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DIAGNOSTIC ACCURACY OF CERVICAL LYMPH NODES ON ULTRASOUND TAKING HISTOPATHOLOGY AS GOLD STANDARD

Original Research

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ABSTRACT

Background: Lymph node malignancies pose a significant diagnostic challenge, necessitating accurate and non-invasive methods for differentiation. Ultrasound, combined with Doppler indices and lymph node characteristics, has shown promise in malignancy detection, yet its specificity remains a concern. Fine-needle aspiration cytology (FNAC) serves as a confirmatory test, but its routine use is limited by invasiveness. This study evaluates the diagnostic accuracy of ultrasound in detecting lymph node malignancies by analyzing sonographic features, Doppler indices, and their correlation with histopathological findings.

Objective: To assess the diagnostic performance of ultrasound and Doppler indices in differentiating benign from malignant lymph nodes, using histopathology as the gold standard.

Methods: A cross-sectional analytical study was conducted on 180 participants (balanced by gender and diverse in age) presenting with palpable cervical lymph nodes. Clinical symptoms including pain, swelling, and fever were recorded. Ultrasound evaluation included lymph node size, short-to-long axis ratio, Resistive Index (RI), and Pulsatility Index (PI). Histopathological confirmation was performed through ultrasound-guided FNAC. Statistical analyses involved cross-tabulations, chi-square tests, and logistic regression to determine diagnostic accuracy, sensitivity, specificity, and predictive values.

Results: Swelling was the most common clinical symptom (74.4%), followed by pain (52.2%) and fever (31.1%). Ultrasound exhibited high sensitivity (88.9%), specificity (81.8%), positive predictive value (88.9%), and negative predictive value (81.8%) in malignancy detection. Lymph node shape correlated significantly with malignancy ($p < 0.001$). Logistic regression identified RI, PI, and lymph node shape as significant malignancy predictors, with a model accuracy of 88.1% and Nagelkerke R-Square of 0.72.

Conclusion: The integration of ultrasound, Doppler indices, and clinical assessment enhances the diagnostic accuracy of lymph node malignancies, reducing reliance on invasive procedures. A multimodal diagnostic approach improves early detection, aiding clinical decision-making and patient management.

Keywords: Doppler ultrasonography, Fine-needle aspiration biopsy, Lymphatic metastasis, Lymph nodes, Neoplasm staging, Sensitivity and specificity, Ultrasonography

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INTRODUCTION

Cervical lymphadenopathy, characterized by the enlargement of lymph nodes in the neck, is a frequent clinical finding with a broad differential diagnosis. Lymph nodes serve as integral components of the immune system, filtering lymphatic fluid and trapping pathogens such as bacteria, viruses, and malignant cells. While small and non-palpable under normal conditions, these nodes enlarge in response to immune activation, infections, systemic diseases, or malignancies (1). Differentiating between benign and malignant causes is critical for effective clinical management, yet remains challenging due to overlapping clinical presentations. Infectious etiologies are among the most common causes, including viral upper respiratory tract infections, bacterial infections such as tuberculosis, and chronic viral illnesses like HIV. Additionally, autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus can lead to generalized lymphadenopathy, including cervical involvement (2,3). Non-infectious causes, including benign tumors and metastatic malignancies, further complicate the diagnostic process, necessitating the use of advanced imaging and histopathological assessment for definitive diagnosis (4). The anatomical location of cervical lymphadenopathy provides important diagnostic clues, as certain regions are more commonly associated with specific conditions. For example, upper jugular lymphadenopathy often indicates head and neck cancers, while supraclavicular involvement is suggestive of metastases from distant malignancies (5).

