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Decipher prostate biopsy genomic classifier | 18.04.2024

Research Inquiries

What is the pertinent and current medical literature supporting the Decipher test, and could you provide the statistical robustness of the recommendation it offers? Additionally, please elucidate the evidence underpinning its utilization for the results.

Summary of findings

The Decipher Genomic Classifier, established and validated through retrospective analysis of radical prostatectomy cases, is designed to inform treatment decisions rather than serve as a prognostic indicator. Trials have focused on evaluating alterations in treatment approaches rather than direct enhancement of oncologic endpoints. Nevertheless, certain outcomes such as biochemical recurrence and early metastases have been associated with the test results.

- **Research indicates that while the Decipher test plays a role in guiding treatment decisions for prostate cancer, particularly in choosing between radical treatment and monitoring, there is still uncertainty regarding whether adjusting treatment based on this test improves clinical outcomes due to insufficient evidence.**

- **A 2021 systematic review, encompassing 42 studies and over 30,000 patients, demonstrated the Decipher genomic classifier as an independent prognostic factor for various outcomes in prostate cancer, such as adverse pathology, biochemical failure, metastasis, and prostate cancer-specific mortality.**
- **It's important to highlight that most studies assessing the prognostic value of the Decipher test focus on post-radical prostatectomy patients, thus limiting its generalizability to those in the pre-therapy setting, potentially leading to increased oncologic risks.**
- **Research conducted in the pre-therapy context comprises a 2022 study that revealed the Decipher genomic test's significant prediction of shorter times to treatment initiation in newly diagnosed localized prostate cancer patients, with a heightened probability of transitioning to radical therapy during active surveillance.**
- **Another pre-therapy context study from 2019 assessing Decipher's pre-therapy role as an adverse pathology predictor found a 1.29 odds ratio per 10% increase in the test score.**
- **Decipher was primarily assessed in patients undergoing radical prostatectomy, with limited data available on its use in patients in the pre-therapy setting. In addition, the majority of studies examining this test exhibit inclusion bias due to testing being conducted on selective populations. Furthermore, there is a significant risk of confounding by cancer stage, as patients with more severe illness were both more inclined to have elevated test values and more likely to receive aggressive therapy.**

Meta Medical Findings

Introduction

The Decipher Genomic Classifier test was developed and **validated** using a retrospective analysis of 639 radical prostatectomy patients from the Mayo Clinic registry [1]. It uses a microarray to identify a 22-gene signature linked to cell proliferation, differentiation, and modulation of androgen-signaling pathways. The test assigns a score from 0 to 1, which quantifies the risk of adverse clinical outcomes such as biochemical recurrence and early clinical metastases following RP. Its goal is to guide decision-making regarding the use of adjuvant radiotherapy [2].

Most evidence supporting the Decipher Biopsy test originates from studies on radical prostatectomy (RP) specimens. However, in 2016, Knudsen et al. [3] confirmed its applicability to biopsy-derived tissue, showing that nearly 95% of the transcriptomic data from RP specimens could be reliably obtained from biopsy tissue, with a high correlation of 0.96.

The Decipher test has been evaluated in numerous completed, ongoing, and planned prospective randomized trials. **Despite its widespread use, it remains uncertain whether changes in treatment based on this risk-adapted approach result in clinically favorable outcomes, both oncologically and functionally.** Trials evaluating the Decipher Genomic Classifier focus on assessing changes in management strategies. The primary objective is not for the biomarker to directly improve hard oncologic endpoints, but rather to influence downstream therapeutic decisions that could potentially impact these outcomes [4].

The role of the Decipher test was shown to affect therapy-related decisions:

- For example, a systematic review [5] published in *European Urology Oncology* (Q1, IF 8.2, unregistered in PROSPERO) in 2024 evaluated the impact of tumor molecular profiling on treatment choice for prostate cancer patients.
    - Patients in the NCCN **favorable intermediate-risk** group experienced an increase in risk after genomic testing in approximately 31–65% of the cases.
    - The changes in risk classification correlated with a wide spectrum of treatment modifications, affecting 5 to 65% of cases.
    - The authors conclude that in the pretherapy context, molecular tests appeared to guide the choice between radical treatment and monitoring. **However, it was uncertain whether these risk-adjusted treatment modifications led to better clinical outcomes.**
      It is worth noting that the majority of studies examining this test exhibit inclusion bias due to testing being conducted on selective populations. Furthermore, there is a significant risk of confounding by cancer stage, as patients with more severe illness were both more inclined to have elevated test values and more likely to receive aggressive therapy.
    - The review's limitations stem from its inclusion of studies with small patient populations, typically ranging up to several hundred patients, and lacking a validation cohort. Additionally, certain sections of the review do not adhere to established guidelines.

