Type 2 diabetes and cardiovascular diseases: How biomarkers can support more tailored based approaches?

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Abstract

The rapid increase in type 2 diabetes mellitus (T2DM) and metabolic syndrome (MetS) prevalence is alarming, affecting all age groups across most ethno-geographical boundaries. This increased prevalence of T2DM and MetS, which constitutes a health threat to the individual and a major burden for health economy, is due to population growth, ageing, urbanization, unhealthy lifestyles, and reduced muscle mass. Among the vast array of associated co-morbidities, T2DM and MetS are associated with higher risk for developing cardiovascular complications and microangiopathy, and patients with these condition often require throughout life multi-target pharmacological interventions as a result of overlapping occurrence of truncal fat distribution, overweight, hypertension, atherogenic dyslipidemia, systemic inflammation, insulin resistance (IR), a pro-coagulant/hypofibrinolytic state, and hyperglycaemia in the subset of subjects with impaired fasting glucose, impaired glucose tolerance and T2DM.

T2DM and MetS are significant risk factors for micro and macrovascular complications. Yet despite the well-established epidemiological association between MetS and heightened cardiovascular disease risk, little is known about the underlying relationship between MetS and neurohormonal profile in T2DM patients. This is an especially relevant issue in regards to the known effects of insulin on the production and release of key vascular tone regulators and the potential role of vasoconstrictor peptides in the pathogenesis of vascular complications.

Circulating neurohormonal biomarkers are increasingly used to stratify patients at risk or with established cardiovascular disease, as well as for predicting morbidity and mortality outcomes. The use of these non-invasive markers for assessing cardiovascular risk is also advocated to stratify high-risk patients into primary or secondary prevention. This is of particular importance in T2DM subjects with or without MetS who are recognized to be a high-risk population.

The role of peptides involved in vascular remodelling such as galectin-3, aldosterone and endothelin-1, in the pathogenesis and progression of various cardio-metabolic and renal conditions is well established. Recent studies have underlined their putative role in human atherosclerosis progression. Thus, measurement of their plasma levels might contribute to the risk stratification of T2DM patients.

Osteocalcin (OC) has also demonstrated recently a new face that might allow its integration in the management of T2DM patients. OC, one of the osteoblast-specific proteins, has several hormonal features and is secreted in the general circulation from osteoblastic cells. Recent data have suggested that OC might act as hormone that regulates glucose metabolism and fat mass and Lee et al. have showed that mice lacking OC display decreased beta-cell proliferation, glucose intolerance, and insulin resistance. Iglesias and coworkers have reported that patients with T2DM exhibited OC serum levels significantly lower than those found in subjects with normal glucose tolerance. They also showed that OC concentration was independently related to 2-h plasma glucose. Hwang et al. have demonstrated that OC levels were inversely associated with the development of T2DM independent of age, gender, body mass index, and fasting plasma glucose and plasma adiponectin levels. Furthermore, serum OC levels were independently associated with glucose intolerance and abdominal obesity as the components of metabolic syndrome and T2DM in postmenopausal women. The link between OC and atherosclerosis is also emerging in T2DM patients as serum OC levels were associated with parameters of atherosclerosis, such as intima-media thicknesses, carotid plaques and aortic calcifications.

Therefore, several biomarkers appear as potential cardio-metabolic risk marker/factor in subjects with T2DM and/or MetS. Such biomarkers might also help strategizing the treatment selection of T2DM patients. The understanding of their regulation allows the identification of new therapeutic targets.

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