METABOLIC SYNDROME AS A CARDIOVASCULAR DISEASE RISK FACTOR: PATIENTS EVALUATED IN PRIMARY CARE IN SPAIN

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The metabolic syndrome (MS) was first described in 1988 by Reaven as “syndrome X.” Although previously alluded to by several authors (Kylin, Marañón, Avogaro, Crepaldi, and others) and termed a multi-metabolic syndrome or insulin resistance, it represented a known risk factor in the development of cardiovascular disease events and was associated with accelerated atherosclerosis [1-12]. The relationship between MS and cardiovascular disease has been well documented in the biomedical literature [13-21]. References in primary care (PC) are available and seem to highlight a high-risk population in developed countries. As such, MS constitutes a multi-pathology frequently encountered in PC consulting rooms and its high prevalence would indicate the need for alertness in identifying the syndrome and treating its components in order to minimize the risk of subsequent cardiovascular disease.

Prevalence of Metabolic Syndrome

To determine the prevalence of MS in the population receiving attention in PC, and to indentify factors or components of MS that independently influence cardiovascular disease prognosis related to MS and to analyse the impact of each component on the appearance of cardiovascular disease events, we performed a study in PC [22].

This prospective, multi-centered cohort study to observe the appearance of cardiovascular disease events with a 2-year follow-up, was performed in patients who were attending 5 basic health-care areas (BHA) in Catalonia, Spain. The catchment area of the PC centers has a total of approximately 72,000 individuals.

The selected subjects were contacted and informed of the study and their written consent to participate was solicited. The tests included blood constituent analyses and a 75 g glucose tolerance test (except for known diabetics). The exclusion criterion was that of having suffered any cardiovascular disease complication prior to recruitment to the present study.

MS criteria were defined according to the NCEP-ATPIII, IDF and WHO sets. Cardiovascular disease complications were defined as ICD-9 codes corresponding to: coronary heart disease, cerebrovascular disease, peripheral vascular disease, diabetic retinopathy, nephropathy, and neuropathy. Also considered as a complication are those deaths related to cardiovascular disease e.g. myocardial infarction that causes death.

Of the 750 subjects selected, 30 were excluded due to having had previous cardiovascular disease events. With respect to MS, the study detected 166 subjects (23.1%; 95%CI: 20.0-26.3) who fulfilled the MS diagnostic criteria according to the WHO, and 210 (29.2%, 95%CI: 26.9-32.6) according to the NCEP-ATPIII criteria; 141 individuals fulfilled both definitions. Two hundred fifty-two subjects (35.0%; 95%CI: 31.5-38.6) fulfilled IDF criteria; 210 of which fulfilled the NCEP criteria as well. The \( \kappa \) index of concordance between the first two
sets of criteria defining MS was 0.66 (p < 0.001) and between the second two sets was 0.87 (p < 0.001).

**Cardiovascular Disease Associated with Metabolic Syndrome**

Cardiovascular disease complications appeared in 113 (15.7%) subjects during the follow-up of 2 years. Overall, there were 142 different complications: 35 (4.9%) were peripheral vascular disease; 30 (4.2) coronary artery disease; 29 (45) nephrotic syndrome; 24 (3.3%) cerebrovascular disease; 18 (2.5%) were classified as having retinopathy; and 6 (0.8%) developed neuropathy. Segregated by cohort, the group with MS suffered 15 coronary complications, 12 cerebrovascular complications (or stroke), 18 peripheral artery disease, 11 retinopathies, 25 nephropathies, and 5 neuropathies. Conversely, in the group without MS, the complications were 15 coronary disease, 12 cerebrovascular, 17 peripheral vascular disease, 7 retinopathies, 4 nephropathies and 1 neuropathy.

Forward stepwise multiple logistic regression analyses of the factors that influenced the appearance of the cardiovascular disease events are summarized in Table 1. As observed in these multivariate analyses, the WHO criteria are more predictive of cardiovascular disease events than those of the IDF. This is evident when the complications are considered globally (OR = 3.48) as well as individually (i.e. cases of coronary artery disease, vascular disease, and nephropathy). Conversely, the NCEP criteria predict the cerebrovascular, arteriopathy, nephropathy, and neuropathy complication. IDF criteria predict the globally complications, as well as coronary, retinopathy, and nephropathy.

Table 1. Logistic regression of component factors in cardiovascular disease risk, adjusted for age and gender.

<table>
<thead>
<tr>
<th>CVD complication</th>
<th>B exponential = Odds Ratio(95%CI)*</th>
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<tbody>
<tr>
<td>All complications</td>
<td>Females; OR = 2.26(1.48-3.47)</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome (WHO criteria); OR = 3.48(2.26-5.37)</td>
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<tr>
<td></td>
<td>Metabolic syndrome (IDF criteria); OR = 2.28(1.84-4.90)</td>
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<tr>
<td>Coronary</td>
<td>Metabolic syndrome (WHO criteria); OR = 3.10(1.48-6.49)</td>
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<tr>
<td></td>
<td>Metabolic syndrome (IDF criteria); OR = 1.96(1.15-4.89)</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>Females; OR = 2.46(1.06-5.37)</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome (NCEP criteria); OR = 2.59(1.26-5.27)</td>
</tr>
<tr>
<td>Peripheral vascular</td>
<td>Females; OR = 3.61(1.72-7.55)</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome (WHO criteria); OR = 2.26(1.11-4.61)</td>
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<tr>
<td></td>
<td>Metabolic syndrome (NCEP criteria); OR = 2.74(1.82-5.33)</td>
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<tr>
<td>Retinopathy</td>
<td>Metabolic syndrome (NCEP criteria); OR = 2.80(1.07-7.34)</td>
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<tr>
<td></td>
<td>Metabolic syndrome (IDF criteria); OR = 3.63(2.27-7.94)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>Females; OR = 2.97(1.32-6.66)</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome (WHO criteria); OR = 11.78(4.91-28.3)</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome (IDF criteria); OR = 3.51(2.07-12.2)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Metabolic syndrome (NCEP criteria); OR = 12.41(1.44-106.9)</td>
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</table>
* For each component are indicated those components included in the regression equation. The rest of the components did not reach statistical significance and, as such, have not been included in the table.

The $\chi^2$ analysis of the number of components of MS (NCEP criteria) indicated significant differences ($p < 0.001$) between the subjects with 0, 1, or 2 components (absence of MS) and those that had 3, 4, or 5 (presence of MS). The prevalence of events was 10.78% in subjects free of MS and 27.61% in subjects suffering from MS (OR = 2.56).

The differences were, as well, significant with the $\chi^2$ test ($p < 0.001$) between individuals who did, and did not, fulfill the criteria using the WHO criteria. The prevalence of CVD events was 10.8% in the group without MS and 31.9% in the group with MS (OR = 2.95).

The rate of cardiovascular disease events during the first 2 years of follow-up was 98.6 events/1,000 patient-years.

**Conclusions**

In conclusion, we believe that MS diagnosis is a simple and easy clinical tool to assess potential cardiovascular risk and, as such, can identify those patients who can benefit most from the prioritization of health-care resources, and we conclude that MS and concomitant CVD risk is high in ostensibly normal populations attending primary care clinics.

**References**


