In univariate analysis, upgrading (to either pGS 3+4 or 4+3) remains a barrier to confidently offering patients AS. Many believe that patients candidates for AS, whereas cGS 6 patients who upgrade to pGS 4+3 do not. We sought to assess how upgrading affects prognosis after radical prostatectomy (RP), and if prognostic discrimination for upgraded patients could be improved through incorporation of a genetic cell cycle progression (CCP) score.

METHODS

Men treated by radical prostatectomy from three centers (UCSF, Martin Clinic, and Durham VAMC) were included in this study if cGS < 7. We compared the clinical utility for predicting biochemical recurrence (BCR) of pGS (6, 3+4, or 4+3), standard clinicopathologic variables, and CCP score using a Cox proportional hazards model stratified by cohort. The CCP score was derived from RP specimen (UCSF), simulated biopsy (MC), and diagnostic biopsy (DVA). Gleason scores were from original pathology reports except at the Durham VA where they were centrally re-reviewed.

RESULTS

In univariate analysis, upgrading (to either pGS 3+4 or 4+3) was predictive of BCR; however, outcomes of pGS 3+4 and pGS 4+3 were not different (Table 2 and Figure 1). In multivariable analysis (Table 3), including CCP score and post-surgical pathology, upgrading was prognostic (P = 0.044), but there was no difference between pGS 3+4 and pGS 4+3. Statistically significant predictors of BCR were surgical margins (p = 0.001), CCP score (p = 0.001), ECE (p = 0.008), and PSA (p = 0.025).

The difference between pGS 4+3 and pGS 3+4 appears to be greater for patients with cGS = 7 (HR = 1.9, 95% CI 1.2-3.1, p = 0.013) than for patients with cGS < 7 (HR = 1.1, 95% CI 0.5-2.4, p = 0.76), as shown in Figure 2. In the subset of patients who upgrade to pGS = 7, CCP score is a statistically significant univariate predictor of outcomes (HR = 1.8, 95% CI 1.3-2.5, p = 0.001), as shown in Figure 3.

CONCLUSIONS

Patients with cGS ≤ 6 who upgrade to pGS = 7 are at increased risk for BCR after surgery. However, the prognosis of patients who upgrade to either pGS 3+4 or 4+3 is similar. This may reflect small tumor volumes among patients who upgrade. However, the CCP score does provide risk stratification in patients who upgrade. These findings are based on a relatively small number of events, so additional studies are needed.