) Fasting glucose (0.22/0.33) Triglycerides (0.53/0.44) HDL-c (-0.37/-0.26) SBP (0.25/0.37) DBP (0.37/0.36)	445.5 [30] (<0.001)	0.07	0.07	(0.06–0.07)	529.5	0.93
USA (847 men)	Original 4-factor Shen et al. model (24)‡ Obesity factor BMI (0.78) Waist-hip ratio (0.59)	101.8 [27] (<0.01)	NA	0.06	NA	159.4§	0.97

	IR factor Fasting insulin (0.83) Glucose (0.38) PGC insulin (0.78) PGC glucose (0.37) Lipids factor Triglycerides (0.78) HDL-c (-0.65) Hypertension factor SBP (0.71) DBP (0.81) Range of correlations between factors (0.17–0.66)						
USA (847 men)	Original 1-factor Shen et al. model (24)‖ MetS factor BMI (0.58) Waist-hip ratio (0.46) Fasting insulin (0.79) PGC insulin (0.76) Fasting glucose (0.33) PGC glucose (0.38) Triglycerides (0.46) HDL-c (-0.35) SBP (0.26) DBP (0.25)	631.4 [32] (<0.01)	NA	0.15	NA	681.5§	0.74
USA (847 men)	Modified 1-factor Shen et al. model (different residual correlations) with the same variables as in the original 1-factor model[#] MetS factor BMI (0.59) Waist-hip ratio (0.46) Fasting insulin (0.72) PGC insulin (0.68) Fasting glucose (0.36) PGC glucose (0.41) Triglycerides (0.46) HDL-c (-0.34) SBP (0.26) DBP (0.24)	103.4 [29] (<0.01)	0.03	0.06	(0.04–0.07)	155.4	0.97
Mauritian (3061)	Original 4-factor Shen et al. (model (24)‡ Obesity factor: BMI (0.88/0.81) Waist-hip ratio (0.66/0.63) IR factor: Fasting insulin (0.93/0.87) Glucose (0.23/0.25) PGC insulin (0.65/0.54) PGC glucose (0.31/0.26)	612.2 [54] (<0.001)	0.07	0.06	(0.05–0.06)	724.2	0.94

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Study population (N)	Model tested (Men/Women or Men standardized weights)	Goodness of Fit Indices: χ^2 [df] (P value)	SRMR	RMSEA	RMSEA (90% CI)	AIC	CFI
Hypothetical (X)	One- or 4-factor hypothetical model with perfect fit	0[−] (1.00)	0	0	(0.00–0.05)	lowest	1.00
	Lipids factor: Triglycerides (0.59/0.55) HDL-c (-0.47/-0.35) Hypertension factor: SBP (0.74/0.89) DBP (0.99/0.83) Range of correlations between factors (0.21–0.74/0.21–0.72)						
Mauritian (3061)	Original 1-factor Shen et al. model (24)‖ MetS factor BMI (0.77/0.74) Waist-hip ratio (0.62/0.62) Fasting insulin (0.75/0.63) PGC insulin (0.59/0.46) Fasting glucose (0.24/0.32) PGC glucose (0.33/0.34) Triglycerides (0.52/0.44) HDL-c (-0.37/-0.27) SBP (0.31/0.45) DBP (0.40/0.43)	3127.6 [66] (<0.001)	0.11	0.12	(0.12–0.13)	3125.6	0.67
Mauritian (3061)	Modified 1-factor Shen et al. model (different residual (correlations) with the same variables as in the original 1-factor model# MetS factor BMI (0.75/0.77) Waist-hip ratio (0.56/0.63) Fasting insulin (0.75/0.62) PGC insulin (0.55/0.40) Fasting glucose (0.24/0.31) PGC glucose (0.34/0.33) Triglycerides (0.52/0.43) HDL-c (-0.37/-0.26) SBP (0.25/0.36) DBP (0.36/0.35)	601.7 [58] (<0.001)	0.06	0.06	(0.05–0.06)	705.7	0.94

