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# Atherosclerosis

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## Letter to the Editor

### Farewell to the metabolic syndrome? Not too soon

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The metabolic syndrome (MS) has received much attention over the last years [1–3]. Almost every scientific society has developed an unique definition of the metabolic syndrome. Most of the definitions are based on the premise that insulin resistance/visceral obesity is the basis for the development of the metabolic syndrome. While the concept of insulin resistance has been a controversial issue in clinical science, it has never reached clinical utility. The metabolic syndrome as the clinical presentation of this pathophysiological derangement may be the only advantage to use this syndrome.

Many investigators have criticised the use of the metabolic syndrome in clinical practice. The controversy is related to the use of this terminology to estimate the risk for the development of type 2 diabetes mellitus and the risk of coronary artery disease (CAD) [4]. Most workers agree upon the former, but conflicting data on the predictive value for the development of CAD have led to a vivid discussion [5–7].

The majority of the scientists agree that the clustering of the components of the metabolic syndrome is more or less equal to the sum of the individual risk factors [8]. The concern could be that by using the metabolic syndrome as a clinical entity, the attention could be distracted from diabetes [1]. Furthermore, for the estimation of CAD risk the use of the individual classical risk factors combined with apolipoprotein measurements seems to be sufficient as the INTERHEART study clearly has shown [9]. In addition, the SCORE tables already help to estimate the mortality risk of CAD in clinical practice [10].

Others, however, advocate the use of the metabolic syndrome because of its simplicity and the power to detect individuals at high risk to develop type 2 diabetes and CAD. Another argument has a more didactic background. The use of the definition with rather simple parameters is within the reach of every clinical (general) practitioner [11].

The paper by Solbu et al. in this issue of the Journal, deals with the question whether the metabolic syndrome is a stronger predictor of cardiovascular mortality than the presence of microalbuminuria [12]. The authors used the Tromsø database to answer this question. They used the IDF definition for the metabolic syndrome which includes the waist circumference as the most important factor, blood pressure and fasting plasma lipids and glucose [11]. Their data suggest that microalbuminuria indeed is a

stronger predictor of mortality than the metabolic syndrome. This is an interesting finding, which may be considered as a reason not to use of the metabolic syndrome to estimate risk. However, the metabolic syndrome was a strong predictor of myocardial infarction in this study, independent from the urinary albumin-creatinine ratio (ACR) since increased risk was found in both high ACR/MetS (75%) and low ACR/MetS (82%). Furthermore, the authors did not show data in relation to the development of diabetes.

What do clinicians and researchers gain from this message? Microalbuminuria as an important predictor of CAD risk has already been reported by many groups. Some would argue that this comparison should have included risk calculations with the SCORE tables [10]. The IDF definition is based, among others, on fasting lipid and glucose levels [11]. The authors did, however, not have fasting samples. One could argue that the use of the IDF definition was not used adequately here. Especially, triglyceride concentrations can vary enormously even in the fasting state [13]. HDL-C concentrations may also be lower in non-fasting samples [14]. Are there any data suggesting that non-fasting lipids and glucose are just as sensitive to detect the metabolic syndrome as fasting levels?

The question also is what would happen if other cardiovascular risk factors would have been analyzed such as LDL-C or apoB? Once again, for LDL-C fasting measurements are necessary and therefore, the analysis performed may not be reliable using non-fasting samples.

Although the present paper by Solbu et al. confirms the notion that microalbuminuria is an important risk indicator that should be considered in risk equations, the comparison with the metabolic syndrome can not lead to discarding this syndrome as an important identifier for both diabetes and atherosclerosis. This is especially the case if the components of the metabolic syndrome are not being used as in the original (IDF) definition. Finally, microalbuminuria reflects vascular damage and may be a consequence of the metabolic syndrome [15] but its presence depends most likely on the duration of the metabolic syndrome.

#### References

- [1] Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia* 2005;48: 1684–99.

- [2] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415–28.
- [3] Opie LH. Metabolic syndrome. *Circulation* 2007;115:e32–5.
- [4] McConnachie A, Shaper AG, Blauw GJ, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. *Lancet* 2008;371:1927–35.
- [5] Dekker JM, Girman C, Rhodes T, et al. Metabolic syndrome and 10-year cardiovascular disease risk in the Hoorn Study. *Circulation* 2005;112:666–73.
- [6] Hu G, Qiao Q, Tuomilehto J, Balkau B, Borch-Johnsen K, Pyorala K. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. *Arch Intern Med* 2004;164:1066–76.
- [7] Sattar N, McConnachie A, Shaper AG, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. *Lancet* 2008;371:1927–35.
- [8] Sundström J, Vallhagen E, Risérus U, et al. Risk associated with the metabolic syndrome versus the sum of its individual components. *Diabetes Care* 2006;29:1673–4.
- [9] Yusuf S, Hawken S, Opunpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937–52.
- [10] De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice. *J Cardiovasc Prev Rehab* 2003;10:S1–10.
- [11] International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. April 14, 2005: [http://www.idf.org/webdata/docs/Metac\\_syndrome\\_def.pdf](http://www.idf.org/webdata/docs/Metac_syndrome_def.pdf).
- [12] Solbu M, Kronborg J, Jenssen TG, et al. Albuminuria, metabolic syndrome and the risk of mortality and cardiovascular events. *Atherosclerosis*, doi:10.1016/j.atherosclerosis.2008.11.002, in press.
- [13] Delawi D, Meijssen S, Castro Cabezas M. Intraindividual variation of fasting plasma lipids, apolipoproteins and postprandial lipemia in familial combined hyperlipidemia. *Clin Chim Acta* 2003;328:139–45.
- [14] De Bruin TWA, Brouwer CB, Gimpel JA, Erkelens DW. Postprandial decrease in HDL-cholesterol and HDL-associated apolipoprotein A-I in normal subjects in relation to triglyceride metabolism. *Am J Physiol* 1991;260:E492–8.
- [15] Bianchi C, Penno G, Daniele G, et al. The metabolic syndrome is related to albuminuria in type 2 diabetes. *Diabetic Med* 2008;25:1412–8.

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