Relationship between sphingomyelinase, ceramide and clinical presentation, extent and severity of atherosclerotic coronary artery disease

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Objectives Background and objective Matrix metalloproteinases (MMPs) and Tissue Inhibitor of Matrix Metalloproteinases (TIMPs) associated with atherogenesis and plaque rupture. Sphingomyelinase has a potential regulator role in the activation of MMP via induced ceramide formation. So we evaluated the relationship between sphingomyelinase, ceramide levels and presentation, extent and severity of atherosclerotic coronary artery disease (CAD).

Methods Consecutive patients who underwent coronary angiography were randomly included. The serum concentrations of sphingomyelinase, ceramide, MMP-2, MMP-9 and TIMP-1 were analysed with ELISA method in 274 patients. Participants were divided into 5 groups; stable angina pectoris (SAP; n=64), unstable angina pectoris (USAP; n=67), non-ST elevation myocardial infarction (NSTEMI; n=56), acute ST elevation myocardial infarction (STEMI; n=55) and controls (n=30). Coronary angiographic Gensini score was calculated, and the correlation between sphingomyelinase, ceramide, MMP-2, MMP-9 and clinical presentation, extent and severity of atherosclerotic coronary artery disease were analysed.

Results Sphingomyelinase, ceramide, MMP-2 levels were higher in STEMI and NSTEMI groups compared with USAP, SAP and control groups (STEMI vs USAP p=0.001; STEMI vs SAP p=0.001; STEMI vs control p<0.001; NSTEMI vs USAP p=0.005; NSTEMI vs SAP p=0.016; NSTEMI vs control p<0.001). In STEMI group, MMP-9 levels were higher than USAP and control groups (p=0.001; p<0.001). TIMP-1 levels were not significantly different within all 5 groups. Higher sphingomyelinase, ceramide, MMP-2, MMP-9 levels were correlated with severe Left Anterior Descending artery (LAD) stenosis and higher angiographic Gensini Score (for severe LAD stenosis; r=0.783, 0.339, 0.561, 0.633 p<0.001; for Gensini score; r=0.723, 0.371, 0.678, 0.525 p<0.001).

Conclusions Serum levels of sphingomyelinase, ceramide are elevated in patients with CAD; more so in acute coronary syndromes. Sphingomyelinase, ceramide are associated with more extensive and severe CAD (as represented by Gensini score).