Transitional Cell Carcinoma of the Urinary Bladder with Regional Lymph Node Involvement Treated by Cystectomy

Clinicopathologic Features Associated with Outcome

Igor Frank, M.D. 1
John C. Cheville, M.D. 2
Michael L. Blute, M.D. 1
Christine M. Lohse, B.Sc. 3
Ajay Nehra, M.D. 1
Amy L. Weaver, M.S. 3
R. Jeffrey Karnes, M.D. 1
Horst Zincke, M.D., Ph.D. 1

1 Department of Urology, Mayo Clinic, Rochester, Minnesota.
2 Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.
3 Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota.

BACKGROUND. Patients with transitional cell carcinoma (TCC) of the urinary bladder metastatic to regional lymph nodes (LN) typically have a poor prognosis. However, some patients are cured by radical cystectomy alone. The goal of this study was to identify predictors of survival in this cohort.

METHODS. The authors identified 154 patients with TCC metastatic to regional LNs treated by cystectomy between 1970 and 1998. Clinical characteristics collected included age, gender, and preoperative computed tomographic or magnetic resonance image scan findings, as well as neoadjuvant and adjuvant therapy. Pathologic features evaluated included multifocality, size, pathologic stage, grade, and margin status of the primary tumor, as well as the number, location, and bilaterality of the positive LNs. Capsular penetration, greatest linear extent, and surface area of the largest metastatic LN deposit were also recorded. The Kaplan–Meier method was used to evaluate survival rates. Cox proportional hazards models were used to identify predictors of outcome.

RESULTS. The mean follow-up was 4.5 years (range, 0.1–13.9 years). In a multivariate setting, only adjuvant chemotherapy and the number of positive LNs were associated significantly with death from TCC. Patients treated adjuvantly with chemotherapy were 2.1 times less likely to die of their disease (P = 0.005). Each increase in one positive LN increased the risk of death from TCC by 20% (P < 0.001). Recursive partitioning indicated that the optimal cutoff point to predict death from TCC was five or more positive LNs.

CONCLUSIONS. Adjuvant chemotherapy and the number of positive LNs were associated significantly with death from TCC. Cancer 2003;97:2425–31. © 2003 American Cancer Society.

DOI 10.1002/cncr.11370

KEYWORDS: urinary bladder, transitional cell carcinoma, regional lymph nodes, staging, outcome prediction.

Radical cystectomy with pelvic lymphadenectomy is undertaken with curative intent for patients with invasive transitional cell carcinoma (TCC) of the urinary bladder. However, it is not clear if patients with TCC metastatic to regional lymph nodes benefit from radical cystectomy and lymphadenectomy, although studies indicate that some of these patients are cured by surgery alone.1–13 In addition, the clinicopathologic features predictive of outcome in these patients are not well defined, including the pathologic features of the lymph node metastases, such as capsular penetration and extent of lymph node involvement. Identification of the clinicopathologic features
predictive of outcome is especially important when analyzing adjuvant chemotherapy regimens for metastatic TCC of the bladder.

The objective of this study was to evaluate the clinicopathologic features of a large cohort of patients with TCC of the bladder metastatic to regional lymph nodes treated by cystectomy and pelvic lymphadenectomy with and without adjuvant chemotherapy to identify which features were predictive of outcome. This study also evaluated the 1997 American Joint Committee on Cancer (AJCC) pathologic lymph node classification system (Table 1) and its ability to predict death from TCC.\textsuperscript{14}

