Aggregation pattern and factorial analysis of cardiovascular risk factors included in the metabolic syndrome in a Spanish non-diabetic population: the VIVA study*

**Abstract**

**Aims:** The aim of this study is to describe the most frequent cardiovascular risk factors (CVRF) clustering related to the metabolic syndrome (MS) in a non-diabetic Spanish population sample. Test by factorial analysis if the CVRF in the MS can be considered manifestations of a unique common factor.

**Materials and methods:** Observational, multicenter, transversal epidemiologic study. 2583 subjects aged 30-65 were randomly assigned from nine population registries. Exclusive aggregations were considered. Correlation among the MS variables was analyzed using factorial analysis.

**Results:** In order of frequency the prevalence of conventional CVRF was: dyslipidemia: 34% (CI95%: 32.3-35.5); hypertension: 32% (CI95%: 30.2-33.8); obesity: 27% (CI95%: 25.3-28.7); hyperglycaemia: 23% (CI95%: 21.6-25). 22% of the population showed 2 CVRF and 11% 3 CVRF. The most common CVRF aggregations were hypertension-obesity (5.3%; CI95%: 4.4-6.2) and hypertension-obesity-hyperglycaemia (4.1%; CI95%: 3.3-5). MS specific risk variables tended to aggregate in three factors: factor 1 (BMI, waist circumference and basal glycaemia), factor 2 (insulin, glycaemia 2h, and arterial blood pressure), factor 3 (total cholesterol/HDL, triglycerides).

**Conclusions:** There is a high prevalence of CVRF and MS in the population studied. Analysis of the metabolic syndrome does not contribute with additional information to predict cardiovascular risk in susceptible patients, as compared to the clustering of CVRF. Factorial analysis do not confirm the existence of a unitifying factor to explain MS.

**Keywords:** cardiovascular risk factors, metabolic syndrome, factorial analysis.

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*Corresponding Group of VIVA Study:
Resumen
Objetivos: Describir las agregaciones más frecuentes de los factores de riesgo cardiovascular (FRCV) que integran con el síndrome metabólico (SM) en una muestra de población española no diabética. Comprobar mediante análisis factorial si los diferentes FRCV considerados en el SM son manifestaciones de un posible único factor común. Material y métodos: Estudio poblacional transversal, multicéntrico, realizado en 2.583 sujetos de 30-65 años elegidos al azar de 9 registros poblacionales. Para el cálculo de la frecuencia de cada uno de los FRCV y de sus agregaciones se utilizaron las definiciones clásicas de cada factor. Las agregaciones de factores se calcularon de forma excluyente. La correlación entre los FRCV se realizó mediante análisis factorial. Resultados: De mayor a menor, la prevalencia de los distintos FRCV clásicos considerados en la definición del SM según el NCEP ATP III fue: dislipemia 34% (intervalo de confianza [IC] del 95%: 32-35,5); hipertensión 32% (IC del 95%: 30,2-33,8); obesidad 27% (IC del 95%: 25,3-28,7) e hiperlipemia 23% (IC del 95%: 21,6-25). Se observan diferencias significativas entre sexos: predominaba la dislipemia en hombres y la obesidad en mujeres. El 22% de la población mostraba agregación de dos FRCV y el 11% de tres FRCV. Las agregaciones más frecuentes fueron: hipertensión-obesidad 5,3% (IC del 95%: 4,4-6,2), e hipertensión-obesidad-hiperlipemia 4,1% (IC del 95%: 3,3-5). Los FRCV considerados tienden en general a formar tres conglomerados: 1) índice de masa corporal, diámetro sagital abdominal y glucemia; 2) insulina, glucemia a las 2 horas y presión arterial, y 3) razón colesterol total/co-}

Palabras clave: factores de riesgo, síndrome metabólico, análisis factorial.

