Oncotype DX for Prostate Cancer

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.

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<th>Procedures addressed by this guideline</th>
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<td>OncotypeDX Genomic Prostate Score</td>
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What are gene expression profiling tests for prostate cancer

Definition

Prostate cancer (PC) is the most common cancer and a leading cause of cancer-related deaths worldwide. It is considered a heterogeneous disease with highly variable prognosis.¹

- At the time of diagnosis of localized PC, patients typically undergo a prognostic risk assessment with routine clinical and pathological tests to assess the probability of subsequent progression or metastasis. These prognostic assessments help to identify lower risk patients with indolent disease who may opt for active surveillance (AS), or higher risk patients with more aggressive disease who would benefit from a treatment intervention.

- High-risk prostate cancer (PC) patients treated with radical prostatectomy (RP) also undergo risk assessment to assess future disease prognosis and determine optimal treatment strategies. Post-RP pathology findings, such as disease stage, baseline Gleason score, time of biochemical recurrence (BCR) after RP, and PSA doubling-time, are considered strong predictors of disease-associated metastasis and mortality. Following RP, up to 50% of patients have pathology or clinical features that are considered at high risk of recurrence and these patients usually undergo post-RP treatments, including adjuvant or salvage therapy or radiation therapy, which can have serious risks and complications. According to clinical practice guideline recommendations, high risk patients should undergo 6 to 8 weeks of radiation therapy (RT) following RP. However, approximately 90% of high-risk patients do not develop metastases or die of prostate cancer, and instead may be appropriate candidates for alternative treatment approaches, including AS. As such, many patients may be subjected to unnecessary follow-up procedures and their associated complications, highlighting the need for improved methods of prognostic risk assessment.²,³
Several genomic biomarkers have been commercially developed to augment the prognostic ability of currently available routine clinical and pathological tests and identify those patients either at the time of diagnosis of localized PC or after radical prostatectomy (RP) most and least likely to benefit from a specific treatment strategy. Prognostic genomic tests, including gene expression profiling tests, may help to avoid overtreatment by reclassifying those men originally identified as high risk, but who are unlikely to develop metastatic disease. Genomic biomarkers may also play a role in assisting clinicians to tailor personalized and more appropriate treatments for subgroups of PC patients, and improve overall health outcomes.\textsuperscript{2,3}

**Test information**

- Gene expression profiles (GEPs) evaluate the expression of several genes using one sample. Gene expression is determined through RNA analysis, using either reverse transcriptase (RT) polymerase chain reaction (PCR) or DNA microarrays.\textsuperscript{4}
- Oncotype DX GPS uses quantitative RT-PCR for 12 prostate cancer-related genes and 5 control genes (total of 17 genes). It was developed for use with fixed paraffin-embedded (FPE) diagnostic prostate needle biopsies (≥1 mm prostate tumor).\textsuperscript{5}
- Results are expressed as a genomic prostate score (GPS), ranging from 0-100, representing tumor aggressiveness. The Oncotype DX GPS provides risk stratification to properly classify patients with regard to their risk of metastasis and death from prostate cancer. This test is designed to help patients with newly diagnosed, early-stage PC make informed treatment decisions, including active surveillance.\textsuperscript{5}

**Guidelines and evidence**

**National Comprehensive Cancer Network**

- The National Comprehensive Cancer Network (NCCN) 2019 Clinical Practice Guidelines on Prostate Cancer state the following regarding molecular assays:\textsuperscript{6}
  - “Men with low or favorable intermediate risk disease may consider the use of the following tumor-based molecular assays: Decipher, Oncotype DX Prostate, Prolaris, and Promark. Retrospective studies have shown that molecular assays performed on prostate biopsy or radical prostatectomy specimens provide prognostic information independent of NCCN or CAPRA risk groups. These include, but are not limited to, likelihood of death with conservative management, likelihood of biochemical progression after radical prostatectomy or external beam therapy, and likelihood of developing metastasis after radical prostatectomy or salvage radiotherapy.”
  - “Although full assessment of their clinical utility requires prospective randomized clinical trials, which are unlikely to be done, the panel believes that men with with low or favorable intermediate disease may consider the use of..."
Decipher, Oncotype DX Prostate, Prolaris, or ProMark during initial risk stratification.”

- According to NCCN, the Molecular Diagnostic Services Program (MolDX) recommendations stated the following:\(^6\)
  - Oncotype DX Prostate: “Cover post-biopsy for NCCN very-low, low-risk, and favorable intermediate-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.”

**American Association of Clinical Urologists**

The American Association of Clinical Urologists has issued a position statement on genomic testing in prostate cancer that states the following:\(^7\)
- “The AACU supports the use of tissue-based molecular testing as a component of risk stratification in prostate cancer treatment decision making.”

**American Urological Association, ASTRO, and the Society of Urologic Oncology**

The AUA/ASTRO/SUO guideline for clinically localized prostate cancer states the following:\(^8\)
- “Among most low-risk localized prostate cancer patients, tissue based genomic biomarkers have not shown a clear role in the selection of candidates for active surveillance.”

**Peer Reviewed Literature**

The proposed use of Oncotype DX GPS varied across available studies.\(^9\)\(^-\)\(^31\) Two older clinical validity studies primarily included patients with NCCN-very low to favorable-intermediate risk disease to demonstrate the use of Oncotype DX GPS as an adjunct to confirm decisions regarding active surveillance. In contrast, recently published studies sought to evaluate the clinical validity of Oncotype DX GPS in NCCN-intermediate-risk patients to identify a subset of these patients who harbor aggressive tumors undetected by biopsy and who may benefit from treatment intervention instead of active surveillance.

Several studies reported that Oncotype DX improved prediction of adverse pathology beyond currently used clinical parameters and nomograms in patients with very low, low-, and intermediate risk disease; however, these studies did not consistently report precision estimates, and when reported, wide confidence intervals suggested inadequate precision. One study conducted at a single institution evaluated long term survival outcomes of distant metastasis and disease-related mortality (~10 years). Analyses assessing the ability of Oncotype DX GPS to detect tumor aggressiveness in NCCN intermediate risk groups versus other risk groups mostly reported results with very wide confidence intervals (imprecise estimates) or P values showing no statistical significance between risk groups. In addition, across the majority of studies, the use of...
adverse pathology as a surrogate for survival outcomes (disease-related mortality and metastasis at 10 years) is an inadequate indicator of the performance of Oncotype DX GPS to detect aggressive tumors that necessitate treatment. In addition, it is not clear if the available study results of Oncotype DX in patient populations who underwent RP would reliably translate to newly diagnosed, untreated patients in clinical practice, with very low-, low-, or intermediate risk of disease per NCCN risk classification.

Direct evidence of clinical utility of Oncotype DX is lacking. Indirect clinical utility studies suggest that Oncotype DX GPS has an impact on physician and patient decision making; however, there is no evidence whether these changes lead to relevant improvements in overall health. As such, clinical utility studies in real-world urologic clinical practice are needed to evaluate if treatment practices change with test use, and if these changes result in improved patient-important outcomes, including overall survival and disease-specific survival. Evidence is also lacking regarding how to conduct ongoing monitoring of men who are determined to be low risk with Oncotype DX testing, but high risk with clinical assessment.

Clinical trials may be ongoing. Additional information can be found at www.clinicaltrials.gov.

Criteria

- This test is considered investigational and/or experimental.
  - Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.
  - In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

References


