PCA3 Testing for Prostate Cancer

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Introduction

PCA3 testing for prostate cancer is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedure addressed by this guideline	Procedure code
PCA3 Score	81313

Criteria

Introduction

Requests for PCA3 testing are reviewed using these criteria.

Prostate cancer antigen testing (PCA3) is medically necessary 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.

What is prostate cancer antigen 3 (PCA3)?

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]

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Test information

Introduction

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]

PCA3 Testing for Prostate Cancer Detection

- 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, 2023) guideline on the early detection of prostate cancer stated:[4]

- "When screening for prostate cancer, clinicians should use PSA as the first screening test. (Strong Recommendation; Evidence Level: Grade A)"
- "For people with a newly elevated PSA, clinicians should repeat the PSA prior to a secondary biomarker, imaging, or biopsy. (Expert Opinion)"
- "Clinicians may use adjunctive urine or serum markers when further risk stratification would influence the decision regarding whether to proceed with biopsy. (Conditional Recommendation; Evidence Level: Grade C)"
- "After a negative biopsy, clinicians may use blood, urine, or tissue-based biomarkers selectively for further risk stratification if results are likely to influence the decision regarding repeat biopsy or otherwise substantively change the patient's management. (Conditional Recommendation; Evidence Level: Grade C) Blood, urine, or tissue-

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based biomarkers may provide additional information for risk stratification in patients with a prior negative biopsy and with ongoing suspicion for GG2+ prostate cancer."
- "While there are a plethora of serum, urine, tissue, and imaging biomarkers to assess the likelihood of high-grade prostate cancer, there is little knowledge on comparative effectiveness, how they may complement or supplement each other, and how various stepwise algorithms perform."

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2024) guidelines for prostate cancer early detection recognized the FDA-approved use of PCA3 testing and stated:[5]

- "Results were reported from an NCI Early Detection Research Network (EDRN) validation study of the PCA3 urinary assay in 859 individuals 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 individuals aged ≥50 years 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. The panel also includes PCA3 as an option in the post-biopsy 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

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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]

Note: This benefit/harm statement only applies to those jurisdictions that do not have Medicare guidance. Based upon the guidelines and evidence provided in the clinical policy, following EviCore's criteria for PCA3 testing for prostate cancer will ensure that testing will be available to those members most likely to benefit from the information provided by the assay. For those not meeting criteria, it ensures alternate management strategies are considered. However, it is possible that some members who would benefit from the testing, but do not meet clinical criteria, will not receive an immediate approval for testing.

References

1. Freedland SJ. Screening, risk assessment, and the approach to therapy in patients with prostate cancer. *Cancer*. 2011;117:1123-35.
2. PCA3.org website. Patient information. Available at: **https://web.archive.org/web/20220120223445/http://www.pca3.org/sites/default/files/pdf/Progensa-Patient-Brochure.pdf**
3. Gittelman MC, Hertzman B, Bailen J, et al. PCA3 molecular urine test as a predictor of repeat prostate biopsy outcome in men with previous negative biopsies: a prospective multicenter clinical study. *J Urol*. 2013 Jul;190(1):64-9. Available at: **http://www.jurology.com/article/S0022-5347(13)00287-5/fulltext** .
4. Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part I: prostate cancer screening. *J Urol*. 2023;210(1):45-53. doi: 10.1097/JU.0000000000003491
5. Moses KA, Sprenkle PC, Bahler C, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024 – March 6, 2024. Prostate Cancer Early Detection, available at: **http://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf** . Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer Early Detection V2.2023 – March 6, 2024. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines®, go online to NCCN.org
6. U.S. Food and Drug Administration. Progensa PCA3 Assay. Approval, summary, and labeling. Available at: **https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100033b.pdf**
7. Crawford ED, Rove KO, Trabulsi EJ, et al. Diagnostic performance of PCA3 to detect prostate cancer in men with increased prostate specific antigen: a prospective study of 1,962 cases. *J Urol*. 2012;188:1726-31.
8. Luo Y, Gou X, Huang P, Mou C. The PCA3 test for guiding repeat biopsy of prostate cancer and its cut-off score: a systematic review and meta-analysis. *Asian J Androl*. 2014;16:487-92.
9. Shinohara K, Nguyen H, Masic S. Management of an increasing prostate-specific antigen level after negative prostate biopsy. *Urol Clin North Am*. 2014;41:327-38.