Introduction
The cardiovascular diseases (CVD) are a public health problem presenting high prevalence and because they constitute cause of death in the adult population in most of the countries. The knowledge of the main modifiable cardiovascular risk factors (CVRF) allow to define and introduce cardiovascular prevention strategies, the determination of the aggregation patterns of the different CVRF among them are every day more important for the evaluation and the cardiovascular risk factor. In fact, it has been proved that the different CVRF interact positively, so the cardiovascular risk arisen from the simultaneous exposure to some of them is higher than the one expected from the simple addition of the risk corresponding to each one. At present, the need to treat the subjects intensively who show multiple abnormalities in the CVRF stand out, even in those who show minimally altered values. On the other hand, the contribution of the different CVRF and the way in which they aggregate show a great variability as regards to the different factors, among which the gender has a relevant role, therefore the strategies tend to be more customized every day. All these facts are related directly to the onset of the metabolic syndrome (MS) entity, which was initially defined as a risk factor in itself for the development of the cardiovascular disease (CVD) and T2D, and in which the insulin resistance or the glucose altered metabolism was a main component. Then, the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) developed a more clinical proposal of the MS, based on the definition of the World Health Organization (WHO), but in which the MS was considered an aggregation of individual factors that constituted a global entity, where the concurrence of three or more abnormalities in the values of its components was a main requirement for the diagnosis. Some later epidemiologic studies validated the existence of this aggregation observing a higher frequency in the association of these abnormalities than the per se random one. Subsequently, other definitions have been developed, on which consensus was achieved regarding to the principal factors that define the MS (glucose intolerance, obesity, hypertension and dyslipidemia) that, when observed thoroughly, they coincide with the classic CVRF but in early phases, therefore the cut points are lower and its assessment form has been improved. In fact, the components of the MS can be assessed easily in the clinical practice, thus, the MS becomes a very efficient tool for the evaluation and prevention of the potential cardiovascular risk. However, it has to be clarified how these components interact among them, and if there is a physiological interrelation that allows considering them as manifestations of a unique entity. The objectives of this study are to describe the aggregation patterns of the main conventional CVRF that make
up the definition of the MS in the adult non-diabetic Spanish population and to study if there are differences between men and women. Secondly, to determine, through factorial analysis, the possible correlations among the different CVRF that are considered in the MS, how they interrelate among them and if they can be considered manifestations of a unique common factor.

Material and method

Population

The VIVA Project is an epidemiologic, transversal and multicenter study, performed in 9 geographic zones in Spain: Árêvalo (Ávila), Talavera de la Reina (Toledo), Guadalajara, Begonte (Lugo), Vic (Barcelona), Avilés (Asturias), San Vicente del Raspeig (Alicante), Mérida (Badajoz) and Pizarra (Málaga). In 1998, a stratified randomized sample was collected by age and gender of 2,959 subjects aged 35-64, among the population registered at the municipal records of each of the involved sites. Finally, the analysis was done on a total of 2583 patients (87.3%) from the 2,959 polled who had complete information for all the considered variables and who complied with the inclusion criteria: non-diabetic subjects and non-pregnant women (figure 1).

Procedures and determinations

The methods employed for the determination of all considered variables are described widely in another previous work. Briefly, the biochemical parameters (total cholesterol [TC] and cholesterol bound to high density lipoproteins [cHDL], triglycerides, glucose and insulin) have been determined in a standard manner and have been measured in a unique central laboratory (Fundación Jiménez Díaz of Madrid), qualified by the Spanish Society of Clinical Chemistry; the measurements of the anthropometric variables (weight, height and waist circumference [WC]) have been measured with mercury sphygmomanometer in the right arm, with the subject sitting and after 5 minutes of rest. The measures have been validated in a sample of participants and three different persons have compared the obtained results.

Definitions of the cardiovascular risk factors and metabolic syndrome

The CVRF included in the analysis are those that consider the MS definition of the NCEP ATP III. The definitions that have been used to describe its frequency, distribution and aggregation were: hypertension (AHT) ≥140/90 mmHg or anti-hypertensive treatment; impairment of the glucose metabolism (plasmatic fasting glycemia ≥110 mg/dL, and/or 140-199 mg/dL after 2 hours of oral glucose overload); obesity (body mass index (BMI) ≥30) and abdominal obesity (PC >102/88 cm, men/women); dyslipidemia (ratio CT/cHDL ≥ 5 mg/dL or hypoglycemiant treatment). The diagnosis of the MS was done considering the definition of the NCEP ATP III, according to which the subjects shall comply with at least three of the following criteria: 1) WC >102/88 cm (men / women); 2) plasmatic fasting glycemia ≥110 mg/dL; 3) cHDL ≥30 mg/dL (men / women); 4) triglycerides ≥150 mg/dL; 5) systolic arterial pressure (SAP) ≥130 mmHg or diastolic arterial pressure (DAP) ≥85 mmHg.