**MATERIALS AND METHODS**

Between 1970 and 1998, 154 patients at the Mayo Clinic (Rochester, MN) underwent a radical or partial cystectomy or an anterior/total exenteration for lymph node-positive TCC of the urinary bladder. All patients had a conventional pelvic lymphadenectomy including removal of obturator and iliac lymph nodes. Every female patient with the uterus still present underwent a hysterectomy at the time of cystectomy. Only patients with poor performance status who would not be able to tolerate a radical cystectomy and who had an easily accessible tumor were selected for partial cystectomy. Patients with evidence of previous or concurrent systemic disease (pM1) were excluded. The clinical characteristics collected included age, gender, the presence of enlarged lymph nodes as determined by preoperative computed tomographic (CT) or magnetic resonance imaging (MRI) scan, and preoperative and adjuvant treatment. Adjuvant chemotherapy was defined as treatment given within 3 months of surgery. Salvage chemotherapy administered to patients who subsequently developed widespread metastatic disease was not evaluated. The pathologic features of the primary tumor examined included the number of tumors in the bladder, maximum tumor size, 1997 AJCC tumor stage,\textsuperscript{14} tumor grade, and margin status. The lymph nodes were examined for the number of positive lymph nodes, the percentage of positive lymph nodes, the location and bilaterality of the positive lymph nodes, 1997 AJCC lymph node classification, and capsular penetration defined as tumor extending beyond the lymph node capsule into perinodal soft tissue. The percentage of the lymph node replaced by the largest metastatic deposit and the greatest linear extent and surface area of the largest lymph node metastasis were also recorded. All primary tumor and lymph node specimens were reviewed by the study pathologist (J.C.C.) without knowledge of patient outcome. The 1997 AJCC TNM classification for TCC is summarized in Table 1.

The retrospective nature of this study precluded any standardized surveillance protocol for these patients. In addition, the radiologic studies available changed during the study period. However, the majority of patients underwent a physical examination and, when available, a CT scan of the abdomen and pelvis, and a chest X-ray or chest CT scan every 3–6 months for the first 2–3 years and every 6–12 months thereafter. Bone scans and brain CT scans were performed only if symptoms were present. The Kaplan–Meier method was used to estimate cancer-specific, metastasis-free, and local recurrence-free survival rates. The duration of follow-up was calculated from the date of surgery to the date of death or last follow-up. Univariate and multivariate Cox proportional hazards models were fit to assess which clinicopathologic features were associated with death from TCC, metastasis, and local disease recurrence. Multivariate models were built using stepwise and backward selection procedures with the \( P \) value for a variable to enter the model set at 0.05. The relationships between the clinicopathologic features studied and outcome were summarized with risk ratios and 95\% confidence intervals (95\% CI). Recursive partitioning was used to determine the optimal cutoff point

---

**TABLE 1**

The 1997 AJCC TNM Tumor Staging System

| Stage | Definition |
|-------|------------|
| Primary tumor | |
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Ta | Noninvasive papillary carcinoma |
| Tis | Carcinoma in situ: “flat tumor” |
| T1 | Tumor invades subepithelial connective tissue |
| T2a | Tumor invades superficial muscle (inner half) |
| T2b | Tumor invades deep muscle (outer half) |
| T3a | Tumor microscopically invades perivesical tissue |
| T3b | Tumor macroscopically invades perivesical tissue |
| T4a | Tumor invades prostate, uterus, or vagina |
| T4b | Tumor invades pelvic wall or abdominal wall |
| Regional lymph nodes | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in a single lymph node, 2 cm or less in greatest dimension |
| N2 | Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in greatest dimension; or multiple lymph nodes, none more than 5 cm in greatest dimension |
| N3 | Metastasis in a lymph node more than 5 cm in greatest dimension |
| Distant metastasis | |
| MX | Distant metastasis cannot be assessed |
| M0 | No distant metastasis |
| M1 | Distant metastasis |

AJCC: American Joint Committee on Cancer.

Data adapted from American Joint Committee on Cancer (AJCC), Urinary bladder. In: Fleming ID, Cooper JS, Henson DE, et al., editors. AJCC cancer staging manual, 5th ed. Philadelphia: Lippincott-Raven, 1997: 241-243.\textsuperscript{14}
for the number of positive lymph nodes to predict death from TCC. 15

RESULTS
Clinicopathologic Features
The clinicopathologic features collected for the 154 patients studied are summarized in Tables 2–4. Of the 127 males, 122 (96.1%) underwent a radical cystoprostatectomy, 3 (2.4%) underwent a partial cystectomy, and 2 (1.6%) underwent a total pelvic exenteration. Eleven of the 27 females (40.7%) underwent a radical cystectomy, 3 (11.1%) underwent a partial cystectomy, and 13 (48.2%) underwent an anterior exenteration.

