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Prostate-specific antigen for prostate cancer screening

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This month's column is devoted to recent papers discussing prostate cancer screening with prostate-specific antigen (PSA).

Hugosson et al. conducted a randomized trial to evaluate whether targeting MRI-positive lesions alone and omitting systemic prostate biopsies for men with an elevated PSA would result in a reduced risk of detecting clinically insignificant disease while still detecting clinically significant cancers. Their reference group consisted of 405 men with PSA elevated above 3.0 ng/mL who underwent MRI. All these men had biopsies regardless of the MRI findings. Those with negative MRI studies underwent systemic biopsies alone, while those with positive MRI findings underwent both systemic and targeted biopsies. Men in the experimental group (n = 796) also underwent MRI. Those men with a suspicious lesion underwent prostate biopsy. Those with negative MRI findings were not biopsied. Sixty-six men in the experimental group and 72 men in the reference group were diagnosed with a clinically insignificant cancer, yielding a relative risk in favour of the experimental group of 0.46 (95% CI 0.33–0.64). Clinically significant cancers were detected in 68 men in the reference group and 110 men in the experimental group, resulting in an insignificant relative risk of 0.81 (95% CI 0.60–1.10). Ten participants in the reference group had clinically significant cancers detected only by systematic biopsies. All the men had Gleason 3 + 4 disease and, in six men, Gleason pattern 4 involved 5% or less of the biopsy specimen. The authors concluded that by performing biopsies only on men with MRI-positive lesions they reduced the risk of overdiagnosis by half, at the cost of delaying the detection of intermediate-risk tumours in a small proportion of patients.

> *"Performing biopsies only on men with MRI-positive lesions reduced the risk of overdiagnosis by half"*

Hao et al. evaluated the cost-effectiveness of prostate screening using MRI with combined targeted and standard biopsies compared with standard biopsies alone. They used a microsimulation model in adult Swedish men to evaluate various screening strategies. Input parameters were obtained from the STHLM-3 MRI study. Compared with no screening, the screening strategies were associated with reduced lifetime prostate cancer-related deaths by 6%–9%. Screening with MRI and the combined biopsies resulted in a moderate cost per quality-adjusted life-year gained. MRI-based screening reduced the number of lifetime biopsies and overdiagnosis by approximately 50%.

Finally, Kim et al. explored subsequent healthcare utilization and spending after PSA tests used for prostate cancer screening. Specifically, they were interested in 'low-value' care associated with testing asymptomatic men over age 70 years, a practice discouraged by multiple guidelines. They conducted a cross-sectional analysis of men over age 70 years without pre-existing prostate conditions and who were enrolled in a Medicare Advantage plan from January 2016 to December 2018. De-identified medical billing claims data stored in the Optum Labs Data Warehouse were used to evaluate the utilization and costs of care cascades that followed at least one PSA claim. They found that 39% of men over age 70 years had been tested for PSA and 63% of these men subsequently underwent at least one follow-up test. A repeated PSA test was most common, but 7.1% incurred high-cost follow-up services including imaging, radiation therapy and prostatectomy. Utilization and spending associated with care cascades increased from 2016 to 2018 such that for every $1 spent on a PSA test an additional $6 were spent on follow-up care.

Hugosson J, Månsson M, Wallström et al. Prostate cancer screening with PSA and MRI followed by targeted biopsy only. *N Eng J Med* 2022; 387:2126–37.

Hao S, Ciscacciati A, Eklund M et al. Cost-effectiveness of prostate cancer screening using magnetic resonance imaging or standard biopsy based on the STHLM3-MRI study. *JAMA Oncol* 2022; doi:10.1001/jamaoncol.2022.5252.

Kim D, Daly AT, Koethe BC et al. Low-value prostate specific antigen test for prostate cancer screening and subsequent health care utilisation and spending. *JAMA Network Open* 2022; doi:10.1001/jamanetworkopen.2022.43449.

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