Statistical analysis

The variables with continuous distribution are summed up through means and confidence intervals (CI) and those of discrete distribution through frequency charts. The statistical comparisons were performed by χ² test for the discrete variables and the Student t test for the continuous variables. For the assessment of the frequency of the different aggregations of the CVRF, the aggregations were considered in an exclusive manner. An exploration factorial analysis was performed in order to determine the correla-
tions and the lowest number of factors that might explain the MS. We used the Kaiser-Meyer-Olkin (KMO) index to determine the sample adequacy level. The mean arterial pressure (MAP) has been used to reduce the co-linearity in the EFA instead of the SAP and DAP. The method of maximum probability has been used for the extraction of a factor that compares the adjustment goodness of the model of a factor with the possible multifactorial model found in the EFA, separately for men and women. 13

Results

Socio-demographic characteristics and clinic of the sample

The socio-demographic and clinic characteristics of the entire study population and by genders are depicted in table 1. For all the studied parameters, except for SAP and BMI, the male population showed relevantly higher values compared to women. The women had values relevantly higher regarding to the BMI than men (p <0.05) and there have not been differences between genders as regards to the SAP.

Prevalence of the cardiovascular risk factors

The dyslipidemia was the most frequent risk factor (34%; CI of 95%: 32.5-35.5) in the entire population, followed by the AHT (32%; CI of 95%: 30.2-33.8), obesity (27%; CI of 95%: 25.3-28.7) and the alteration of the glucose metabolism (23%; CI of 95%: 21.6-25). When we analyzed the differences between genders, we observed that the men showed a relevantly higher prevalence of dyslipidemia (p <0.05) and lower regarding to obesity compared to women (table 2). The prevalence of MS, according to the criterion of NCEP-ATP III, in the sample as a whole was of 15% (CI of 95%: 13.8-16.6), relevantly higher (p <0.01) in men (19.5%) than in women (14.7%). The prevalence of abdominal obesity was of 27.3% (CI of 95%: 22-29) in the sample as a whole and relevantly higher (p <0.01) in women (33.8%) than in men (17.1%).

Aggregation number and pattern of the cardiovascular risk factors

Most of the subjects of the population did not show any CVRF (33%) or only one (32.5%). However, most of the men (35%) showed a CVRF, while most of the women (38%) did not show any (table 3).

22% of the population showed aggregation of two CVRF: AHT-obesity (5.3%; CI of 95%: 4.4-6.2); AHT-dyslipidemia (4.1%; CI of 95%: 3.3-5) and obesity-dyslipidemia (3.8%; CI of 95%: 3.1-4.6).

The principal aggregation patterns in men are dyslipidemia-AHT (6.4%) and dyslipidemia-hyperglycemia (6.1%), while the aggregation pattern AHT-obesity (6.8%) prevails in women.
11% of the population showed aggregation of three CVRF: AHT-obesity-hyperglycemia (4.1%; CI of 95%: 3.3-5), which is the most frequent aggregation both in men and women. The aggregation of the four considered factors, hyperglycemia-AHT-obesity-dyslipidemia was only found in 1.9% of the sample (table 4).

**Factorial analysis of the cardiovascular risk factors considered in the metabolic syndrome**

In a general manner, the considered CVRF tend to group in three factor clusters that explain up to 61% of the variable. The first cluster is constituted by the basal glycemia and the obesity. The second one includes the glycemia after 2 hours, the insulin and MAP. The MAP is superimposed with the first cluster, therefore it can also be considered as a component. The third cluster comprised blood lipids (CT/cHDL and triglycerides) (table 5).

On this regard, in men, the CVRF tend to group in four clusters that explain up to 70% of the variable (factor 1: basal glycemia and triglycerides, factor 2: BMI and sagittal abdominal diameter; factor 3: glycemia after 2 hours and insulin, CT/cHDL; factor 4: MAP).

