Introduction/Aims: Matrix metalloproteinases (MMPs) are physiological regulators of the extracellular matrix, participating in plaque instability. MMP-9, regulated by a specific inhibitor (TIMP-1), has been localized in the vulnerable plaque area. Pregnancy-associated plasma protein A (PAPP-A), an insulin-like growth factor metalloproteinase has been detected in ruptured plaques. Although a predominant role of these molecules in plaque degradation has been suggested, the exact role in atherosclerosis is not known. The aim of the study was to assess the levels of soluble MMP-9, TIMP-1 and PAPP-A in a high-risk population, and relate the levels to the degree of atherosclerosis assessed by carotis intima media thickness (IMT), and to different disease entities.

Materials and methods: Individuals participating in DOIT (Diet and Omega-3 Intervention Trial)*; elderly men (n=563) with longstanding hyperlipidemia, were included. IMT was assessed by ultrasound, and fasting blood samples were analyzed for MMP-9, TIMP-1 and PAPP-A, determined by commercial ELISA methods.

Results: MMP-9 was significantly correlated with LDL-C and inversely with HDL-C (both p<0.0001) whereas TIMP-1 was correlated with ox-LDL (p=0.001) and inversely with LDL-C (p=0.012). PAPP-A showed a negative correlation to systolic blood pressure (p=0.006). There were no significant correlations between the measured variables and IMT. TIMP-1 levels were lower in subjects with previous AMI (p=0.021). In smokers significantly higher levels of MMP-9 (p<0.0001) compared to the non-smokers were observed.

Conclusion: The present results may strengthen the suggestion that MMP-9 and TIMP-1 play a pathogenic role in atherosclerosis.