LOOKING FOR A POPULATION-BASED DEFINITION OF THE METABOLIC SYNDROME

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The Metabolic Syndrome: The Concept

The publication of several definitions of the metabolic syndrome made this topic popular, but highly controversial. Nevertheless the concept of the metabolic syndrome has theoretical and practical advantages. The metabolic syndrome integrates, in a single diagnosis, the clinical manifestations of insulin resistance and/or abdominal obesity that lead to increased cardiovascular morbidity and precede type 2 diabetes [1]. The combination of the components of the metabolic syndrome gives the epidemiologist an instrument with a good predictive power for future complications. For example, in the Botnia Study [2], a 6.9 year follow up study of 4,483 first degree relatives of patients with type 2 diabetes, the relative risk for having CHD was greater in patients with the metabolic syndrome (relative risk [RR] = 2.96) compared to that found for obesity (RR = 1.44), dyslipidemia (RR = 1.73), hypertension (RR = 1.57), microalbuminuria, and insulin resistance by themselves. The same is true for incident diabetes [3]. Thus, the relative risk for having coronary heart disease (CHD) is greater in cases with the metabolic syndrome compared to the risk associated with each component alone. It provides the primary care physician an integrative view linking conditions frequently seen together but thought unrelated in the past (e.g. hypertension and low high density lipoprotein [HDL] cholesterol). However, this field remains contentious due to the significant limitations of the available definitions of the disease. We will discuss an adaptation of the most frequently used definition of the metabolic syndrome (i.e. that proposed by the National Cholesterol Education Program [4,5]); the proposal reflects the continuous nature of the metabolic syndrome and was adapted to the characteristics of Hispanic subjects, using population-based data.

The Metabolic Syndrome: The Definitions

Every group that has embraced the task of defining the metabolic syndrome has confronted difficult questions. These include which traits have to be included, the importance given to each trait, the methods selected to define the traits, and the thresholds for identifying abnormal cases. Each trait can be evaluated using different parameters. As a result, the number of possible components of the metabolic syndrome has grown significantly. In addition, the categorical approach of the current criteria oversimplifies the complexity of the syndrome. The need for having thresholds for defining abnormality for every trait has lead to arbitrary decisions; their selection should be based on the associated risk of the identified phenotype. Hence, the current definitions include, in the “affected” category, a heterogeneous group of cases with a broad range of relative risks for future complications.

The NCEP criteria are the most widely used definition of the metabolic syndrome. The major strength of the criteria is the simplicity of the components; the parameters can
be measured in almost every setting. However, the NCEP approach has been heavily criticized because the criteria have a low sensitivity for detecting insulin resistance (0.2) [6]; this finding is not in agreement with the original concept of the metabolic syndrome. In addition, the cutoff values for the waist circumference and the HDL cholesterol may vary between ethnic groups [7]. This issue was recognized by the International Diabetes Federation that proposed ethnic-specific thresholds for the waist circumference [8]. However, the adaptation of the waist circumference threshold has a remarkable impact on the prevalence of the syndrome.

The metabolic syndrome should be viewed as a progressive process that over time leads to major complications (Figure 1). Its expression depends heavily on age and exposure to an unhealthy lifestyle. The diagnosis of the metabolic syndrome should not be managed as an acute event; a “yes or no” approach is not valid in chronic-degenerative disorders such as this. The metabolic syndrome incorporates the clinical entities in which insulin resistance plays a major pathophysiological role. This concept results in a group of subjects with a spectrum of long-term risk for having the final outcomes. In addition, the risk will depend on the characteristics of the population being treated. Thus, the metabolic syndrome definition should take into account the heterogeneity of the disease and it may be adaptable to the ethnic group in which it will be applied.