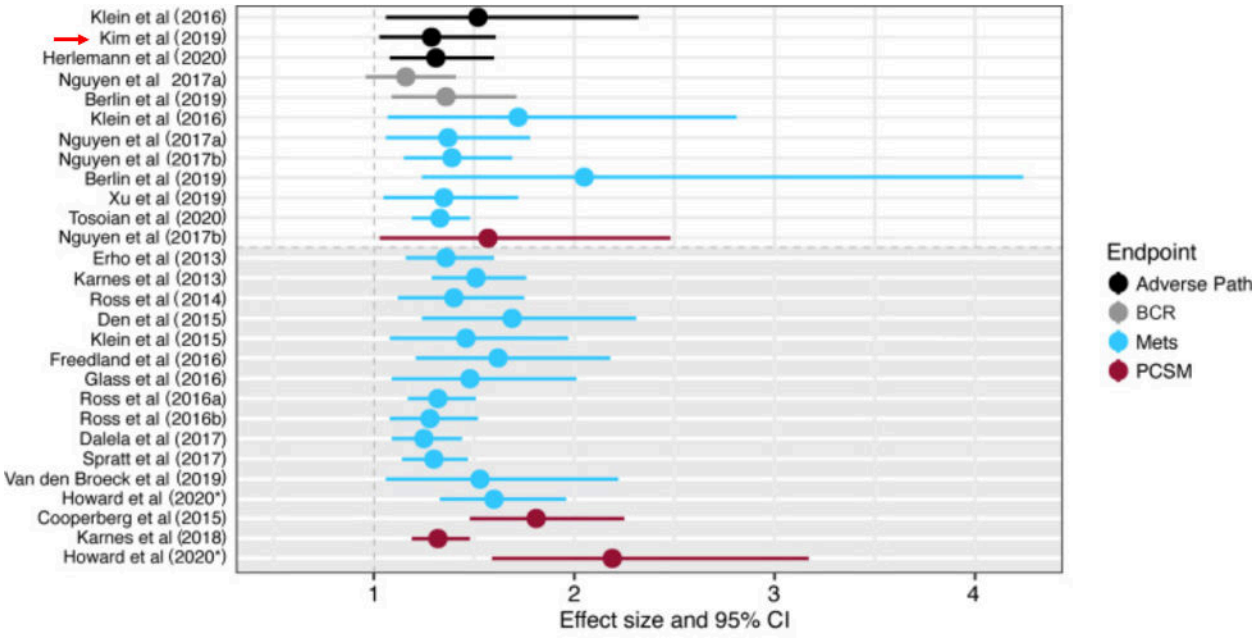
- A study [6] published in *JNCI Cancer Spectrum in 2023 (Q1, IF 3.7)* analyzed 8,927 prostate cancer patients who underwent decipher testing.
    - Overall, biopsy-tested (Decipher test from biopsy) patients were more likely to undergo active surveillance or watchful waiting than untested patients (OR =2.21, 95% CI = 2.04 to 2.38, P < .001).
    - Among patients with NCCN low and favorable-intermediate risk, a **higher GC risk class was associated with greater use of local therapy** (OR = 4.79, 95% CI = 3.51 to 6.55, P < .001).
    - In the group of patients who underwent prostatectomy following the test, a high Decipher risk was linked to the presence of adverse pathological findings (OR = 2.94, 95% CI = 1.38 to 6.27, P = .005).

The impact of the Decipher test on clinically favorable outcomes is currently being examined in the ongoing G-MAJOR prospective trial [7], which includes patients with favorable-risk prostate cancer. Results are expected in the upcoming years.

Systematic Review of the prognostic value of Decipher

- **A Systematic Review of the Evidence for the Decipher Genomic Classifier in Prostate Cancer-** a systematic review [4] published in 2021 in *European Urology* (Q1, IF 24, unregistered in PROSPERO) included 42 studies and 30,407 patients and evaluated the clinical utility of the Decipher genomic classifier among patients with prostate cancer.

