



The Main Determinant of Operative Time in Diagnostic Lymphadenectomy: Lymph Node Depth

Tanısal Lenfadenektomide Ameliyat Süresinin Ana Belirleyicisi: Lenf Nodu Derinliği

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ABSTRACT

Objective: We evaluated patients who underwent excisional peripheral lymph node biopsy in terms of histopathologic findings, palpability of lymph nodes, incision depth, and surgery duration, together with demographic and clinical characteristics of the patients.

Methods: This prospective study was conducted over an 18-month period at a university research hospital. The total number of 42 patients who attended the oncologic surgery outpatient clinic for excisional lymph biopsy was included in the study.

Results: Reactive lymph nodes were found in most benign cases (n=15/25), but the most common malignancy in the malignant group was B-cell lymphoma (n=5/17). When the lymph node was clinically non-palpable and had a size of up to 3.5 cm, the incision was deeper (p<0.05).

Conclusion: It would be a useful approach to add the depth of peripheral lymph nodes to the ultrasound reports together with other necessary data to assist the surgeon so that the exact location of the node can be more precisely predicted, and unnecessary incision size, depth, elongation of the duration of the surgery, and complications can be avoided. Collaboration between the surgeon, radiologist, and pathologist is a very important corner stone not to underdiagnose a malignancy and to avoid complications.

Keywords: Lymphadenopathy, complications, biopsy, surgical duration

ÖZ

Amaç: Eksizyonel periferik lenf nodu biyopsisi yapılan hastalar histopatolojik bulgular, lenf nodlarının palpabilitesi, insizyon derinliği ve ameliyat süresi ile hastaların demografik ve klinik özellikleri açısından değerlendirildi.

Gereç ve Yöntem: Bu çalışma prospektif bir araştırma olarak tasarlanmış ve bir üniversite araştırma hastanesinde 18 aylık bir süre boyunca yürütülmüştür. Eksizyonel lenf biyopsisi için onkolojik cerrahi polikliniğine başvuran toplam 42 hasta çalışmaya dahil edildi.

Bulgular: Benign olguların çoğunda reaktif lenf nodları (n=15/25) saptanırken, malign grupta en sık görülen malignite B-hücreli lenfoma (n=5/17) idi. Klinik olarak palpe edilemeyen lenf nodu ve boyutu 3,5 cm'ye kadar olan grupta insizyon daha derindi (p<0,05).

Sonuç: Cerraha yardımcı olmak için gerekli diğer verilerle birlikte ultrason raporlarına periferik lenf nodu derinliğinin eklenmesi çok yararlı bir yaklaşım olacaktır, böylece nodun tam yeri daha kesin olarak tahmin edilebilir ve gereksiz kesi boyutu, derinliği, ameliyat süresinin uzaması ve komplikasyonlardan kaçınılabılır. Cerrah, radyolog ve patoloğun işbirliği, bir maligniteye eksik tanı koymamak ve komplikasyonlardan kaçınmak için çok önemli bir köşe taşıdır.

Anahtar Kelimeler: Lenfadenopati, komplikasyonlar, biyopsi, ameliyat süresi

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Cite as: Şentürk A, Mutlu F. The Main Determinant of Operative Time in Diagnostic Lymphadenectomy: Lymph Node Depth. Med J Bakirkoy. 2024;20:203-209

Received: 01.03.2024

Accepted: 14.06.2024



INTRODUCTION

Human secondary lymphoid organs consist of approximately six hundred lymph nodes, spleen, tonsils, adenoids, and Peyer's patches. These sites are tissues where B and T-cells interfere with antigens (1,2). More than one centimeter enlargement and changes in lymph node consistency are generally defined as lymphadenopathy (3,4). The most common location of lymphadenopathies is the head and neck region, followed by the inguinal region, and axilla. Nearly 25% of patients have generalized lymphadenopathies, which may be a sign of systemic and serious pathology (5). Reactive lymph node hyperplasia, lymphadenopathy due to infection (viral, bacterial, fungal or parasitic), granulomatous lymphadenitis, local or distant metastatic lymphadenopathies, and primary lymphoproliferative disorders, such as B-cell lymphoma and Hodgkin's lymphoma, are the most common clinical manifestations of peripheral lymphadenopathy. All peripheral lymphadenopathies should be evaluated carefully not to under diagnose a malignant disease. Patient history, physical examination, laboratory test, and radiologic imaging results should be requested. The characteristics of swollen lymph nodes often provide valuable clues about the nature of the underlying diseases. Acute, painful, and soft lymphadenopathy is a common sign of localized or systemic infection. In cases of elastic, conglomerated, and painless enlarged lymph nodes, primary lymphomas should be suspected. Metastatic peripheral lymphadenopathies are usually hard in texture and generally painless, and are attached to surrounding tissues. When the specific cause of the peripheral lymph congestion is not determined, excisional peripheral lymph node biopsy should be executed. Although this approach is the most reliable method for diagnosing underlying diseases, the excision procedure is inconvenient, time-consuming, and difficult for patients (6). In a retrospective study, excisional peripheral lymph node biopsies in the cervical area were regarded as unnecessary because 45% of the cases were benign (7).