Cancer-Specific Survival
Seventy-eight patients died of TCC of the bladder. The average time from surgery to death from TCC was 1.8 years (median, 1.3 years; range, 0.2−6.9 years). The average time from surgery to last follow-up for the patients still alive at last follow-up was 4.5 years (median, 4.3 years; range, 0.1−13.9 years). Cancer-specific survival for this cohort is shown in Figure 1. The estimated cancer-specific survival rates (standard error [SE], number still at risk) at 1 year, 3 years, 5 years, 7 years, and 10 years were 76.1% (3.6%, 101), 53.0% (4.5%, 57), 39.4% (4.7%, 27), 31.8% (5.2%, 14), and 31.8% (5.2%, 5), respectively.

Features univariately significantly associated with death from TCC are summarized in Table 5. Patients with 1997 N2 tumors were more likely to die of TCC compared with patients with N1 tumors, but this difference was not statistically significant (risk ratio 1.60; 95% CI 0.99−2.57; P = 0.053). The estimated cancer-specific survival rates at 5 years for patients with N1 and N2 tumors were 47.0% and 34.6%, respectively.

When all the clinicopathologic features were allowed to compete in a multivariate model, only adjuvant chemotherapy and the number of positive lymph nodes were associated significantly with death from TCC (Table 6). Patients treated adjuvantly with chemotherapy were 2.1 times less likely to die of TCC compared with patients who did not receive adjuvant treatment (P = 0.005; Fig. 2). Each increase in one positive lymph node increased the risk of death from TCC by 20% (P < 0.001). Recursive partitioning indicated that the optimal cutoff point for the number of positive lymph nodes to predict death from TCC was less than than five versus five or more. After adjusting for adjuvant chemotherapy, patients with five or more positive lymph nodes were 5.1 times more likely to die

### TABLE 2
Clinical and Radiologic Features

| Feature                        | No. of patients (%) |
|--------------------------------|---------------------|
| Age at surgery (yrs)           |                     |
| Mean (SD) = 69 (33−68)         |                     |
| Median (range) = 69 (33−68)    |                     |
| Gender                         |                     |
| Male                           | 127 (82.5)          |
| Female                         | 27 (17.5)           |
| Yr of surgery                  |                     |
| 1970s                          | 20 (13.0)           |
| 1980s                          | 67 (43.5)           |
| 1990s                          | 67 (43.5)           |
| Abdominal CT or MRI result     |                     |
| Negative                       | 95 (90.5)           |
| Enlarged lymph nodes           | 10 (9.5)            |
| Preoperative treatment         |                     |
| None                           | 117 (76.0)          |
| Chemotherapy                   | 3 (1.9)             |
| Radiation                      | 34 (22.1)           |
| Adjuvant treatment             |                     |
| None                           | 105 (68.2)          |
| Chemotherapy                   | 43 (27.9)           |
| Radiation                      | 6 (3.9)             |
| Type of adjuvant chemotherapy  |                     |
| CMV                            | 21 (48.8)           |
| MVAC                           | 15 (34.9)           |
| VP-16, CDDP                    | 2 (4.7)             |
| Paclitaxel, Cisplatin          | 2 (4.7)             |
| Cisplatin                      | 1 (2.3)             |
| CTX                            | 1 (2.3)             |
| Cisplatin, doxorubicin, cisplatin | 1 (2.3)         |

CT: computed tomographic scan; MRI: magnetic resonance imaging scan; CMV: cisplatin, methotrexate, and vincristine; MVAC: methotrexate, vincristine, doxorubicin, and cisplatin; VP-16: etoposide; CTX: cyclophosphamide.

### TABLE 3
Pathologic Features of the Primary Tumor

| Feature                        | No. (%) |
|--------------------------------|---------|
| Tumor size (cm)                |         |
| Mean (SD) = 4.1 (2.0)          |         |
| Median (range) = 3.5 (0.8−10.0)|         |
| Multifocality                  |         |
| No                             | 132 (85.7)|
| Yes                            | 22 (14.3)|
| 1997 AJCC tumor classification |         |
| Tis                            | 3 (1.9)  |
| T1                             | 4 (2.6)  |
| T2a                            | 18 (11.7)|
| T2b                            | 30 (19.5)|
| T3                             | 80 (51.9)|
| T4a                            | 18 (11.7)|
| T4b                            | 1 (0.6)  |
| Tumor grade                    |         |
| Missing                        | 7 (4.5)  |
| 2                              | 8 (5.2)  |
| 3                              | 139 (90.3)|
| Margin status                  |         |
| Negative                       | 143 (92.9)|
| Positive                       | 11 (7.1) |

AJCC: American Joint Committee on Cancer.
of TCC compared with patients with less than five positive lymph nodes ($P < 0.001$; Fig. 3).

