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LETTER TO EDITOR

The Osteoprotegerin - Von Willebrand Factor Complex: Protagonist Or Bystander In Atherothrombosis?

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Two important cardiovascular risk factors, osteoprotegerin and Von Willebrand Factor form complex in endothelial cells and in circulating blood. The pathophysiological role of the complex is unknown. We give a brief review of the relevant literature and confront it with some of our recent findings regarding the OPG-VWF correlation.

Keywords: osteoprotegerin, Von Willebrand Factor

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To the editor:

Endothelial dysfunction characterizes all of the main manifestations of atherosclerosis: coronary artery disease, carotid stenosis and peripheral arterial disease. The endothelium in atherosclerosis shifts to a pro-coagulant, cell-harboring, secretory biological surface with specific molecular patterns. Atherothrombosis is one of the most important complications of the vulnerable atheromatous plaque, and Von Willebrand Factor (VWF), a multimeric glycoprotein that mediates the adherence of platelets to the denudated endothelial surface, is implicated in this process (1). The grade of multimerization, and the activitity of its degrading protease, " a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13" (ADAMTS-13) largely influence VWF's biological activity (2).

Osteoprotegerin (OPG) is a cytokine produced in many cell types, with a variety of biological roles: regulates the homeostasis of the bone, mediates cell survival, prevents T-cell mediated inflammatory reactions (3). OPG is expressed throughout the cardiovascular system and can be detected in the heart tissue, the arterial wall, but also in veins (3). In human venous endothelial cells, osteoprotegerin, together with VWF and P-selectin resides in the secretory granules called the Weibel-Palade bodies. The OPG binding site on the VWF A1 domain has been identified and the co-secretion of the two molecules from the endothelial cells was documented (4,5). Each of the two molecules increase in sera of patients with unstable coronary artery disease and critical limb ischemia, conditions with a high atherothrombotic risk (6-8). The circulating fraction of osteoprotegerin has a yet unknown commitment. OPG possibly exerts a protective role in the complex, but this still remains a hypothesis. Vinholt et al developed an enzyme-linked immunosorbent assay (ELISA) to determine the circulating OPG-VWF complexes and found that their levels do not correlate with the grade of coronary calcification in coronary artery disease patients (9). However, this is a single observation that cannot rule out the pathological importance of the OPG-VWF complex.

In a cohort of peripheral arterial disease patients (n=105), we observed that cases with a positive history for acute myocardial infarction (n=11) have a stronger correlation of plasma VWF and OPG, than those without infarction. Moreover, patients with a previous stroke history (n=12) also possessed stronger VWF-OPG correlations, than those with no stroke (Nagy E et al, unpublished data). Since the subgroups were with a limited number, we have to interpret these findings carefully; however, due to the plenty of data concerning the cardiovascular risk factor role of osteoprotegerin, the association is worthwhile to be investigated on larger patient cohorts.

Conflict of interest

The authors hereby declare no conflict of interest.

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