Test Specific Guidelines

PCA3 Testing for Prostate Cancer

MOL.TS.215.A
v1.0.2023

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedure addressed by this guideline	Procedure code
PCA3 Score	81313

What Is Prostate Cancer Antigen 3 (PCA3)?

Definition

Prostate cancer antigen 3 (PCA3) is a non-protein-coding messenger RNA (mRNA) that is highly overexpressed in >95% prostate cancer tissue compared with normal prostate tissue or benign prostatic hyperplasia.[1]

The strong association between PCA3 mRNA levels and prostate cancer led to the development of a urinary assay to measure this analyte to aid in cancer detection.[1]

Test Information

Following a digital rectal examination, first-void urine is collected, rapidly processed, and the mRNAs for the PCA3 gene and the PSA gene are quantified. A PCA3 score is calculated from the ratio of PCA3 RNA to PSA RNA.

A high (>25) PCA3 Score indicates an increased likelihood of a positive biopsy. A low (<25) PCA3 Score is associated with a decreased likelihood of a positive biopsy.[2]

A multi-center study which included a total of 466 men found that at a score cutoff of 25 for men with at least one previous negative biopsy, PCA3 demonstrated 77.5% sensitivity, 57.1% specificity, and negative and positive predictive values of 90% and 33.6%, respectively. Men with a PCA3 score of <25 were 4.56 times more likely to have a negative repeat biopsy than men with a score of >25.[3]

Guidelines and Evidence

Introduction

This section includes relevant guidelines and evidence pertaining to PCA3 testing.

American Urological Association

The American Urological Association (AUA, 2018) guideline on the early detection of prostate cancer stated:[4]

"While the benefits of PSA-based prostate cancer screening have been evaluated in randomized- controlled trials, the literature supporting the efficacy of digital rectal exam (DRE), PSA derivatives and isoforms (e.g. free PSA, -2proPSA, prostate health index, hK2, PSA velocity or PSA doubling time) and novel urinary markers and biomarkers (e.g. PCA3) for screening with the goal of reducing prostate cancer mortality provide limited evidence to draw conclusions. While some data suggest use of these secondary screening tools may reduce unnecessary biopsies (i.e. reduce harms) while maintaining the ability to detect aggressive prostate cancer (i.e. maintain the benefits of PSA screening), more research is needed to confirm this. The Panel recognizes that these tests can be used as adjuncts for informing decisions about the need for a prostate biopsy –or repeat biopsy- after PSA screening, but emphasizes the lack of evidence that these tests will increase the ratio of benefit to harm."

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2021) guidelines for prostate cancer early detection recognize the FDA-approved use of PCA3 testing and state:[5]

"Results were reported from an NCI Early Detection Research Network (EDRN) validation study of the PCA3 urinary assay in 859 men scheduled for a diagnostic prostate biopsy in 11 centers. The primary outcomes were reported at a PPV of 80% (95% CI, 72%–86%) in the initial biopsy setting and an NPV of 88% (95% CI, 81%–93%) in the repeat biopsy setting. Based on the data, use of PCA3 in the repeat biopsy setting would reduce the number of biopsies by almost half, and 3% of men with a low PCA3 score would have high-grade prostate cancer that would be missed. In contrast, the risk of high-grade disease in men without prior biopsy with a low PCA3 is 13%. Thus, the panel believes that this test is not appropriate to use in the initial biopsy setting."

"The FDA has approved the PCA3 assay to help decide, along with other factors, whether a repeat biopsy in men aged 50 years or older with one or more previous negative prostate biopsies is necessary. This assay is recommended for men with previous negative biopsy in order to avoid repeat biopsy by the Molecular

Diagnostic Services Program (MolDX) and is therefore covered by CMS (Centers for Medicare & Medicaid Services) in this setting."

U.S. Food and Drug Administration

The U.S Food and Drug Administration (FDA, 2012) approved the Progensa PCA3 assay with the following intended use:[6]

"The PROGENSA PCA3 Assay is indicated for use in conjunction with other patient information to aid in the decision for repeat biopsy in men 50 years of age or older who have had one or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended by a urologist based on current standard of care, before consideration of PROGENSA PCA3 Assay results."

"The Clinical Study only included men who were recommended by urologists for repeat biopsy. Therefore, the performance of the PROGENSA PCA3 Assay has not been established in men for whom a repeat biopsy was not already recommended."

"Black Box Warning: The PROGENSA PCA3 Assay should not be used for men with atypical small acinar proliferation (ASAP) on their most recent biopsy. Men with ASAP on their most recent biopsy should be treated in accordance with current medical guidelines."

Selected Relevant Publications

Data from many peer-reviewed publications suggest that PCA3 gene testing, when used with other patient information, may help address some of the well-known challenges urologists face, such as identifying prostate cancers while reducing unnecessary repeat biopsies.[7-9]

Criteria

Prostate cancer antigen testing (PCA3) may be indicated in males with ALL of the following:

Age >50 years, and

One or more previous negative prostate biopsies, and

Continued clinical suspicion of prostate cancer based on digital rectal exam (DRE) or elevation of prostate specific antigen (PSA) of >3 ng/mL, and for whom a repeat biopsy would be recommended by a urologist based on current standard of care, and

Atypical small acinar proliferation (ASAP) was NOT identified on the most recent biopsy.

References

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