Prostate Diseases and the Metabolic Syndrome

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet, kommer att offentligen försvaras i hörsal Hjärtats Aula, Sahlgrenska universitetssjukhuset, fredagen den 8/5 kl. 13:00.

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Avhandlingen baseras på följande delarbeten:

I. M.A. Haghsheno, D. Mellström, R. Peeker, J. Hammarsten, M. Lorentzon, V. Sundh, M. Karlsson, C. Ohlsson and J.E. Damber. *Lower urinary tract symptoms are associated with low levels of serum serotonin, high levels of adiponectin and fasting glucose, and benign prostatic enlargement.*
Scand J Urol, 2014. 25: p. 1-7

II. M.A. Haghsheno, D. Mellström, C.J. Behre, J.E. Damber, H. Johansson, M. Karlsson, M. Lorentzon, R. Peeker, E. Barret-Connor, E. Waern, V. Sundh, C. Ohlsson and J. Hammarsten. *Low 25-OH vitamin D is associated with benign prostatic hyperplasia.*
J Urol., 2013. **190**(2): p. 608-14

III. M.A. Haghsheno, D. Mellström, R. Peeker, J. Hammarsten, M. Lorentzon, Ö. Ljunggren, M. Karlsson, H. Johansson, C. Ohlsson and J.E. Damber.
Is *there an Association between Components of the Metabolic Syndrome and incident Prostate Cancer?A prospective cohort study in Sweden.*
Submitted

IV. M.A. Haghsheno, J-E. Damber, R. Peeker, H. Johansson, M. Karlsson, C. Lewerin, J. Hammarsten, M. Lorentzon, U. Smith U. Lerner, C. Ohlsson and D. Mellström.
High plasma octeocalcin predicts incident prostate cancer.
Submitted

Prostate Diseases and the Metabolic Syndrome

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ABSTRACT

The overall aim of this thesis was to explore the association between the components of the metabolic syndrome (MetS), including vitamin D, and lower urinary tract symptoms (LUTS). The focus was on the relationship between diseases of the prostate, mainly benign prostatic enlargement (BPE) and prostate cancer (PC).

The study cohort consisted of 3,014 Swedish men aged 69-81 enrolled in the Swedish arm of the Osteoporotic Fractures in men (MrOs) study. The study participants were randomly selected using population registries and then contacted and asked to participate in the study. The selected men were asked to fill in questionnaires regarding a variety of items such as daily activities and physical exercise, eating-, drinking- and smoking habits, medication, past and present history of diseases, voiding habits, surgery and current treatment. They underwent investigations regarding bone mineral density, measurements of body composition such as height, weight, body mass index, body fat mass and lean mass and blood samples were obtained for analyses of a variety of variables. In a subgroup of this cohort (1,010 individuals) more extended analyses were performed. Furthermore, in a small cohort (184 individuals), the prostate gland volumes were measured through transrectal ultrasonography. Lower urinary tract symptoms were measured by the International Prostate Symptom Score and urinary incontinence (UI) was evaluated by a questionnaire. The cohort has been followed for more than 10 years. The MrOs register was coordinated with the Swedish Death Register, the Swedish Cancer Register, and the National Prostate Cancer Register.

This investigation showed that LUTS and UI were neither associated with any major component of the MetS, nor associated with serum levels of vitamin D. However, serum levels of serotonin were negatively associated with LUTS and UI, while fasting glucose and adiponectin were positively associated with LUTS. Benign prostatic enlargement was associated with low levels of vitamin D, serum calcium, sex hormone- binding globulin and high-density lipoprotein cholesterol. Individuals with type 2 Diabetes mellitus (T2DM) had a decreased risk of being diagnosed with incident prostate cancer. Increased levels of vitamin D were associated with increased risk of being diagnosed with PC. Individuals with low serum c-reactive-protein levels and taller individuals had a higher risk of developing PC. Plasma levels of osteocalcin, a protein produced by osteoblasts, were lower in individuals with T2DM, and higher in individuals with incident PC.

The overall conclusions in the present thesis were that vitamin D was negatively associated with BPE and positively associated with PC, however, not associated with LUTS. In addition, the end-point component of MetS, T2DM, was positively associated with BPE but inversely associated with incident PC, and finally, that osteocalcin was positively associated with incident PC.

Keywords: Metabolic syndrome, lower urinary tract symptoms, urinary incontinence, benign prostatic enlargement, prostate cancer, serotonin, vitamin D, osteocalcin

ISBN: 978-91-628-9378-1 (Printed edition)

ISBN: 978-91-628-9379-8 (Electronic edition)