Aim: The natural history of prostate cancer is highly variable and difficult to predict accurately. Better markers are needed to guide management and avoid unnecessary treatment.

Methods: We evaluate the predictive value of a cell cycle progression (CCP) score and a pre-specified linear combination of this score with standard clinical variables (CAPRA) as a combined clinical risk (CCR) score, for predicting prostate cancer death in two retrospective cohorts of conservatively managed patients diagnosed by needle biopsy. The first cohort consisted of 180 men diagnosed between 1990-96 and the second consisted of 585 men diagnosed mostly from 1997-2003 giving a combined cohort of 765 men. The primary endpoint was prostate cancer death within 10 years of diagnosis. Clinical variables consisted of centrally reviewed Gleason score, baseline PSA, age, clinical stage, and extent of disease; these were combined into a single predefined risk assessment (CAPRA) score.

Results: In univariate analyses, the hazard ratio (HR) for a one unit change in CCP was 2.05 (95% CI: 1.76, 2.46, $\chi^2 = 78.7, P < 10^{-19}$); for CAPRA it was 1.36 (95% CI: 1.27, 1.47, $\chi^2 = 78.3, P < 10^{-19}$); and for the combined score it was 2.16 (95% CI: 1.86, 2.5, $\chi^2 = 118.5, P < 10^{-27}$). Thus the CCP score was of similar predictive value as CAPRA, but was largely independent of it ($\rho = 0.4$) and added a substantial amount of information to the CAPRA score (HR = 1.8, $\Delta \chi^2 = 44.5, P < 10^{-13}$). The predictive value of the CCP score was maintained for 10 years, and there was no significant interaction with other prognostic factors. No heterogeneity was seen between the two cohorts ($p = 0.9$).

Conclusions: The CCP score provides substantially more pre-treatment prognostic information than available from clinical variables and is useful for determining which patients can be safely managed by a conservative policy avoiding radical prostatectomy. In particular the combined score would have upgraded 18 patients with CAPRA $\leq 2$ to have a higher risk, and downgraded 53 patients with CAPRA > 2 to have a low risk.

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