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Invited commentary

Is it time to implement a standardized oral glucose and fat load test to detect high risk patients? Probably not yet…

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The relationship between plasma triglyceride level and common carotid artery intima-thickness (CCA-IMT) is strongly debated and the available data have not yet confirmed an unequivocal relationship [1]. In this issue of Atherosclerosis, Batluk et al. reports an association between CCA-IMT and fasting triglyceride levels, but not the post-challenge one with a standardized combined oral glucose and fat tolerance test performed 3–7 days after first ever ischemic stroke. The glucose load was a standard oral glucose tolerance test (OGTT), in this case associated to a lipid charge (i.e. 250 mL cream, ingested within 30 min), with measurement of triglycerides level 3, 4 and 5 h post-challenge. Slow triglyceride metabolizers were defined as patients whose triglyceride levels rose until 5 h post-challenge, while fast triglycerides metabolizers as patients whose triglyceride values that rose sharply from 0 to 3 h post-challenge and thereafter declined. For all metabolism categories (fast, medium, and slow), a rise in triglyceride levels was defined as a >10% increase in triglyceride values from one consecutive time-point to the next (e.g. fasting to 3 h post-challenge; 3 h–4 h post-challenge, and 4–5 h post-challenge) [2].

From a pathophysiological point of view, both fat and sugar intake determines a dose-related increase in serum triglycerides and, at the same time, a series of vascular effect finally leading to intima-media thickening. The OGTT has been used largely as model of post-prandial state [3]. When mimicing a condition of high sugar intake with an OGTT, we could in fact observe an increase in laboratory biomarkers of vascular inflammation and endothelial dysfunction such as soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), interleukin-6 (IL-6), high-sensitivity C reactive protein (hsCRP), and tumor necrosis factor-alpha (TNF-alpha) [4], and of parameters related to vascular remodeling such as matrix metalloproteinases (MMP) 9 [5], especially in diabetics who are usually hypertriglyceridemic. On the other hand, the use of drugs which can reduce the increase of glycemia during an OGTT, such as acarbose and pioglitazone, are associated with an improvement of almost all the above cited laboratory parameters [6].

When considering the effect of an oral fat load (OFL) to mimic post-prandial hypertriglyceridemia mainly related to the assumption of dietary lipids, there is a linear trend between increasing numbers of metabolic syndrome components and the magnitude of the post-prandial triglycerides [7] and also an increase in laboratory markers of vascular inflammation such as sICAM-1, IL-6, hsCRP, sVCAM-1, Soluble E-selectin, and TNF-alpha [8], a decrease in biomarkers of endothelial dysfunction such as nitrites/nitrates and ADP and of parameters related to vascular remodeling such as MMP-2 and MMP-9 [9]. Once again, the changes in the plasma level of the most part of these parameters during an OFL are attenuated by the use of drugs reducing the peak of triglycerides, such as omega 3 polyunsaturated fatty acids [10] or acarbose [11].

So, from one side, it appears that the application of a standardized glucose and fat tolerance test could help to identify subjects with higher post-prandial increase in plasma triglycerides who could be target of a more intensive lipid-lowering treatment. On the other side, it seems from the current study [2], that this test is not able to detect subjects with more advanced vascular aging. Before to finally exclude that the proposed test is able to detect those patients potentially treatable with the drugs associated with a greater modulation of post-prandial lipemia (polyunsaturated fatty acids [12] and fibrates [13]), it has to be remembered that recent data have strongly reduced the relevance of carotid intima-media thickness as a predictor of cardiovascular disease [14].

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Thus, further studies based on different instrumental markers of vascular damage (as for instance flow-mediated dilation or carotid-femoral pulse wave velocity) are needed to evaluate the association of vascular damage with higher level of post-prandial triglycerides compared to other dyslipidaemic subjects, before to exclude the usefulness of the proposed standardized combined oral glucose and fat tolerance test.

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