Endotrophin, a fragment of collagen type VI, is correlated to IMT and associated with cardiovascular events in patients with atherosclerosis and diabetes: the IMI-SUMMIT cohort

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Topic(s):
Carotid Disease

Citation:

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Background/Introduction: Patients with micro- and macrovascular diseases, including atherosclerosis, have increased risk of cardiovascular events and early mortality. The atherosclerotic disease is characterised by accumulation of lipids, cells and proteins in the arterial wall, which includes remodelling of the extracellular matrix (ECM). Collagen type VI (COL6) is known to be over-expressed in patients with atherosclerosis. The biomarker PRO-C6, known as endotrophin, is a COL6 fragment that reflects formation of collagen type VI, and possess pro-inflammatory and pro-fibrotic activities.

Purpose: We explored whether increased endotrophin levels, measured by PRO-C6, were associated with intima-media thickness (IMT) and mortality in the IMI-SUMMIT cohort.

Methods: Circulating protein levels of PRO-C6 were measured in EDTA plasma from 1500 patients enrolled at four European University Hospitals, using an enzyme-linked immunosorbent assay. Follow-up data were available up to three years after sample collection. Associations between PRO-C6 and incidence of cardiovascular (CV) events and all-cause mortality were assessed by Kaplan-Meier curves and Cox proportional hazard regression analyses. Pearson correlation was performed to explore the association of PRO-C6, IMT and clinical variables. Known confounders defined by the Framingham Heart study (age, gender and diabetes) were included in the Cox proportional hazard regression analysis.

Results: Plasma PRO-C6 was significantly correlated with IMT in both the common carotid artery and the carotid bulb (r=0.09, p=0.002 and r=0.11, p=0.0003, respectively), HbA1c (r=0.11, p<0.0001) and C-reactive protein (r=0.14, p<0.0001). A total of 145 patients suffered from fatal or non-fatal cardiovascular events during the three-year follow-up period. Patients in the highest PRO-C6 tertile had a two-fold increased risk of experiencing a CV event during follow-up (p=0.002), independently of age, presence of CVD at baseline, type 2 diabetes, smoking and statin treatment in a regression model.

Conclusion: The present findings demonstrate that circulating levels of PRO-C6 are associated with atherosclerosis severity and increased incidence of cardiovascular events. Since PRO-C6 detects the signaling molecule endotrophin, the results may indicate that endotrophin is not only a biomarker of atherosclerotic disease, but may have a role in promoting disease progression.
Abstract:
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