

Re: Detection of Life-Threatening Prostate Cancer with Prostate-Specific Antigen Velocity during a Window of Curability

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Expert's summary:

The authors use data from the Baltimore Longitudinal Study of Ageing to identify prostate-specific antigen velocity (PSAV) cut-off levels, which might predict potential death from prostate cancer hopefully still during a phase of curability. PSAV was evaluated in 856 men without prostate cancer, 104 with prostate cancer who were alive or died from other causes, and 20 who died from prostate cancer. Duration of follow-up amounted to a maximum of 39 yr. PSAV was evaluated 10–15 yr and 5–10 yr prior to diagnosis. At this time most men had PSA levels <4.0 ng/ml. PSAV measured during both time periods was related to prostate cancer-specific survival. Men who presented with a PSAV \leq and $>$ 0.35 ng/ml/yr experienced a prostate cancer-specific survival of 92% as opposed to 54%, respectively. The authors conclude that PSAV identifies men with life-threatening disease and hope that PSAV will be suitable to identify men with high velocities in time for potentially curative management.

Expert's comments:

This is an important paper that potentially leads the way to the identification of aggressive disease early during its clinical course and, if used as a biopsy indicator, may prevent large numbers of unnecessary biopsies and unnecessary treatments in otherwise overdiagnosed cases. Here follow some suggestions and critical notes.

1. The authors state that the PSAV cut-off 0.35 ng/ml/yr was found on the basis of a receiver operating characteristic (ROC) analysis. It is regrettable that the ROC analysis is not presented

in the paper. Table 3 allows the calculation of the specificity and sensitivity for the periods of 10–15 and 5–10 yr prior to diagnosis. The sensitivity for 10–15 yr is only 33% and for 5–10 yr, 58.3%. Specificities in both situations exceed 90%. Would it not make sense to sacrifice some specificity to improve the sensitivity of the PSAV cut-off? This would slightly decrease the proportion of men who received a reassuring message but increase the number of those who are correctly identified as having a high risk.

2. Fig. 2 of the paper compares total PSA levels and PSAV among the three study groups. It is not obvious from this figure that PSAV would perform better than total PSA. It would be good to see a multivariate analysis comparing both parameters.
3. Treatment is not mentioned in the paper. Could, for example, cure by radical prostatectomy or radiotherapy have affected outcome? The time period between two determinations of PSA amounts to about 3 yr. This is unrealistic for the daily use of PSAV. How should PSAV be used in a clinical setting to produce similar results?

Obviously, the data of this important paper need to be confirmed, preferably in a prospective setting. Attention is drawn to the paper by Fall et al [1]. This group carried out a similar analysis for the control group participants of the SPG4 randomized radical prostatectomy trial. Their results and conclusions using different techniques for assessment are slightly different.

Reference

- [1] Fall K, et al. J Natl Cancer Inst 2007;99:526–32.

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