



Novel and Traditional Risk Factors for Coronary Artery Disease:

Role of Coronary Artery Calcium, Lipidomics, Psychosocial Factors and Diet

av

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Akademisk avhandling

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Abstract

Demir Djekic (2020): Novel and Traditional Risk Factors for Coronary Artery Disease: Role of Coronary Artery Calcium, Lipidomics, Psychosocial Factors and Diet. Örebro Studies in Medicine 215.

Background: The aim of the research reported in this thesis was to determine the association of novel and traditional risk factors with coronary artery calcium (CAC), a marker of subclinical coronary artery disease (CAD) in healthy individuals. In addition, we investigated the effects of a vegetarian, compared to a meat diet, on novel and traditional risk factors in patients with diagnosed CAD.

Methods: Studies I-II evaluated the inter-laboratory reproducibility of liquid chromatography-mass spectrometry (LC-MS) lipid analysis and the association of serum lipidome with CAC in a cohort of 70 patients. Studies III and IV analysed data of 1067 participants in the pilot study of the Swedish CardioPulmonary bioImage Study to determine associations of psychosocial (residential area, education, housing, and social support) and traditional risk factors with CAC. Cardiac computed tomography was used to obtain a coronary artery calcium score (CACS) (Studies I-IV). Study V employed a crossover design in which 31 patients with CAD were randomly allocated to a four-week vegetarian diet alternating with four weeks of an isocaloric meat diet. Enzyme-linked immunosorbent assay was used to measure oxidised LDL-cholesterol. Plasma metabolome, including choline, trimethylamine N-oxide, L-carnitine, and acetyl-carnitine, as well as plasma lipidome were determined with LC-MS. Gut microbiota and faecal short- and branched-chain fatty acids were analysed with 16S rRNA gene sequencing and gas chromatography-MS, respectively.

Results: In Study I, two laboratories independently identified six lipids in common that differentiated serum of patients with CACS >250 from that of those with CACS=0. Study II, revealed higher levels of phosphatidylcholine(PC)(16:0/20:4) and lower levels of PC(18:2/18:2), PC(36:3) and phosphatidylethanolamine(PE)(20:0/18:2) in patients with CACS >250 than found in those with CACS=0. Study III showed a CACS >0 prevalence of 46.3% and 36.6% in low and high socioeconomic residential areas, respectively, but the traditional risk factor-adjusted odds ratio for CACS >0 was not significantly higher in subjects living in low socioeconomic areas. In Study III, the traditional risk factor-adjusted odds ratio for CACS >100 relative to CACS=0 was significantly higher in women with low education level and living in a rented apartment. Studies III and IV showed traditional risk factor-adjusted odds ratios for CACS >0 to be significantly higher in women with a family history of premature cardiovascular disease and low social support. No relationship of psychosocial factors with CAC was observed in men. The vegetarian diet implemented in Study V significantly lowered mean oxidized LDL-cholesterol (-2.73 U/L), total cholesterol (-0.13 mmol/L), LDL-cholesterol (-0.10 mmol/L), and body mass index (-0.21 kg/m²), as well as the relative abundance of PCs, PEs, and several microbial genera compared with the meat diet. The effect of the vegetarian diet on oxidized LDL-C was associated with higher relative abundance of *Ruminococcaceae* genera and of *Barnesiella* and reduced abundance of *Flavonifractor*. The vegetarian diet lowered the relative abundance of ceramide(d18:1/16:0) and triacylglycerols with saturated fatty acyl chains and raised the relative abundance of triacylglycerols with high carbon and polyunsaturated fatty acyl chains compared with the meat diet.

Conclusions: Novel and traditional cardiovascular risk factors are associated with subclinical CAD. Psychosocial factors are associated with subclinical CAD in women, but not in men. Short-term intervention with a vegetarian diet in individuals with CAD can positively impact novel and traditional factors that have been associated with risk of future cardiovascular events.

Keywords: Novel risk factors, coronary artery calcium, lipidomics, lipidome, psychosocial factors, vegetarian diet, gut microbiota, metabolome.

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