

Endogenous sex hormones and cardiometabolic risk factors

-Population-based studies within the Skaraborg Project

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i sal 2118, Arvid Wallgrens Backe, hus 2, plan 1, den 20:e januari 2023, klockan 09:00.

av

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Avhandlingen baseras på följande delarbeten

I: **Ottarsdottir, K**, Nilsson AG, Hellgren M, Lindblad U and Daka B. The Association between Serum Testosterone and Insulin Resistance: A Longitudinal Study. *Endocrine Connections*, 2018, Vol. 7, Iss. 12, Pp. 1491-1500 7.12 (2018): 1491-500. Print

II: **Ottarsdottir, K**, Hellgren M, Bock D, Nilsson AG, Lindblad U, and Daka B. Longitudinal Associations between Sex Hormone-binding Globulin and Insulin Resistance. *Endocrine Connections*, 2020, Vol. 9, Iss. 5, Pp. 418-425 9.5 (2020): 418-25. Print.

III: **Ottarsdottir, K**, Tivesten Å, Li Y, Lindblad U, Hellgren M, Ohlsson C, and Daka B. Cardiometabolic Risk Factors and Endogenous Sex Hormones in Postmenopausal Women: A Cross-Sectional Study. *Journal of the Endocrine Society* 6.6 (2022): Bvac050. Web.

IV: **Ottarsdottir, K**, Tivesten Å, Ohlsson C, Li Y, Hellgren M, Lindblad U and Daka B. Endogenous sex hormones levels are associated with the revised Framingham Stroke Risk Profile in postmenopausal women – a cross sectional study in a Swedish cohort. Manuscript.

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Endogenous sex hormones and cardiometabolic risk factors – population-based studies within the Skaraborg project

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Abstract

Cardiovascular diseases are the major contributors to mortality in Sweden and globally. Men have a higher incidence of cardiovascular diseases compared to women, until women reach the menopause. Levels of sex hormones might explain these sex differences beyond known differences in risk factors. The overall aim of this thesis was to investigate the associations between sex hormones and known cardiometabolic risk factors.

Cohort studies in Vara and Skövde, based on a random sample of the population, were conducted. The first visit took place in 2002-2005 including 2,816 participants aged 30-74 years (50% men). The second visit in 2012-2014 included a representative sample of 1,327 participants. Papers I-II are based on this cohort. In 2018 we analyzed eight different sex hormones by a validated high sensitivity liquid chromatography-tandem mass spectrometry in a subset of 240 women who were ≥ 50 years of age at visit 1. Papers III-IV are studying this sub-cohort.

Study I showed a significant inverse association between testosterone and insulin resistance in men, both in the cross-sectional analysis and after approximately 10 years' follow-up. However, no significant association between insulin resistance at visit 1 and testosterone levels at visit 2 was found. Study II found a strong and significant inverse association between levels of sex hormone-binding globulin and insulin resistance in both men and women, also when the female group was stratified for age ($</\geq 50$ years old) or menopausal status. Study III addressed the association between known cardiometabolic risk factors and sex hormones in postmenopausal women. The waist-to-hip ratio was mainly associated with androgens and BMI was associated with estrogens. Study IV showed significant positive associations between estrone, progesterone and testosterone and the revised Framingham stroke risk profile after adjustments were made for confounders.

These studies found significant associations between levels of sex hormones and cardiometabolic risk factors. This new knowledge will contribute to the understanding of sex differences in the development of cardiovascular diseases and may contribute to add further precision to the risk stratification of individuals.

Keywords: Sex hormones, sex hormone binding globulin, cardiometabolic risk factors, insulin resistance, post-menopause, cardiovascular diseases