Early diagnosis and treatment of prostate cancer

Observational studies in the National Prostate Cancer Register of Sweden and the Västerbotten Intervention Project

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Prostate-specific antigen (PSA) testing has caused a steep increase in the incidence of prostate cancer, especially the incidence of localised low risk disease. In order to decrease the overdiagnosis accompanied by PSA testing, analysis of inherited genetic variants have been suggested as potential tools for clinical assessment of disease risk. With the aim of minimizing overtreatment and postpone side-effects of curative treatment for low risk prostate cancer, active surveillance, a treatment strategy with initial surveillance and deferred radical prostatectomy at the time of progression has evolved. The aim of this thesis was to study the validity of PSA (paper I) and inherited genetic variants (paper II) for early diagnosis of prostate cancer, to assess the extent of PSA testing in Sweden (paper III), and to study the safety of deferred radical prostatectomy in localised low to intermediate risk prostate cancer (paper IV). The study designs were i) case-control studies nested within the Västerbotten intervention project (paper I and II), ii) observational study in the Cancer Register of Sweden (paper III), and iii) observational study in the NPCR Follow-up study (paper IV).

PSA had a high validity in predicting a prostate cancer diagnosis with an area under the receiver operating characteristics (ROC) curve of 0.86 (95% CI, 0.84 to 0.88). A combined test, including PSA, the ratio of free to total PSA, and 33 single nucleotide polymorphisms (SNPs) in a genetic risk score, increased the area under curve to 0.87 (95% CI, 0.85 to 0.89). The estimated uptake of PSA testing among men aged 55 to 69 years increased from zero to 56% between 1997 and 2007 and there were large variations in the uptake of PSA testing between counties in Sweden. After a median follow-up time of eight years there was no significant difference in presence of any one or more adverse pathology features or prostate cancer specific mortality after primary compared to deferred radical prostatectomy in localised low to intermediate risk prostate cancer. Results from these studies indicate that PSA and the hitherto identified SNPs are not suitable biomarkers in single-test prostate cancer screening. It is possible to estimate the uptake of PSA testing on a population level. Initial surveillance and deferred radical prostatectomy represent a feasible treatment strategy in localised low to intermediate risk prostate cancer.

Key words
Prostate cancer, prostate-specific antigen, single nucleotide polymorphism