What is the role of adjuvant chemotherapy in locally advanced and lymph node-positive bladder cancer after radical cystectomy?

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SUMMARY

Within a study group of 958 patients treated with radical cystectomy (RC), the authors identified 274 (29.0%) with a high risk of progression due to pT3 or pT4 and/or pN1-3 stages. Of these, 129 (46.6%) received adjuvant chemotherapy (ACHT), [Methotrexate, Vincristine, Adriamycin, Cyclophosphamide(MVAC) in 103, Gemcetabine and Cis-platin (GC) in 26]. These patients were then matched with the remaining patients who were unexposed to ACHT. Exact matches were made for age year of surgery, pT stage, tumor grade, pN stage and lymphovascular invasion (LVI). Matching resulted in 62 patients treated with RC/ACHT and 65 treated with RC alone.
The median (range) follow-up in event-free patients was 2.4 (0.1-11.6) years. Cancer-specific mortality was documented in 115 patients (41.5%) during the follow-up. The median actuarial cancer-specific survival (CSS) was 5.3 years (mean 7.1). In the overall cohort, the mean (95% confidence interval) CSS probabilities were 64.2 (58.2-70.8), 51.3 (44.6-59.1) and 37.7% (29.5-48.2), respectively, at 2, 5 and 10 years after RC. The median actuarial overall survival (OS) was 3.7 years (mean 10.1). The OS probabilities were 60.7 (54.8-67.3), 44.9 (38.3-52.7) and 25.9% (18.4-36.6), respectively, at 2, 5 and 10 years after RC in the overall cohort.

There was no statistically significant difference in age (P = 0.8), year of surgery (P = 0.7), tumor grade (P = 0.9), tumor stage (P = 0.7), rate of LVI (P = 0.2) and rate of lymph node invasion (P = 0.2) between the groups. CSS and OS were not significantly different between the overall cohort and the matched cohort (P = 0.6 and 0.7, respectively). There was no statistically significant difference in CSS (relative risk 1.2; log-rank P = 0.5) or in OS (relative risk 1.1; log-rank P = 0.7) between the groups, nor was there a statistical significance in the CSS (log rank P = 0.9) or in the OS (log-rank P = 0.9) between the two ACHT regimens.1

**COMMENTS**

The rational for adjuvant chemotherapy is that patients with pathologically staged tumors with evidence of metastatic disease may benefit from systemic therapy, which could reduce the likelihood of local recurrence or distant metastatic relapse. Translating the high response seen in locally advanced disease into long-term survival in the locally advanced carcinoma bladder has not been proved consistently.2

This is a multiinstitutional, well-matched, case-control study in which the authors have taken OS and CSS as endpoints that are considered to be more important for any trial addressing cancer control. Because of the well-matched design of the study, no further statistical adjustment for the variable was needed. The authors have concluded that adjuvant chemotherapy does not improve either CSS or OS in high-risk patients. The results are comparable to previous studies.3,4 The advanced bladder cancer metaanalysis collaboration has also concluded about insufficient evidence on which to reliably base treatment decisions.5

The study has its own shortcomings due to the retrospective nature of this study. The study population comprises 62 and 65 patients respectively in the ACHT and the no-ACHT arms thus lacking power. This limitation is shared by all the previous studies. The case-control study inherits certain flaws, which is another important limitation. The study duration of 20 years is another limitation as contemporary patients have better prognosis. Certain limitations are due to the multiinstitutional design and lack of unified protocol for administration of chemotherapy and absence of central pathological service. The study did not give any data on salvage chemotherapy.

In view of the evidence from the literature, it may be prudent to review our treatment protocols for locally advanced bladder tumor. This study also highlights the need for a multiinstitutional randomized control trial with statistical power to further clarify the status of adjuvant chemotherapy for advanced bladder cancer.

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