Abstract: half-time seminar

Therese Ohlsson
190523

Title: Genetic causes and prediction of hypertension

Background: Hypertension, caused by an interaction of genetic and environmental factors, constitutes one of the major risk factors for cardiovascular disease and mortality. The genetic background appears to be a mix of multiple common genetic variants with small effect sizes on blood pressure (BP), and rare variants with large effect sizes. In addition, hormonal regulation of blood pressure is of importance, and in this work we focus especially on adrenomedullin.

Aim: We aim to evaluate genetic and endocrine predictors of hypertension and cardiovascular disease (CVD).

Method: In subproject 1 we created a genetic risk score for BP (BP-GRS) including 29 blood pressure elevating genetic variants, and prospectively evaluated the impact of this score on CVD and mortality in 27 000 individuals in Malmö Diet and Cancer Study (MDCS).

In subproject 2 we searched for BP associated gene variants introducing premature stop-codons, on the Illumina exome chip, which was genotyped in 5400 individuals from MDCS. These were analyzed for associations with BP, measures of obesity and risk of ischemic stroke.

In subproject 3 we studied midregional pro-adrenomedullin (MR-proADM) in fasting plasma in 3000 individuals from the MDCS, and related baseline levels to cardiometabolic risk factors cross-sectionally and longitudinally.

Results: In subproject 1 we found the BP-GRS significantly associated with incident cardiovascular morbidity and mortality, but when adjusting for traditional cardiovascular risk factors, only the associations with CVD remained significant.

In subproject 2, we identified 19 stop-codon variants with significant BP associations. One of these, located in the phosphodiesterase 11A gene, was
significantly associated with higher levels of BP, measures of obesity, and risk of ischemic stroke.

In subproject 3, we found that baseline levels of MR-proADM were significantly associated with higher BP and measures of obesity cross-sectionally. Over time, MR-proADM predicted significantly reduced progression of BP but greater increase of obesity markers.

**Significance:** As cardiovascular disease remains the most common cause of death globally, prediction and prevention is of great significance. In this project, we continue the search for the genetic background and prediction of hypertension, constituting one of the main risk factors for cardiovascular morbidity and mortality.

**Published manuscripts:**

   *J Hypertens.* 2014 Jul;32(7):1424-8


3) Midregional proadrenomedullin predicts reduced blood pressure and glucose elevation over time despite enhanced progression of obesity markers. *Ohlsson T, Nilsson PM, Persson M, Melander O.*