A New Approach to Define the Metabolic Syndrome

We published a population-based definition of the metabolic syndrome derived from the distribution of the majority of the components of the NCEP definition found in a Mexican population [9]. The age/sex distribution curve for each variable was divided into deciles. An increasing number of points were given per decile of each curve. The sum of the points is considered a new variable (the maximal number being 60) that is used to define the metabolic risk for each case. This example clarifies the method: a 28-year-old man with a BMI of 27.7 kg/m² (BMI 70-80th percentile = 8 points), HDL cholesterol of 0.63 mmol/l (> 90th percentile = 10 points), triglycerides of 3.37 mmol/l (> 90th percentile = 10 points), fasting glycemia of 5.38 mmol/l (70-80th percentile = 8 points), systolic blood pressure of 120 mmHg (20-30th percentile = 3 points), and diastolic pressure of 80 mmHg (30-40th percentile = 4 points) collects 43 points. This subject falls within the 80th and 90th percentile when classified according to the total number of points accumulated; he would not be considered affected by the NCEP definition. However, as it will be shown, his risk for having incident diabetes is equal or greater than a large proportion of the cases considered as affected with the NCEP criteria. Thus, this approach provides an integrative view of the disease and avoids the use of arbitrary thresholds.

The data source was the National Survey of Chronic Diseases [10-11], a population-based study representative of the Mexican adults aged 20 to 69 living in urban areas in 1992-93. The body mass index was used instead of waist circumference because only the distribution of the former was available. This population-based definition was validated using the prospective data from the Mexico City Diabetes Study (a population-based study designed to characterize the prevalence and natural history of type 2 diabetes in a low income urban population located in Mexico City) [12,13].

We compared the predictive power for incident diabetes of the NCEP and the population-based method in the Mexico City Diabetes Study. Incident diabetes was diagnosed in 7.6% of the participants. The incidence of diabetes was directly proportional to the total number of points accumulated. The risk became significant above the 40th percentile (≥ 30 points) when compared to the reference group (6-18 points). In order to have a reasonable comparison against the NCEP criteria, we selected the cases with ≤ 1
component of 2004 version (n = 457) as the reference group for all methods. The population-based definition had a significantly better prognostic power compared to the original and the updated NCEP criteria, based on a greater area under the ROC curve (0.746 versus 0.697 and 0.723 respectively, p < 0.05). Also the odds ratio was greater in the upper quartile of the sum of points (≥ 39 points): OR 12.71 (95%CI 5.67-28.49) compared to that found for the original (OR 9.52 95%CI 4.69-19.31) and the updated (OR 11.14, 95%CI 5.33-23.30) NCEP definitions.

The population-based definition provides complimentary information to the NCEP definitions. This approach allows us to distinguish subjects with a 7-year incidence of diabetes as low as 7.5% (original NCEP with less than 30 points) from others with rates above 25% (original NCEP with ≥ 43 points). All cases with incident diabetes that had a total number of points in the upper quintile were identified by both NCEP versions. In contrast, incident diabetes cases that had a total number of points at baseline in the middle of the range were frequently missed by both NCEP definitions. In conclusion, our points system allows us to categorize metabolic syndrome cases with varying metabolic risk. Furthermore, cases missed by the current NCEP criteria that are still at significant risk for incident diabetes can also be identified.

Conclusion

The metabolic syndrome should be viewed as a progressive process over time that leads to major complications (i.e. type 2 diabetes and CHD). Here we have described a strategy to avoid some drawbacks of the NCEP definition. Instead of interpreting each variable in a dichotomous fashion, each is analyzed as a continuous variable. Individual results are compared against the distribution of the variables encountered in population-based data. Our approach had a better prognostic power for incident diabetes compared to previous versions of the NCEP definition. We recognize that the clinical application of our method may be limited by the necessity for a decile distribution of the variables. However, this tool may be useful for research and epidemiological studies.

References


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Figure 1. The metabolic syndrome: an heterogeneous and progressive long-term process that leads to major complications (type 2 diabetes and CHD).

WHO= World health Organization criteria
NCEP= National Cholesterol Education Program definition

Number of traits of the metabolic syndrome
(abdominal obesity, arterial hypertension, dyslipidemia, impaired glucose tolerance)

Accumulation of intra-abdominal fat
Insulin resistance
Genetic predisposition
Undernourishment early on life

Life span

Type 2 diabetes
Atherosclerosis
Other outcomes (i.e. non-alcoholic steatohepatitis)