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Diagnostic Accuracy of Imaging and Biopsy Techniques Compared with Surgical Excisional Lymph Node Biopsy in Cervical Lymphadenopathy

Servikal Lenfadenopatide Görüntüleme ve Biyopsi Yöntemlerinin Cerrahi Eksizyonel Lenf Nodu Biyopsisiyle Karşılaştırmalı Tanısal Değerlendirmesi

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ABSTRACT Objective: Accurate and timely diagnosis of cervical lymphadenopathy is essential for effective management. This study aimed to assess the diagnostic performance of various imaging modalities and biopsy techniques compared to surgical excisional lymph node biopsy (SEB). **Material and Methods:** A retrospective review of 115 patients who underwent SEB was performed. Preoperative diagnostic methods including fine-needle aspiration biopsy (FNAB), ultrasound-guided core needle biopsy (USCNB), ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography-CT (PET-CT) were evaluated for sensitivity, specificity, and concordance with SEB results. **Results:** Among 115 patients (61 males, 54 females; mean age 48.6±19 years), FNAB and USCNB were performed in 62 and 37 patients, respectively. Ultrasound identified pathological nodes in 71.3% of 82 patients but had a 31% false-positive rate. CT correctly diagnosed 66.6% of 30 patients, and MRI identified true positives in 53.8% of 39 patients. PET-CT achieved 83% true-positive results in 59 patients. USCNB matched SEB in 64.8% of cases, with a non-diagnostic rate of 21.6% and a 13.5% error rate. In malignancy detection, USCNB had a sensitivity of 90% and specificity of 77.7%, with 2 false positives and 2 false negatives. **Conclusion:** PET-CT and USCNB demonstrated high diagnostic accuracy in cervical lymphadenopathy. PET-CT achieved the highest correct diagnosis rate, while USCNB showed strong sensitivity and acceptable specificity. CT and MRI were less reliable, highlighting the need for clearer diagnostic protocols, particularly in cases involving lymphoma and other head and neck tumors.

Keywords: Lymphadenopathy; lymphoma; squamous cell carcinoma; cytology; fine needle aspiration cytology

ÖZET Amaç: Servikal lenfadenopatinin doğru ve zamanında tanısı, etkili bir tedavi süreci için hayati öneme sahiptir. Bu çalışma, cerrahi eksizyonel lenf nodu biyopsisi (SEB) ile karşılaştırıldığında çeşitli görüntüleme yöntemleri ve biyopsi tekniklerinin tanısal doğruluğunu değerlendirmeyi amaçlamaktadır. **Gereç ve Yöntem:** SEB uygulanan 115 hastanın geriye dönük analizi yapıldı. İnce iğne aspirasyon biyopsisi (FNAB), ultrason eşliğinde yapılan kor biyopsi (USCNB), ultrason, bilgisayarlı tomografi (BT), manyetik rezonans görüntüleme (MRG) ve pozitron emisyon tomografi-BT (PET-BT) gibi preoperatif tanı yöntemleri; duyarlılık, özgüllük ve SEB sonuçlarıyla uyumluluk açısından değerlendirildi. **Bulgular:** 115 hastanın (61 erkek, 54 kadın; ortalama yaş 48,6±19 yıl) 62'sine FNAB, 37'sine USCNB uygulandı. Ultrason, 82 hastanın %71,3'ünde patolojik lenf nodlarını saptadı ancak %31 oranında yanlış pozitif sonuç verdi. BT, 30 hastanın %66,6'sında doğru tanı koydu; MRG ise 39 hastanın %53,8'inde doğru pozitif sonuç sağladı. PET-BT, 59 hastanın %83'ünde doğru pozitif sonuç verdi. USCNB, SEB ile %64,8 oranında uyum gösterdi; %21,6 oranında tanı konulamayan, %13,5 oranında ise hatalı sonuçlar izlendi. Malignite saptanmasında USCNB'nin duyarlılığı %90, özgüllüğü ise %77,7 olarak hesaplandı (2 yanlış pozitif, 2 yanlış negatif). **Sonuç:** PET-BT ve USCNB, servikal lenfadenopati tanısında yüksek doğruluk oranları sergilemiştir. PET-BT en yüksek doğru tanı oranına ulaşırken, USCNB yüksek duyarlılık ve kabul edilebilir özgüllük sunmuştur. BT ve MRG ise daha düşük güvenilirliğe sahiptir. Özellikle lenfoma ve diğer baş-boyun tümörleri vakalarında daha net tanı protokollerine ihtiyaç olduğu görülmektedir.

