Vickers et al. (1) reported that prostate-specific antigen velocity (PSAV) was associated with a 5.2-fold increased risk of prostate cancer on biopsy, adjusting for age, PSA, family history, digital rectal examination, and prior biopsy. However, it led to only a modest improvement in area under the receiver operating characteristic curve, leading the authors to conclude that PSAV does not add “important” predictive value.

Numerous aspects of the study design limit the applicability of these results. Contrary to the authors’ suggestion that the Prostate Cancer Prevention Trial (PCPT) represents the “ideal population,” prior studies have shown that PSAV has the best performance characteristics at a younger age (2). Unfortunately, 79% of the Vickers study population was aged 65 years or older, and the largest proportion (47%) were 70 years or older, an age group for which the US Preventive Services Task Force recommends against PSA screening (3). Even for men in their 70s with a sufficient life expectancy to undergo screening, we have previously demonstrated that those with a PSA less than 3 ng/mL at age 70 have virtually no risk of lethal prostate cancer (4). Thus, elderly men with low PSA levels (a major proportion of the PCPT) are not an ideal population in which to study the association between PSAV and the presence of life-threatening prostate cancer.

Another important consideration is that the endpoint of the study was prostate cancer detection on biopsy. However, the majority of biopsies were performed empirically (without cause) at the end of the 7-year trial. Using empiric biopsy data from a heavily prescreened population leads to an inflation in the proportion of indolent tumors that would not have been clinically apparent. Therefore, end-of-study biopsies from the PCPT also do not provide an ideal population to study the utility of PSAV for the prediction of life-threatening disease.

Vickers et al. (1) reported only small increases in discrimination using PSAV to predict “clinically significant” and high-grade disease on biopsy. However, pathological data were missing for one-fourth of participants, and the criteria for clinically significant disease using biopsy data are an imperfect proxy for disease-specific outcomes. Because follow-up data were not available in the Vickers study, their data cannot address the utility of PSAV for the prediction of lethal disease.

This issue has, however, been examined by numerous studies with long-term follow-up, including the Baltimore Longitudinal Study of Aging (5). In 786 men with 3474 PSAV observations, PSAV reclassified men with regard to the risk of life-threatening prostate cancer beyond PSA alone. For example, for observations at PSA less than 3 ng/mL, the probability of life-threatening prostate cancer was 3%, which increased to 13.6% if PSAV was greater than 0.4 ng/mL per year.

If the recommendations of the Vickers study were followed, there would be no reason to record PSA measurements in the medical record. However, there is no incremental cost associated with an evaluation of existing clinical data and to disregard it would be inconsistent with standard medical practice. Instead, emphasis should be placed on determining the best way to make use of a PSA history for the prediction of life-threatening prostate cancer.

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References
Notes

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