Test Specific Guidelines

ConfirmMDx for Prostate Cancer Risk Assessment

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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
ConfirmMDx for Prostate Cancer	81551

What Is ConfirmMDx Testing for Prostate Cancer?

Definition

The ConfirmMDx™ test (MDx Health) is a proprietary epigenetic assay that measures gene methylation associated with the presence of cancer. Results are intended to assist in determining which patients likely have a true negative biopsy, and which patients are at increased risk for occult cancer. Results may prevent unnecessary repeat biopsies in unaffected men, and triage higher risk patients for repeat biopsies and treatment, as needed.[1]

Prostate cancer is the most common cancer among men, with over 200,000 new cases identified each year in the United States.[2,3] The median age at diagnosis is 67 years.[4] Older men are more likely to be affected than younger men, and African American men have higher rates compared to men of other ethnic backgrounds.[4]

Screening programs for prostate cancer may allow for its early detection. Screening is typically performed by prostate-specific antigen (PSA) test and/or digital rectal examination (DRE).[3]

Diagnosis is confirmed by prostate biopsy.[5-7] Biopsy is typically performed by collecting approximately 12 needle biopsy cores.[7]

Initial biopsies only detect 65-77% of prostate cancers, and repeat biopsies are frequently performed.[8,9] The false negative rate of biopsy may be as high as 25%.[10]

Test Information

ConfirmMDx measures the methylation levels (using quantitative methylation PCR) of 3 genes (GSTP1, APC and RASSF1) associated with prostate cancer. The

test is performed on formalin-fixed, paraffin-embedded prostate specimens from a 12-core biopsy.

Results are reported with methylation positive/negative for each biopsy core, along with a map of the regions where methylation is distributed.[1]

Negative predictive value of the test is approximately 90%, based on results of a large, blinded clinical evaluation study.[11]

Guidelines and Evidence

National Comprehensive Cancer Network (NCCN)

The National Comprehensive Cancer Network (NCCN, 2021) Clinical Practice Guidelines in Oncology for Prostate Cancer Early Detection state the following:[7]

"It is well known that a negative prostate biopsy does not preclude a diagnosis of prostate cancer on subsequent biopsy. Those patients with negative prostate biopsies should be followed with DRE and PSA with consideration of multiparametric MRI and biomarker tests that improve specificity of PSA testing."

"Tests that improve specificity in the post-biopsy setting—including percent-free PSA, 4Kscore, PHI, PCA3, and ConfirmMDx—should be considered in patients thought to be higher risk despite a negative prostate biopsy."

"The panel believes that ConfirmMDx can be considered as an option for individuals contemplating repeat biopsy, because the assay may identify individuals at higher risk of prostate cancer diagnosis on repeat biopsy."

"Therefore, the panel recommends that, as for patients with HGPIN, follow-up with PSA and DRE at 6- to 24-month intervals is appropriate. The use of biomarker tests that improve the specificity of screening (see Biomarker Testing: PSA Derivatives and Other Tests, above) and/or multiparametric MRI can also be considered in these patients, although it is not known whether these patients receive as much (or more) benefit from these approaches as patients with a completely negative biopsy."

Selected Relevant Publications

A number of peer-reviewed expert-authored studies that evaluate ConfirmMDx for detection of prostate cancer are available.[8-17] Most of these studies demonstrate the potential for the assay to help urologists accurately determine which patients likely have a true negative biopsy, and which patients are at increased risk for occult cancer.

Multiple factors have been reported in the literature that contribute to an individual being considered high risk for prostate cancer:

Positive family history:

1st degree relative with prostate cancer younger than 65 years of age[7,18,19,20]

two or more 1st degree relatives with prostate cancer at any age[19]

Being of African descent (including African American and Caribbean of African ancestry)[7,18,19,20]

Having a known mutation in a gene associated with increased risk of prostate cancer (e.g., BRCA1/2, HOXB13 (G84E mutation carriers), MLH1, MSH2, MSH6, PMS2, EPCAM)[7,18]

PSA levels:

greater than 10 ng/ml[21]

not greater than 10 ng/ml but increasing more than 0.35 ng/ml/year[7,22]

doubling in less than 3 years, when initial PSA level is greater than or equal to 4 ng/ml (if doubling occurs in under 2 years, other causes such as infection and inflammation have been excluded)[23,24]

Criteria

Coverage for ConfirmMDx will be granted when the following criteria are met:

No previous ConfirmMDx testing on the same sample when a result was successfully obtained, AND

No previous 4Kscore testing performed after the most recent negative biopsy when a result was successfully obtained, AND

Member is not under active surveillance for low stage prostate cancer, AND

Negative prostate biopsy (including individuals with unifocal high-grade prostatic intraepithelial neoplasia (HGPIN)) within the past 24 months, AND

Member is considered at higher risk for prostate cancer by one or more of the following:

Family history of 1st degree relative with prostate cancer diagnosed younger than age 65 years, and/or

Family history of two or more first-degree relatives with prostate cancer diagnosed at any age, and/or

African descent (including African American and Caribbean of African ancestry), and/or

Known mutation in a gene associated with increased risk of prostate cancer (e.g., BRCA1/2, HOXB13 (G84E mutation carriers), MLH1, MSH2, MSH6, PMS2, EPCAM), and/or

PSA level of greater than 10 ng/ml, and/or

PSA level increase of greater than 0.35 ng/ml/year if PSA level less than or equal to 10 ng/ml, and/or

PSA doubling time of less than 3 years, when initial PSA level is greater than or equal to 4 ng/ml and other causes of rising PSA (i.e., infection, inflammation) have been ruled out for individuals whose PSA doubling occurred in less than 2 years

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