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Brief Correspondence

Relationship of the Number of Removed Lymph Nodes to Bladder Cancer and Competing Mortality After Radical Cystectomy

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Abstract

The extent of lymph node dissection in radical cystectomy is a subject of controversy. A more extended dissection has been reported to be associated with superior survival. We analyzed the relationship between the lymph node count and different causes of death in a sample of 735 patients who underwent radical cystectomy for recurrent or muscle-invasive urothelial or undifferentiated carcinoma of the bladder. The median follow-up was 7.8 yr. The median lymph node count was 17, and the median age was 67 yr. Although there was a clear association between lymph node count and overall survival ($\geq$21 vs $<$10 lymph nodes: 10-yr rates: 59% vs 32%, respectively; hazard ratio: 0.63; 95% confidence interval, 0.46–0.87; log-rank test: $p = 0.0056$), there was no detectable relationship between bladder cancer mortality and lymph node count (narrowly congruent cumulative mortality curves, Pepe-Mori test, p values ranging between 0.40 and 0.93). The differences were virtually entirely attributable to differences in competing mortality. These observations indicate that serious bias may occur when the lymph node count is used to stratify patients undergoing radical cystectomy. The results of the ongoing randomized trials should be awaited to reliably answer the question of the degree to which more extensive dissection may improve outcome.

Patient summary: Survival differences in patients stratified by lymph node count may be attributed to competing mortality. The results of ongoing randomized trials should be awaited to answer the question of the degree to which more extensive lymph node dissection may improve outcome.

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The extent of lymph node dissection in radical cystectomy is a subject of controversy [1–3]. Results from randomized trials (Appendix) are still pending. Extended and super-extended dissection have been reported to be associated with superior survival outcome. The potential for meaningful bias, however, prohibits drawing definite conclusions [1,3].

We studied 796 consecutive patients who underwent radical cystectomy between January 1, 1993, and December 31, 2010, for recurrent or muscle-invasive urothelial or undifferentiated carcinoma of the bladder. Standard lymph node dissection [1] was performed with modifications on the decision of the surgeon, taking into account the

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individual clinical constellation. Thirty-nine patients (5%) had received neoadjuvant chemotherapy prior to surgery. If considered feasible, adjuvant cisplatin-based chemotherapy was usually offered to patients with locally advanced or node-positive disease. Patients without a documented number of removed lymph nodes ($n = 61$) were excluded, leaving 735 patients for analysis. The median age was 67 yr. The median follow-up in the censored patients was 7.8 yr, and the median lymph node count was 17. Until the time of analysis, 241 patients had died from bladder cancer

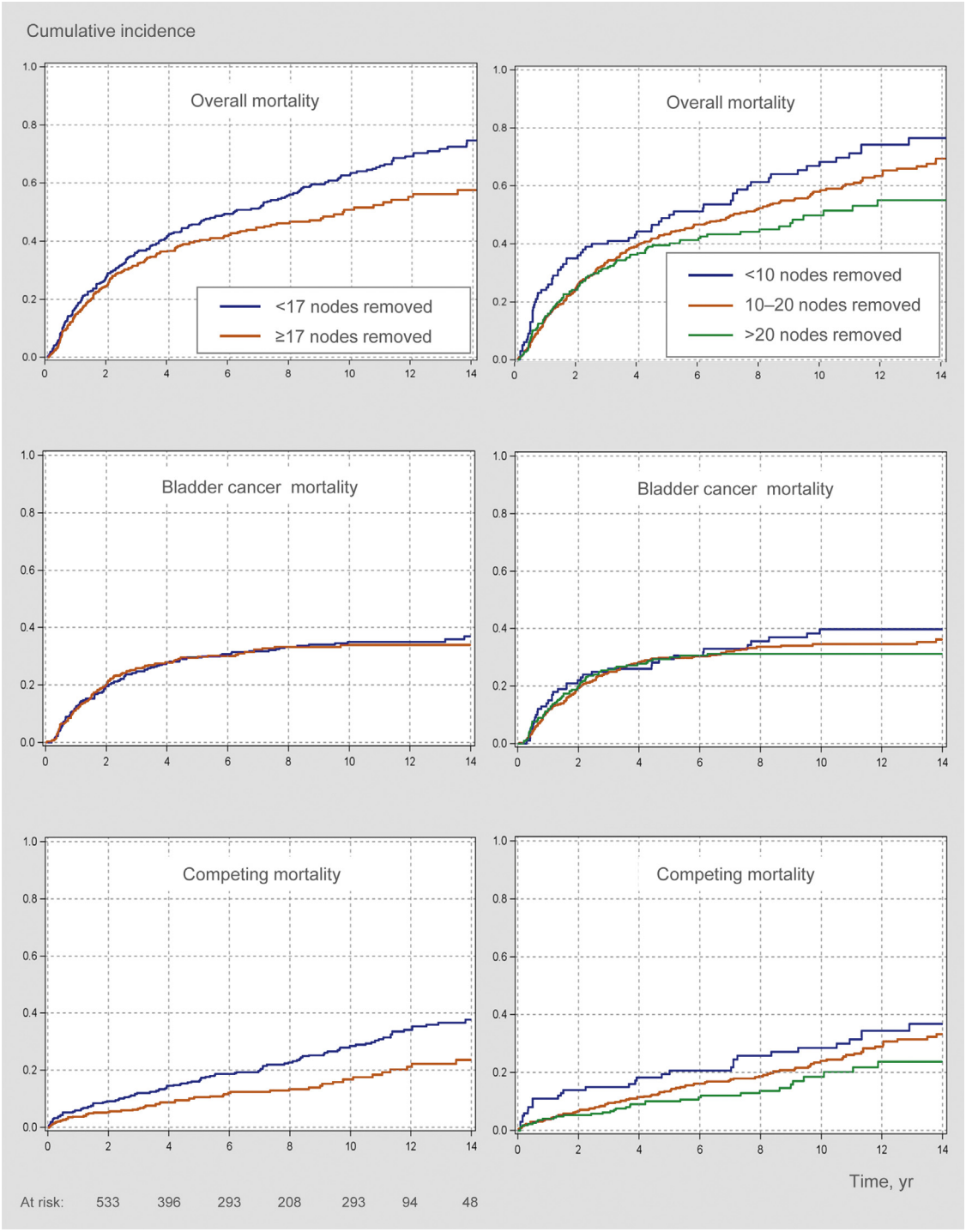

Fig. 1 – Overall mortality, bladder cancer (BCa) mortality, and competing mortality stratified by lymph node count using the median lymph node count as the threshold and a three-sided stratification, respectively. In the left column, threshold is given for overall mortality (log-rank test, $p = 0.0342$), BCa mortality (Pepe-Mori test, $p = 0.8785$), and competing mortality (Pepe-Mori test, $p = 0.1047$). In the right column, three-sided stratification, is shown for overall mortality (log-rank test: <10 vs 10–20 nodes, $p = 0.0576$; <10 vs ≥20 nodes, $p = 0.0056$; 10–20 vs ≥20 nodes, $p = 0.1774$), BCa mortality (Pepe-Mori test: <10 vs 10–20 nodes, $p = 0.3973$; <10 vs ≥20 nodes, $p = 0.3905$; 10–20 vs ≥20 nodes, $p = 0.9342$), and competing mortality (Pepe-Mori test; <10 vs 10–20 nodes, $p = 0.3272$; <10 vs ≥20 nodes, $p = 0.0588$; 10–20 vs ≥20 nodes, $p = 0.1178$).