# Separate Submission of Standard Lymphadenectomy in 6 Packets Versus En Bloc Lymphadenectomy in Bladder Cancer

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**Introduction:** Our aim was to evaluate detection of nodal metastasis during radical cystectomy with standard pelvic lymph node dissection versus en bloc lymphadenectomy for the treatment of bladder cancer.

**Materials and Methods:** Hospital records of a total of 77 patients with radical cystectomy and either standard pelvic lymph node dissection or en bloc lymphadenectomy were reviewed. Nodal dissection specimens during standard lymphadenectomy were sent for pathology examination in 6 separate containers marked as external iliac, internal iliac, and obturator groups from both sides. En bloc dissection specimens were sent in 2 containers marked as the right and the left pelvic nodes. Clinical and pathological findings of these two groups were compared in terms of the number of dissected lymph nodes, number of nodes with metastasis, lymph node density, and clinical outcomes.

**Results:** There were 34 patients with standard lymph node dissection and 43 with en bloc lymphadenectomy (anterior pelvic exenteration). Age, sex, duration of the disease, number of transurethral resections prior to cystectomy, pathological grade at cystectomy, and stage of the primary tumor were comparable in the two groups of patients. The median numbers of nodes removed per patient were 15.5 (range, 4 to 48) and 7.0 (range, 1 to 24) in those with standard and en bloc lymphadenectomy, respectively ($P < .001$). Nodal involvement was detected in 10 (29.4%) and 9 (20.9%) patients, respectively ($P = .43$).

**Conclusion:** Although nodal involvement was not significantly different between the two groups, standard lymphadenectomy submitted in 6 different containers significantly improved the nodal yield over en bloc resection. Obturator nodes were the most commonly involved nodes in our study.

*Keywords: urinary bladder neoplasms, cystectomy, lymph node excision*

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## INTRODUCTION

Transitional cell carcinoma (TCC) of the bladder originates from the mucosa, invades the lamina propria, and involves the muscularis propria, perivesical fat, and pelvic structures with increasing incidence of lymph node involvement during progression.[1] On cystectomy, 14% to 28 % of the patients show evidence of lymph node metastasis.[2] Radical cystectomy (RC) is the standard management of high-grade and muscle-invasive bladder tumors. Bilateral pelvic lymphadenectomy is now an

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essential part of RC. A combination of these two provides excellent local control and long-term survival rate for most of the patients with tumors in stage pT2 or higher.[3,4] Thus, accurate staging is decisive in terms of choosing the treatment option and reducing local recurrence. Preoperative imaging modalities may miss microscopic nodal metastasis in up to 70% of the patients.[5] Lymph node involvement is associated with increased risk of local recurrence and disease progression with survival rates varying from 20% to 40% in patients with and without lymph node metastasis, respectively.[6,7]

The practice of lymphadenectomy is not standardized. It has been shown that the number of nodes retrieved could vary from 0 to 53 per patient.[8] Recent studies suggest that both the number of nodes removed and the method of submission of lymph node specimens affect the treatment outcome.[3, 9-11] Some recent papers have also indicated that the lymph node specimens separately retrieved and submitted for pathology have a greater number of nodes compared to *en bloc* resection.[9-11] Studies have shown that the incidence of positive lymph nodes increased with higher stage, higher pathological grade, and greater number of transurethral resections prior to RC.[10-12] In the present study, we sought to identify if there was a difference in the number of nodes retrieved between separately retrieved and submitted pathologic specimens and specimens from *en bloc* resection.

## MATERIALS AND METHODS

Hospital records of all patients with TCC of the bladder treated by RC or anterior pelvic exenteration (APE) at our institution between 1995 and 2007 were retrospectively studied. During this period, 95 patients had undergone RC or APE for primary bladder cancer. We excluded 18 patients because their lymph nodes could not been evaluated. The hospital was not a referral center for oncological surgery. There are 3 trained oncological urologists and all types of urinary diversions including orthotopic bladder replacements are performed.

Of 77 patients, 34 (44.2%) had undergone standard lymphadenectomy (group 1; lymph nodes submitted in 6 separate nodal packets) and 43 (55.8%) had undergone en bloc dissection (group 2). The extent and operative field in the two groups were similar. The field of standard lymph node dissection extends caudally, up to the lacunar ligament; cranially, to the angle of Marcille; laterally, to the genitofemoral nerve; and medially, up to the obturator nerve. Nodal dissection specimens during standard lymphadenectomy had been sent for pathology examination in 6 separate containers marked as external iliac, internal iliac, and obturator groups from both sides. En bloc dissection specimens had been sent in 2 containers marked as the right and the left pelvic nodes.

The patients in the two surgical groups were compared in terms of the number of dissected lymph nodes, number of nodes with metastasis, lymph node density, and other clinical outcomes. Lymph node density was defined as the ratio of positive nodes for metastasis to the total number of nodes examined. Operative mortality was defined as death within 30 days after the procedure. Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA). Continuous variables were compared between the groups using the independent sample *t* test or the Mann Whitney U test. The chi-square test and the Fischer exact test were used to compare categorical and dichotomous variables. A *P* value less than .05 was considered significant.