Anahtar Kelimeler: Lenfadenopati; lenfoma; skuamöz hücreli karsinom; sitoloji; ince iğne aspirasyon sitolojisi

Cervical lymphadenopathies associated with head and neck squamous cell carcinoma (HNSCC) and lymphomas require distinct approaches in terms of etiology and management. In HNSCC, lymphadenopathy typically arises from metastatic lymph node involvement secondary to a primary tumor. The diagnostic process prioritizes identifying the primary tumor's location through clinical examination, imaging

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ing modalities [e.g., contrast-enhanced computed tomography (CT) or positron emission tomography-CT (PET-CT)], and, when necessary, fine-needle aspiration biopsy (FNAB) or ultrasound-guided core needle biopsy (USCNB).¹⁻³

In cases of HNSCC, excisional lymph node biopsy is generally contraindicated as it may disrupt the anatomical integrity of lymphatic drainage pathways, hinder accurate staging, and complicate optimal treatment planning.⁴ Conversely, lymphomas, as primary lymphoid malignancies, require more extensive tissue sampling for accurate diagnosis.⁵ Immunohistochemical, cytogenetic, and molecular analyses are essential to classify lymphoma subtypes, making excisional biopsy the gold standard for diagnosis.^{6,7}

The diagnostic accuracy of preoperative procedures, such as FNAB and CNB, varies significantly, highlighting the need for a comprehensive evaluation of their effectiveness.^{1,5,6}

While surgery, radiotherapy, and chemotherapy are the cornerstone treatment modalities for HNSCC, the management of lymphomas primarily relies on chemotherapy and targeted therapies.

Comprehensive guidelines for managing HNSCC-related lymphadenopathy provide detailed recommendations on staging, diagnostic approaches (e.g., biopsy techniques, imaging), and treatment planning (e.g., surgery, radiotherapy, chemotherapy).⁸⁻¹⁰

However, for cervical lymphadenopathy due to lymphoma, general hematology and oncology guidelines predominate. For instance, organizations such as the National Comprehensive Cancer Network, the European Society for Medical Oncology, and the British Society for Hematology provide frameworks for the diagnosis, staging, and management of lymphomas.¹¹⁻¹³

These guidelines typically focus on the systemic nature of lymphoma rather than specific anatomical regions, which may lead to confusion in cases of cervical lymphadenopathy with an unknown primary origin.

When the clinical differentiation between HNSCC and lymphoma is challenging, selecting the appropriate biopsy technique becomes critical. Ex-

tensive radiological and pathological investigations frequently delay diagnosis and treatment initiation.

Thus, the primary aim of this study was to reveal the results of surgical excision of cervical lymph nodes in patients referred to an otolaryngology clinic from hematology, oncology, internal medicine, and infectious disease clinics at a tertiary care hospital. The secondary aim was to evaluate the clinical utility of preoperative diagnostic techniques, including FNAB, USCNB, and various imaging modalities.

MATERIAL AND METHODS

STUDY DESIGN AND INCLUSION CRITERIA

This retrospective cross-sectional study was conducted at the Clinic of Ear Nose Throat, Ankara Bilkent City Hospital. The study protocol was approved by the Institutional Ethics Committee of Ankara Bilkent City Hospital (date: January 24, 2024; no: E2-24-6128) and adhered to the principles of the Helsinki Declaration. All patients agreed to participate and signed the informed consent. This study included patients aged 16 years and older who underwent surgical excisional biopsy (SEB) in our clinic over the past 5 years. These patients were referred from hematology/oncology, internal medicine, and infectious diseases clinics.

DATA COLLECTION

The patient records, along with the radiology and histopathology reports, were reviewed. The diagnostic tests used before the decision for surgical excision -USCNB, FNAB, magnetic resonance imaging (MRI), CT, PET-CT- were identified. The results of FNAB and USCNB were evaluated for diagnostic yield, non-diagnostic findings, and concordance with radiological imaging and excisional biopsy results. In our clinic, USCNB and FNAB procedures for head and neck lesions are performed under ultrasound guidance. Biopsy guns of 14-18 gauge are used, depending on the size of the swelling area. Standard procedures are applied to tissue biopsies in the histopathology laboratory. Immunohistochemical analyses are performed by histopathologists using monoclonal antibodies. Additional immunohistochemical tests, molecular genetic analyses and PCR

typing are used in the diagnosis of lymphoma. In our study, the WHO guidelines were used for classifying malignant lymphomas.¹⁴

STATISTICAL ANALYSIS

Statistical analysis of the data collected within the scope of the investigated variables was performed using the SPSS 20.0 for Windows (IBM SPSS Inc., Chicago, IL, USA) software. Quantitative variables were expressed as means $\pm$ standard deviations, while categorical variables were presented as percentages.

