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How many components for the metabolic syndrome? Results of exploratory factor analysis in the FIBAR study

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Abstract *Background and aims:* Factor analysis can be used as a basis for the determination of diagnostic criteria for the metabolic syndrome (MS). This approach can be used as a basis for the determination of diagnostic criteria for MS.
Methods and results: Exploratory factor analysis of Adult Treatment Panel (ATP)-III and International Diabetes Federation (IDF) criteria for MS, entered as dichotomic variables, was performed on 2945 patients enrolled in a screening programme for diabetes. The ability of calculated factors to identify patients with MS-related conditions (glucose intolerance, hyperuricaemia, and elevation of alanine aminotransferase; ALT) was assessed through Receiver Operator Characteristics (ROC) curve analysis. Alternative sets of criteria based on ATP-III and IDF definitions of MS were also assessed. A two-factor structure was found for both ATP-III and IDF criteria. Factor 1 (associated with fasting hyperglycaemia, hypertension, and elevated waist circumference) was capable of identifying subjects with MS-related conditions to a greater extent than factor 2 (low HDL-cholesterol and hypertriglyceridaemia). When a composite variable (low HDL-cholesterol and/or hypertriglyceridaemia) was used for dislipidaemia, a single factor structure was obtained both for ATP-III and IDF definitions; this factor structure was retained when hyperuricaemia was added as a fifth component of MS. Such a modified definition of MS was not inferior to original ATP-III and IDF criteria in the identification of subjects with glucose intolerance and elevated ALT.

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Conclusions: A modification of current ATP-III or IDF criteria is necessary in order to obtain a single-factor structure. Alternative definitions of MS, including additional features, such as hyperuricaemia, can maintain a monofactorial structure, and an association with related conditions not inferior to that of original criteria.

Introduction

The choice of what parameters are needed for the diagnosis of metabolic syndrome (MS) has been criticized as arbitrary by several authors [1—3]. In fact, several conditions known to be associated with insulin resistance and increased cardiovascular risk, such as hyperuricaemia [4], non-alcoholic fatty liver disease (NAFLD) [5], and polycystic ovary syndrome (PCOS) [6], have not been included among components of MS by Adult Treatment Panel (ATP)-III [7] or International Diabetes Federation (IDF) [8]. In fact, ATP-III criteria allow the diagnosis of MS when three of the following conditions are satisfied: elevated waist circumference ($>$102 cm and $>$88 cm in men and women, respectively), elevated blood pressure (systolic blood pressure $\geq$130 mmHg and/or diastolic blood pressure $\geq$85 mmHg and/or treatment with antihypertensive drugs) low HDL-cholesterol ($<$40 mg/dL and $<$50 mg/dL in men and women, respectively), triglyceride $\geq$150 mg/dL, fasting glycaemia $\geq$110 mg/dL. Conversely, IDF recommends to perform diagnosis of MS when waist exceeds 93 cm and 79 cm in men and women, respectively, and two of the following are present: elevated blood pressure (see above), low HDL-cholesterol (see above), triglyceride $\geq$150 mg/dL, fasting glycaemia $\geq$100 mg/dL (or diabetes mellitus). Furthermore, current ATP-III criteria confer the same diagnostic weight to the different components of MS, despite the fact that they show a different strength of association with insulin resistance and cardiovascular risk.

Factor analysis is a technique derived from social sciences and psychometric investigations, which is commonly used to detect heterogeneous areas explored by interviews and questionnaires and to identify related scales accordingly. This analysis identifies a small number of virtual variables (termed ''factors'') related to a larger number of measured parameters, and capable of explaining most of their variance.

Factor analysis has been used to assess the homogeneity or heterogeneity of pathogenetic mechanisms underlying a series of clinically detectable alterations, which are associated in epidemiological studies. In this case, each identified factor can be assumed to correspond to a different pathophysiological mechanism. In other words, a multifactorial structure of a syndrome strongly suggests a pathogenetic heterogeneity of components of the syndrome, despite their epidemiological association; conversely, a single factor structure supports the hypothesis of a common pathogenetic background underlying all clinical manifestations of the syndrome. In particular, factor analysis has been applied to components of the metabolic syndrome in several studies [9], identifying from one to seven distinct factors [10—12]. Most investigations performed so far have identified three or four factors, suggesting a possible heterogeneity of the metabolic syndrome [10—12]. Differences in results among different studies can be partly due to heterogeneity of the populations enrolled; however, a major reason for discrepancies could be the difference in the list of parameters considered. In fact, some studies include insulin levels or other indexes derived from insulinaemia [13], while others do not; the inclusion of hyperuricaemia [13] is also variable. It has also been observed that the use in factor analysis of two parameters closely related to each other, such as diastolic and systolic blood pressure, could interfere with factor analysis, as the two variables tend to identify a distinct factor [9]; this phenomenon can also be observed with fasting and post-load glycaemia, body mass index and waist circumference, and low HDL-cholesterol and hypertriglyceridaemia.

Available studies on factor structure of the metabolic syndrome usually considered each parameter of the syndrome as a continuous variable. This procedure increases the sensitivity of the analysis, but it may cause some problems in interpretation of results. In fact, some of the parameters included in the metabolic syndrome, such as high blood pressure, hyperglycaemia, and hypertriglyceridaemia, are the target of specific pharmacological treatments; if values under treatment are considered, this produces a distortion in the analysis. Conversely, if patients receiving any pharmacological treatment for one or more of the components of the metabolic syndrome are excluded, this introduces a relevant selection bias in the sample. Notably, factor analysis can be easily