Figure 3—*Comparison of the four-factor CFA models with one-factor CFA models of the metabolic syndrome (MetS) in three study populations from Spain, Mauritius, and the U.S. *Triglycerides and insulin were log transformed. Residuals correlation between BMI and waist-to-hip ratio, triglycerides and HDL cholesterol (HDL-c), systolic blood pressure (SBP) and diastolic blood pressure (DBP), between fasting glucose and insulin, and between glucose and triglycerides. †Residuals correlation between fasting glucose and triglycerides. All possible correlations among the four factors were allowed. ‡Glucose, postchallenge glucose, insulin, postchallenge insulin, and triglycerides were log transformed. Residuals correlation between glucose and post-glucose challenge (PGC) glucose and between PGC insulin and PGC glucose. All possible correlations among the four factors were allowed. §AIC obtained from analyzing the published variance-covariance matrix. The index was not available in the original publication. ‖Glucose, PGC glucose, insulin, PGC insulin, and triglycerides were log transformed. Residuals correlation between glucose and PGC glucose and between PGC insulin and PGC glucose. #Glucose, PGC glucose, insulin, PGC insulin, and triglycerides were log transformed. Residuals correlation between BMI and waist-to-hip ratio, triglycerides and HDL cholesterol, SBP and DBP, and insulin resistance (IR) measures (fasting insulin and PGC insulin, PGC glucose and PGC insulin, and glucose and PGC glucose). CFI, comparative fit index; NA, not available; SRMR, standardized root mean-square residual; RMSEA, root mean-square error of approximation.*

to HDL for the dyslipidemia trait (29), and waist circumference for central obesity (9,30,31). Since there seem to be sex differences in the genetic factors involved in the metabolic syndrome (32,33), we modeled the metabolic syndrome correlation structure allowing for different values between men and women (two-group CFA).

Data analysis

The triglycerides-to-HDL ratio and HOMA-IR were log transformed in the Spanish And Mauritian data to more closely adhere to the normality assumptions of the model. Significance level was set at $P \leq 0.05$.

CFA. Figure 1 shows the hypothesized model. The hypothesized model ("standard model") included waist circumference, HOMA-IR, triglyceride-to-HDL ratio, and MAP as core metabolic syndrome components. An "expanded model" included the addition of leptin and uric acid. We looked for substantial (values >0.4) and statistically significant standardized weights to support the notion that a common factor was influencing how each of the metabolic syndrome traits is expressed. The weights can be used to quantify the amount of variability in the measured variable that can be explained by the underlying factor; the higher the standardized weight, the greater the influence of the factor. The weights have an interpretation similar to that of correlation coefficients and they estimate the degree of association between the factor(s) and the measured variables. Identical models were analyzed separately for men and women using two-group CFA (23). The CFA used maximum likelihood estimation methods and was performed with AMOS 5.0 (23). Several measures of fit were used to test the models. The χ^2 test tests whether a model significantly deviates from a perfect fit of the data, whereby a larger χ^2 (i.e., a lower *P* value) indicates a greater difference from a perfect fit. However, this test is highly dependent on sample size and cannot be used in isolation to test model fit. The following model fit indexes were also used: comparative fit index, standardized root mean-square residual, and root mean-square error of approximation. A comparative fit index of one indicates a perfect fit with values >0.9 indicating a good fit. For standardized root mean-square residual, the closer the value to 0, the better the model fit. For root mean-square error of approximation, values ≤0.05 indicate a good fit. Finally, the Akaike information criterion (AIC) was used for comparisons among models that included different variables. Models with the smallest AIC are considered to have the best fit (23).