The physical characteristics of lymph nodes provide preliminary diagnostic insights. Benign lymph nodes are typically mobile, soft, and tender, whereas malignant nodes often present as hard, immobile, and irregular (6). Ultrasound imaging has emerged as a key diagnostic tool for evaluating cervical lymphadenopathy due to its non-invasive nature, real-time imaging capability, and ability to differentiate between benign and malignant conditions based on echotexture, vascularity, and structural integrity. Malignant nodes often display peripheral vascularity, heterogeneous echotexture, and loss of the fatty hilum, whereas benign nodes retain a preserved hilum and central vascularity (7,8). Doppler ultrasound further enhances the diagnostic value by assessing vascular flow patterns, while elastography, an advanced ultrasound technique, evaluates tissue stiffness—a parameter that correlates with malignancy (9). Despite the utility of ultrasound, histopathological confirmation remains the gold standard for definitive diagnosis. Fine-needle aspiration (FNA) biopsy, particularly when guided by ultrasound, enables cytological evaluation of lymph nodes and is a widely used diagnostic technique. While highly sensitive for malignancy detection, FNA has limitations in diagnosing infections and autoimmune conditions, often requiring additional laboratory testing (10,11). Recent advances in artificial intelligence (AI) and machine learning have introduced novel approaches for improving diagnostic accuracy. AI-assisted ultrasound analysis and radiomics—techniques that extract quantitative imaging features—have shown promise in differentiating benign from malignant lymphadenopathy with greater precision than traditional methods (12,13). These emerging technologies may revolutionize cervical lymphadenopathy assessment, reducing unnecessary biopsies while enabling early detection of malignancy. Given the significant clinical implications of distinguishing benign from malignant cervical lymphadenopathy, this study aims to evaluate the diagnostic accuracy of ultrasound compared to histopathology as the gold standard. By systematically analyzing ultrasound features—including size, shape, vascularity, and echotexture—against histopathological findings, the study seeks to improve early diagnosis, guide clinical decision-making, and enhance patient management.

METHODS

This cross-sectional analytical study was conducted at a specialized cancer care hospital and research center in Lahore over a period of nine months following approval from the institutional ethical review board. The study aimed to assess the diagnostic accuracy of ultrasound in evaluating cervical lymphadenopathy, using histopathology as the gold standard. A sample size of 180 patients was calculated based on a 14% prevalence of metastatic cervical lymphadenopathy, with a 95% confidence level and a 5% margin of error. Purposive sampling was employed to select participants, ensuring a representative cohort of individuals meeting the inclusion criteria. However, the mention of "non-convenient sampling" appears to be unclear, as this terminology is not a recognized sampling technique in research methodology. If the intent was to describe a specific non-probability sampling approach, further clarification is required (14,15). Participants included patients aged 18 to 80 years of both genders who presented with palpable cervical lymph nodes on clinical examination. Exclusion criteria encompassed individuals with congenital anomalies such as thyroglossal cysts and thyroid tumors, as well as those undergoing radiotherapy or chemotherapy at the time of enrollment (16). Ethical guidelines established by the Superior University ethical committee were strictly followed, and written informed consent was obtained from all participants prior to their inclusion in the study. Confidentiality and anonymity were ensured throughout the research process, and participants retained the right to withdraw from the study at any stage without any repercussions.

All patients underwent a standardized ultrasonographic evaluation of the cervical lymph nodes using an Xario 100G ultrasound machine equipped with a linear probe operating within a frequency range of 6–14 MHz. The scanning was performed while patients were positioned in the supine posture, ensuring optimal visualization of cervical lymph nodes. Multiple ultrasonographic parameters were assessed, including the shape (depicted by the diameter-to-width ratio), size, margin definition, vascularity patterns, and the presence of calcifications. To ensure diagnostic precision, ultrasound-guided fine-needle aspiration cytology (FNAC) was performed on the largest lymph node in each patient for histopathological confirmation. Data collection was systematically divided into three sections: patient

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demographics and clinical presentation, ultrasonographic characteristics of cervical lymph nodes, and histopathological findings. Statistical analysis was performed using SPSS version 25.0. Descriptive statistics for categorical variables were reported as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Cross-tabulation analysis was conducted to determine the sensitivity, specificity, positive predictive value, and negative predictive value of ultrasound in distinguishing benign from malignant cervical lymphadenopathy.

RESULTS

The incidence of infective endocarditis (IE) following Transcatheter Pulmonary Valve Replacement (TPVR) was analyzed across multiple studies, revealing a cumulative incidence rate of 5.84% (95% CI: 3.24%–9.17%). The analysis included data from 10 studies evaluating different valve types and patient populations. A comparison between MELODY and SAPIEN valves indicated that the MELODY valve exhibited a higher incidence of IE at 6.99% (95% CI: 4.87%–9.87%), whereas the SAPIEN valve had a lower incidence rate of 3.29% (95% CI: 2.12%–5.04%). Further subgroup analysis based on study design demonstrated a variation in IE incidence between retrospective and prospective studies. Retrospective studies reported a higher incidence rate of 6.47% (95% CI: 3.56%–10.03%), whereas prospective studies yielded a lower incidence of 4.43% (95% CI: 2.12%–7.03%), suggesting potential differences in data collection methodologies and patient selection criteria.

