Intravenous adipocyte-secreted IL-18 and markers of body fat composition. We hypothesized that adipose tissue is not a major contributor to circulating IL-18. This is not in contrast with data on IL-18 expression in adipocytes, since the reported amount of in vitro secreted IL-18 was rather low (2). This finding does not preclude a role for adipocyte-expressed IL-18 in adipose tissue since higher concentrations, which are relevant for the cross-talk between adipocytes and infiltrating immune cells, might be reached locally. Furthermore, we did not find a sex difference in the relation between IL-18 and markers of body fat composition, whereas this has been demonstrated for C-reactive protein and other inflammatory mediators (5). We conclude that the reported impact of weight loss on IL-18 levels (3) is indirect, as long-term caloric restriction (3) can be assumed to attenuate systemic immune activation and therefore also reduce IL-18 in the circulation. On the other hand, extensive weight loss is associated with a substantial increase in insulin sensitivity. The data linking increased IL-18 with reduced insulin sensitivity (4) and elevated type 2 diabetes risk (1) indicate that insulin resistance and not obesity per se may be the major determinant of circulating IL-18 concentrations.

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The Metabolic Syndrome: Time for a Critical Appraisal: Joint Statement From the American Diabetes Association and the European Association for the Study of Diabetes

We read with interest the American Diabetes Association statement about the metabolic syndrome (1). The idea that the aggregation of borderline risk factors could result in cardiovascular damage equal or superior to that occurring in individuals carrying a full-blown risk factor disease was intriguing. However, this intuition was soon polluted by inclusion of patients with frank diseases. If the philosophy of the metabolic syndrome is to draw firm attention upon “at very high risk” subjects, then the time has come to capture only subjects falling into borderline categorical zones using the Adult Treatment Panel III criteria: fasting glucose levels between 110 and 126 mg/dl, triglycerides between 150 and 200 mg/dl, HDL cholesterol between 30 and 40 mg/dl for men and between 40 and 50 mg/dl for women, blood pressure between 130/80 and 140/90 mmHg, and similar waist circumference values in the absence of obesity (BMI > 30 kg/m²). If, however, the basilar concept is the construct of an algebraic hierarchy of risk, the reflections of Kahn et al. (1) claim for the noninferiority of the sum of components versus the whole syndrome. The concept of a “pure” metabolic syndrome, i.e., identifying subjects without frank diseases such as diabetes, obesity, atherogenic dyslipidemia, and hypertension, would have some benefits: 1) to avoid double-labeled diagnosis, for example diabetes and the metabolic syndrome; 2) to give the real number of subjects at risk and to trace the natural history of the syndrome; and 3) to interfere with its evolution with lifestyle or pharmacological interventions. In the National Health and Nutrition Examination Surveys III sample, ~8% of coronary heart disease events occurred in people with only borderline levels of multiple risk (2). Moreover, intensive lifestyle intervention (3), diet (4), and drugs (5) have all been shown to be effective in reducing the prevalence of metabolic syndrome, although interventions based on diet, physical activity, and weight reduction seem to work better than drugs. Lastly, it would be easier to force a labeled patient (that with a pure syndrome) to follow advice for lifestyle changes than for unlabeled subjects with one or more borderline risk factors. Since the way to disseminate healthy practices is all but easy, any help is welcome.

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The Metabolic Syndrome: Time for a Critical Appraisal: Joint Statement From the American Diabetes Association and the European Association for the Study of Diabetes

Response to Kahn et al.

The joint statement from the American Diabetes Association and the European Association for the Study of Diabetes (1) takes issue with the entity of the metabolic syndrome, criticizing it on a number of levels, including the seemingly arbitrary selection of its component risk factors and their corresponding cutoff values, the lack of concordance between competing definitions of the metabolic syndrome, and, fundamentally, that the syndrome itself conveys no greater information than the sum of its component risk factors.

Unfortunately, these criticisms detract from the primary utility of the metabolic syndrome as a means of assisting the front-line practitioner in identifying risk factors that require clinical attention. This is especially pertinent for mental health practitioners who have become increasingly aware of the vulnerability of the seriously and persistently mentally ill in developing diabetes and cardiovascular disease and the potential impact of psychotropic medication on this risk (2). The initial focus of attention had been on monitoring for obesity, but body weight is only one of many parameters that need to be assessed on a routine basis. The concept of the metabolic syndrome allows for a discussion of other important traditional cardiovascular risk factors that require ongoing monitoring such as blood pressure, lipid profile, and glucose. Furthermore, unlike most of the existing cardiovascular risk algorithms, the metabolic syndrome includes consideration of central obesity and serum triglyceride levels. Most psychiatrists are unlikely to calculate Framingham risk scores. Hence, the pragmatic value of the metabolic syndrome is not in studying pathophysiology per se or in designing clinical trials for those who rigidly meet its criteria, but rather the usefulness of the concept is in the ongoing education of practitioners and, ultimately, in the improvement of overall health care (3).

References


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