

Prognostic impact of tumor-associated immune cell infiltrates at radical cystectomy for bladder cancer

ABSTRACT

Objectives: To assess whether the presence and location of tumor-associated immune cell infiltrates (TAIC) on histological slides obtained from cystectomy specimens impacts on oncological outcomes of patients with bladder cancer (BC). **Material and methods:** A total of 320 consecutive patients staged with cM0 bladder cancer underwent radical cystectomy (RC) between 2004 and 2013. The presence of TAIC (either located peritumorally [PIC] and/or intratumorally [IIC]) on histological slides was retrospectively assessed and correlated with outcomes. Kaplan-Meier analyses were used to estimate the impact of TAIC on recurrence-free (RFS), cancer-specific (CSS), and overall survival (OS). Multivariable Cox-regression analysis was carried out to evaluate risk factors of recurrence. The median follow-up was 37 months (IQR: 10-55). **Results:** Of the 320 patients, 42 (13.1%) exhibited IIC, 141 (44.1%) PIC and 137 (42.8%) no TAIC in the cystectomy specimens. Absence of TAIC was associated with higher ECOG performance status ($P = 0.042$), histologically advanced tumor stage ($\geq pT3a$; $P < 0.001$), lymph node tumor involvement (pN+; $P = 0.022$), positive soft tissue surgical margins ($P = 0.006$), lymphovascular invasion ($P < 0.001$), and elevated serum C-reactive protein levels ($P < 0.001$). The rate of never smokers was significantly higher in the IIC-group (64.3%) compared to the PIC-group (39.7%, $P = 0.007$) and those without TAIC (35.8%, $P = 0.001$). The 3-year RFS/CSS/OS was 73.9%/88.5%/76.7% for patients with IIC, 69.4%/85.2%/70.1% for PIC and 47.6%/68.5%/56.1% for patients without TAIC ($P < 0.001$ / <0.001 / 0.001 for TAIC vs. no TAIC). In multivariable analysis, adjusted for all significant parameters of univariable analysis, histologically advanced tumor stage ($P = 0.003$), node-positive disease ($P = 0.002$), and the absence of TAIC ($P = 0.035$) were independent prognosticators for recurrence. **Conclusions:** In this analysis, the presence and location of TAIC in cystectomy specimens was a strong prognosticator for RFS after RC. This finding suggests that the capability of immune cells to migrate into the tumor at the time of RC is prognostically important in invasive bladder cancer.

Keyword: Bladder cancer; Immune cell; Infiltrate; Radical cystectomy; Recurrence; Survival