RESULTS

A total of 115 patients (61 male, 54 female) who underwent excisional lymph node biopsy in the head and neck region between 2019-2024 (5-year period) were included in this study.

The patients' ages ranged from 14 to 87 years, with a mean age of 48.6 $\pm$ 19 years. Demographic data are presented in Table 1.

Preoperative radiological imaging requests varied due to differences in clinical approaches among hematology, oncology, internal medicine, and infectious diseases clinics, leading to multiple radiological examinations for some patients. A total of 210 radiological examinations were conducted on 115 patients.

Before surgery, neck ultrasound was requested for 82 patients (71.3%). According to the ultrasound reports, there were pathological findings in 58 patients. When the sonographic findings evaluated as malignant on ultrasound were compared with the pathology results, we found that 18 ultrasound reports (31%) were false positives. Four cases initially misinterpreted as malignancy were diagnosed as Castleman's disease in the excisional biopsy. In 7 cases, the pathology specimen was diagnosed with caseous necrosis. Additionally, in 7 cases, although ultrasound revealed pathologically enlarged lymph nodes and conglomerations, the pathology results were benign. The sensitivity of ultrasound was determined to be 97.5%, with a specificity of 55%.

Thirty patients (26.1%) underwent neck CT. When the CT findings were compared with the pathological results of SEB in terms of malignancy, 20 CT reports were identified as true positives (66.6%),

TABLE 1: Demographic data of patients	
	Total (n=115)
Age	48.6 ($\pm$ 19.03)
Gender	
Female	54 (39.9%)
Male	61 (60.1%)
Hypertension	21 (%18.3)
Hypothyroidism	7 (%6.1)
Diabetes	10 (%8.7)
Renal disease	1 (%0.9)
Astma	3 (%2.6)
Lymphoma in remission	14 (%12.2)
Head and neck tumor in remission	2 (%1.7)

while 3 were falsely identified as positive (10%). Seven patients were correctly identified as negative, and no patient was falsely diagnosed as negative in terms of malignancy.

Thirty-nine patients (33.9%) underwent neck MRI. When the MRI findings were compared with the pathological results of SEB regarding malignancy, 21 (53.8%) were correctly identified as positive, 6 (15.3%) were falsely identified as positive, 1 (2.5%) was falsely identified as negative, and 11 patients (28.2%) were correctly identified as negative. Among the neck MRIs reported falsely as malignant, 2 showed lymph nodes with diffusion restriction, 2 showed conglomerated lymph nodes, 11 showed central necrosis, and 1 showed multiple pathologically enlarged lymph nodes. In the patient who had a falsely negative FNAB result, the final pathology of the lymph nodes-identified through SEB-revealed metastasis from the prostate carcinoma.

For 59 (51.3%) patients, PET-CT was requested. Pathological lymph nodes were detected in the 58 patients who underwent PET-CT. Of these, 9 (15.2%) were found to have false positives. Among these false positives, 5 (8.4%) had a history of cured lymphoma.

SEB was conducted on 56 patients on the right side of the neck, 56 patients on the left side of the neck, and 3 on the midline neck. The excised neck regions are detailed in Table 2.

The largest lymph node removed measured 8 cm, while the smallest measured 0.5 cm ($\pm$ 2.3).

All patients underwent SEB, whose results are presented in Table 3.

Of these patients (n=115), 62 underwent preoperative FNAB. Among these, the results were consistent with SEB in 30 (48.3%) cases, non-diagnostic in 20 (32.2%) cases, and falsely diagnosed in 12 (19.3%) cases. The FNAB results are presented in Table 4.

Of the total number of patients (n=115), 37 underwent preoperative USCNB. Of these, 24 (64.8%) had results consistent with SEB, 8 (21.6%) were non-diagnostic, and 5 (13.5%) were incorrectly diagnosed. Malignancy was diagnosed in 18 patients (48.6%) through USCNB, with 2 false positives (5.4%) and 2 false negatives (5.4%). The sensitivity of USCNB for diagnosing malignancy was determined to be 90%, with a specificity of 77.7%. The USCNB results are presented in Table 5.