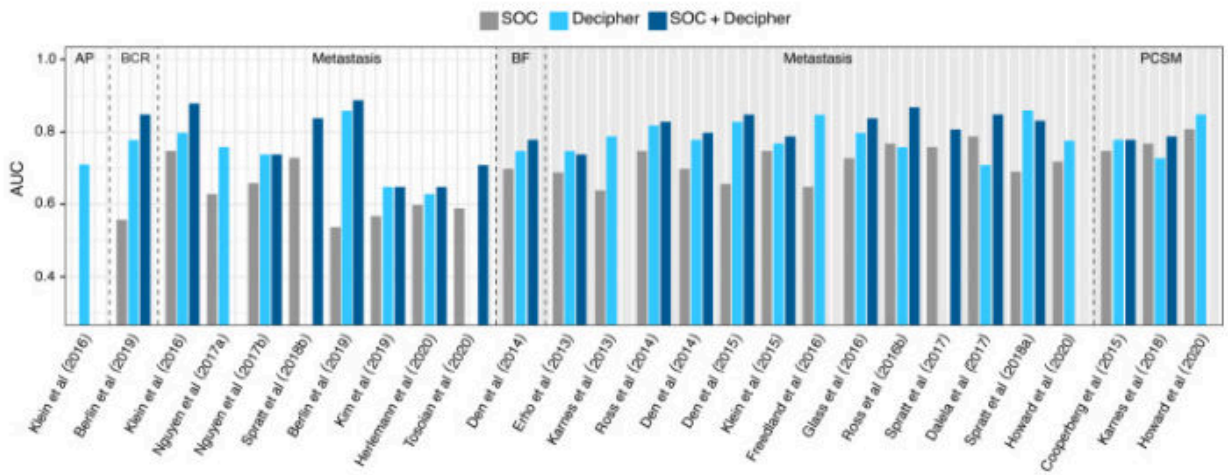
    - **Decipher was found to be an independent prognostic factor for different study outcomes, including adverse pathology, biochemical failure, metastasis, and survival**. The following figure presents the Hazard Ratio (HR) from multivariate analysis for each study endpoint associated with Decipher. The HR is reported per 0.1 unit increase on the continuous scale of the Decipher score.



Jairath et al. 2021

The white background indicates that the genomic test was performed from biopsy tissue, while the gray background indicates that it was from prostatectomy tissue.

- The subsequent figure illustrates the Discrimination performance, as indicated by AUC calculations for each study endpoint, comparing the performance of standard of care (SOC) clinicopathologic multivariable models, Decipher (GC) alone, and the combination of SOC + GC.



Jairath et al. 2021

Guidelines for biomarker endorsement have been inconsistent. The latest ASCO guidelines from 2022 [8] rated the genomic classifier score as "intermediate" for evidence quality and "moderate" for recommendation strength in postprostatectomy patients. Conversely, for the same patient group, advanced imaging techniques like MRI or molecular PET imaging received a "high" evidence quality rating and a "strong" recommendation [9], despite the evidence being largely retrospective. This is even though the evidence for these imaging biomarkers is primarily based on their ability to change management, similar to what is shown for the genomic classifier.

Only one trial included in the review (marked with arrow) has evaluated the role of the Decipher test in risk stratifying and guiding therapy in the pretherapy setting:

- **Validation of the Decipher Test for predicting adverse pathology in candidates for prostate cancer active surveillance-** A retrospective study [10] of 266 with very low/low and favorable-intermediate risk prostate cancer, was published in *Prostate Cancer and Prostatic Diseases (Q1, IF 4.3) in 2019.* Decipher was evaluated as a predictor of adverse pathology (AP).
    - The odds ratio for adverse pathology was 1.29 per 10% increase (95% CI 1.03–1.61, p= 0.025).
    - The sensitivity and specificity for predicting AP with the cutoff of Decipher score of 45, were 28% and 84%, respectively.

Studies published since (not included) the systematic review

- **Decipher has a prognostic value in intermediate-risk prostate cancer -** a study [11] published in the International *Journal of Radiation Oncology, Biology, Physics in 2023 (Q1, IF 7)* retrospectively analyzed the results of RTOG 01-26, a phase 3 trial of men with intermediate-risk prostate cancer randomized to different doses of radiotherapy.
    - On multivariable analysis, the **Decipher test (per 0.1 unit) was independently prognostic for various endpoints**, including disease progression (HR 1.12; 95% CI, 1.00-1.26; P = .04), biochemical failure (HR 1.22; 95% CI, 1.10-1.37; P < .001), distant metastasis (HR 1.28; 95% CI, 1.06-1.55; P = .01), and prostate cancer-specific mortality (HR 1.45; 95% CI, 1.20-1.76; P < .001)

- The prognostic value of the Decipher genomic test in prostate cancer management was investigated in a study [12] published in *Prostate Cancer and Prostatic Diseases (Q1, IF 4.8)* in 2022. The study conducted a retrospective analysis using a prospective cohort of 855 patients with newly diagnosed localized prostate cancer undergoing active surveillance or radical therapy.

    - **The Decipher test significantly predicted shorter times to treatment initiation and treatment failure in patients with high-risk scores.**

    - For patients on active surveillance, a high-risk Decipher score was associated with a higher likelihood of transitioning to radical therapy (HR 2.51; 95% CI, 1.52-4.13; P < .001).

- An ancillary study [13] from the STAMPEDE abiraterone Phase 3 trial, published as a preprint in 2023 and involved 1,824 prostate cancer patients, was conducted following a pre-specified statistical plan that evaluated Decipher score as a prognostic factor.
    - **Every 0.1 unit increase in Decipher score was associated with a significant worsening of metastasis-free survival** in high-risk localized patients (HR 1.20 [1.10–1.31], $p=2\times10^{-5}$).

Note: This is a preprint and It has not yet been peer-reviewed by a journal. The National Library of Medicine is running a pilot to include preprints that result from research funded by NIH in PMC and PubMed.

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