

Metabolic Syndrome

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Evolution of the metabolic syndrome

In 1939, the English author, H. Himsworth, in his Goulstonian Lecture at the Royal College of Physicians, in London, showed that the absorption of glucose varied from one individual to another according to cell sensitivity to insulin (greater or lesser resistance), suggesting a mechanism that later would explain diabetes mellitus type 2¹.

In 1968, twenty years after establishment of the Framingham Heart Study Project, it became evident that certain factors could be deleterious, in one way or another, to proper function of the arteries. The important concept of risk factors was born and, in the following 30 years, it would revolutionize the natural history of atherosclerosis.

Therefore, a risk factor is defined as a means that can lead an individual to a greater likelihood of developing a disease.

In spite of Himsworth's article having been published in 1939, it was only in 1979 that De Fronzo, in the United States, described an adequate and precise technique to measure insulin resistance, which was called Glucose Clamp Technique, making it possible for this resistance to be intensely and extensively studied².

In 1988, G. Reaven, from the Department of Cardiovascular Medicine at Stanford University, in California, in a memorable conference (Banting Lecture), drew attention to the fact that in certain individuals, some risk factors frequently appear as a cluster. He called this condition the insulin resistance syndrome, since these individuals had a low sensitivity to insulin^{3,4}.

In 1998, the World Health Organization (WHO) developed a criterion to define this condition, and for the first time called it the Metabolic Syndrome, including in the definition arterial hypertension, dyslipidemia, obesity, and microalbuminuria⁵.

In 2001, by means of the National Cholesterol Education Program (NCEP), the National Institute of Health assembled the Third Adult Treatment Panel (ATP III) and suggested another criterion to define the metabolic syndrome, different from that of the WHO. The American definition was simpler and more practical since it did not use weight and microalbuminuria; but, on the other hand, it required

at least three abnormal components for a diagnosis⁶. The metabolic syndrome, then, would be a multiple prediction system for cardiovascular risk based on some risk factors that were not considered in other systems.

In 2002, Lakka et al, showed that cardiovascular diseases and overall mortality rates were higher in middle-aged men with metabolic syndrome, even in individuals with no established coronary artery disease or diabetes⁷.

In April 2005, the First Brazilian Guideline for Diagnosis and Treatment of Metabolic Syndrome was published with the support of the Brazilian Society of Cardiology [Sociedade Brasileira de Cardiologia]^{8,9}.

Critical evaluation of metabolic syndrome

Definition

1) The metabolic syndrome is not yet well defined and well characterized, as some suppose; each existing definition presents different components, variables, or risk factors, frequently causing confusion and ambiguity¹⁰⁻¹²;

2) The medical value of diagnosis of the syndrome is not yet evident¹³;

3) For these reasons, currently, certain authors prefer to call this entity metabolic risk or cardiometabolic risk, instead of metabolic syndrome¹³.

General aspects

1) Since the metabolic syndrome is a cardiovascular risk prediction score, is it necessary to include in it patients with prior clinical diagnoses of diabetes or cardiovascular disease, even though they would have nothing to gain as to benefits of knowing about the risks or a recognized treatment?

2) There are studies suggesting that, as a cardiovascular risk score, Framingham's coronary score is superior to that of Metabolic Syndrome^{10,12,13}; nevertheless, the ARIC Study compared these two methods by means of "receptor operating curves" and found identical predictive values¹⁴.

Pathophysiology of metabolic syndrome

1) Although insulin resistance may be the best proposal for the pathophysiological basis of metabolic syndrome, there are considerable doubts as to its presence in all patients¹²;

2) There are several other suggestions for the pathophysiological substrate of the metabolic syndrome, such as inflammation, obesity, and hyperglycemia, all of them requiring further research in order to confirm them as substrates¹²;

Key words

Metabolic syndrome; hypertension; dyslipidemias; diabetes mellitus.

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3) Proinflammatory and prothrombotic states are already often associated with metabolic syndrome.

Components, variables or risk factors in defining metabolic syndrome

1) The risk factors that were grouped to define the metabolic syndrome are not based on any defined criterion. A rational criterion is needed for choosing syndrome components;

2) The metabolic syndrome is not yet, as supposed, a cardiovascular risk marker superior to the risk of each of its components. Therefore, the predictive value of the syndrome seems to be lower than that of the sum of its parts¹²;

3) The criteria to define metabolic syndrome generally includes four or five components; would they have the same value or the same weight in a risk assessment? In other words, would some combinations of components or factors carry the same risk as other combinations? The predictive value of each risk factor for cardiovascular disease is, therefore, variable, and depends on each specific risk present¹⁴;

4) Treatment of metabolic syndrome is not different from treatment for each of its components¹²;

5) In order to be effective, metabolic syndrome should be analyzed as the need for adding other risk factors to the roll of its components, such as age, sex, high sensitive C-reactive protein (hsCRP), family history or insulin resistance¹⁵;

6) It is known that the presence of diabetes or insulin resistance determines a risk greater than that of any other component¹⁶.

Research agenda

1) There is an urgent need, in metabolic syndrome, for more fundamental data that are clinically significant and critically evaluated¹²;

2) All aspects of the metabolic syndrome, including its name, poor understanding of its pathophysiology, inclusion or exclusion of certain components, validity of making a clinical diagnosis, and nonexistence of a treatment for the syndrome, demand further research, even if just to call it syndrome or disease, and to clarify if knowledge of it is truly useful.

Conclusion

We have seen throughout this exposition how this brilliant idea has been evolving, even though it is still under progress and does not have a precise definition or a known substrate as its basis. As I mention in my book, these ideas are revolutionary and have changed our traditional way of thinking. We can now consider it possible that hypertension is also a metabolic disease, and that diabetes mellitus type 2 is a vascular condition, in which a high glucose level would be a late manifestation of the disease¹⁷.

Metabolic syndrome continues to be a brilliant idea with many controversial data.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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