Extranodal Extension Is a Powerful Prognostic Factor in Bladder Cancer Patients with Lymph Node Metastasis

Introduction and Objective: Lymph node metastasis is the most powerful pathological predictor of disease recurrence after radical cystectomy. However, the outcomes of patients with lymph node metastasis (LNM) are highly variable. We sought to assess the prognostic value of extranodal extension (ENE) and other lymph node (LN) parameters and to test whether they improve the performance of predictive models constructed without ENE.

Materials and Methods: Retrospective analysis of 748 patients with LNM treated with radical cystectomy (RC) and lymphadenectomy for UCB without neoadjuvant therapy at 10 European and North American centers (median follow-up: 27 months). Microscopically, each LNM was evaluated for presence of ENE, defined as a clear-cut perforation of lymph node capsule by tumor. Number of LN removed, number of positive LN, and LN density were recorded and calculated.

Results: Overall, 375 patients (50.1%) had ENE. The median number of LN removed, number of positive LN, and LN density were 15, 2, and 15%, respectively. The rate of ENE increased with advancing pT stage (p<0.001). In multivariable Cox regression analyses that adjusted for the effects of established clinicopathologic features and LN parameters, ENE was associated with disease recurrence (HR: 1.95, 95% CI: 1.59-2.40, p<0.001) and cancer-specific mortality (HR: 1.90, 95% CI: 1.52-2.37, p<0.001). Addition of ENE to a multivariable model that included pT stage, tumor grade, age, gender, lymphovascular invasion, surgical margin status, LN density, number of LN removed, number of positive LN, and adjuvant chemotherapy improved its accuracy for predicting disease recurrence and cancer-specific mortality from 70.3% to 77.8% (p<0.001) and from 71.8% to 77.8% (p=0.007), respectively.

Conclusions: ENE is an independent predictor of both cancer recurrence and cancer-specific mortality in RC patients with LNM. Knowledge of ENE status could help with patient counseling, clinical decision-making regarding inclusion in clinical trials of adjuvant therapy, and tailored follow-up scheduling after RC.