New approaches are being developed regarding the use of molecular and serologic markers, as well as advanced imaging methods, such as ultrasound and computed tomography, in the diagnosis of peripheral lymph node pathologies. With the increase in technological and interventional opportunities, the use of less invasive methods, such as fine-needle aspiration biopsy and ultrasound-guided fine-needle aspiration biopsy, compared with excisional biopsy has been brought to the agenda. However, there is no consensus on a diagnostic method that can be used in place of the reliability of excisional biopsy

and its ability to guide correct diagnosis among clinicians and clinical guidelines (6).

In this research article, we evaluated patients who underwent excisional peripheral lymph node biopsy in terms of histopathologic findings, palpability of the lymph nodes, incision depth, and surgery duration, together with demographic and clinical characteristics of the patients.

METHODS

The data for this study were prospectively collected over an 18-month period between September 2021 and May 2023 at a university research hospital and evaluated retrospectively. This research was carried out in accordance with the Principles of the Declaration of Helsinki. This study was approved by Sakarya University Faculty of Medicine Non-Invasive Ethics Committee (no: E-71522473-050.01.04-241712-159, date: 02.05.2023). Patients attending an oncologic surgery outpatient clinic for excisional lymph biopsy were included in the study. Demographic and clinical data of the patients together with comorbidities such as smoking and diabetes mellitus were questioned. Lymph node location, surgical duration, and incision depth were recorded during the excision procedure. All surgical procedures were performed by one surgeon. In all cases, peripheral lymph node excision was performed under local anaesthesia. Histopathological reports of the lymph nodes were also examined.

Statistical Analysis

Data were analyzed using SPSS version 26 (IBM Corporation). The descriptive statistics on the distribution of responses to independent variables are presented as numbers and percentages for categorical variables and mean, standard deviation, and median for numerical variables. The conformity of continuous variables to the normal distribution assumption was evaluated by Kolmogorov-Smirnov test. For binary and multiple comparisons, the chi-square test, Fisher's Exact test for categorical variables, One-Way ANOVA test or Kruskal-Wallis method for quantitative variables were used. The results were interpreted as significant when $p < 0.05$ with 95% confidence interval.

RESULTS

A total of 42 patients were included in the study, including 19 (45.2%) females and 23 (54.8%) males. The mean age of the patients was 53.7 ± 16.8 years. Palpable lymph nodes were detected in 19 (45.2%) of the patients. When the characteristics of peripheral lymph nodes and surgery were examined; the mean diameter of the lymph node was

2.61±1.14 cm, the mean incision size was 3.95±1.29 cm, the mean depth of the incision was 4.27±1.45 cm. and the mean operation time was 34.48±11.25 minutes. The peripheral lymph nodes were mostly located in the inguinal region in 18 (42.9%) and in the axillary region in 18 (42.9%) of the patients (Table 1).

Histopathological examination revealed that 17 (40.5%) patients had malignancies. The most relevant comorbidities were diabetes mellitus 11 (26.2%) and smoking 11 (26.2%). In addition, complications developed in 8 (19.0%). All demographic, clinical, and surgical data are presented in

Table 1. Reactive lymph nodes (n=15) were identified in most benign cases (n=25), whereas B-cell lymphoma (n=5) was a common malignancy (n=17) in the malign group of patients (Table 2).

