The prognostic effect of tumour-infiltrating lymphocytic subpopulations in bladder cancer.

Intratumoural lymphocytic infiltration is strongly associated with the outcome of many human epithelial cancers. The current paper investigated whether subpopulations of tumour-infiltrating T lymphocytes are associated with certain clinicopathological parameters and the prognosis of patients with invasive bladder cancer (BCa). The infiltration densities of the adaptive immune markers CD3 (the whole T cell population), FOXP3 (regulatory T cells; Tregs), CD8 (T effector cells) and CD45R0 (T effector memory cells) were analysed by immunohistochemistry and image analysis with tissue microarrays of tumour tissues from 149 patients with invasive BCa treated with radical cystectomy. The findings were correlated with certain clinicopathological parameters. Higher FOXP3/CD3 [OS: p = 0.016, HR 1.29, 95% confidence intervals (95% CIs 1.05-1.59)] and FOXP3/CD8 (OS: p = 0.013, HR 1.32, 95% CIs 1.06-1.65) ratios were significantly associated with briefer overall survival and time to cancer-specific death; the latter ratio represented an independent prognostic factor according to a multivariate analysis adjusted for pathological T and N stages (HR 1.32, 95% CIs 1.05-1.67, p = 0.018). The infiltration densities of individual markers (CD3, CD8, FOXP3 and CD45R0) were not significantly
associated with clinicopathological parameters or survival; however, a trend towards a better outcome was observed for higher log-transformed CD8 (p = 0.070, HR 0.80, 95 % CIs 0.63-1.02) and CD3 (p = 0.113, HR 0.84, 95 % CIs 0.68-1.04) infiltration values. A high fraction of Tregs amongst CD3- and CD8-positive lymphocytes indicated a poor prognosis, thereby emphasising the important role that Tregs play in the suppression of the anti-tumour immune response. No single lymphocytic marker was significantly correlated with clinical outcomes, but high CD3 and CD8 infiltration showed trends towards better prognosis.