TABLE 2: Lymph node areas subjected to surgical excision

	Frequency (n=115)	%
Level 1	26	22.6
Level 2	36	31.3
Level 3	14	12.2
Level 4	10	8.7
Level 5	25	21.7
Posterior neck	2	1.7
Multiple neck level	2	1.7

TABLE 3: SEB results

	Frequency (n=115)	%
Diffuse large B cell	12	10.4
Metastatic carcinoma	14	12.2
Non-malignant findings, others	6	5.2
Castelman disease	4	3.5
Caseification findings	7	6.1
Reactive lymph node	34	29.6
Follicular	3	2.6
Mantle cell	2	1.7
Nodal marginal zone	2	1.7
Small B cell lymphoma	4	3.5
Hodgkin lymphoma, classic	15	13.0
Hodgkin lymphoma, nodular lymphocyte predominant	7	6.1
Nodal peripheral T cell lymphoma	4	3.5
Anaplastic large cell lymphoma	1	0.9

TABLE 4: Fine needle aspiration biopsy results

	Frequency (n=65)	%
Reactive	3	2.6
Non-diagnostic	20	17.4
Malignancy negative	12	10.4
Suspected malignant	5	4.3
Suspected lymphoproliferative disease	15	13.0
Lymphoma	5	4.3
Infective	1	0.9

A wide variety of diagnostic algorithms were observed. The same sequence of tests was not performed for every patient. At least one preoperative radiological imaging procedure was conducted on 111 patients, of whom 20 (18%) had benign radiology reports that did not correlate with the malignancy diagnosis. Metastatic carcinoma was present in 14 (12.2%) patients who underwent SEB.

DISCUSSION

This retrospective study evaluated the outcomes of SEB in patients aged 16 years and older who presented with cervical lymphadenopathy. Patients were referred from the hematology, oncology, internal medicine, and infectious diseases clinics at a tertiary care hospital. Our findings underscore both the essential role of SEB as the gold standard and the potential utility of preoperative diagnostic tests (FNAB,

TABLE 5: Ultrasound core needle biopsy results

	Frequency (n=37)	%
Reactive	3	2.6
Granulomatous lymph node	2	1.7
Non-diagnostic	8	7.0
Malignancy negative	4	3.5
Lymphoma	4	3.5
Suspected lymphoma	12	10.4
Carcinoma	2	1.7
Suspected carcinoma	1	0.9
Patients who did not undergo CNB before surgery	78	67.8
Metastatic lymph node	1	0.9

CNB: Core needle biopsy

USCNB, and various imaging modalities) in guiding clinical decision-making. Our findings highlight several challenges in the diagnostic process.

The management of neck lymphadenopathy can be challenging due to the variety of tests in the diagnostic algorithm. There are few evidence-based clinical practice guidelines to assist clinicians in the management of neck masses in adults.⁸⁻¹⁰

DIAGNOSTIC ROLE OF SEB AND OTHER BIOPSY TECHNIQUES

SEB remains the gold standard for diagnostic confirmation in cases of uncertainty, especially for lymphoma subtyping, where complete lymph node excision is necessary for in-depth immunohistochemical and architectural analysis.¹⁵ Despite its high diagnostic yield, SEB introduces increased costs and potential complications, including those related to hospitalization, anesthesia, and the technical complexity of the head and neck region.^{16,17} For patients at high risk of head and neck malignancies, a pan-endoscopic examination is typically recommended.⁸ Meanwhile, less invasive techniques such as FNAB and USCNB are considered before proceeding to SEB, particularly when the malignant potential is not yet confirmed.^{8,18}

Before SEB, evaluation of the upper respiratory and upper digestive systems under anesthesia is recommended. Following SEB in patients with HNSCC, there is a need for more aggressive complementary surgery and chemoradiotherapy to ensure disease control. In our study, SEB identified metastatic carcinoma in 12.2% of the cases. In a study including patients requiring neck dissection after SEB, the rate of tumor cell accumulation around the incision scar was reported to be 7%.¹³ These findings underscore the limitations of SEB, including the possibility of tumor seeding and the subsequent need for more aggressive surgical interventions in head and neck squamous cell carcinoma. Consequently, there is a pressing need to optimize preoperative diagnostic strategies to minimize risks and improve diagnostic efficiency.

