

Is the pN category in radical cystectomy dependent on the pathologist dissection?

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Abstract

A correlation exists between the number of lymph nodes (LNs) detected in radical cystectomy specimens and the accuracy of pathologic nodal (pN) staging. In this context, correct handling of pathology specimens is crucial, but there is currently no consensus on the optimal methodology. The objective of the present study was to compare two main methods: palpation and complete embedding of all fat tissue.

Palpation of LNs and complete embedding of remaining fat tissue were performed in 42 patients. In 33.3% of the patients, no LNs were observed in the remaining fat tissue. The mean number and size of LNs detected were, respectively, 14 and 9 mm with palpation and 2.9 and 5 mm with complete embedding of remaining fat tissue. All positive LNs (30.9%) were detected by palpation. The mean pN density was 12.9% with palpation and 10.7% with complete embedding. All patients with a LN density higher than 20% were already observed by manual palpation.

In conclusion, the complete embedding of fat tissue does not have a crucial impact on evaluation of the pN category.

Introduction

The importance of lymphadenectomy (LND) during radical cystectomy has increasingly been recognized in international guidelines [1]. Although further supportive evidence is required, an increasing number of studies have shown that the number of metastatic lymph nodes (LN) and the LN density (positive LN/total LN) are independent predictors of disease evolution [2]. Thus, appropriate detection of LN is crucial in the evaluation of radical cystectomy specimens.

The number of LN detected by the pathologist may depend on the extent of the LDN [3], the inter-individual variability among patients [4], and the handling and interpretation of the pathological specimen [5]. Currently, consensus is lacking on the optimal handling and reporting of LDN specimens [6], which may explain differences in the interpretation between an LN and a simple lymphoid aggregate and in the methodology used to evaluate LN and the corresponding final count [5]. LDN pathological dissection is one variable that can be standardized. This can be done by manual palpation, with or without fat clearing, or submitting entirety of fat tissue.

The objective of the present study is to compare manual palpation and the complete embedding of all fat tissue with a view to assessing the impact on evaluation of the pN category.

Materials and methods

Lymphadenectomies (LDNs) obtained by cystectomy from 42 patients diagnosed with urothelial carcinoma of the bladder were included in the study. The number of lymph node packets from each LDN was registered and embedding of nodes detected by palpation (without fat clearing) was performed. Thereafter, complete embedding of the remaining tissue was also carried out.

Lymph nodes were considered to be all clearly defined lymph node and aggregates of lymphocytes totally or partially surrounded by a band

of fibrous tissue. LN count and size were measured. The maximum diameter was measured as the mean diameter when LN were similar in size or as the diameter from the smallest to the largest in LN with different sizes. Pathological findings observed in the cystectomy tissues were also registered (Table 1).

Results

Of the 42 patients, 36 were men and six, women. Their age ranged from 39 to 84 years (mean 65.7). Six of the 42 (14.2%) were classified as pT0 at cystectomy, and in another six (14.2%) only carcinoma “in situ” was observed. In five patients (11.9%) residual bladder tumor had not infiltrated the muscular layer, while 25 patients (59.5%) showed a high-grade urothelial carcinoma with infiltration of the muscular propia.

The number of LN identified by palpation was 14 (range 5-33), with a mean size of 9 mm (2-35 mm). Upon embedding of the remaining fat tissue, no additional LN were found in 14 patients (33.3%), while in the remaining 28 patients (66.6%) the number of LN removed from fat tissue was 2.9 (range 1-8), with a mean size of 5 mm (1-15 mm).

Thirteen patients (30.9%) presented LN metastases in the LN detected by palpation (no LN metastases were detected in the remaining fat tissue). The LN density was 12.9% (4%-27.2%) with palpation and 10.7% (3.4%-21.9%) with complete embedding of remaining fat tissue. Five patients with positive LN had a LN density higher than 20%, and only one of them (case number 10) presented more negative LN in the

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Table 1. Patients with cystectomy and lymphadenectomy