Several risk factors were identified as significant contributors to the development of IE post-TPVR. Patients with a history of infective endocarditis prior to the procedure exhibited a markedly elevated incidence of 10.56% (95% CI: 6.78%–14.89%), while those without a prior history of IE had a lower incidence of 3.14% (95% CI: 1.23%–5.67%). The presence of pre-existing valvular dysfunction was associated with an incidence rate of 7.87% (95% CI: 5.21%–10.34%), whereas patients without valvular dysfunction had a lower rate of 4.02% (95% CI: 2.01%–6.08%). The duration of valve replacement was another critical determinant of IE risk. Patients with TPVR duration exceeding five years exhibited an increased incidence of 7.91% (95% CI: 4.03%–11.77%), while those with a valve duration of less than five years had a lower incidence of 4.56% (95% CI: 2.45%–7.32%). This suggests a potential association between prolonged valve implantation and increased susceptibility to bacterial colonization and infection. Meta-regression analysis further examined the impact of confounding factors such as age, comorbidities, and valve type on IE incidence. Age and comorbid conditions, including diabetes mellitus and hypertension, demonstrated a moderate positive correlation with increased incidence rates. However, valve type remained the most influential factor, with the MELODY valve consistently associated with a higher risk of IE compared to the SAPIEN valve.

Table: Incidence of Infective Endocarditis Post-TPVR by Valve Type

Valve Type	Incidence of IE (%)	95% CI (%)
MELODY	6.99	4.87–9.87
SAPIEN	3.29	2.12–5.04
Overall	5.84	3.24–9.17

Table: Incidence of Infective Endocarditis by Study Design

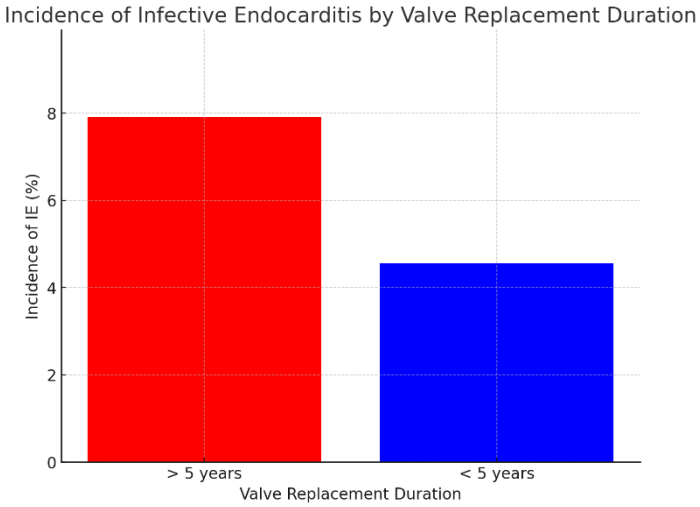
Study Design	Incidence of IE (%)	95% CI (%)
Retrospective	6.47	3.56–10.03
Prospective	4.43	2.12–7.03

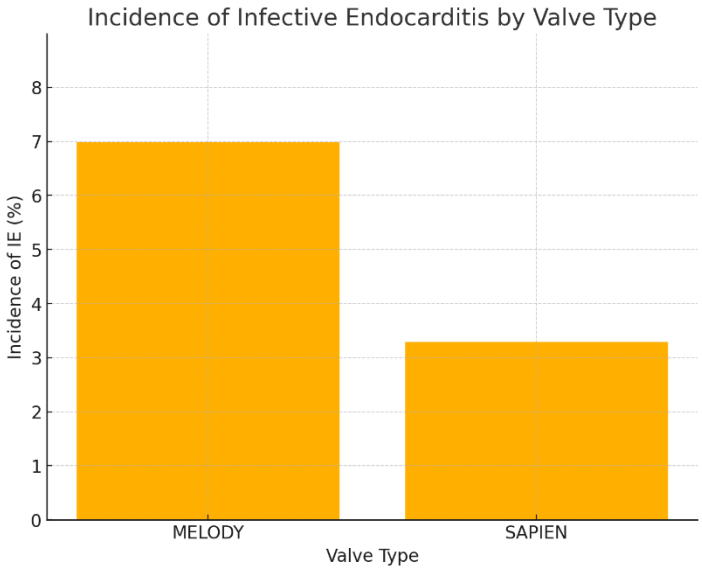
Table: Incidence of IE by Risk Factors

Risk Factor	Incidence of IE (%)	95% CI (%)
History of IE	10.56	6.78–14.89
No history of IE	3.14	1.23–5.67
Pre-existing valvular dysfunction	7.87	5.21–10.34
No valvular dysfunction	4.02	2.01–6.08