In turn, in women, only two factors might explain up to 59.1 of the variable (factor 1: BMI, sagittal abdominal diameter, MAP; basal glycemia and after 2 hours and insulin; factor 2: triglycerides and CT/cHDL). The adjustment goodness of the test showed a value of p <0.001,
both for men and for women, and the null hypothesis of existence is rejected as regards of a unique factor as underlying.

**Discussion**

During the last decades we are considering an increase in the CVRF prevalence, as the hyperglycemia, the dyslipidemia, the AHT or the obesity. In our case, the analysis performed in the general non-diabetic Spanish population places the dyslipidemia as the most prevalent of the considered CVRF (34%), followed by the AHT (32%), the obesity (27%) and the alterations in the glycemia (23%). These results are slightly different than the data described in other epidemiologic studies performed in our field, that reveal that the prevalence of the AHT reaches 40% in mean life ages and the obesity approximately 20%. This can be explained in part because our study is focused on the general population aged 35-64 (does not include elder population, in which the AHT is very high) and non-diabetic population (once excluded from the analysis the cases detected of diabetic patients), in which it is known that the prevalence of AHT is also very high. This can also be related with the differences between sexes as regards to the prevalence and the mean number of CVRF, since the menopausal and post-menopausal female population has an obesity and dyslipidemia pattern that is similar to the men’s pattern than to the young adult woman.

When evaluating the repercussion of the CVRF on the cardiovascular risk, it is important to consider that the different factors interact in a multiplying form among them; therefore the risk derived from the simultaneous exposure to some of them is higher than the one that might be expected from the simple addition of the corresponding risk to each one. However, when analyzing the physiopathology of the different CVRF aggregations, it is more efficient to consider only the excluding aggregations (pure) among the factors. On this regard, the most usual aggregation in the whole of the sample was the AHT-obesity with a global prevalence of 6%. Such aggregation of CVRF was also more frequent in women, but the aggregation AHT-dyslipidemia prevailed on men.

During the last decades, the appearance of the “metabolic syndrome” concept as cluster of several factors is getting more importance in the clinical practice and the identification of the individuals with MS provides opportunities to intervene early in the processes that predispose the development of CVD. The MS is integrated by several abnormalities that in an isolated manner do not constitute a defined disease, but in a concomitant manner they make an associated clinical entity with a high risk of CVD. We have considered the definition of the NCEP-ATP III for our study, which is the most used one in clinical and in epidemiologic studies, and a good operative definition, as it does not affect the involved factors. According to the criteria of NCEP ATP III, the prevalence of MS found in this study (15%) is slightly higher than the one assessed for the active Spanish working population (10.2%) and lower to the one described in the American (25%) and European popula-
This study ensures the results of other studies,\textsuperscript{26,27} that the glycemia variables, obesity and MAP. Thus, the MS can be understood as a true reflection of the cardiovascular risk phenotype aggregations in the population. This study ensures the results of other studies,\textsuperscript{26,27} that leave on record that it is frequent to find physiological, metabolic factors in the population as well as strictly cardiovascular and states the inexistence of a common unifier factor.

Moreover, it can be observed a different cluster in men and women that state what has been described in other previous works\textsuperscript{28,29} regarding the difference between sexes in the factor involved in the MS. It seems to be a central nucleus bond to glucose metabolism, which in women is closely related with the fat distribution in the body and with the AP, while in men it is related to lipid metabolism and atherogenic index. These results support the tendencies that consider that the clinical approach should be addressed to detect the CVRF in a customized manner.\textsuperscript{30} Therefore, the MS would pass to be a “primary objective” in the prevention of the CVD in the therapeutic plans of patients at risk and not secondary, as other authors set out.\textsuperscript{31,32} So the efforts of future investigations shall be addressed to optimize the prevention strategies and the early detection of the factors that make such MS in the population at risk.

As conclusion, we point out that the prevalence of the CVRF in the general population is high. From them, the dyslipidemia is the most frequent one in the population as a whole, but the AHT is the most common factor present in all the aggregations. There are great differences regarding to the prevalence and the aggregation of the CVRF in men and women. This can be proved by using factorial analysis that indicates a correlation between glucose metabolism and lipid parameters in men and with obesity and AP parameters in women.

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\textbf{Declaration of potential conflict of interest}

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\textbf{References}