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Review – Bladder Cancer

Lymph Node Metastasis in Bladder Cancer

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Abstract

Objective: We reviewed the literature on nodal staging in patients with bladder cancer treated with radical cystectomy and lymphadenectomy.
Results: Fractionating the lymph node specimen significantly increases the node count, whereas results are contradictory as to whether that increase improves detection of positive nodes. Pathoanatomic data indicate that extending lymph node dissection to the aortic bifurcation improves nodal staging. That approach might be beneficial, especially in cases of T3/T4a tumours, which more often have lymph node metastases above the iliac bifurcation as compared to less advanced tumours. In node-negative patients, extended lymph node dissection probably removes undetected micrometastases and thereby increases disease-free survival. Four studies suggested that a minimum of 8, 10, 10–14, and 16 nodes must be removed, to improve survival, and in another investigation aortic bifurcation was proposed as the upper limit for dissection. Some patients with positive nodes can be cured by surgery alone, even those with gross adenopathy. There is no evidence that extended lymphadenectomy increases surgery-related morbidity. The TNM classification is apparently insufficient for stratifying node-positive patients because several larger cystectomy series could not verify differences in survival between N groups.
Conclusions: Fractionating the lymphadenectomy specimen increases the lymph node count. In node-negative patients, more meticulous and extended lymph node dissection (8–16 nodes or to the aortic bifurcation) probably improves disease-free survival by removing undetected micrometastases. Patients with positive lymph nodes should also be offered radical cystectomy.

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1. Introduction

The pathological stage of the primary bladder tumour and the presence of lymph node metastasis are the most important determinants of survival in patients with bladder cancer undergoing radical cystectomy [1]. There has been a continuous search for reliable and robust methods for preoperative assessment of lymph node status. Lymphangiography with fine needle aspiration has been evaluated in several studies, but it is not reliable due to a high false-negative rate [2]. Only a few investigations have appraised positron emission tomography (PET) and its capacity to detect lymph node metastases in bladder cancer, and the results have been largely disappointing [3]. Also, with computed tomography (CT) a high (21%) false-negative rate has been observed [4]. Some investigators [5] have recently claimed that new ferumoxtran-enhanced magnetic resonance imaging (MRI) for nodal staging offers 91% sensitivity and a 98% negative predictive rate. Nonetheless, open surgery is still the standard for nodal staging, although one report has indicated that limited laparoscopic lymphadenectomy offers equivalent efficacy and a shorter postoperative stay [6].

In the 2002 TNM classification, patients with positive lymph nodes are stratified into three stages (N1, N2 and N3) based on the number of positive nodes and the size of the metastatic nodes. However, Fleishmann and colleagues [7] found no difference in survival between patients at stages N1 and N2 in an analysis of extracapsular extension of pelvic lymph node metastases. Similarly, in a retrospective study Herr [8] found no significant variation in survival among patients in the three N stages.

Surgical treatment of invasive bladder cancer by cystectomy and regional lymphadenectomy evolved >70 years ago [9]. In 1950, Kerr [10] reported long-term survival of 2 patients who had node-positive disease and underwent cystectomy, and that investigator also observed that the local recurrence rate decreased after pelvic lymphadenectomy. Based on those results, Kerr advocated that such dissection be added to the procedure. More than a decade later, Whitmore and Marshall [11] noted that radical cystectomy and pelvic lymph node dissection led to 5-year survival in 16% (2 of 13) of node-positive patients.

In 1950, Leadbetter [12] described a technique for ''regional gland dissection'' that is still in use today. The optimal extent of the lymph node dissection for accurate staging, the curative potential of the method and the prognosis of lymph node-positive disease after such treatment are matters of debate that are discussed in this review.

2. Classification of lymph node dissections

Perivesical lymph nodes are identified in cystectomy specimens from 16% of patients with bladder cancer who have not undergone pelvic lymphadenectomy [13]. Thus, a patient can be classified as node positive without a formal lymph node dissection. The *limited lymph node dissection* is generally described as an extirpation of the lymphatic tissue in the obturator fossa (ie, between the obturator nerve and the external iliac vein), which provides a maximum of 10 nodes for examination [14]. Another method of limited dissection usually referred to as a *conventional pelvic dissection* [15] or a *standard dissection* [16] includes the area stretching laterally as far as the genitofemoral nerve and posteriorly to the internal iliac vessels. A median of 14 nodes are excised within these boundaries [17], and reports indicate that surgeons using this template have removed from 8 to 26 nodes [16,18]. Thalmann et al. [19] have used an approach that also includes presacral nodes medial to the internal iliac vessels and common iliac nodes, as far up as the ureteral junction. In a technique that is commonly called *an extended dissection* [18,20,21], the lymphadenectomy is expanded to the aortic bifurcation, as in the regional gland dissection described by Leadbetter [12] (Fig. 1), or even up to the inferior mesenteric artery (IMA). Extending the dissection to the aortic bifurcation increases the number of nodes that are harvested, and yields reported in the literature vary between 15 (mean) and 39 (median) nodes [16,17,22–24]. Corresponding results in series using the IMA as the upper limit of dissection are 43 (mean) and 56 (median) nodes [18,21,25]. However, even within the same study and using standardized dissection templates, there is substantial intersurgeon variability in terms of lymph node retrieval. Leissner et al. [22] found significant variation in the number of nodes obtained (range 10–21) by 16 surgeons who used the aortic bifurcation as the upper limit of dissection.

3. Current practices in pelvic lymph node dissection performed in conjunction with radical cystectomy

In a large study representing 12% of the population of the United States in 1988–1998, it was found that