	LN (cm) palpation	LN (cm) fat tissue	Total LN	pN positive LN	packets	LNdensity palpation	LNdensity Total
1	22 (1-0.3)	3 (0.3)	25	pN2-3	2	13.6%	12%
2	9 (1.5-0.3)	4 (0.6-0.2)	13	pN0	4		
3	7 (0.4-2)	4 (0.1-1.5)	11	pN0	2		
4	15 (0.5-2)	4 (0.3)	19	pN0	2		
5	9 (0.5-1)	0	9	pN2-4	2	44.4%	
6	11(3.5-03)	1 (0.3)	12	pN0	5		
7	12 (0.5-1)	3 (0.2-1)	15	pN0	5		
8	17 (0.2-0.7)	6 (0.3)	23	pN0	2		
9	25 (1.3-0.3)	4 (0.3)	29	pN1-1	8	4%	3.4%
10	33 (0.5-1)	8 (0.4)	41	pN3-9	8	27.2%	21.9%
11	10 (0.5-1)	1 (0.2)	11	pN0	2		
12	16 (0.3-1)	3 (0.3)	19	pN0	4		
13	8 (1)	3 (0.6)	11	pN1-1	2	12.5%	9%
14	5 (1-0.5)	0	5	pN2-2	2	40%	
15	27(1.5-0.4)	2 (0.4)	29	pN0	2		
16	10 (1-0.3)	1 (0.3)	11	pN0	4		
17	15 (0.5-1.5)	3 (0.3)	18	pN0	2		
18	19(0.3-1.5)	3 (0.5)	22	pN1-1	6	5.2%	4.5%
19	5 (0.3-1.5)	1 (0.1)	6	pN0	3		
20	11 (1.2)	1 (0.5)	12	pN2-2	4	18.1%	6.6%
21	21(0.5-1.5)	4 (0.2)	25	pN0	2		
22	19 (0.2-3)	0	19	pN0	8		
23	14 (0.3-1.2)	2 (0.4)	16	pN0	4		
24	10 (0.5-1.4)	0	10	pN2-2	5	20%	
25	10 (0.5-2)	3 (0.3)	13	pN1-1	6	10%	7.6%
26	13 (0.4-1.2)	0	13	pN0	2		
27	8 (0.5-2)	0	8	pN0	2		
28	14 (0.3-2)	0	14	pN0	2		
29	23 (1)	7 (0.4)	30	pN0	2		
30	14 (0.8-0.2)	0	14	pN0	8		
31	9 (0.3-1)	0	9	pN2-2	3	22.2%	
32	11 (1.5)	2 (0.3)	13	pN0	2		
33	14 (1.5)	1 (0.3)	15	pN0	2		
34	22(1.5-0.5)	1 (0.4)	23	pN0	5		
35	6 (0.5-1)	0	6	pN2-2	2	33.3%	
36	13 (0.3-1)	2 (0.3)	15	pN0	2		
37	10 (0.5-2)	0	10	pN1-1	2	10%	
38	22 (0.2-1)	1 (0.4-1.3)	23	pN0	2		
39	11 (0.4-1.7)	0	11	pN0	2		
40	21(0.5-1.5)	5 (0.7)	26	pN0	2		
41	7 (0.4-1)	0	7	pN0	2		
42	15 (0.3-1.2)	0	15	pN0	2		

(LN- Lymph nodes; cm-diameter LN)

remaining fat tissue but continues with a LN density > 20% (went from 21.9% to 27.2%).

Two LN packets were sent in 25 patients (59.5%) and in three to eight LN packets in the remaining 17 (40.5%). In the case of LDN with two LN packets, the mean number of LN identified by palpation was 13.2 (range 5-27), while the mean rose to 15.6 (range 5-29) when the LN identified in all the fat tissue were also considered. Six (24%) of these patients presented positive LN, with a mean of 15.1 dissected LN.

In the case of LDN with more than two LN packets, the mean number of LN identified by palpation was 14.6 (range 5-33), and the mean rose to 16.8 (range 6-41) when the LN identified in all the fat tissue were also considered. Seven patients (41%) presented positive LN, with a mean of 19.4 dissected LN.

Discussion

The minimum number of LN needed for more accurate bladder cancer pN staging is still uncertain. To date, nine LN have been considered sufficient [7], but in routine clinical practice it is usual to obtain from 4 to 16 [6], and the American Joint Committee on Cancer recommends more than 12 LN [8]. Nevertheless, in general, authors agree that as more tissue is studied, more LN are found. A common observation is that when LDN is carried out in multiple separate containers the number of LN increases [9,10], probably due to more accurate surgical dissection. This observation is in accordance with the results of the present study, where positive LN were observed in 24% of patients in whom two LN packets were sent, compared to 41% when more packets were remitted, although there was an average increase of only 1.2 LN.

The objective of the present study was to explore the utility of the two main methods for pathological handling of specimens in patients undergoing radical cystectomy, manual palpation and complete embedding of all fat tissue. Because, all findings were made by only one person, the interpersonal differences in LN counting were avoided and all results were obtained using the same criteria.

Our results show that in 33.3% of patients no additional LN were detected after the evaluation of fat tissue. In the remaining 66.6% a small number of additional LN were detected (average 2.9), and their size was smaller (5 mm) than that of the LN identified by palpation (9 mm), none of them with metastasis thus the inclusion of the remaining fat tissue had no impact on either the pN category or the LN density [11].

This issue has also been discussed for other neoplasia. Although in some studies, micrometastases were detected in 1%-3% of LN when the remaining fat tissue was embedded after palpation [12,13], these findings have a low prognostic impact [14]. Moreover, even if more LN are found when a complete embedding of the remaining tissue is performed, most of them are negative or were already positive at palpation [15-17].

Conclusion

The results of this study suggest that the manual palpation is sufficient LN search method, and that complete embedding of fat tissue does not provide additional crucial information. Use of manual palpation only would save time and material. Probably the best recommendation, for a better definition of the pN category, is to send the LDN in separated packets from the different lymph nodes regions [18].

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