Comparison of the depth of the incision applied to the patients during surgery with the demographic and clinical characteristics of the patients is presented in Table 3. The incision depths of female patients were deeper than that of male patients, but the differences were not significant. Interestingly, statistical analyses yielded that the incision depth was significantly different in patients between the

Table 1. Demographic and clinical characteristics of patients (n=42)

Age		53.69±16.78 (min-max: 19-91)	
Body mass index (kg/cm ²)		23.76±1.96 (min-max: 19-28)	
Lymph node diameter (cm)		2.61±1.14 (min-max: 1-6)	
Duration of surgery (min)		34.48±11.25 (min-max: 17-52)	
Length of incision (cm)		3.95±1.29 (min-max: 2-6.3)	
Depth of incision (cm)		4.27±1.45 (min-max: 2.3-6.5)	
		n	
		%	
Gender, (n, %)	Female	19	45.2
	Male	23	54.8
Age group, (n, %)	18-50 years	17	40.5
	51 years and older	25	59.5
Excision area (n, %)	Neck	6	14.3
	Axilla	18	42.9
	Inguinal	18	42.9
Lymph node location(s) (n, %)	Neck	5	11.9
	Axilla + inguinal	8	19.0
	Inguinal	7	16.7
	Neck + axilla + inguinal	12	28.6
	Axilla + inguinal	6	14.3
	Neck + axilla	1	2.4
Palpabl, (n, %)	Neck + inguinal	3	7.1
	Yes	19	45.2
Lymph node size (cm), (n, %)	No	23	54.8
	0-3.5 cm	36	85.7
Malignancy, (n, %)	3.6 and above	6	14.3
	Yes	17	40.5
Diabetes mellitus (n, %)	No	25	59.5
	Yes	11	26.2
Smoking frequency (n, %)	No	31	73.8
	Where	11	26.2
Complication(s), (n, %)	No	31	73.8
	Yes	8	19.0
	No	34	81.0

Min-max: Minimum-maximum

Table 2. Histopathological results of the excised lymph nodes

Histopathology	n	%	
Malign n=17, 40.5%	B-cell lymphoma	5	11.9
	Hodkin lymphoma	4	9.5
	Follicular lymphoma	3	7.1
	Mantle cell lymphoma	2	4.8
	High grade prostate adeno Ca	1	2.4
	Marginal zone lymphoma	1	2.4
	Urothelial carcinoma metastasis	1	2.4
Benign n=25, 59.5%	Reactive lymph node	15	35.8
	Follicular hyperplasia	2	4.8
	Chronic lymphadenitis	2	4.8
	Dermatopathic lymphadenopathy	1	2.4
	Granulomatous lymphadenitis	1	2.4
	Caseous granuloma	1	2.4
	Necrotizing granulomatous lymphadenitis	1	2.4
	Non-necrotizing granulomatous lymphadenitis	1	2.4
	Non-specific	1	2.4

Ca: Cancer

Table 3. Comparison of the demographic and clinical characteristics of patients with incision depth

		Incision depth (avg ± std)	p-value
Gender	Woman	4.37±1.5	0.698
	Male	4.19±1.39	
Age (years)	18-50	4.83±1.45	0.048
	51 years and over	4.02±1.42	
Body mass index		23.76±1.96	0.232
Excision area	Neck	3.58±1.26	0.035
	Axilla	3.88±1.41	
	Inguina	4.89±1.36	
Lymph node size (cm)	0-3.5 cm	4.43±1.46	0.043
	3.6 and above	3.85±1.45	
Palpability	Palpable	2.76±0.58	<0.001
	Non-palpable	5.52±0.47	
Incision length (cm)		3.95±1.29	<0.001
Duration of surgery (min)		34.48±11.25	<0.001
Malignancy	Yes	3.89±1.45	0.066
	No	4.53±1.41	
Diabetes mellitus	Yes	4.49±1.46	0.565
	No	4.19±1.45	
Smoking	Yes	4.87±1.22	0.052
	No	4.05±1.48	
Complication(s)	Yes	5.47±0.35	0.008
	No	3.99±1.47	

Avg ± std: Average ± standard

ages of 18-50, patients with peripheral lymph nodes mostly located in the neck area. It was clearly observed that patients with greater incision depth were more likely to develop complications ($p<0.008$). One of the most remarkable findings was that when the lymph node was clinically non-palpable and its size was up to 3.5 cm, the incision was deeper ($p<0.001$). In addition, statistically significant differences were found between the incision depth, the size of the incision and the duration of the surgery ($p<0.05$).