Adjuvant chemotherapy use increased throughout the study from 0% in the 1970s to 13.4% in the 1980s and 50.8% in the 1990s. However, even after adjusting for chemotherapy use and year of surgery, the number of positive lymph nodes was still associated significantly with death from TCC. There were no other significant changes over time in the pathologic features (i.e., TNM tumor stage, lymph node stage, and the number of positive lymph nodes).

**Metastasis-Free Survival**

Eighty-nine patients experienced metastases. Of these, 73 patients died of TCC, 4 died of other causes, and 12 were still alive at the last follow-up. The average time from surgery to disease metastasis was 1.3 years (median, 0.7 years; range, 0.1–6.4 years). The estimated metastasis-free survival rates (SE, number still at risk) at 1 year, 3 years, 5 years, 7 years, and 10 years were 63.6% (4.1%, 84), 43.8% (4.4%, 48), 34.1% (4.4%, 24), 32.1% (4.6%, 14), and 32.1% (4.6%, 5), respectively.

---

**TABLE 4**

Pathologic Features of the Lymph Node Metastasis

| Feature                           | Values                        |
|-----------------------------------|-------------------------------|
| No. of lymph nodes sampled        |                               |
| Mean (SD)                         | 13.6 (6.3)                    |
| Median (range)                    | 12 (6–39)                     |
| No. of positive lymph nodes       |                               |
| Mean (SD)                         | 2.8 (2.5)                     |
| Median (range)                    | 2 (1–15)                      |
| Lymph nodes positive (%)          |                               |
| Mean (SD)                         | 22.4 (18.9)                   |
| Median (range)                    | 16.7 (3.7–100.0)              |
| Percent of lymph node replaced by |                               |
| largest metastatic deposit        |                               |
| Mean (SD)                         | 55.8 (36.0)                   |
| Median (range)                    | 60 (1.0–100.0)                |
| Greatest linear extent of largest |                               |
| lymph node metastasis (mm)        |                               |
| Mean (SD)                         | 7.4 (5.2)                     |
| Median (range)                    | 5.5 (0.25–27.0)               |
| Surface area of largest lymph node |                               |
| metastasis (mm$^2$)               |                               |
| Mean (SD)                         | 40.7 (57.2)                   |
| Median (range)                    | 16.0 (0.006–270.0)            |
| No. of positive lymph nodes       |                               |
| 1                                 | 54 (35.1%)                    |
| 2                                 | 49 (31.8%)                    |
| 3                                 | 21 (13.6%)                    |
| 4                                 | 6 (3.9%)                      |
| $\geq$ 5                          | 24 (15.6%)                    |
| Positive perivesical lymph nodes  |                               |
| No                                | 140 (90.9%)                   |
| Yes                               | 14 (9.1%)                     |
| Positive bilateral lymph nodes    |                               |
| No                                | 111 (72.1%)                   |
| Yes                               | 43 (27.9%)                    |
| 1997 AJCC lymph node classification$^{14}$ |     |
| N1                                | 54 (35.1%)                    |
| N2                                | 100 (64.9%)                   |
| N3                                | 0 (0.0%)                      |
| Capsular penetration              |                               |
| Missing                           | 6 (3.9%)                      |
| No                                | 96 (62.3%)                    |
| Yes                               | 52 (33.8%)                    |

$^{14}$AJCC: American Joint Committee on Cancer.
Features univariately significantly associated with metastasis are summarized in Table 7. After adjusting for the number of positive lymph nodes, no other feature was associated significantly with metastasis. Patients treated adjuvantly with chemotherapy were less likely to experience disease metastasis, even after adjusting for the number of positive lymph nodes, but this difference was not statistically significant (risk ratio 0.67; 95% CI = 0.42–1.07; P = 0.096). Patients with 1997 N2 tumors were more likely to experience metastasis compared with patients with N1 tumors, but this difference was not statistically significant (risk ratio 1.29; 95% CI = 0.83–2.00; P = 0.258). Each increase in one positive lymph node increased the risk of metastasis by 14% (P = 0.002). Patients with five or more positive lymph nodes were 2.7 times more likely to experience metastasis compared with patients with less than five positive lymph nodes (P < 0.001). At 3 years, the estimated metastasis-free survival rates (SE, number still at risk) for patients with less than five positive lymph nodes and for patients with five or more positive lymph nodes were 45.9% (4.8%, 44) and 29.0% (10.8%, 4), respectively. No patients with five or more positive lymph nodes were left at risk for metastasis 5 years postsurgery.

