OUTCOME OF PATIENTS WITH GROSSLY NODE POSITIVE BLADDER CANCER AFTER PELVIC LYMPH NODE DISSECTION AND RADICAL CYSTECTOMY

HARRY W. HERR AND S. MACHELE DONAT

From the Department of Urology, Memorial Sloan-Kettering Cancer Center, New York, New York

ABSTRACT

Purpose: Should the surgeon proceed with surgery when grossly positive nodes are found at cystectomy? To answer this question, we determine the outcome of patients after radical surgery alone for grossly node positive bladder cancer.

Materials and Methods: A total of 84 patients with grossly node positive (N2-3) bladder cancer found at cystectomy underwent extended pelvic lymph node dissection and have been followed for up to 10 years. The end point of study was disease specific survival.

Results: Of the 84 patients 20 (24%) survived and 64 (76%) died of disease. Median survival time was 19 months for all patients and 10 years for surviving patients. Of 53 patients with clinical stage T2 (organ confined) tumors 17 (32%) survived versus 3 of 31 (9.7%) with stage T3 (extravesical) tumors.

Conclusions: A proportion of patients with grossly node positive bladder cancer can be cured with radical cystectomy and thorough pelvic lymph node dissection.

KEY WORDS: bladder neoplasms, lymph nodes, outcome assessment (health care), dissection, cystectomy

Should the urologist proceed with pelvic lymph node dissection and cystectomy for bulky node positive bladder cancer? We1, 2 and others3–5 have demonstrated surgical curability of some patients, especially when nodal metastasis is unsuspected and microscopically involves 1 node (N1). Surgical cure is rare in patients with extensive node positive (N2-3) bladder cancer. Patients with positive nodes who are most likely to benefit from surgery have primary tumors that are pathologically confined (stage P0–P2) to the bladder rather than extravesical (stage P3–4) disease.6 However, the pathological stage of a bladder tumor is unknown at laparotomy and provides little help to the surgeon who must decide whether to proceed with surgery when faced with grossly positive nodes. We address the dilemma from this perspective by analyzing the long-term outcome of patients who underwent cystectomy and resection of bulky node positive bladder cancer.

MATERIALS AND METHODS

From 1980 to 1990 a total of 792 patients with transitional cell carcinoma of the bladder were examined with intent to undergo cystectomy. Of these patients 29 (4%) were not able to undergo resection and 763 underwent pelvic lymph node dissection and radical cystectomy. Of the 763 patients 193 (25%) had nodal metastases, including 82 with grossly normal but surgically unsuspected, microscopic positive nodes and 111 with multiple, palpably enlarged, firm and pathologically confirmed positive nodes resected. Of these 111 patients 27 had received planned neoadjuvant cisplatin based chemotherapy before cystectomy and were excluded from analysis because of the confounding effect chemotherapy may have had on pathological stage and survival. The outcome of the 84 patients treated with surgery alone for extensive node positive bladder cancer forms the basis of this analysis.

Of the 84 patients 63 were men and 21 were women, with an average age of 62 years (range 40 to 81). Clinical staging was based on bimanual examination with patient under anesthesia, histological analysis of repeat transurethral biopsies of the primary bladder tumor and computerized tomography in select cases. All patients were candidates for cystectomy, and computerized tomography findings in the absence of obvious retroperitoneal or visceral metastases did not exclude them from surgery. The primary tumor was staged according to the 1997 revision of the TNM classification as organ confined (stage T2) or nonorgan confined (stage T3) disease.7

Resection of grossly positive nodes found during cystectomy represented the collective experience and philosophy of our institution from 1980 to 1990. Pelvic lymph node dissection and radical cystectomy were performed as previously described.8 Variations in the extent of node dissection depended on surgical findings, which included thorough resection of the common iliac, external iliac, obturator, hypogastric, presacral and paravesical nodes. The obturator vessels were usually sacrificed, and in some cases the hypogastric vein and its ramifications were resected to facilitate removal of all involved nodal tissue. Final pathological stage of the primary bladder tumor was defined as organ confined (stage P2) or extravesical (stage P3) disease. Grossly positive lymph nodes at surgery were classified pathologically as N2 (multiple positive nodes greater than 2 cm. but less than 5 cm.) or N3 (multiple positive nodes greater than 5 cm. in greatest dimension). Patients were followed expectantly, and none received adjuvant chemotherapy. Chemotherapy or radiation therapy was reserved for treatment of tumor relapse.

