Lipocalin-2 is associated with aneurysm development and can possibly be used as a biomarker for rupture

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Abdominal aortic aneurysm (AAA) pathophysiology involves deterioration of the medial layer by mechanisms such as smooth muscle cell (SMC) apoptosis and extracellular matrix (ECM) degradation. Reactive oxygen species (ROS) and matrix metalloproteinase-9 (MMP-9) have been suggested to play an important role in these mechanisms. A protein that is possibly involved in regulation of ROS production, MMP-9 expression and SMC apoptosis, is lipocalin-2. Our aim is to determine the role of lipocalin-2 in aneurysm development and its possible role as a biomarker for AAA rupture.

Full thickness aortic wall biopsies of ruptured (n=13) and non-ruptured (n=26) AAA as well as non-dilated aortas (n=3) were investigated for lipocalin-2 concentration and expression by ELISA and immunofluorescence microscopy, respectively. Also, expression of nitrotyrosine (marker of ROS), MMP-9 and caspase-3 (marker of apoptosis) were measured. In addition, lipocalin-2 blood plasma concentration was analyzed by ELISA.

Median lipocalin-2 concentration in the aneurysm wall of ruptured AAA (4.7 µg/ml [1.4–25.0;107.8]) was higher than in non-dilated aortas (1.8 µg/ml [1.2–2.7;14.2]; p=0.04). Expression of lipocalin-2 correlated positively with nitrotyrosine (Rs=0.80; p<0.01), MMP-9 (Rs=0.56; p=0.02) and caspase-3 expression in the medial layer (Rs=0.75; p=0.01). Lipocalin-2 blood concentration in ruptured AAA (46 µg/ml [range: 22-122]) was higher than in non-ruptured AAA (26 µg/ml [range: 6-55]); p<0.01.

The present study demonstrates that lipocalin-2 expression in ruptured AAA is higher than in non-dilated AAA. In the medial layer of the aneurysms lipocalin-2 was associated with factors of vessel wall deterioration, namely oxidative stress, ECM degeneration and apoptosis. We therefore suggest that lipocalin-2 might play a role in the pathologic cascade leading to rupture of aortic aneurysms. As lipocalin-2 is also increased in blood of ruptured AAA patients, it can possibly be a biomarker for AAA rupture.