## RESULTS

Of 77 patients with TCC of the bladder, 67 (87.0%) were men and 10 (13.0%) were women. The two groups were comparable in terms of age, sex, primary tumor stage, grade of the tumor, duration of the disease, and number of transurethral resections (Table 1).

The median number of nodes removed per patient were 15.5 (range, 4 to 48) in group 1 and 7 (range, 1 to 24) in group 2 ($P < .001$). There were 10 patients (29.2%) and 9 patients (20.9%) with involved nodes in groups 1 and 2, respectively ($P = .43$). The obturator lymph nodes were the most commonly involved nodes followed by internal and external iliac node groups in patients

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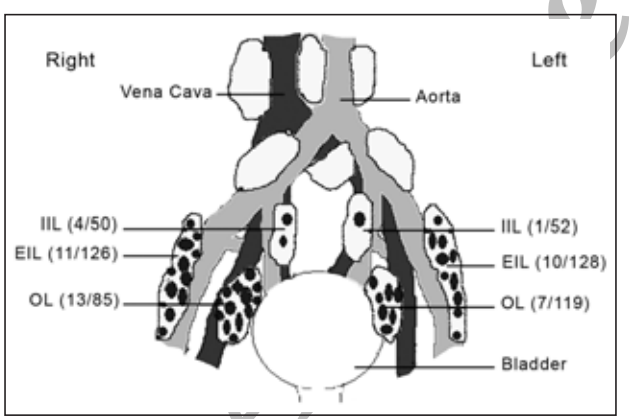
**Table 1.** Demographic and Clinical Profile of Patients With Bladder Cancer Who Underwent Either Radical Cystectomy and Standard Lamyphadenectomy or En Bloc Cystectomy*

| Characteristics | Surgical Treatment | | *P* |
|---|---|---|---|
| | Standard Lymphadenectomy (Group 1) | En Bloc Cystectomy (Group 2) | |
| Number of patients | 34 (44.2) | 43 (55.8) | |
| Mean age, y | 56.5 ± 13.3 | 64.0 ± 12.4 | .51 |
| Sex | | | |
| Male | 28 (82.4) | 39 (90.7) | |
| Female | 6 (17.6) | 4 (9.3) | .32 |
| Duration of disease, d† | 76.0 ± 946.8 | 147.0 ± 927.0 | .97 |
| Tumor stage | | | |
| T0 | 3 (8.8) | 4 (9.3) | |
| T1 | 1 (2.9) | 2 (4.7) | |
| T2 | 16 (47.1) | 23 (53.5) | |
| T3 | 9 (26.5) | 6 (14) | |
| T4 | 5 (14.7) | 8 (18.6) | .74 |
| Tumor grade | | | |
| 1 | 0 | 1 (2.3) | |
| 2 | 5 (14.7) | 12 (27.9) | |
| 3 | 29 (85.3) | 30 (69.8) | .19 |
| Number of resections | 1.0 ± 1.0 | 1.0 ± 1.1 | .90 |

*Values in parentheses are percents.
†Duration of disease was defined as the time from diagnosis to cystectomy.

of group 1 (Figure). Lymph node density was significantly higher in the patients of group 1 than those of group 2 ($P < .001$; Table 2).




Location of 46 metastatic nodes in 34 patients with anatomical dissection (standard lymphadenectomy). IIL indicates internal iliac lymph node; EIL, external iliac lymph node; and OL, obturator lymph node.

Early complications, including lymphocele, were noted in 7 patients (20.6%) in group 1 and 4 (9.3%) in group 2; however, none of the patient required surgical intervention. No other complication or peri-operative death was attributed directly to the lymph node dissection in neither of the groups (Table 2).

## DISCUSSION

Lymph node metastasis is detected in 14% to 28% of the patients undergoing pelvic lymphadenectomy during RC for bladder cancer.[2] It is associated with an increased risk of local recurrence, regional disease progression, and overall poorer outcome. Extended standard lymphadenectomy is important for accurate

**Table 2.** Outcomes of Standard Lamyphadenectomy and En Bloc Cystectomy

| Characteristics | Surgical Treatment | | *P* |
|---|---|---|---|
| | Standard Lymphadenectomy (Group 1) | En Bloc Cystectomy (Group 2) | |
| Median number of removed nodes | 15.5 | 7 | < .001 |
| Patients with involved lymph nodes | 10 (29.4) | 9 (20.9) | .43 |
| Median lymph node density, % | 23.5 | 11.0 | < .001 |
| Operative mortality | 1 (2.9) | 1 (2.3) | .70 |
| Patients with early complications | 7 (20.6) | 4 (9.3) | .16 |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staging and provides direct survival benefit.[2] Recent evidence has shown that node involvement is a significant and independent prognostic factor.[3-5]

