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## MicroRNA Signatures Predict Early Major Coronary Events in Middle Aged Men and Women

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**Background:** The role of microRNA as biomarkers able to predict major coronary events (MACE) has not been fully elucidated, reproducibility being a critical issue.
**Aim:** To identify circulating microRNA signatures able to predict MACE.
**Methods:** We employed a PCR-based method to screen 754 microRNAs in a cohort of 60-year-olds (60YOs) from Stockholm, using a nested case-control design (100 cases vs 100 matched controls). The association of microRNAs and their interaction with the risk of MACE (myocardial infarction (MI), angina and sudden cardiac death) was estimated with random-effect logistic regression and expressed as OR with 95% CI. A bioinformatics approach identified microRNA clusters based on predicted targets. Main findings were tested in 58 MI and 60 age and sex matched referents from the the Nord-Trøndelag Health (HUNT) Study, a longitudinal population health study conducted in Norway.
**Results:** Fifty-five microRNAs were found to be associated with risk of MACE in the 60YO. MicroRNA-145-3p was associated with the largest estimated risk increase of MACE after adjustment for the common CV risk factors (OR: 2.18; 95% CI: 1.27–3.75). Interaction analysis revealed that increasing plasma levels of microRNA-320b modulated the association of 16 microRNAs with risk of MACE. As an example the estimated MACE risk associated with microRNA-145-3p was 1.47 (0.87–2.47) in the presence of low (<25th percentile) and 4.00 (1.79- 8.93) in the presence of high (>75th percentile) miRNA 320b expression levels. Sixteen microRNA pairs could be classified in 4 functional clusters with 492 predicted gene targets, mainly involved in the regulation of inflammation, thrombosis and lipid metabolism. Eight miRNAs interacting pairs belonging to cluster 2 and 4 showed a similar association trend with MI risk in the HUNT study.
**Conclusions:** We report the identification of microRNA signatures predicting risk of MACE in middle-aged Scandinavian men and women. These signatures could be a valuable tool to improve CV disease prediction in the aged.