The end point of study was disease specific survival and was calculated as months from cystectomy to death from bladder cancer. Patients who died of other causes or were alive at last followup were censored. Surviving patients have been followed for a minimum of 10 years. Survival curves were constructed using the Kaplan-Meier method and were compared using the log-rank test. Statistical analysis was performed with commercial software.
RESULTS

Of the 84 patients with resected, grossly positive, pelvic lymph nodes 53 had clinical stage T2 and 31 had stage T3 tumors. The pathological stage was P2 in 12 patients and P3 in 72. Of the 84 cases 74 were classified as N2 and 10 as N3. Because of the small number of N3 cases, these 2 groups (N2-3) were considered together.

Figure 1 shows disease-free survival distribution after cystectomy and resection of bulky node positive bladder cancer. Of the 84 patients 20 (24%) survived with surgery alone and 64 (76%) died of disease. Median survival time was 19 months (95% confidence interval [CI] 12 to 26 months) for all patients and 10 years (range 3 to 14) for surviving patients. Survival distribution of patients with grossly positive nodes stratified by whether the primary tumor was clinically staged as confined to the bladder (stage T2) or had spread beyond the bladder (stage T3) is shown in figure 2. Of the 53 patients with T2 tumor 17 (32%) survived after surgery alone versus 3 of 31 (9.7%) with T3 tumors. Median survival time was 27 months (95% CI 14 to 30 months) for patients with T2 tumors versus 14 months (95% CI 8.5 to 19.4 months) for those with T3 tumors (p = 0.002).

Survival distribution based on final pathological stage of the bladder tumor is summarized in figure 3. Of 12 patients with tumor pathologically confined (stage P2) to the bladder 6 (50%) survived versus 14 of 72 (19.5%) with extravesical (P3) disease. Median survival time for patients with P2 tumors was 30 months (95% CI 26 to 39 months) versus 18 months (95% CI 12 to 24 months) for those with P3 tumors (p = 0.07). Figure 4 shows survival distribution of the 53 cases clinically staged as having organ confined tumor (stage T2) stratified by pathological stage (stage P2 versus P3) of the primary bladder tumors. Of the 41 patients whose disease was up staged to P3 tumor 11 (27%) survived compared with 6 of 12 (50%) who had tumor pathologically confined (P2) to the bladder (p = 0.1).

Virtually all patients died of metastatic bladder cancer, except 4 who died of other causes. Surgical morbidity after lymph node dissection for grossly positive nodes was similar to a more limited dissection when nodes appeared normal. There was 1 (1.2%) postoperative death, and 9 patients (11%) had pelvic recurrence in the operative site. Median time to local relapse was 9 months (range 3 to 36).

DISCUSSION

Prior series suggest that most patients with node positive bladder cancer who benefit from pelvic lymph node dissection and cystectomy have microscopic nodal disease usually involving only 1 node. Such nodes appear normal at surgery, and when gross nodal disease is present, radical surgery alone is unlikely to improve outcome. Our recent study shows that for all stages the 5-year survival rate was 44% for N1, 26% for N2 and 0% for N3 resected nodes.2

Translating pathological information into individual clinical decision making becomes problematic when the surgeon encounters bulky positive lymph nodes during cystectomy. Our experience suggests that the prevailing opinion that radical surgery in such circumstances is of limited value needs to be modified. Among the 84 patients with grossly positive nodes 24% survived for 10 years after cystectomy and complete pelvic lymph node dissection. The majority of surviving patients (32%) had tumors clinically staged as con-
fined to the bladder (stage T2), although a fraction (10%) survived who had clinical extravesical (stage T3) disease. Of the patients with clinical stage T2 tumors in whom disease was pathologically up staged to microscopic P3 on the cystectomy specimen 27% survived 10 years with surgery alone. These patients would have undoubtedly died of disease without radical surgery.

