



European Association of Urology



Letter to the Editor

Re: Henrik Grönberg, Martin Eklund, Wolfgang Pickler, et al. Prostate Cancer Diagnostics Using a Combination of the Stockholm3 Blood Test and Multiparametric Magnetic Resonance Imaging. Eur Urol 2018;74:722–8

We would like to address some questions regarding the recently published paper by Grönberg and colleagues [1]. The authors evaluate whether the combination of the Stockholm3 (STHLM3) blood test and magnetic resonance imaging (MRI)-targeted biopsies improve diagnosis in terms of reducing the number of biopsies and detection of Gleason grade group (GG) 1, while maintaining the sensitivity for detection of GG ≥ 2 prostate cancer.

We commend the authors for their intention to reduce overdiagnosis. However, several aspects regarding the study design need clarification, most importantly patient selection. Furthermore, we believe that their conclusion is vague and largely unsupported by the results.

Several factors indicate a high degree of selection bias in this study. First, the rate of negative MRI was only 1% in Oslo, compared to 26% in Tønsberg, and 40% in Stockholm. Furthermore, the rate of previous systematic biopsies was 49% in Stockholm, 23% in Oslo, and only 8% in Tønsberg. No details regarding the number of previous biopsy sessions or results are presented. The cancer detection rate of systematic biopsies will surely be reduced by the fact that systematic biopsies were previously performed in a considerable proportion of the patients. This is problematic since systematic biopsy is used as the reference standard in the study.

Selection bias is clearly reflected in the results, with large variation in STHLM3 test results between the three sites (median 8% in Stockholm compared to 22% in Oslo and 20% in Tønsberg) and cancer detection rates (69% in Oslo, 57% in Tønsberg, and 32% in Stockholm).

The authors claim that performing only targeted biopsies in STHLM3-positive patients reduces detection of GG 1 while maintaining detection of GG ≥ 2 cancer. We agree that the results show that the STHLM3 test reduces detection of GG 1 cancer, but we are not convinced that detection of GG ≥ 2 is maintained. This conclusion is only valid if systematic biopsies are used as the reference standard (relative sensitivity 0.98,

95% confidence interval [CI] 0.88–1.07). However, the authors seem to ignore that the combination of systematic and targeted biopsies showed the highest detection rate for GG ≥ 2 , and should be used as the reference standard. When using the combination of systematic and targeted biopsies, the STHLM3 test significantly *lowered* the detection rate of GG ≥ 2 (relative sensitivity 0.92, 95% CI 0.88–0.95). Furthermore, with the proposed strategy of omitting systematic biopsies, the detection rate for GG ≥ 2 was reduced even further (relative sensitivity 0.81, 95% CI 0.76–0.87).

Owing to the unrecognized selection bias, the added value of a positive or negative STHLM3 test remains uncertain. Since a large proportion of patients had already undergone systematic biopsies, the true diagnostic value of systematic biopsies is surely underestimated in this study.

In conclusion, we believe that this study does not provide any evidence for changing prostate biopsy practice for patients with clinical and radiological suspicion of prostate cancer.

Conflicts of interest: The authors have nothing to disclose.

Reference

- [1] Grönberg H, Eklund M, Pickler W, et al. Prostate cancer diagnostics using a combination of the Stockholm3 blood test and multiparametric magnetic resonance imaging. *Eur Urol* 2018;74:722–8.

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