EDITORIAL

Emerging Biomarkers for the Optimal Assessment of Global Cardiovascular Risk: where do we Stand?

Atherosclerotic vascular disease remains an enormous public health problem [1]. The estimation of risk for cardiovascular events is traditionally based on factors such as age, sex, cholesterol, high density lipoprotein (HDL)-cholesterol, blood pressure levels, presence of diabetes mellitus, and cigarette smoking history. As our understanding of the vascular biology of atherosclerosis grows, the list of potential mediators and markers of the disease process increases. There is increasing evidence that these biomarkers may be sensitive, specific and reliable in identifying individuals at risk [2].

This supplemental issue of the Open Clinical Chemistry Journal focuses on recent advances in the assessment of cardiovascular risk with the implementation of newer risk factors such as inflammatory markers, newer lipid measurements, and factors associated with the oxidative stress, thrombosis and hemostasis [2]. Distinguished authors in the field were invited to give answers as to whether these novel risk factors should be incorporated into cardiovascular risk estimation.

It is established that inflammatory processes play a fundamental role in the development of cardiovascular disease (CVD). Current evidence suggests that high sensitivity C-reactive protein (hsCRP) is a strong prognostic factor for CVD events. A direct involvement of CRP in the pathogenesis of atherosclerosis has also been implied. Nakou *et al.* review contemporary relevant literature and suggest that determination of hsCRP levels may be useful in therapeutic considerations help guiding medical treatment initiation and adjustment in certain groups of subjects both in the primary and secondary prevention.

Serum total homocysteine (tHcy) has been implicated in promoting venous thromboembolic events and coronary, cerebral and peripheral artery atherosclerosis. In this respect, it was anticipated that dietary supplementation with B complex vitamins by lowering tHcy concentrations would result in risk reduction of CVD events. However, this was not shown in randomized controlled trials. Athyros *et al.* analyse recent evidence on the impact of tHcy on health status as well as the potential role of vitamin B supplementation.

Hemostatic and thrombotic factors, such as fibrinogen, factor VII, von Willebrand factor, tissue plasminogen activator, plasminogen activator inhibitor - 1, and D-dimers, have been reported to be related with CVD. However, their contribution to the prediction of future CVD events on top of conventional risk factors remains to be established. Lioudaki and Ganotakis suggest that further investigation is required to clarify whether and which of these factors may claim a position in everyday clinical practice.

Lipoprotein (a) [Lp(a)] is considered a strong and independent predictor of many forms of vascular disease. Evidence from cross-sectional and prospective studies is conflicting with regard to its role in the development of stroke. An important issue to be resolved concerns the methodology of Lp(a) measurement. Christogiannis *et al.* are in favour of an aggressive management of established CVD risk factors in subjects exhibiting elevated serum Lp(a) levels.

Several studies have reported that elevated serum uric acid levels are related independently to increased morbidity due to vascular events and mortality. However, other studies yielded conflicting results. Tziomalos *et al.* review epidemiological data, and discuss the associations of serum uric acid levels with established vascular risk factors and the potential benefits of its lowering.

Until recently, vitamin D has been considered in close association with bone health. In a state-of-the-art review, Michos *et al.* claim that a direct causal relationship between 25(OH)D deficiency and the risk of CVD has not been completely established. Current evidence suggests that vitamin D may have a role in the risk of malignancy, infection, autoimmune disease, renal disease, and CVD. Intriguing data indicate that low vitamin D levels are associated with increased risk of congestive heart failure, left ventricular hypertrophy, peripheral arterial disease, subclinical vascular disease, myocardial infarction, stroke, and mortality independently of traditional and lifestyle risk factors.

Several large-scale, prospective studies have shown that both plasma lipoprotein-associated phospholipase A_2 (Lp-PLA_2) mass and activity represent important predictors of future CVD risk both in primary and secondary prevention. Of interest, the enzyme bound to apolipoprotein-B-containing lipoproteins may play a proatherogenic role, whereas Lp-PLA_2 associated with HDL may play an antiatherogenic role since it protects low-density lipoprotein (LDL) from oxidation and diminishes the biological functions of oxidized LDL. Tsimihodimos and Tselepis review pertinent information that could help clinicians to design safe and effective therapeutic strategies for the prevention and treatment of atherosclerotic disease.

Despite achieving targets for LDL-cholesterol, blood pressure, and glycemia in accordance with current standards of care, patients remain at high so-called 'residual risk' of vascular events [3]. Newer risk factors such as inflammatory markers, newer lipid measurements, and factors associated with the oxidative stress, thrombosis and hemostasis are common among patients with established CVD and may be of help in identifying residual risk. To date, there is increasing interest in utilizing novel biomarkers of CVD risk, and consequently, there is a need to assess the value of their use [2, 4]. Which of these biomarkers

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will survive the test of time as useful clinical tools and whether some of them will serve as targets for effective lifestyle changes and/or pharmacotherapy remains to be verified in future studies.

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