Characteristics of Screening Failures in Prostate Cancer Screening

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten:

I. Robool, M, Grenabo, A, Schröder, FH, Hugosson, J. Interval Cancers in Prostate Cancer Screening: Comparing 2- and 4-Year Screening Intervals in the European Randomized Study of Screening for Prostate Cancer, Gothenburg and Rotterdam. J Natl Cancer Inst 2007; 99: 1296-303.

II. Grenabo Bergdahl, A, Aus, G, Lilja, H, Hugosson, J. Risk of Dying From Prostate Cancer in Men Randomized to Screening: Differences between Attendees and Nonattendees. Cancer 2009; 115: 5672-9.

III. Grenabo Bergdahl, A, Holmberg, E, Moss, S, Hugosson, J. Incidence of Prostate Cancer After Termination of Screening in a Population-Based Randomised Screening Trial. Eur Urol. 2013; 64: 703-9.

IV. Grenabo Bergdahl A, Wilderäng, U, Aus, G, Carlsson, S, Damber, JE, Frånlund, M, Geterud, K, Khatami, A, Socratous, A, Stranne, J, Hellström, M, Hugosson J. Role of MRI in Prostate Cancer Screening: Results from a Pilot Study Nested Within the Göteborg Randomized Screening Trial *(in manuscript)*.

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ABSTRACT

Although prostate-specific antigen (PSA)-based screening has been shown to reduce prostate cancer (PC)-specific mortality with large variations in mortality reduction with different screening algorithms, the optimal screening strategy has not yet been established. This thesis aims at exploring aspects of underdiagnosis in PC screening, focusing on the impact of screening failures on screening effectiveness. All of its papers are based on the Göteborg randomized PC screening trial except for Paper I, which also includes data from the Dutch center of the European Randomized Study of Screening for Prostate Cancer (ERSPC).

Paper I analyzes the frequency of interval cancers (IC) between a 2- and a 4-year screening interval, as high IC rates are recognized as a limitation for screening effectiveness in screening for other cancers. Extremely few IC cases were detected and no difference was found in cumulative incidences of IC with a 2- and 4-year interval. In Paper II, the risk of PC death is compared between attendees and nonattendees in screening. A large proportion of PC deaths occurred in nonattendees, and the majority of attendees dying from PC were men aged ≥60 years when detected at their first (prevalence) screen. Paper III analyzes the PC incidence after screening cessation (due to upper age limit). Compared to the control arm, the incidence of potentially aggressive PC was reduced in the screening arm up to 9 years post-screening but thereafter approached the incidence of the control group. In Paper IV, multiparametric magnetic resonance imaging (mpMRI) was evaluated as a screening tool. A lowered PSA cut-off (1.8 ng/ml) + mpMRI followed by targeted biopsy yielded a higher detection rate of clinically significant PC compared with "conventional" screening (PSA, cut-off ≥3 ng/ml followed by systematic biopsy), requiring a decreased number of biopsies.

In conclusion, better screening strategies are needed to improve on screening failures. One option may be to lower the PSA cut-off and introduce sequential testing with mpMRI to decide which men to refer for biopsy. Age at screening start and cessation greatly impacts efficiency; starting at age 60 is probably too late, and stopping at age 70 for all men is probably too early.

Keywords: screening failures, age, prostate-specific antigen, interval cancer, non-attendees, multiparametric magnetic resonance imaging, prostate cancer screening

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