The clinical cell-cycle risk score is associated with metastasis after radiation therapy and may identify men with prostate cancer who can forgo combined androgen deprivation therapy.

INTRODUCTION

- This study evaluated the ability of the combined clinical cell-cycle risk score (CCR) to prognosticate the risk of prostate cancer metastasis in men receiving dose-escalated radiation therapy (RT) with or without androgen deprivation therapy (ADT).

BASIC CLINICAL QUESTION: Can we identify individuals with intermediate, high, or very-high risk localized prostate cancer who have a risk of metastasis that is so low after treatment with dose-escalated radiation therapy that the relative benefit of adding ADT no longer makes clinical sense?

METHODS

- The CCR score is a validated model that combines the cell cycle progression score (CCP) with the UCSF Cancer of the Prostate Risk Assessment score (CAPRA).

The CCR score and a CCR-based multimodality threshold score (2.112) were evaluated in a retrospective, multi-institutional cohort of men with National Comprehensive Cancer Network (NCCN) intermediate or high-risk localized disease (N=741) who received single (RT) or multimodality therapy (ADT with RT).

Effects of prognostic variables were analyzed using Kaplan-Meier and Cox regression methods.

RESULTS

- CCR is a more precise prognosticator of metastasis.

- Median follow-up was 5.6 years. CCR predicted metastasis (Table 1).

- The CCR score was a better prognosticator of metastasis than either NCCN-risk group, CAPRA score, or CCP score alone (Table 1).

- In bivariate analyses, the CCR score remained highly prognostic for metastasis when comparing any ADT vs none, ADT duration as a continuous variable, or ADT use given as less than or at the recommended duration for each NCCN risk group (Table 1).

- Men with CCR scores either below or above the threshold (2.112) had a 10-year risk of metastasis of 4.1% and 25.3%, respectively (Figure 1).

- For men below the threshold receiving RT alone versus RT+ADT, the 10-year risk of metastasis was 4.2% and 3.9%, respectively (Figure 2).

CONCLUSIONS

- CCR is a highly precise and accurate predictor of metastasis in men undergoing dose-escalated RT, with or without ADT.

- CCR adds clinically actionable information relative to guideline recommended therapies that are based on NCCN risk groups or CAPRA alone.

- Men with scores below the multimodality threshold may not significantly reduce their 10-year risk of metastasis with the addition of ADT.
The Basic Clinical Question:

- Can we identify individuals with intermediate, high, or very-high risk localized prostate cancer who have a risk of metastasis that is so low after treatment with dose-escalated radiation therapy that the relative benefit of adding ADT no longer makes clinical sense?

Key Points:

- CCR is Prognostic for Metastases in both RT alone and RT+ADT contexts.
- CCR is prognostic for metastases no matter how you account for how ADT was given.
- CCR is a more precise and accurate prognosticator of metastasis than NCCN Risk, CAPRA, or CCP Score alone.
- The CCP Score adds additional useful prognostic information even when accounting for NCCN Risk, CAPRA, or ISUP Grade Group.
Below the threshold the risk of metastasis is less than 5% at ten years in any context.
Performance below the threshold by NCCN Risk and ADT use

- Men with a CCR score ≤2.112 (below or at the threshold) receiving dose-escalated EBRT have a 10-year risk of metastasis of only 4.1% overall. (RT alone 4.2%, RT+ADT 3.9%).
- The relative risk reduction ADT provides translates to a minimal absolute difference.
- NCCN Risk Groups are no longer metastasis “risk” prognosticators below the multimodality threshold.

**CONCLUSIONS:**
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- CCR adds clinically actionable information relative to guideline recommended therapies that are based on NCCN risk groups or CAPRA alone.
- Men with scores below the multimodality threshold may not significantly reduce their 10-year risk of metastasis with the addition of ADT.