PCA3

Background Information

Serum prostate specific antigen (PSA) is the standard marker for diagnosis and management of prostate cancer. While PSA is a useful marker available for this disease, its utility is limited in many common clinical situations. For screening purposes, PSA utility is limited because it is prostate specific but not cancer specific; consequently, there is no PSA lower limit of detection for which the risk of prostate cancer is zero. For predicting biologically significant disease, the predictive value of PSA is limited because higher grade tumors often express little PSA. Decisions regarding the need for re-biopsy in men with an elevated PSA are limited because PSA usually is more reflective of prostate volume rather than the risk of carcinoma.

mRNA of the prostate cancer antigen 3 (*PCA3*) gene has been shown to be over-expressed (median 66-fold) in >95% of prostate cancer tissue compared with normal or benign prostate tissue.[1,2] PCA3 is prostate cancer specific, and the PCA3 assay is unaffected by prostate volume. Therefore, the PCA3 assay addresses many of the issues related to PSA screening, improves the sensitivity and specificity of PSA interpretation and may add other information more reflective of tumor biology. Low levels of PCA3 mRNA have been shown to correlate with a low probability of biopsy-proven prostatic adenocarcinoma.[3,4]

Clinical Indications

PCA3 is useful:

1. in conjunction with PSA screening of high-risk individuals (those with positive family history), where serum PSA may be normal and not reflect true cancer risk;
2. in deciding on the need for re-biopsy in men with elevated PSA and prior negative biopsy, as published studies have demonstrated that, in this setting, PCA3 improves diagnostic accuracy;
3. in the selection of men for active surveillance, as published studies have demonstrated that PCA3 correlates with tumor volume and can help identify those with biologically insignificant tumors.

Interpretation

PCA3 results are reported as a score ranging from 4 to 125, the ratio of PCA3 mRNA to PSA mRNA.

Likelihood of a positive biopsy increases as the score increases.

A score of 35 is considered the cutoff for positive vs. negative PCA3 result.

Methodology

The PROGENSA PCA3 assay (Gen-Probe, San Diego, Calif.) is performed on a first-catch urine sample collected following digital rectal examination of the prostate gland. The assay combines RNA target capture, transcription mediated amplification and hybridization protection for both PCA3 and PSA RNA.

Limitations of the Assay

An international standard for the assay has not been established. The test utilizes urine obtained immediately after a digital rectal examination of the prostate sufficient to yield a sufficient number of prostate gland cells for reliable analysis.

References

1. Bussemakers MJ, van Bokhoven A, Verhaegh GW *et al.* DD3: a new prostate-specific gene, highly overexpressed in prostate cancer. *Cancer Res.* 1999;59:5975-9.
2. Hessels D, Klein Gunnewiek JM, van Oort I *et al.* DD3^{PCA3}-based molecular urine analysis for the diagnosis of prostate cancer. *Eur Urol* 2003;44: 8-16.
3. Marks, LS, Y Fradet *et al.* PCA3 molecular urine assay for prostate cancer in men undergoing repeat biopsy. *Urology*. 2007;69:532-535.
4. Wang, R, Chinnaiyan, AM, Dunn, RL, Wojno, KJ *et al. Cancer*. 2009;115:3879-3886.

Test Overview

Test Name	Prostate Cancer Biomarker (PCA3)
Reference Range	A score of 35 or more is considered a positive PCA3 result.
Specimen Requirements	20-30 mL first-catch urine after digital rectal exam of prostate
Ordering Mnemonic	PCA3
Billing Code	87736
CPT Codes	83891 (x2); 83896 (x2); 83902 (x2); 83892 (x2); 83898 (x2); 83913

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