To validate the robustness of the proposed one-factor structure, several comparisons were performed with the Spanish (18) and Mauritian (10) datasets. Using these data we compared the "standard" one-factor model (Fig. 1) with an "expanded" one-factor model that also included uric acid and leptin. Moreover, we also evaluated the four-factor model postulated by Novak et al. (27) and compared its fit to the fit of a one-factor model. Finally, a similar comparison was performed with a different four-factor model postulated by Shen et al. (26) using their original and the Mauritian datasets (10). To allow direct comparisons with the original four-factor models, those one-factor models had to include exactly the same variables as the original four-factor models and therefore included more than one variable per metabolic syndrome component (Figure 3). However, both the Novak et al. and the Shen et al. modified one-factor models included correlations between the error terms (residuals) of the variables measuring the same trait (insulin resistance, blood pressure, dyslipidemia, and fat measurements). Those correlation terms represent shared sources of variability by those variables that would not be explained by the metabolic syndrome factor (23). The modeling makes sense both clinically and statistically because correlations among those variables exist even among individuals without the metabolic syndrome.

RESULTS

Model estimation and evaluation

The goodness of fit of the standard one-factor model was excellent in both Spanish and Mauritian datasets. Moreover, the standard one-factor model had better fit indexes than the expanded one-factor model in both datasets. The expanded model had a better fit in the Spanish dataset when compared with the Mauritian dataset (Figure 2).

The Spanish dataset did not fit the four-factor CFA model proposed by Novak et al. (27), and a direct comparison between the four-factor model and the one-factor model was not possible. However, the one-factor model had a good fit in the Spanish data (Figure 3). The comparisons performed using data from the Mauritian study population showed that the goodness-of-fit indexes of the one- and four-factor Novak et al. models were similar but both unsatisfactory. For the Shen et al. model (26), the comparisons in both the U.S. and Mauritian study populations showed similarly good goodness-of-fit indexes for the modified one-factor and the four-factor models (Figure 3). If any difference, they were slightly better for the one-factor than for the four-factor models. Overall, since the four-factor model fit the Spanish data so poorly that no solution was obtainable and the one-factor models had better AIC indexes than the four-factor models in the three populations, the results suggest that the one-factor model structure best explains the data over a wide variety of populations.

CONCLUSIONS — Based in part on the results of prior factor analyses, the existence of the metabolic syndrome as a distinct entity has recently been questioned (34). However, this study shows that insulin resistance, MAP, triglyceride-to-HDL ratio, and waist circumference cluster together under a single latent factor, suggesting that there may indeed be a common causal factor that underlies these different components of the metabolic syndrome. This was further supported by the finding that the simpler (more parsimonious) one-factor model had the best goodness-of-fit indexes. Moreover, the direct comparisons, using the same variables, between the previously published four-factor models and the one-factor models showed that the one-factor model had goodness-of-fit indexes at least as good as those of the four-factor model.

There is evidence supporting a role for both leptin and uric acid in the metabolic syndrome. For example, animal and human data suggest that leptin resistance is involved in promoting and aggravating the consequences of obesity and insulin resistance (35). Uric acid predicts both weight gain and hypertension (17), and hyperuricemia can be detected before the development of hyperinsulinemia (36). However, although the expanded one-factor model, which included leptin and uric acid, demonstrate a good fit of the Spanish data, the comparison and validation results suggest that the standard one-factor model has the best fit. Therefore, although both one-factor models are plausible statistically and biologically, our results seem to favor the robustness and simplicity of the standard one-factor

model, which happens to be consistent with the currently accepted definitions of the metabolic syndrome (7–9).

The models tested in our data were based on an extensive literature review (see online appendix) and also with a critical view of the previous EFAs. This critical view, recently supported by others (24,28), highlights that it is unnecessary to introduce either highly correlated indicators to measure blood pressure (i.e., systolic and diastolic blood pressure) or redundant insulin resistance measurements when conducting factor analysis for the metabolic syndrome. Moreover, key to the fit of the one-factor modified models from previously published CFAs (26,27) was the allowance of correlations between the error terms (residuals) of variables measuring the same trait (systolic and diastolic blood pressure, insulin resistance measures, waist-to-hip ratio and BMI, and triglycerides and HDL cholesterol). As shown in Fig. 3, those one-factor models had goodness-of-fit indexes at least as good as the ones of the published four-factor models. The model specification of the previous CFAs was based on the results of the previously published EFAs (see online appendix) that did not show a single latent factor but rather three or four factors in most cases. Overall, our results would suggest that the failure to identify a one-factor model of previous EFAs and CFAs could be explained by variable selection for the EFAs and by model specification for the CFAs. This analysis suggests that the one-factor model has a good fit across several populations and thus is plausible statistically and consistent with recent studies (28,37,38). Although some of the four-factor CFA models also had good fit indexes, it would be misleading to interpret the good fit of four-factor models as evidence against the existence of a single factor explaining the clustering of metabolic syndrome components.

