Prostate cancer (pCA) is the most common solid neoplasm among European men, with an incidence of 214 per 1000, outnumbering lung and colorectal cancer [1]. The mortality rate of pCA, however, is significantly lower as compared to the aforementioned cancer types, suggesting that many men harbour nonaggressive pCA without the need for immediate treatment. Therefore, many groups have attempted to identify prognostic risk factors based on clinical, serological, and pathohistologic parameters to predict the biologic aggressiveness of pCA and to identify patients who will need active treatment [2,3].

In the current paper, Loeb et al [4] evaluated the clinical utility of prostate-specific antigen (PSA) doubling time (PSA DT) and PSA velocity (PSAV) to predict the presence of biologically aggressive pCA as defined by PSA >20 ng/ml at diagnosis, a Gleason score >8, or cancer-specific death. Among a series of 681 men from the Baltimore Longitudinal Study of Aging, 98 and 583 men with and without pCA, respectively, were detected. Among the pCA patients, 27 men belonged to the high-risk group and 71 men belonged to the nonaggressive group. Using multivariate comparisons and analysis of receiver operator characteristics (ROC), the authors identified PSAV as the most significant parameter for predicting fatal disease, whereas PSA DT had no significant impact on the prediction models. The authors concluded that PSAV could be used in the routine clinical setting to predict fatal disease outcome.

The data presented are in line with several other reports that have identified PSAV as a clinically useful marker to either predict the presence of highly aggressive pCA independent of the type of primary local therapy or to improve the detection rate of life-threatening pCA and to reduce the most pressing problem of screening: overdetection and overtreatment of nonaggressive pCA [3–13]. The findings of Loeb et al [4] imply that PSAV might be used to identify men who might benefit from prostate biopsy independent of PSA serum levels in order to detect clinically significant and potentially lethal pCA. Despite the promising results, however, there are some arguments that question the use of PSAV in routine pCA screening.

Prospective screening studies have not demonstrated an additional informative role for PSAV compared to PSA alone [5–8]. PSAV independently predicted high-grade disease, but it only minimally increased the area under the curve (AUC) for the prediction of high-grade disease from 0.626 to 0.646. The true role of PSAV in predicting survival and prognosis remains unclear because the study of Loeb et al [4] includes a heterogeneous group of patients with clinical and screened, detected pCA, with most of the pCA-related deaths having developed in the clinically detected subgroups.
It has yet to be demonstrated in the findings of a prospective randomised trial that more cancers will be cured if the indication for a prostate biopsy will be based on PSAV >0.35 ng/ml per year.

Although no published clinical trials have answered the question of whether PSAV will be helpful in population screening for pCA, the correlation of PSAV with pCA-specific mortality requires further clinical attention. Considering the relatively high frequency of overdiagnosed pCA, reliable clinical parameters allowing the treating physician to stratify patients with regard to the need for active therapy versus active surveillance are urgently needed.

Although the exact role of PSAV in the management of patients with already diagnosed pCA has to be validated in prospective randomised trials, several aspects might be integrated in the process of counselling patients. First, pretreatment PSAV has been shown to correlate with the development of distant metastases and pCA-specific mortality after radical prostatectomy (RP), radiation therapy (RT), and androgen-deprivation therapy (ADT) [9–13]. Following RP, PSAV >2 ng/ml is associated with a significantly reduced 5-yr relapse-free survival (89% vs 73%) and a significantly increased pCA mortality [9,10]. In patients undergoing RT, a low PSAV was associated with a higher overall survival rate and a longer time interval until biochemical relapse [11,12]; furthermore, Palma et al [12] reported on a significantly increased risk of distant metastasis and pCA-specific mortality in men with high PSAV. Even in men with nonmetastatic castrate pCA, PSAV is a significant predictor of time to first bone metastasis, metastasis-free survival, and overall survival [13]. Based on the general finding of a worse therapeutic outcome in men with PSAV >2 ng/ml independent of the mode of primary local treatment, PSAV should be integrated in the decision-making process for the most accurate primary local treatment considering pathohistologic variables and preexisting comorbidities.

Second, PSAV might be helpful to identify patients with a high risk of disease recurrence who might be candidates for experimental, intensive adjuvant treatment regimes. The use of PSAV will help to homogenise treatment groups and to generalise treatment results more easily and more objectively, since PSAV reflects the biology of pCA independent of stage and grade.

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References


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