The palpability of peripheral lymph nodes was compared with the demographic and clinical characteristics of the patients (Table 4). When the lymph node was nonpalpable, the lymph node size was smaller as expected ($p=0.043$).

It was also clearly determined that the duration of the surgery, depth of the incision, and size of the incision were significantly associated with nonpalpable lymph nodes ($p<0.001$).

The comparison of the presence of malignancy in peripheral lymph nodes with the demographic and clinical characteristics of the patients were given in Table 5. The mean age of the malign patients was 60.82 ± 17.43 years ($p<0.021$) and patients who were older than 51 years had significantly more malign cases compared to the younger age group ($p<0.013$). In malign lymph nodes, the node diameter was larger ($p<0.03$).

Table 4. Comparison of the demographic and clinical characteristics of patients with the palpability of the lymph nodes

		Non-palpable	Palpable	p-value
		n (%)	n (%)	
Gender	Woman	10 (23.81)	9 (21.43)	0.523
	Male	13 (30.95)	10 (23.81)	
Age (years)		52.53±19.89	55.11±12.43	0.626
Age group	18-50	11 (26.19)	6 (14.29)	0.227
	51 years and over	12 (28.57)	13 (30.95)	
Body mass index		23.48±2.35	24.11±1.33	0.308
Excision area	Neck	3 (7.14)	3 (7.14)	0.129
	Axilla	7 (16.67)	11 (26.19)	
	Inguinal	13 (30.95)	5 (11.90)	
Lymph node location(s)	Neck	3 (7.14)	2 (4.76)	0.783
	Axilla	4 (9.52)	4 (9.52)	
	Inguinal	5 (11.90)	2 (4.76)	
	Neck + axilla + inguinal	5 (11.90)	7 (16.67)	
	Axilla + inguinal	4 (9.52)	2 (4.76)	
	Neck + axilla	0 (0.00)	1 (2.38)	
Lymph node diameter (cm)		2.41±0.89	2.86±1.39	0.123
Lymph node size (cm)	0-3.5 cm	21 (50.00)	15 (35.71)	0.043
	3.6 and above	2 (4.76)	4 (9.52)	
Duration of surgery (min)		44.09±3.93	24.84±2.89	<0.001
Depth		5.52±0.47	2.76±0.58	<0.001
Incision (cm)		5.03±0.55	2.66±0.44	<0.001
Malignancy	Yes	7 (16.67)	10 (23.81)	0.152
	No	16 (38.10)	9 (21.43)	
Diabetes mellitus	Yes	7 (16.67)	4 (9.52)	0.051
	No	16 (38.10)	15 (35.71)	
Smoking	Yes	9 (21.43)	2 (4.76)	0.038
	No	14 (33.33)	17 (40.48)	
Complication(s)	Yes	8 (2.38)	1 (2.38)	0.004
	No	15 (35.71)	18 (42.86)	

Table 5. Comparison of demographic and clinical characteristics between patients with and without histopathological results

		Benign	Malign	p-value
		n (%)	n (%)	
Gender	Woman	13 (30.95)	6 (14.29)	0.227
	Male	12 (28.57)	11 (26.19)	
Age (years)		48.84±14.78	60.82±17.43	0.021
Age group	18-50	13 (30.95)	4 (9.52)	0.013
	51 years and over	12 (28.57)	13 (30.95)	
Body mass index		23.68±2.04	23.88±1.91	0.747
Excision area	Neck	3 (7.14)	3 (7.14)	0.696
	Axilla	12 (28.57)	6 (14.29)	
	Inguinal	10 (23.81)	8 (19.05)	
Lymph node location(s)	Neck	3 (7.14)	2 (4.76)	0.388
	Axilla	6 (14.29)	2 (4.76)	
	Inguinal	4 (9.52)	3 (7.14)	
	Neck + axilla + inguinal	7 (16.67)	5 (11.90)	
	Axilla + inguinal	3 (7.14)	3 (7.14)	
	Neck + axilla	0 (0.00)	1 (2.38)	
	Neck + inguinal	2 (4.76)	1 (2.38)	
Lymph node diameter (cm)		2.30±0.88	3.09±1.36	0.030
Palpability	No	16 (38.10)	7 (16.67)	0.152
	There is	9 (21.43)	10 (23.81)	
Lymph node size (cm)	0-3.5 cm	23 (54.76)	13 (30.95)	0.168
	3.6 and above	2 (4.76)	4 (9.52)	
Duration of surgery (min)		36.52±10.61	31.47±11.80	0.056
Depth		4.53±1.41	3.89±1.45	0.066
Incision (cm)		4.14±1.29	3.69±1.27	0.275
Diabetes mellitus	Yes	8 (19.05)	3 (7.14)	0.061
	No	17 (40.48)	14 (33.33)	
Smoking	Yes	4 (9.52)	7 (16.67)	0.041
	No	21 (50.00)	10 (23.81)	
Complications	Yes	7 (16.67)	1 (2.38)	0.044
	No	18 (42.86)	16 (38.10)	

