Institutionen för folkhälsovetenskap

Early and later life mechanisms in the aetiology of cardiovascular disease

AKADEMISK AVHANDLING
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av

Kristiina Rajaleid
MSc

Huvudhandledare:
Professor Johan Hallqvist
Karolinska Institutet
Institutionen för folkhälsovetenskap

Bihandledare:
Professor Denny Vågerö
CHESS
Stockholm University/Karolinska Institutet

Fakultetsopponent:
Professor Amanda Sacker
University of Essex
Institute for Social and Economic Research

Betygsnämnd:
Professor Maj-Lis Hellénius
Karolinska Instututet
Institutionen för medicin
Enheten för kardiologi

Professor Christina Hultman
Karolinska Institutet
Institutionen för medicinsk epidemiologi och biostatistik

Docent Tomas Faresjö
Linköpings Universitet
Institutionen för medicin och hälsa

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ABSTRACT

Evidence over the recent decades indicates that susceptibility to cardiovascular disease (CVD) may be established already prenatally and in early childhood, and that the aetiological processes of the disease involve biological and social influences occurring throughout a person's life span. Numerous studies have shown that small size at birth is associated with increased risk of CVD later in life. This finding is suggested to reflect the influence of poor foetal nutrition on the body's organ structure, physiology and metabolism. Surprisingly, there is little empirical evidence available to support the proposed causal mechanisms. The aim of this thesis is to study the mechanisms underlying the inverse association of size at birth with CVD.

Three studies in the thesis are based on Uppsala Birth Cohort Study (UBCoS), a prospective cohort study which includes men and women, who were born at the Uppsala Academic Hospital between 1915 and 1929. Information from birth records, school catalogues, Hospital Discharge Register, Cause of Death Register and Censuses is used. One study is based on Stockholm Heart Epidemiology Program (SHEEP), a population based case-control study of risk factors for acute myocardial infarction (AMI) with study base including all Swedish citizens aged 45-70 years with no prior clinically diagnosed AMI, who lived in Stockholm County during 1992-1994. Data from birth records, questionnaire, health examination and blood sampling is used.

In both data materials small size at birth was associated with increased risk of disease. Further analyses showed that birth weight for gestational age in men was associated with ischemic heart disease (IHD) mortality within the non-manual class but not among the manual workers, even if the overall mortality rate was higher in the latter. There was no difference in the association by the men's family's social class at birth. For women, social class neither at birth nor in adulthood modified the association between birth weight for gestational age and IHD mortality.

We found that there was a synergistic interaction between low weight for gestational age and overweight in adulthood on risk of AMI.

The simultaneous analysis of foetal growth, cognitive ability and IHD mortality suggested that there is an indirect association between foetal growth and cognitive ability through childhood cognitive ability.

Finally, men with very low and very high birth weight for gestational age had a higher risk of dying after an AMI than men with intermediate birth size. Case fatality in women was not associated with their size at birth.

The results suggest that the effect of poor foetal nutrition on CVD may be modified by social exposures later in life. The synergistic interaction between small size at birth and high adult body mass index with respect to AMI risk supports the thrifty phenotype hypothesis according to which a mismatch between foetal and adult nutrition is causing the disease. The existence of an indirect association between foetal growth and IHD mortality through childhood cognitive ability implies that mechanisms related to brain development are contributing to the association between poor foetal nutrition and IHD, in addition to the effects on physiology and metabolism. As the association of size at birth with case fatality was different from the associations with incidence and mortality, the mechanisms that operate after the AMI event and determine the prognosis might partly be different from the mechanisms that drive the development of the disease.