A growing body of evidence suggests that an extended lymph node dissection may provide prognostic information and therapeutic benefits for patients with or without lymph node involvement undergoing RC for TCC. Boundaries of the lymphadenectomy are still a subject of controversy. Abol-Enein and colleagues reported that extended lymphadenectomy up to the origin of the inferior mesenteric vessels showed 37% and 60% bilateral and unilateral node involvement, respectively.[13] Dissection of only internal iliac nodes will miss 85% of positive nodes, whereas dissection of the internal and external iliac and obturator nodes will pick two-thirds of the nodes. Dissection up the aortic bifurcation picks four-fifth of the nodes.[13]

Guidelines for the treatment of muscle-invasive bladder cancer by the *European Association of Urology* recommend limited pelvic node dissection, consisting of removal of the tissue in the obturator fossa in patients undergoing surgery with a curative intent.[14] Several authors have noted an improved 5-year survival rate with extensive pelvic lymph node dissection in the patients with node-involved bladder cancer.[5,15] Herr and colleagues studied the number of nodes removed and its effect on the outcome of the patient after RC.[3] They found that a minimum of 9 nodes was needed to be examined to accurately assess nodal involvement. They also found that survival improved in both patients with and without node involvement as the number of the removed nodes increased. They also evaluated the impact of submitting nodes en bloc or as separate packages and suggested that submitting nodes as separate packages not only is easier, but also optimizes the evaluation and number of the lymph nodes retrieved.[3] Some studies indicate that lymphadenectomy in combination with RC can cure a small fraction of node-positive patients.[9]

## CONCLUSION

We found that the number of the nodes retrieved per specimen increases significantly if dissection and submission of the nodes is done in the anatomically defined areas rather than en bloc submission.

## CONFLICT OF INTEREST

None declared.

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## REFERENCES

1. Ather MH, Fatima S, Sinanoglu O. Extent of lymphadenectomy in radical cystectomy for bladder cancer. World J Surg Oncol. 2005;3:43.
2. Vieweg J, Gschwend JE, Herr HW, Fair WR. Pelvic lymph node dissection can be curative in patients with node positive bladder cancer. J Urol. 1999;161:449-54.
3. Herr HW, Bochner BH, Dalbagni G, Donat SM, Reuter VE, Bajorin DF. Impact of the number of lymph nodes retrieved on outcome in patients with muscle invasive bladder cancer. J Urol. 2002;167:1295-8.
4. Steven K, Poulsen AL. Radical cystectomy and extended pelvic lymphadenectomy: survival of patients with lymph node metastasis above the bifurcation of the common iliac vessels treated with surgery only. J Urol. 2007;178:1218-23.
5. Ghoneim MA, el-Mekresh MM, el-Baz MA, el-Attar IA, Ashamallah A. Radical cystectomy for carcinoma of the bladder: critical evaluation of the results in 1,026 cases. J Urol. 1997;158:393-9.
6. Frazier HA, Robertson JE, Dodge RK, Paulson DF. The value of pathologic factors in predicting cancer-specific survival among patients treated with radical cystectomy for transitional cell carcinoma of the bladder and prostate. Cancer. 1993;71:3993-4001.
7. Leissner J, Hohenfellner R, Thüroff JW, Wolf HK. Lymphadenectomy in patients with transitional cell carcinoma of the urinary bladder; significance for staging and prognosis. BJU Int. 2000;85:817-23.
8. Koppie TM, Vickers AJ, Vora K, Dalbagni G, Bochner BH. Standardization of pelvic lymphadenectomy performed at radical cystectomy: can we establish a minimum number of lymph nodes that should be removed? Cancer. 2006;107:2368-74.
9. Bochner BH, Herr HW, Reuter VE. Impact of separate versus en bloc pelvic lymph node dissection on the number of lymph nodes retrieved in cystectomy specimens. J Urol. 2001;166:2295-6.
10. Stein JP, Penson DF, Cai J, et al. Radical cystectomy with extended lymphadenectomy: evaluating separate package versus en bloc submission for node positive bladder cancer. J Urol. 2007;177:876-81.

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11. Honma I, Masumori N, Sato E, et al. Removal of more lymph nodes may provide better outcome, as well as more accurate pathologic findings, in patients with bladder cancer--analysis of role of pelvic lymph node dissection. Urology. 2006;68:543-8.

12. Wiesner C, Pfitzenmaier J, Faldum A, Gillitzer R, Melchior SW, Thüroff JW. Lymph node metastases in non-muscle invasive bladder cancer are correlated with the number of transurethral resections and tumour upstaging at radical cystectomy. BJU Int. 2005;95:301-5.

13. Abol-Enein H, El-Baz M, Abd El-Hameed MA, Abdel-Latif M, Ghoneim MA. Lymph node involvement in patients with bladder cancer treated with radical cystectomy: a patho-anatomical study--a single center experience. J Urol. 2004;172:1818-21.

14. van der Meijden AP, Sylvester R, Oosterlinck W, et al; for the EAU Working Party on Non Muscle Invasive Bladder Cancer. EAU guidelines on the diagnosis and treatment of urothelial carcinoma in situ. Eur Urol. 2005;48:363-71.

15. Poulsen AL, Horn T, Steven K. Radical cystectomy: extending the limits of pelvic lymph node dissection improves survival for patients with bladder cancer confined to the bladder wall. J Urol. 1998;160:2015-9.

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