Our results must be interpreted in light of the study limitations. First, analyses used cross-sectional data. Therefore, our results do not establish a temporal relationship between the studied metabolic syndrome components. Second, inflammatory and procoagulant variables, such as C-reactive protein, plasminogen activator inhibitor-1, and fibrinogen, which have also been proposed as components of the metabolic syndrome (38), were not measured in the current study. Lastly, although the HOMA-IR is considered an acceptable measure of insulin resistance, other methods of measuring insulin resistance, such as the hyperinsulinemic-euglycemic clamp technique, are considered to be more valid (39). However, a recent EFA study (28) of the metabolic syndrome demonstrated that fasting insulin levels and waist circumference give similar results to insulin sensitivity measured directly by the hyperinsulinemic-euglycemic clamp and intra-abdominal fat assessed by computerized tomography, respectively, and the latter methods are hardly feasible in epidemiological studies.

Why is the current study using CFA relevant for clinicians? Although there is no direct way clinicians can use the factor scores generated by factor analysis to identify patients with the metabolic syndrome (24), the current study supports the simplicity and applicability of some of the current clinical metabolic syndrome definitions (8,9). Those definitions were created on the basis of different cutoff points of CVD risk factors, but doing so does not take into account the fact that CVD risk factors are continuous variables. Factor analysis overcomes this limitation, and this study confirms the validity of the components included in the current metabolic syndrome definitions. HOMA-IR is the only measure included in the proposed standard one-factor model that is not available in routine clinical practice, and it is also omitted in some of the metabolic syndrome definitions (30). However, HOMA-IR is the simplest insulin resistance measure and probably the one that holds most potential to be introduced in routine clinical practice (2).

Although insulin resistance is the most accepted unifying hypothesis to describe the pathophysiology of the metabolic syndrome, the worldwide obesity epidemic has been the most important driving force in the increase in the metabolic syndrome (38). Despite the presence of insulin resistance among nonobese individuals (38), a common link could still exist between visceral adiposity and insulin resistance. Recent studies suggest that an overabundance of circulating fatty acids could play a major role in the metabolic syndrome. Visceral or central obesity increases the flux of free fatty acids to the liver, and free fatty acids play an important role in the genesis of insulin resistance (38,40). Inflammation is an alternative candidate for the common link between central obesity and insulin resistance. Obesity is a proinflammatory state (41), and animal data suggest that inflammation may underlie the metabolic disorders of insulin resistance and type 2 diabetes (12,42). Recent studies suggest that central obesity might precede the development of other metabolic syndrome components and that preventing this weight gain could be the best way of preventing the metabolic syndrome and its complications (43,44). This could be because Western life style (diet/sedentariness) inducing central obesity is the underlying etiologic factor. Alternatively, the metabolic syndrome is likely to have a genetic basis, and environment-induced obesity and other behavioral risk determinants trigger the expression of other metabolic syndrome components such as dyslipidemia, hypertension, and insulin resistance (20,35,37) (see online appendix).

In this study, using CFA, we show that the concept of a single underlying factor is not only plausible but best explains the observed correlations between the core metabolic syndrome components. This suggests the metabolic syndrome is a distinct entity. Moreover, we show how variable selection and model specification may have contributed to the failure of prior factor analyses to identify a single factor. The components of the metabolic syndrome occur together with a frequency greater than that expected by chance alone (1). Therefore the concept of a single underlying factor that influences the expression of all these traits is plausible, and further investigation is needed to determine whether it is genetic or environmental.

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