Over the last decades, inflammation and obesity have deserved particular attention to explain the etiopathogenesis of atherosclerosis. (1, 2)

White adipose tissue produces tumor necrosis factor-alpha and specific neutralizing antibodies reverse insulin resistance in obese animals. (3) Therefore, the study of adipose tissue has attracted great interest, as it has been recognized as a real endocrine organ. (2)

In most subjects, obesity is associated with changes in adipocytes and macrophage function, expressing a “chronic low-grade inflammation” which leads to insulin resistance (IR) and to the development of diabetes mellitus (DM). (4)

Adipose tissue is the main source of interleukin-6 (IL-6), a potent marker of inflammation. This cytokine is also associated with IR and increases the risk of DM, independently of body weight. (5)

Adipocytes also produce adiponectin, a cytokine with anti-atherosclerotic effects that increases insulin sensitivity by inhibiting the production of hepatic glucose, improves peripheral glucose utilization and increases fatty acid oxidation. Adiponectin in synthesis is reduced in IR, obesity, metabolic syndrome (MS) and DM.

Recently, the key role of IR has lost importance while more attention is being paid to the theory of lipotoxicity due to leptin resistance and ectopic lipid deposition. (6)

Finally, truncal obesity is related to IR, determining a pro-inflammatory condition with increased levels of adipokines as IL-6 and tumor necrosis factor-alpha and adiponectin in reduction. Prothrombotic mechanisms, such as increase in fibrinogen levels and PAI-1 with subsequent inhibition of fibrinolysis, are also activated. All these factors predispose to other major risk factors as DM, hypertension and dyslipidemia. Under this scenario, the development of atherosclerotic disease may be just a matter of time.

Obesity predisposes to the development of DM, one of the main risk factors for cardiovascular disease.

In a multicenter study, Yusuf et al. (7) have insisted on the importance of truncal obesity as a major cardiovascular risk factor.

The MS is a possible intermediary between risk factors and the likelihood of presenting cardiovascular disease. Elevated waist circumference is an essential component of MS. This syndrome has deserved particular attention and its validity for determining the prognostic value or causality of its components has been widely discussed. (8, 9)

The World Health Organization (10) has recently excluded individuals with DM or known cardiovascular disease from the definition of MS as there is no sense in predicting conditions that are already established. The impact of this measure lowers the prevalence of MS to almost 25% and delimits the population for primary prevention. (11) In addition, the role of high sensitivity C-reactive protein (hsCRP) as a necessary mediator of inflammation in the “obesity-metabolic syndrome-diabetes-cardiovascular disease” continuum has been postulated and widely discussed. (12)

In this issue of the Revista Argentina de Cardiología, Benozzi et al. (13) analyze the association of a single determination of hsCRP with obesity and MS in an observational, cross-sectional study. This interesting paper included 467 adults between 18 and 67 years of age who were selected from a population attending a public hospital in the province of Buenos Aires between 2009 and 2011. The authors reported that in subjects with MS, hsCRP levels were significantly higher and increased when the number of MS components increased.

As study limitations, they reported that a cause and effect relationship between MS and hsCRP was not established due to the cross-sectional design of the study, and “only the association between both parameters was verified”.

Undoubtedly, this interesting investigation has the credit of establishing for the first time the profile of an American population of European descent by studying the association of a marker of inflammation with MS and obesity.

However, certain aspects related to the methods and conclusions should be considered. The description of the exclusion criteria is insufficient to understand the characteristics of the sample. As it happens with all non-randomized population-based studies, the possible biases cannot be recognized. Although many diseases have been adequately excluded, a population selected from a hospital surely includes differ-
ent diseases which may bias the results.

The study lacks a reasonable sample size; the low prevalence of MS may be influenced by the type of patients and the small number of patients included over a 2-year period.

The authors should have avoided mentioning in the conclusions of the abstract and full text that “these results show a strong relation between adipose tissue, cardiovascular disease and inflammation” (italics are added by me) or that “hsCRP may be useful to apply prevention and treatment strategies which help to control DM and CVD epidemics affecting the world population”. Conclusions should be in agreement with the objectives of the investigation and the obtained results; following this line, the study demonstrated a significant association between hsCRP, MS and its components.

The importance of hsCRP as determinant of cardiovascular disease has been postulated and widely discussed. (12) Its independent predictive value as determinant of cardiovascular events has been demonstrated, but it is accepted that its contribution to improve the area under the ROC curve is very low. Therefore, new statistical techniques, such as IDI (Integrated Discrimination Improvement Statistics) and NRI (Net Reclassification Improvement) have been developed for reclassification of different risk patients despite lack of improvement of the area under the ROC curve. (14)

In reference to the JUPITER trial (15), Ridker has noted lack of therapies acting selectively on elevated hsCRP to reduce cardiovascular events. (16)

So far, for the recent European guidelines on cardiovascular disease prevention, (17) hsCRP has a low evidence level (class IIb; level of evidence B; grade: weak) and recommend that hsCRP should not be measured in asymptomatic low-risk individuals and high-risk patients to assess 10-year risk of CVD (class III; level of evidence B; grade: strong).

Therefore, there is still a long and winding road of continuous and intense research to better understand the pathophysiology of atherosclerosis. Studies like the one of Benozzi et al. (13) contribute to maintain the interest in inflammation and commit to follow-up these patients, trying to establish the causality between biomarkers of inflammation and CVD.

Conflicts of interest
None declared.

REFERENCES