**BACKGROUND**

- The natural history of newly diagnosed prostate cancer is highly variable and difficult to predict accurately. Improved tools are needed to more appropriately match treatment to a patient’s risk of progression.
- Previously published data showed that a 46 gene cell cycle progression (CCP) RNA signature is a robust predictor of biochemical recurrence after radical prostatectomy and of prostate cancer-specific death in a conservatively managed cohort diagnosed by either needle biopsy or transurethral resection of the prostate.1,2
- Here we report the utility of the CCP score obtained from 3 different cohorts, including initial needle biopsy, TURP, and radical prostatectomy.

**METHODS**

- mRNA was extracted from paraffin embedded tumor sections from 366 U.S. patients after radical prostatectomy, from 337 conservatively managed (i.e. watchful waiting) UK patients after disease diagnosis by TURP, and from 349 conservatively managed UK patients after diagnosis by needle biopsy.
- RNA levels of 31 CCP genes and 15 housekeeper genes were determined and a mean composite score calculated (CCP score).
- Clinical variables consisted of centrally re-reviewed Gleason score, baseline PSA, age, clinical stage and for biopsies extent of disease (proportion of positive cores).
- Primary endpoint was death from prostate cancer in the TURP and needle biopsy cohorts, and biochemical recurrence in the RP cohort.

**RESULTS**

- At time of initial diagnosis the CCP score was the dominant prognostic variable.
- In the TURP cohort, the \( \chi^2 \) for CCP score was 92.7 (p-value < 10^{-2}; HR = 2.92), which was a stronger association than Gleason (\( \chi^2 = 80 \)) or PSA (\( \chi^2 = 57.5 \)).
- In the needle cohort, the \( \chi^2 \) for CCP score was 37.6 (p-value < 10^{-3}; HR= 2.02) compared to Gleason (\( \chi^2 = 36.4 \)) or PSA (\( \chi^2 = 16.8 \)).
- CCP score was highly predictive of biochemical recurrence after prostatectomy (p-value < 10^{-6}; HR = 1.89). From comparison of \( \chi^2 \) values (df =1), the CCP score provides slightly less univariate information than PSA, Gleason, or pathologic stage (33.96 versus 71.12, 54.56, or 67.7).
- In all cohorts, CCP score was at most only moderately correlated with other prognostic variables (highest correlation was with Gleason in TURP cohort, \( r = 0.61 \)).

**CONCLUSIONS**

- An mRNA expression signature based on CCP genes is prognostic in prostate cancer patients at diagnosis and after prostatectomy.
- In both settings, the CCP score provides important prognostic information, and it is the dominant variable at disease diagnosis.
- The CCP signature should be a valuable addition to clinical variables for differentiating aggressive from indolent disease.

**REFERENCES**


**ACKNOWLEDGMENTS**

Supported by Cancer Research UK, The Orchid Appeal, National Institutes of Health (SPORE), the Koch Foundation and Myriad Genetics. We also thank investigators and staff in the cancer registries and participating hospitals for their support.