Letter to the Editor NOT referring to a recent journal article

Preliminary Results of a Novel Method to Estimate the Probability of Prostate Cancer in Men with Elevated Serum PSA Values

Despite its shortcomings—mainly, its lack of specificity—prostate-specific antigen (PSA) testing currently is a widely-accepted clinical tool for diagnosis of prostate cancer. Therefore, various static concepts for improving the PSA specificity have not yet reached a significant level of evidence to justify their inclusion in clinical guidelines. In an effort to address these concerns, we developed a novel mathematical model to estimate the probability of prostate cancer and, subsequently, the need for more extensive evaluation in patients with PSA values ranging from 4.0 ng/ml to 10.0 ng/ml.

The development of our model was based on the following assumptions: (1) Serum PSA values are correlated to patient age and prostate volume [1], (2) free-to-total PSA ratio is a valid predictor of prostate cancer [2], and (3) 50 ng/ml PSA values have a 98.5% positive predictive value (PPV) for prostate cancer diagnosis. Our main study hypothesis was as follows: Correlation of ratios of a given PSA by patient age, prostate volume (U/S), and free-to-total PSA ratio, to the corresponding ratios of 50 ng/ml PSA value (prostate cancer evidently present) by the same parameters (age, prostatic volume), as well as free PSA-to-50 ratio, can operate as a "simulation" model to establish a relationship between these two measures and thus yield an estimate of the probability of cancer [3]. A total of 146 patients were included in the study with 8.13 ng/ml mean PSA (median: 7.65 ng/ml) and were subjected to transrectal ultrasonographic prostate biopsy. Statistical analysis was performed using the SPSS-12 (SPSS Inc, Chicago, IL, USA) and Instat (Pearson correlation coefficient-rho[r], Fisher’s exact test, p < 0.05).

A mean of 1.86 biopsies per patient were performed (median: 2.00 [1–5]), obtaining 12.1 mean cores per biopsy (median: 12 [6–24]). Pathologic examination was positive for prostate cancer in 69 patients (47.3%), negative in 60 patients (41.1%), and showed PIN (I-III) changes in 17 patients (11.6%). Overall, the r statistic (Pearson-rho) was positive [r(+) ] in 83 patients (55.8%) [83.3% positive biopsies and 16.7% negative biopsies for prostatic carcinoma] and negative [r(−) ] in 63 patients (44.2%) [84.21% negative biopsies and 15.8% positive biopsies for prostate cancer] (p < 0.0001 odds ratio (OR) 25.5 [9.9–65.8]). The calculated sensitivity of the method was 86.95%, the specificity was 80.0%, the PPV was 83.3%, and the negative predictive value was 84.21%.

The introduced mathematical model predicted the result of prostate biopsy with high diagnostic accuracy and properly identified (1) eight out of 10 patients who proved to have prostate cancer and (2) eight out of 10 patients without histologic evidence of the disease. These findings suggest that with further investigation and proper validation, this method may become a useful clinical prognosticator that is capable of advancing the diagnostic performance of PSA testing.

Conflicts of interest: The authors have nothing to disclose.

References

Editorial Comment on: Preliminary Results of a Novel Method to Estimate the Probability of Prostate Cancer in Men with Elevated Serum PSA Values
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The advent of prostate-specific antigen (PSA) testing in combination with digital rectal examination (DRE) has revolutionized early prostate cancer detection and consequently resulted in a stage migration at radical prostatectomy [1]. The majority of patients are currently being diagnosed at a localized stage. However, PSA represents an organ-specific but not disease-specific test, resulting in an “unnecessary” biopsy in approximately 60–70% of all men subjected to prostate biopsy [2]. This fact coined the term “PSA dilemma.” Fortunately, numerous efforts are under investigation and have already been made in improving PSA’s specificity, eg, percent free PSA (%fPSA), (−5,−7) proPSA, proenzyme prostate-specific antigen prostate cancer gene 3 (PCA3), early prostate cancer antigen-2 (EPCA2) [3,4].

Spyropoulos and Dellis [5] present an interesting novel statistical approach to estimating an individual’s risk of prostate cancer putting a ratio relative to the acknowledged positive predictive value (PPV) of a PSA value of 50 ng/ml. Specifically, the authors derive three different ratios consisting of PSA, age, prostate volume, and %fPSA. These “individual” ratios are compared to the PSA value of 50 ng/ml ratios to derive the probability of a positive biopsy outcome.

Despite this intriguing concept, some considerations need to be acknowledged regarding its statistical and clinical approach. First, it is limited by the relatively small sample size of only 146 men. Clearly, validation in larger cohorts needs to demonstrate comparable results. Additionally, it would be of interest how these ratios behave in different PSA strata. Moreover, how does this approach behave differently from other established statistical approaches, such as a classification and regression tree analysis (CART) or a logistic regression-based nomogram model?

From a clinical standpoint, this mathematical model relies solely on continuously coded variables. Unlike established models, other risk factors such as DRE cannot be accounted for. Further, the biopsy scheme (extended vs sextant) is not reported and may significantly influence the detection rate [2]. Finally, within this study cohort, individuals subjected to an initial and a repeat biopsy were included. Obviously, these individuals do not share the same risk of harboring prostate cancer at biopsy.

Nevertheless, the authors are to be commended for their work and attempt to risk-stratify men prior to prostate biopsy. Besides allaying patients’ anxiety, these efforts have major implications for health care systems.

References

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