Perineural Invasion and Lethal Prostate Cancer

Introduction and Objective: Perineural invasion (PNI) is believed to be a common route of metastasis in patients with prostate cancer, with recent studies also suggesting that interaction with nerves bestows cancer cells with a survival advantage. However, the prognostic significance of PNI in prostate cancer has not been definitively established.
Materials and Methods: The relationship between PNI and lethal prostate cancer was studied in two population-based cohorts: a Swedish cohort of 615 men diagnosed incidentally on transurethral resection (TURP) and treated with watchful waiting, and a U.S. cohort of 689 men participating in the Health Professionals Follow-Up Study (HPFS) who were treated with radical prostatectomy. All TURP and prostatectomy specimens underwent standardized histopathologic review by dedicated study pathologists for Gleason grade and the presence of PNI. Patients were followed prospectively from the date of diagnosis until the development of metastases or death through 2011, with the cause of death reviewed by endpoint committees. Logistic and proportional hazards regression were used to model the outcome of lethal prostate cancer as a function of PNI, adjusting for age at diagnosis, Gleason grade, tumor volume (Swedish cohort) and tumor stage (HPFS).
Results: The prevalence of PNI was 7% and 38% in the Swedish and HPFS cohorts, respectively. There was a strong correlation between presence of PNI and higher Gleason grade in both cohorts. In the Swedish cohort, PNI was found to be strongly associated with lethal prostate cancer on univariate analysis (crude OR 7.36, 95% CI = 3.46–15.66, $p < 0.0001$), but the association was not significant after adjusting for age at diagnosis, Gleason grade, and tumor volume (OR 2.17, 95% CI = 0.88–5.35, $p = 0.09$). In the HPFS, PNI was found to predict lethal prostate cancer independent of age, Gleason grade, and tumor stage (HR 1.70, 95% CI 1.05–2.76, $p = 0.03$).
Conclusions: Ours is the first study to show the presence of PNI in the surgical specimen to be an independent predictor of prostate cancer-specific mortality in men undergoing radical prostatectomy. Further research is necessary to elucidate the biological mechanisms underlying PNI, and to define the appropriate role of PNI in guiding adjuvant treatment after prostatectomy.