Re: PCA3 Score before Radical Prostatectomy Predicts Extracapsular Extension and Tumor Volume


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Expert’s summary:
Whitman et al examined 72 patients before radical prostatectomy. Following digital rectal examination, urine samples were taken and PCA3 and prostate-specific antigen (PSA) mRNA were measured. The PCA3–PSA ratio is the PCA3 score. The scores were correlated with the histologic result.

The authors found that 71.2% of the patients had cT1c tumors, and the rest had cT2 tumors. Median PSA was 4.7 ng/ml (range: 1.0–31.6). Gleason score was 3 + 3 for 69.4% of patients. All prostatectomy specimens were processed according to a standardized protocol and were assessed by two experienced genitourinary pathologists. All tumors were measured in three dimensions, and tumor volume was estimated. The median test was performed to determine the association between PCA3 score and pathologic characteristics of the tumor.

Upgrading of Gleason score occurred in 21 of 72 cases (29.2%) and downgrading occurred in 11 cases (15.3%) from biopsy to prostatectomy specimens. Similarly, upstaging was found in 29.1% of the cases (20.8% pT3a, 8.3% pT3b).

With a cut-off PCA3 score of 47, the resulting sensitivity, specificity, and accuracy to predict extracapsular extension (ECE) were 57%, 94%, and 83%, respectively, resulting in a area under the curve (AUC) of 0.732. When combined with Gleason score and PSA, PCA3 independently predicted ECE with an AUC of 0.90.

Expert’s comments:
One of the persistent problems in oncology is the lack of prognostic factors to determine the fate of the individual patient. With a better understanding of the molecular base of tumor development and progression, numerous attempts have been made to overcome this hurdle. DNA and mRNA changes have been researched intensively to understand the differences between tumor cells and normal tissue. It turned out, however, that tumor cells of the same tumor can show a wide variety of genetic abnormalities, making it extremely complex to rely on changes of individual genes or single-digit numbers of gene sets. While first attempts with this approach often looked promising [1] in terms of prognostic differentiation, reproduction of the results turned out to be difficult or impossible. Even with the advent of multiple gene analysis using micro tissue arrays and the possibility of developing gene signatures, only modest progress (eg, with breast cancer) has been made to determine the prognosis of individual patients [2].

For prostate cancer, a PCA3 mRNA-based urine test has recently been added to the diagnostic armamentarium [3]. While its ability to enhance early detection seems only modest so far, recent evidence suggests that it may be able to enhance our prognostic assessment of patients with clinically localized prostate cancer.

ECE has recently been shown to be a significant prognostic factor for prostate cancer–related mortality [4]. Moreover, ECE was the most commonly underestimated adverse feature in patients who were theoretically eligible for active surveillance [5].

Thus, when combined with standard prognostic factors in a nomogram or artificial neural network, PCA3 might be able to enhance our ability to better characterize clinically localized prostate cancer. This first report with a limited number of patients needs further confirmation, but cautious optimism seems warranted that we may finally make some progress in differentiating between the tiger and the pussycat.

Conflicts of interest: The author has nothing to disclose.

References
Re: Surveillance and Deferred Treatment for Localized Prostate Cancer. Population Based Study in the National Prostate Cancer Register of Sweden
Stattin P, Holmberg E, Bratt O, Adolffson J, Johansson J-E, Hugosson J; National Prostate Cancer Register
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Experts’ summary:
In this Swedish study, the extent of watchful waiting and active surveillance (ie, deferred treatment for patients with localized prostate cancer) were evaluated. In Sweden, the national prostate cancer registry is mandatory and covers 98% of all tumor patients. Between 1997 and 2007, 8304 patients with incident prostate cancer were identified, including patients with clinically localized tumors T1 or T2, N0 or Nx, and M0 and Mx and a prostate-specific antigen (PSA) level <20 ng/ml. Patients were studied at time of diagnosis and for 4 yr thereafter.

Of all patients, 26% were put on surveillance, whereas 48% underwent radical prostatectomy, 20% underwent radiotherapy, and 5% underwent hormonal treatment. Men on surveillance had significantly fewer aggressive tumors than those treated immediately. After 4 yr, 34% of the men on surveillance had had treatment with radical prostatectomy, radiotherapy, or hormonal treatment, and 66% of the patients initially managed with active surveillance remained untreated. The authors conclude that in Sweden, active surveillance was a relatively common treatment option for patients <70 yr old in the period studied.

Expert’s comments:
Scandinavian countries have a long tradition of conservatively managing men with prostate cancer. While the rest of the world became more and more aggressive in the treatment of even the smallest tumors, a relatively larger percentage of patients were not treated initially in Sweden. It is only in recent times that expectant management or active surveillance have gained attention in other countries for smaller, less aggressive tumors. But what are less aggressive tumors? Clear and uniformly accepted criteria are still lacking for whom to put on watchful waiting or active surveillance. Many would agree that a Gleason score ≤6, a PSA <10 ng/ml, and T1c to T2a represent good-risk tumors. Considering that these criteria are found in approximately 50% of all newly diagnosed prostate cancers, we are talking about a significant number of patients for whom treatment might not, or not immediately, be necessary [1].

Stattin et al did a wonderful job in taking advantage of one of the most complete cancer registries in the world. They add an important set of data on how to manage patients with less aggressive tumors. From earlier studies, we know that good-risk tumors remain so, even up to 20 yr [2].

It is reassuring to urologists and to patients that active surveillance does not mean just postponing treatment for a few years and, consequently, losing precious time. It is rather a long-term option for many patients, given proper tumor selection and close follow-up.

In my opinion, we are still underutilizing surveillance as a management option, thus treating too many men with prostate cancer. Studies like this one may help us to find a better way of handling this frequent tumor.

Conflicts of interest: The author has nothing to disclose.

References

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