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NEWS AND VIEWS

First diagnostic results from Gothenburg-2 screening trial

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Context: The European Randomized Study of Screening for Prostate Cancer trial has revealed that screening for prostate cancer not only can reduce cause-specific mortality but also that a screening based on prostate-specific antigen (PSA) and systematic biopsies leads to unacceptably high rates of overdiagnosis and overtreatment [1]. However, the diagnostic methods have improved and now allow for a more selective detection of potentially lethal prostate cancer. The introduction of MRI and targeted biopsies has reduced the proportion of men who need a prostate biopsy and the detection of low-grade prostate cancer with a maintained detection of Gleason score ≥ 7 cancer [2]. One of the remaining knowledge gaps is whether targeted biopsies should be combined with a systematic biopsy in men who participate in a screening programme, and if yes, in which of these men.

News: The Gothenburg-2 prostate cancer screening trial started recruiting in 2015. The main aim was to investigate whether a screening algorithm using an MRI and targeted biopsies can reduce overdiagnosis without substantial loss of sensitivity for potentially lethal prostate cancer. Diagnostic results from the first screening round for men aged 50–60 years with PSA ≥ 3 ng/mL were reported in December 2022 [3]. The analysis was based on the three screening arms; no results were obtained from the group assigned to no screening. The reference was a screening arm in which all men had a systematic biopsy (those with an MRI lesion also had a targeted biopsy). These biopsy results were compared with the diagnostic pathway in the two experimental arms with targeted biopsies only.

Nearly half (47%) of the 37,887 invited men participated and had a PSA test. Two-thirds of the men with PSA ≥ 3 ng/mL had a non-suspicious MRI. The diagnostic pathway with a pre-biopsy MRI and targeted biopsies detected only half as many Gleason score 6 cancers as the pathway with a systematic biopsy for all men with PSA ≥ 3 ng/mL: relative risk 0.46 (95% confidence interval 0.33–0.64). Detection of Gleason score ≥ 7 cancer was somewhat lower in the targeted versus the systematic biopsy group: 0.8 (95% confidence interval 0.6–1.1). All cancers detected on systematic biopsy in the reference arm (biopsy regardless of MRI) had a Gleason score of 6 ($n = 73$) or 3 + 4 = 7 ($n = 10$). A total of 7 of the 10 Gleason score 3 + 4 = 7 cancers were stage T1c and 6 of them had less than 5% Gleason pattern 4.

Views: These results confirm previous studies reporting that an MRI-based diagnostic pathway reduces the proportion of biopsied men with a raised PSA and that the proportion of non-suspicious MRI scans is greater in screened men (56–65%) than in clinical series (25–40%) [2]. The results also add to the evidence that an MRI pathway can decrease overdiagnosis of Gleason score 6 cancer and support the use of targeted biopsy only without a systematic biopsy (at least in a screening setting) [2].

Do the Gothenburg-2 results justify national screening programmes for prostate cancer? No, they don't. First, the evidence from this and other trials is limited to a single diagnostic evaluation without follow-up testing. Cancers detected in men who have their first PSA test are often different from the cancers detected after repeated testing in an organised screening programme [4]. We therefore need results from repeated screening rounds, not only to estimate the long-term effects of a screening programme but also to estimate the MRI resources required and the programme's cost-effectiveness. Results from the second and third screening rounds in the Gothenburg-2 trial are expected within a year or so.

Another missing piece of the puzzle is the performance of ancillary tests to select men for an MRI. The Finnish ProScreen trial evaluates a screening algorithm with a kallikrein panel (4KScore) as a 'filter' between a raised PSA and an MRI [5], but the trial will not report results from repeated screening rounds until at least 2024. Finally, but very importantly, mortality results are not available.

Nonetheless, important progress is now being made for prostate cancer screening, and many pieces are expected to be added to the puzzle over the next several years.

Disclosure of interests

The authors have no financial conflicts of interest to declare. AA is the PI of the ProScreen trial, with funding from the Finnish Cancer Foundation, Academy of Finland, Competitive State Research Funding administered by the Tampere University Hospital and

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