Expression and cellular localization of metallopeptases ADAMs in high graded carotid artery lesions.

Metalloproteases with a disintegrin domain (ADAM) has already been implicated in various cellular processes such as cytokine and growth factor shedding, proliferation, migration, and degradation of extracellular matrix. Their role in the development and progression of atherosclerosis in carotid lesions is however unknown. The aim of the study was to analyze expression of proteolytic ADAMs (8, 9, 10, 12, 15, 17) and their inhibitors TIMP-1, -3 in patients with high-graded carotid artery stenosis. Atherosclerotic plaques were obtained from 44 patients undergoing carotid endarterectomy (CEA) and analyzed by histochemistry, immunohistochemistry, and SYBR green-based real-time PCR. All ADAMs analyzed in our study were expressed in early as well as in advanced atherosclerotic carotid lesions. The highest expression within the plaque was observed for ADAM15 followed by ADAM8. Furthermore, a significant increase was observed in the expression of ADAM10 and ADAM12 in unstable plaques compared to unstable lesions (p =0.05 and p = 0.036, respectively). In contrast, expression of TIMP-1 was significantly reduced in the same lesions (p = 0.020). Macrophages and smooth muscle cells showed the highest staining intensity and were positive for all ADAMs and TIMPs tested, with the exception of ADAM9. Endothelial cells at the lumen side were positive for ADAM 15 and
TIMP-1, neovessels were positive also for ADAM12. In conclusion, the ADAM family of proteases seems to play an important role in the maintenance of proper vessel physiology and some ADAMs such as ADAM10 and ADAM12 might also contribute to the progression of atherosclerosis.