A number of considerations impact the decision to proceed with radical cystectomy when grossly positive nodes are unexpectedly found at surgery. Can the nodes and bladder be resected completely without leaving gross tumor behind, and can they be resected safely with low morbidity? The surgeon should answer yes to both questions before proceeding with cystectomy. Does the patient suffer bladder symptoms that justify cystectomy and urinary diversion? Cystectomy may be palliative by reducing morbidity of uncontrolled pelvic cancer. Can the patient tolerate full dose systemic chemotherapy? If not, it may be prudent to attempt a surgical cure in such cases. Although success with surgery alone is low, it might be preferable to palliative chemotherapy or radiation therapy, which is associated with significant morbidity and rarely extends survival.

Is patient age a factor? Probably not since octogenarians tolerate radical cystectomy and extended node dissection as well as younger patients. If the bladder cancer is operable and resectable, even with grossly positive nodes, age alone should not deter cystectomy. Obviously the experience of the surgeon and patient status are unquantified variables that may or may not favor radical surgery for grossly node positive bladder cancer. When the anticipated benefit of radical surgery is limited, its morbidity should be acceptably low. It is difficult to fault the surgeon who extends indications for cystectomy in the face of grossly positive nodes for patients who might not be saved by nonoperative treatment strategies.

Finally, an inherent weakness of any retrospective study is the uncontrolled selection bias that may influence outcomes. Nonetheless, despite potential confounding variables in this experience, the practical message is that when presented with unexpected grossly positive nodes, the surgeon has an opportunity to improve survival of some of these patients with aggressive surgery. The decision whether or not to proceed with surgery in patients with extensive, regionally metastatic bladder cancer will probably be modified in the future with improved chemotherapy regimens.

CONCLUSIONS

A minority of patients with grossly node positive bladder cancer can be cured by a visible, complete regional lymph node dissection and radical cystectomy, especially those in whom primary tumor is clinically confined (stage T2) to the bladder. Without effective control of pelvic cancer accomplished by surgery, these patients would in all likelihood die of disease.

REFERENCES


EDITORIAL COMMENT

The results of this large, single institution review of patients with invasive urothelial carcinoma who were found to have grossly positive nodes at the time of planned cystectomy are important for several reasons. The data support an aggressive surgical approach despite the fact that the disease has demonstrated obvious locoregional spread. In fact, in this series 24% (20) of patients treated with surgery alone were without evidence of disease at a median followup of 10 years. These results were most pronounced among those patients whose primary tumors were pathologically confined compared to those with extravesical extension (50% versus 19.5% survival, respectively).

These data, coupled with the indisputable palliative benefit for most patients with locally advanced yet resectable primary tumors, add further to support cystectomy and extended pelvic node dissection when feasible. However, the low surgical morbidity reported in this series may not be directly transferable to surgeons who perform only an occasional cystectomy. Indeed, there is no substitute for experience, and this series represents a subset of almost 800 cystectomies performed during this 10-year period. Not only is it important to assess the resectability of the primary tumor when confronted with this intraoperative scenario, but also the safe performance of an extended pelvic node dissection should not be underestimated. The presence of bulky adenopathy is often technically challenging and may significantly increase the risk of complications, such as obturator nerve injury and excessive bleeding from iliac vessel injury.

Another important point of this series is the limitations of surgery as monotherapy for these patients. While durable cancer-free survival is achievable in a small percentage of patients, it appears to be woefully inadequate in most with node positive urothelial cancer. Among those patients with disease relapse the overwhelming majority will die secondary to metastatic disease and most within 2 years of diagnosis. Unfortunately, despite the fact that more than a decade has passed since these patients were treated, there has been little improvement with respect to effective systemic therapy. Thus, these data likely represent the modest survival benefit of surgical therapy and argue strongly for the search for prognostic markers of disease failure coupled with continued randomized studies to assess the role of effective adjuvant therapy. In the meantime, an aggressive surgical approach appears justifiable as first line therapy in properly selected node positive cases.

Michael S. Cookson
Department of Urologic Surgery
Vanderbilt University Medical Center
Nashville, Tennessee