Our results further highlight the role of USCNB as an intermediary between FNAB and SEB. In detecting malignancy, USCNB demonstrated a 90% sensitivity and 77.7% specificity, making it notably

more reliable than FNAB, which had a higher rate of non-diagnostic and false-negative outcomes. Although FNAB (often performed under ultrasound guidance) remains attractive due to its minimal invasiveness, its limited accuracy can prolong the diagnostic process by necessitating repeat or additional procedures. Nonetheless, SEB continues to be indispensable for the definitive diagnosis of certain lymphoma subtypes where the architectural integrity of the lymph node and the identification of Reed-Sternberg cells are crucial.¹⁸⁻²⁰

ROLE OF PREOPERATIVE IMAGING MODALITIES

Preoperative imaging plays a pivotal role in diagnostic pathways but is not without limitations. Ultrasound demonstrated high sensitivity (97.5%) but low specificity (55%), leading to a substantial number of false-positive findings, particularly in conditions mimicking malignancy, such as Castleman's disease or caseous necrosis.²¹ Similarly, distinguishing benign from malignant lymphadenopathy is particularly challenging in cases of cystic necrosis, which is frequently observed in squamous cell carcinoma metastases and tuberculosis.²¹

Cross-sectional imaging modalities like CT and MRI, particularly recommended in high-risk malignancy scenarios, and PET-CT, frequently utilized in hematology and oncology referrals, have demonstrated complementary diagnostic value.^{22,23} However, PET-CT false positives in lymphoma remission cases contribute to diagnostic inaccuracies and may prolong decision-making.²⁴ These findings highlight the importance of judiciously selecting imaging modalities based on clinical suspicion and correlating radiological findings with histopathological confirmation.

CHALLENGES IN THE DEVELOPMENT OF DIAGNOSTIC ALGORITHMS AND MULTIDISCIPLINARY COORDINATION

A major challenge in the management of cervical lymphadenopathy is the absence of standardized, multidisciplinary guidelines that integrate the distinct perspectives of various specialties. In our cohort, hematology and oncology referrals frequently underwent PET-CT before any tissue biopsy, reflecting a primary concern for lymphomas and other systemic ma-

lignancies. Conversely, patients from internal medicine or infectious diseases clinics often received ultrasonography, CT, or MRI before FNAB. This lack of uniformity can result in unnecessary repetition of imaging, delays in diagnostic confirmation, and increased healthcare costs. Studies have reported diagnostic delays of 3-6 months in malignancies, which can adversely affect survival and treatment outcomes.²⁵⁻²⁷

The lack of standardized, multidisciplinary guidelines for assessing head and neck lymphadenopathy intensifies inconsistencies in the diagnostic approaches. Each specialty tends to prioritize its specific diagnostic approach, often resulting in redundant imaging, avoidable invasive procedures, and prolonged diagnostic timelines—all of which drive up healthcare costs. Furthermore, inadequate coordination among specialties can heighten patient anxiety by delaying a definitive diagnosis, thereby increasing the risk of disease progression and reducing opportunities for timely, optimal treatment. Establishing evidence-based, multidisciplinary guidelines would help streamline diagnostic pathways, minimize redundant testing, and ultimately improve both patient outcomes and the efficiency of healthcare delivery.

LIMITATIONS

Our study has certain limitations. The variability in the diagnostic pathways due to referrals from different specialties restricted the direct comparison of the diagnostic test performance. Additionally, the relatively small sample size may not fully represent the spectrum of lymphadenopathy etiologies encountered in broader clinical practice. Further prospective studies with larger cohorts and standardized diagnostic protocols are warranted to validate our findings and improve the diagnostic accuracy.

CONCLUSION

Our study demonstrates that USCNB and PET-CT offer high diagnostic accuracy for cervical lymphadenopathy and can serve as critical tools before proceeding to surgical excisional biopsy. In particular, USCNB showed superior sensitivity (90%) and acceptable specificity (77.7%) compared with FNAB, supporting its role as an effective intermediary step. However, SEB remains the definitive standard, especially for lymphoma subtyping and cases with inconclusive or conflicting results. To optimize patient care, standardized, multidisciplinary guidelines that integrate clinical, radiological, and histopathological data are urgently needed. Such an approach would reduce diagnostic delays, lower healthcare costs, and ultimately lead to improved patient outcomes in the management of head and neck lymphadenopathy.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Zehra Betül Paksoy, Melih Çayönü; **Design:** Zehra Betül Paksoy; **Control/Supervision:** Melih Çayönü; **Data Collection and/or Processing:** Öznur Gündüz; **Analysis and/or Interpretation:** Melih Çayönü; **Literature Review:** Zehra Betül Paksoy, Öznur Gündüz; **Writing the Article:** Zehra Betül Paksoy, Melih Çayönü, Öznur Gündüz; **Critical Review:** Melih Çayönü, Zehra Betül Paksoy; **References and Fundings:** Melih Çayönü, Zehra Betül Paksoy, Öznur Gündüz; **Materials:** Öznur Gündüz.

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