Local Disease Recurrence-free Survival

Thirty-one patients experienced local disease recurrence. Of these, 26 patients initially had a radical cystectomy or cystoprostatectomy and 5 patients were treated with an anterior exenteration. None of the patients treated with partial cystectomy experienced local disease recurrence. The average time to local disease recurrence was 1.3 years (median, 0.7 years; range, 0.1–5.8 years). The estimated survival-free recurrence rates (SE, number still at risk) at 1 year, 3 years, 5 years, 7 years, and 10 years were 85.5% (3.1%, 91), 72.0% (4.7%, 47), 70.2% (4.9%, 24), 66.7% (5.8%, 13), and 66.7% (5.8%, 5), respectively. Of the 31 patients with local disease recurrence, 10 had concomitant metastatic disease, 14 subsequently developed metastatic disease, 2 died of TCC without disease metastasis, and 5 either died of other causes or were still alive at last follow-up.

Univariately and multivariately, only the presence of enlarged lymph nodes on preoperative CT or MRI scans was associated significantly with this outcome (risk ratio 3.31; 95% CI = 1.08–10.10; P = 0.036). Patients with macroscopically enlarged lymph nodes were more than three times more likely to experience disease recurrence compared with patients with negative CT or MRI scans. No other clinicopathologic feature was associated significantly with local disease recurrence.

DISCUSSION

This study identified that adjuvant chemotherapy and the number of positive lymph nodes were associated significantly with death from TCC in patients with TCC metastatic to regional lymph nodes treated by cystectomy and regional lymphadenectomy. Recursive partitioning indicated that the cutoff point for the number of positive lymph nodes that resulted in the

---

**TABLE 7**

Features Univariately and Significantly Associated with Metastases

| Feature                          | Risk ratio (95% CI) | P value |
|----------------------------------|--------------------|---------|
| Number of positive lymph nodes   | 1.14 (1.05–1.24)   | 0.002   |
| Percent of positive lymph nodes  | 1.15 (1.02–1.28)*  | 0.018   |
| Positive bilateral lymph nodes   | 1.61 (1.08–2.59)   | 0.049   |

* Risk ratio represents a 10% increase in the percent of positive lymph nodes.
best prediction of death from TCC was five positive lymph nodes. Lymph node size and the microscopic features of the lymph node metastasis had no independent predictive value. In addition, the number of positive lymph nodes was a more powerful predictor of death from TCC than the 1997 AJCC lymph node classification, which is based primarily on size. Therefore, the results of this study indicate that the 1997 AJCC lymph node stage classification system should be revised to underscore the importance of the number of positive lymph nodes, not the size of metastasis.

Our findings are similar to the study by Mills et al.\textsuperscript{13} who identified that the number of positive lymph nodes was predictive of death from any cause in 83 patients with metastatic TCC to regional lymph nodes treated by cystectomy and lymphadenectomy. More specifically, in their study, the median overall survival of patients with less than five positive lymph nodes was 27 months compared with 13 months for patients with five or more positive lymph nodes. Other studies also have identified a survival difference related to the number of positive lymph nodes in patients with TCC treated by cystectomy.\textsuperscript{4,10,12} Using the recursive partitioning method, we identified that the optimal cutoff point to predict death from TCC in our cohort of 154 patients was five positive lymph nodes. Patients with less than five positive regional lymph nodes had a 57.7% estimated cancer-specific survival rate 3 years postsurgery compared with a 25.0% rate for patients with five or more positive lymph nodes. The median cancer-specific survival for patients with less than 5 positive lymph nodes and for patients with 5 or more positive lymph nodes were 48 months and 8 months, respectively.