DISCUSSION

Peripheral lymphadenopathies can be classified as localized or generalized (swollen lymph nodes in more than one region). Generalized lymphadenopathies are almost always a sign of serious systemic disease. Diagnostic difficulties are usually observed in localized lymphadenopathies (3,8). Excisional peripheral lymph node biopsy is generally indicated for situations such as the presence of unexplained localized or generalized lymphadenopathies and persistent lymphadenopathy despite antibiotic treatment at the end of 3-4 weeks follow-up period (8,9). Although many studies have tried to develop algorithms that use excisional biopsy

as the last option and highlight other diagnostic methods, no consensus has yet been reached on this issue. Histopathologic evaluation provides important data about the importance of cautious evaluation of peripheral lymphadenopathies. In our patients, malignant cases constituted approximately 40% of the cases, with B-cell lymphoma being the most common malignancy. Gül et al. (9) evaluated 67 excisional peripheral lymph node biopsy cases and reported that the number of malignant cases was 34%.

Fine-needle aspiration biopsy guided by ultrasound provides promising results. The use of immunohistochemical methods and molecular techniques leads to more accurate and specific results for the histopathological evaluation

of fine-needle aspiration biopsy samples (10). It has been reported that the sensitivity and specificity of fine-needle aspiration is between 85-95% and 98-100%, respectively (11,12). Although fine-needle aspiration seems reliable, malignant cases can be missed in cases of heterogeneity and early or partial sampling of the lymph nodes (8). Fine-needle aspiration biopsy may be useful in differentiating between benign and malignant tumors, but diagnosis insufficiency is frequently encountered. In addition, excisional biopsy is required for definitive diagnosis of lymphoma. Therefore, excisional biopsy has been indicated as the "gold standard" in the diagnosis of lymphadenopathy (7,9,13).

Excisional biopsy is a diagnostic method that can be performed safely with minimal morbidity and mortality (7). However, surgical complications are still possible. Therefore, excisional peripheral lymph node biopsy maintains its diagnostic validity even when used in unnecessary situations (3,8,10). We determined that approximately 20% of our patients developed surgical complications associated with increased incision depth and nonpalpable lymph nodes. Furthermore, as previously revealed, elongation of the surgical duration increases the risk of surgical site infections (14). In our research, we found that the presence of nonpalpable lymph nodes was related to the prolonged duration of the surgery, increased size and depth of the incision, and which, in turn, resulted in complications. It would be a useful approach to add the depth of peripheral lymph nodes to the ultrasound reports together with other necessary data to assist the surgeon so that the exact location of the node can be more precisely predicted, and unnecessary incision size, depth, elongation of the duration of the surgery, and complications can be avoided. When lymph nodes are nonpalpable and small in diameter, wire marking can be a useful method to reduce complications. The use of methylene blue, indocyanine green, or tattoo may help shorten the operating time under ultrasound guidance, especially for less experienced surgeons. As a limitation, the data would be more expensive if this research were performed with a larger sample group. Another limitation of this study was that a comparison of wire-marked lymph node excision with regular excision was not performed.

CONCLUSION

Peripheral lymphadenopathy requires very careful evaluation of patient. Collaboration between the surgeon, radiologist, and pathologist is a very important corner stone not to underdiagnose a malignancy and to avoid complications.

ETHICS

Ethics Committee Approval: This study was approved by Sakarya University Faculty of Medicine Non-Invasive Ethics Committee (no: E-71522473-050.01.04-241712-159, date: 02.05.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: A.Ş., F.M., Concept: A.Ş., F.M., Design: A.Ş., F.M., Data Collection or Processing: A.Ş., F.M., Analysis or Interpretation: A.Ş., F.M., Literature Search: A.Ş., F.M., Writing: A.Ş., F.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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