

IS RADICAL CYSTECTOMY INDICATED IN PATIENTS WITH REGIONAL LYMPHATIC METASTASES?

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ABSTRACT—*The records of 21 patients who had radical cystectomies for the treatment of locally advanced bladder cancer and were found to have regional lymphatic metastases have been reviewed. Ten of these patients had only one lymph node involved (N1), and 11 patients had metastases in more than one lymph node (N2–3). Four patients with N1 disease and 1 patient with N2–3 disease survived tumor-free greater than forty months postoperatively. Radical cystectomy can produce long-term disease-free survival in some patients with limited pelvic metastases.*

The treatment of high-stage locally advanced bladder cancer is often radical cystectomy with urinary diversion. Despite a variety of pre-operative imaging techniques, understaging occurs in more than 33 per cent of patients.¹ This is frequently a result of failure to detect small-volume regional lymphatic metastases. The overall survival of patients with lymphatic metastases is low. However, it has been reported that an aggressive lymph node dissection may be associated with improved survival.² We have evaluated our experience with 21 patients who have undergone a therapeutic radical cystectomy and were found to have metastases in regional lymph nodes.

Material and Methods

The records of 21 patients who had radical cystectomies performed for therapeutic intent and were found to have regional lymphatic metastases were reviewed. A bilateral pelvic lymphadenectomy was performed starting at the bifurcation of the common iliac vessels and extending along the external and internal iliac chains. These patients have had their operative procedures performed by multiple attending and resident surgeons at the University of Michigan Medical Center. Similarly, the patho-

logic material was evaluated by a number of different attending and resident pathologists. As a result of this, there was not a uniform technique applied to either the performance of the surgery or the subsequent analysis of the surgical specimens. This situation, we believe, is a reflection of the diversity of surgical and pathologic practice that exists in the United States.

The patients have been followed from two to fifty-eight months. The lymph node staging is that of the American Joint Committee on Cancer.³ Ten patients had lymphatic metastasis confined to one lymph node. Eleven patients had metastases in more than one lymph node. No one has been lost to follow-up. Statistical analysis of the data (survival curves) was performed using the Cox model of survival analysis with covariates by the BMDP statistical software package from the University of California. The Fisher exact test was used for analysis as described here.

Results

The mean ages and number of patients surviving greater than forty months in each group are listed in Table I. Of the patients with only one metastatic lymph node (N1), 4 patients are still alive at two, forty-four, forty-five, and

TABLE I. Patient characteristics

Stage	No. of Pts.	Mean Age	Survival >40 Months
N1	10	61.7	4 (40%)
N2-3	11	67.1	1 (9%)

TABLE II. Survival status at forty months

Stage	Alive, Disease-Free	Dead
N1	4	5
N2-3	1	10

fifty-eight months. All of these individuals are currently free of disease. Furthermore, the 1 patient who survived greater than forty months but subsequently died at forty-five months was free of neoplasm at the time of his death. Only 1 patient with more than one metastatic lymph node (N2-3) has survived beyond forty months (44 months). This patient had three perivesical lymph nodes involved by metastases and is currently disease-free.

The age adjusted survival curves are shown in Figure 1 and demonstrate a survival advantage for the group with only one metastatic lymph node. Although there is a calculated 71 per cent increase in the death rate in the group with more than one lymph node, the data do not reach statistical significance ($p = 0.36$). Seventy-five patients would be required in each group to reliably detect a statistically significant difference in these two groups with the same survival difference! The Fisher exact test

was used to assess the statistical significance between the groups of patients who were disease-free and alive forty months after surgery (Table II). This excluded the 1 patient in the N1 group who is alive at two months. The probability of the data occurring by chance using the Fisher exact test is 0.0975.

Comment

The role of surgery in the treatment of metastatic disease remains controversial. At the very least, lymphadenectomy serves a staging role to differentiate between patients with favorable and unfavorable prognoses. At best, aggressive local treatment with excision of regional metastases may produce surgical cures of high-stage lesions. There exists a large number of clinical reports attesting to the limited success of this approach.⁴⁻⁶ However, there is a suggestion that in certain instances surgical treatment of metastatic disease may effect a cure. Examples of