The Mills et al. study\textsuperscript{13} incorporated the number of positive lymph nodes (less than five vs. five or more positive lymph nodes), the largest size of the lymph node deposit (<0.5 cm vs. ≥0.5 cm), lymph node capsular perforation by tumor, adjuvant chemotherapy, and internal iliac lymph node involvement in a multivariate analysis to predict death from any cause. In this model, only lymph node capsular perforation by the tumor was associated significantly with outcome. In our study, although capsular penetration was univariately significantly associated with death from TCC, it was not associated significantly with this outcome in a multivariate model. In addition, the other pathologic features of lymph node metastasis, including the extent of the lymph node metastasis (other than the number of positive lymph nodes), were not associated with death from TCC in a multivariate setting. The reasons for the differences between our findings and those of Mills et al. may be related to the outcome assessed (overall vs. cancer-specific survival), statistical modeling of the number of positive lymph nodes (dichotomizing at five positive lymph nodes vs. analyzing as a continuous variable), and the number of patients in each study. No other studies have evaluated the pathologic features of lymph node metastasis in patients with TCC of the bladder and the association of these features with outcome.

The 1997 AJCC lymph node classification system is based on the size of the metastasis within involved lymph nodes (Table 1).\textsuperscript{14} Vieweg et al.\textsuperscript{11} studied 193 patients with urinary bladder TCC metastatic to regional lymph nodes treated by cystectomy. They identified that the AJCC lymph node classification system was an independent predictor of death from TCC of the bladder. The study consisted of 75 patients with AJCC N1, 107 patients with N2, and 11 patients with N3 tumors, with 5-year cancer-specific survival rates for each lymph node classification of 41.7%, 22.2%, and 0%, respectively. However, this study did not test for associations between outcome and the number of positive lymph nodes or other pathologic features such as extranodal extension. In our analysis, we identified 54 patients with N1 tumors and 100 with N2 tumors, with 5-year cancer-specific survival rates of 47.0% and 34.6%, respectively. Using a univariate model, patients with N2 tumors were more likely to die of TCC, but this difference was not statistically significant (risk ratio 1.6; \( P = 0.053 \)), although we had 80% power to only detect a risk ratio of 2.0 or greater for lymph node stage. In addition, the 1997 AJCC lymph node classification was not associated significantly with death from TCC after adjusting for adjuvant chemotherapy and the number of positive lymph nodes. Separation of the lymph node classification system by the number of positive lymph nodes was a better discriminator of patient outcome than the current AJCC classification.

We identified that patients who received adjuvant chemotherapy had an improved cancer-specific survival compared with patients who did not receive treatment, even after adjusting for the number of positive lymph nodes. Although greater than 80% of patients treated with chemotherapy received either cisplatin, methotrexate, and vincristine (CMV) or methotrexate, vincristine, doxorubicin, and cisplatin (MVAC) combination chemotherapy, our analysis was retrospective, not a randomized standardized prospective trial, thereby limiting our interpretation of the association of adjuvant chemotherapy and outcome. However, our findings suggest that postoperative chemotherapy has a beneficial effect in patients with TCC metastatic to regional lymph nodes. In similar retrospective analyses, Mills et al.\textsuperscript{13} identified that adjuvant chemotherapy was associated univariately, but not multivariately, with death from any cause, whereas Vieweg et al.\textsuperscript{11} did not find an association.
between adjuvant chemotherapy and death from TCC among 193 patients with lymph node positive TCC treated between 1980 and 1990.

Metastasis-free survival for our cohort mirrored cancer-specific survival because most deaths from cancer resulted from the metastatic tumor and the majority of patients with metastatic cancer died of their disease. However, although patients treated adjuvantly with chemotherapy were less likely to develop metastatic TCC, this difference was not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.

The current study is limited by its retrospective design. Our results show that the number of lymph nodes rather than the size of the positive lymph nodes or the size of the metastasis, is associated more strongly with cancer-specific survival. However, the study cannot address the issues of the extent of lymphadenectomy nor the optimal number of lymph nodes retrieved in cystectomy specimens. This difference is not statistically significant after adjusting for the number of positive lymph nodes. Local disease recurrence rates in this cohort were low. For example, local disease recurrence-free survival rates at 5 years and 10 years were 70.2% and 66.7%, respectively. The only characteristic that was univariately and multivariately predictive of local disease recurrence was the presence of enlarged lymph nodes on preoperative CT or MRI, increasing the risk of local disease recurrence more than threefold.