VALIDATION OF A 46-GENE CELL CYCLE PROGRESSION (CCP) RNA SIGNATURE FOR PREDICTING PROSTATE CANCER DEATH IN A CONSERVATIVELY MANAGED WATCHFUL WAITING NEEDLE BIOPSY COHORT

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INTRODUCTION

- Since the natural history of newly diagnosed prostate cancer is variable and difficult to predict, validated prognostic biomarkers could have a major impact on patient care.
- Previously, a 46 gene cell cycle progression score (CCP score, based on measuring the expression levels of CCP genes) has proven to be a robust predictor of prostate cancer outcomes in various clinical settings, including in a conservatively managed cohort diagnosed by needle biopsy.1
- Here, we present a validation study of both the CCP score and a pre-specified linear combination of the score with standard clinical variables (clinical-cell-cycle-risk (CCR) score) for predicting disease specific mortality (DSM) in a cohort of conservatively managed patients diagnosed by needle biopsy.

METHODS

- CCP score was calculated as previously described.1
- Previously, a 46 gene cell cycle progression score (CCP score) was calculated for patients managed by deferred treatment regimens (i.e. watchful waiting or active surveillance), the CCP score provides significant pre-treatment prognostic information that cannot be provided by clinical variables.2
- For such, the CCP score is a valuable addition for the informed management of newly diagnosed prostate cancer patients.

RESULTS

- In univariate analysis, the CCP score hazard ratio (HR) for DSM was 2.08 (95% CI 1.76, 2.46; P = 6.0 x 10^-11) for a unit change in the score (Figure 2).
- In a multivariate analysis (n = 585) including CAPRA, the CCP score HR was only marginally decreased (1.76; 95% CI 1.44, 2.14), and remained highly significant (P = 4.2 x 10^-10). The score performed similarly across clinical risk groups (Figure 3).
- The Kattan nomogram and the Cuzick score were highly correlated (Kattan nomogram, p = 0.85; Cuzick score, p < 0.0001).
- The hazard ratio for adding the CCP score was similar regardless of which clinical score was used (CAPRA, HR = 1.76; Kattan, HR = 1.70; Cuzick, HR = 1.71).

CONCLUSIONS

- The CCR score was also highly predictive of DSM (P = 5.9 x 10^-10), and accounted for virtually all prognostic information (Figure 4).
- The 10-year risk of prostate cancer death as a function of CCR is shown in Figure 5, and is virtually identical to the 10-year risk curve derived from our previously published conservatively managed biopsy cohort.3

REFERENCES