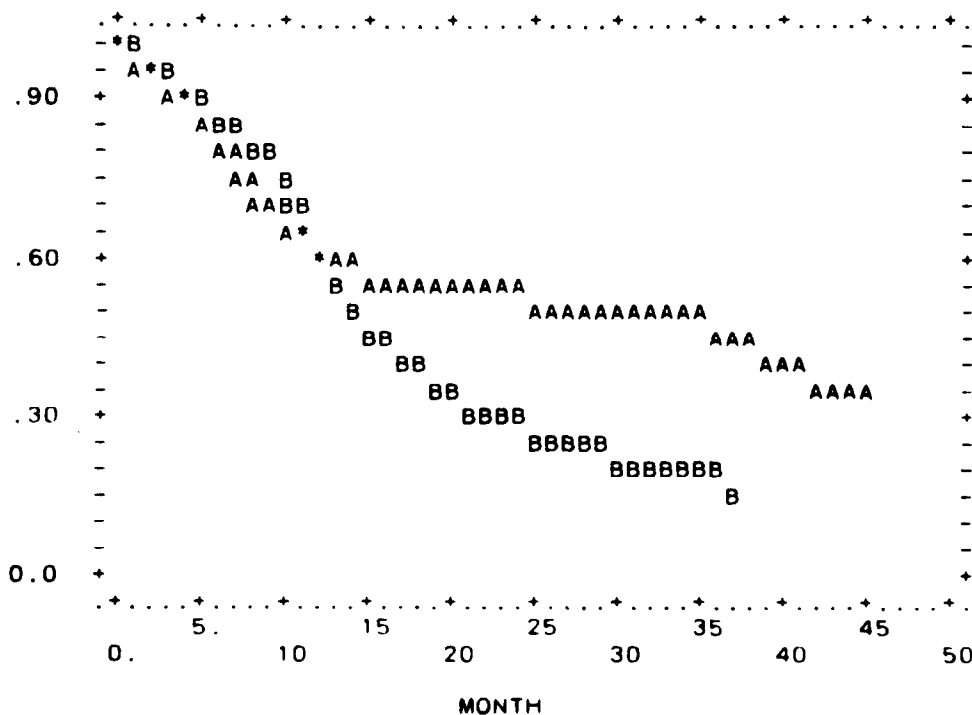


FIGURE 1. Age adjusted survival. A = patients with metastasis to one lymph node; B = patients with metastases to more than one lymph node.

this phenomenon in urologic oncology are seen in carcinomas of the testis and penis.^{7,8} The role of surgery in advanced bladder cancer is less clear. However, aggressive surgical therapy of distant metastases has occasionally resulted in long-term tumor-free survival.^{9,10}

Most reports document poor five-year survival in patients with regional lymphatic metastases at the time of cystectomy. The five-year survival of these patients has generally been reported to be 15 per cent or less. Furthermore, most of these patients die within thirty months of their surgical procedure. An example is the large series of Smith and Whitmore¹¹ in which 5 of 30 patients (17%) with N1 disease survived five years free of disease while only 5 per cent (4/79) patients with Stage N2-3 shared a similarly favorable course. Dretler, Ragsdale, and Leadbetter¹² reported on the five-year survival rates of 35 patients with regional lymphatic metastases who had been treated by cystectomy. Patients with metastases to one or two lymph nodes survived longer than patients with greater than two lymphatic metastases. The respective survival for the two groups was 33 and 9 per cent. In 1982, Skinner² reported the effect of a "meticulous" lymph node dissection on patient survival in a group of patients with regional lymphatic metastases. Thirty-six patients with regional lymphatic metastases had a six-year survival of 35 per cent. Patients with five or fewer involved lymph nodes had a better survival than patients with more diffuse involvement. The survival in these two groups was 46 per cent and 12 per cent, respectively. The improvement in survival in more recent series does not appear to be an artifact of decreased mortality from a general improvement in patient care. McCarron and Marshall⁶ demonstrated that patients with regional lymphatic metastases shared a similar fate regardless of the time of their surgery. The five-year survival for patients treated from 1926 to 1952 and a similar group treated from 1960 to 1971 had five-year survivals of 4 and 9 per cent, respectively.

We have found a significant clinical advantage in the survival of patients with limited regional lymphatic metastasis. The age adjusted three-year survival in the patients with one node and in patients with more than one lymph node involved by metastatic bladder cancer was 45 per cent and 20 per cent, respectively. Although continuing follow-up will be required to be certain that there are no late failures, no patient to date who has survived forty months has

had recurrence of their disease. Four patients are alive and disease-free beyond this point. Three have had one lymph node involved with neoplasm and one had metastases in three perivesical lymph nodes. This clinical improvement in survival cannot yet be demonstrated to be statistically significant. Maintaining the current survival advantage would require approximately 130 more patients to document a statistically significant difference between the N1 and N2-3 survival curves at the 0.05 level.

Our series of patients undergoing radical cystectomy and having regional lymphatic metastasis confirms the findings of Skinner² that some patients can have long-term, disease-free survival after this therapy. The effect of the surgeon and pathologist in determining the extent of the lymph node dissection and the completeness of the histologic examination on long-term, tumor-free survival remains undefined. Although these variables may influence the reported results, the available data strongly suggest that radical cystectomy should be performed when surgically resectable pelvic lymphatic metastases are found.

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