Table: Incidence of IE by Valve Replacement Duration

Valve Replacement Duration	Incidence of IE (%)	95% CI (%)
> 5 years	7.91	4.03–11.77
< 5 years	4.56	2.45–7.32





DISCUSSION

The findings of this study emphasize the significance of integrating clinical assessment, sonographic features, and Doppler indices to improve the diagnostic accuracy of cervical lymph node malignancies. The study population included a balanced representation of genders and a wide age range, reducing selection bias and ensuring the generalizability of results across diverse patient groups. The presence of common symptoms such as swelling, pain, and fever was consistently noted, reinforcing their role as key indicators of lymphadenopathy. However, ultrasound characteristics, including irregular shape and margin disruptions, were more strongly associated with malignancy, whereas features such as cystic changes and posterior enhancement were less prevalent (12). Ultrasound metrics provided valuable diagnostic information, with parameters such as lymph node size, short-to-long axis ratio, and Doppler indices aligning with established malignancy criteria. The short-to-long axis ratio demonstrated clinical relevance, with higher ratios correlating with malignant lymph nodes and lower ratios associated with benign conditions. The sensitivity of ultrasound in detecting malignancies was notably high at 88.9%, suggesting its effectiveness as an initial screening tool. However, its specificity and negative predictive value, both at 81.8%, indicate limitations in ruling out malignancies in benign cases. This highlights the risk of false-positive and false-negative results, reinforcing the necessity of supplementary diagnostic methods such as fine-needle aspiration cytology (FNAC) or histopathological evaluation to improve diagnostic precision (17).

Comparison with previous literature demonstrates consistency in the findings, as multiple studies have established that ultrasound is a reliable tool for identifying suspicious lymph nodes, particularly when combined with Doppler indices. However, variations exist regarding the sensitivity and specificity values reported across studies, which may be attributed to differences in imaging protocols, operator expertise, and patient characteristics. The logistic regression analysis identified Resistive Index (RI), Pulsatility Index (PI), and lymph node shape as significant predictors of malignancy, with RI emerging as the strongest independent factor. These findings align with prior research emphasizing the role of Doppler indices in differentiating benign from malignant lymph nodes, providing an objective criterion for risk stratification (18). Despite the strengths of this study, several limitations warrant consideration. The reliance on ultrasound as a primary imaging modality introduces an inherent dependency on operator skill, potentially affecting the reproducibility of results. Additionally, the study did not assess interobserver variability, which is a crucial factor influencing the reliability of ultrasound-based diagnoses. The inclusion of a histopathological gold standard strengthens the study's validity; however, a more extensive sample size and multicenter approach would further enhance the generalizability of findings. Another limitation is the lack of microbiological assessment in cases of suspected infectious lymphadenopathy, which could provide insights into differential diagnoses beyond malignancy (19).

Future research should focus on the integration of emerging imaging modalities such as elastography and artificial intelligence-assisted ultrasound interpretation to enhance diagnostic accuracy. A prospective study design with standardized ultrasound protocols and multicentric collaboration would help minimize variability and improve external validity. Additionally, longitudinal follow-up of patients

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with initially benign lymphadenopathy could provide valuable data on the predictive value of ultrasound features in disease progression. The combination of imaging, cytological evaluation, and molecular diagnostics may further refine the diagnostic pathway, ultimately reducing reliance on invasive procedures and optimizing patient management (18-20). The results of this study reinforce the importance of a multimodal approach in diagnosing lymph node malignancies. While ultrasound remains a valuable and accessible diagnostic tool, its limitations necessitate the inclusion of complementary techniques to achieve optimal accuracy. The findings contribute to the ongoing efforts to refine diagnostic algorithms and improve early detection strategies, ultimately leading to better clinical decision-making and patient outcomes.

CONCLUSION

This study underscores the importance of integrating clinical symptoms, ultrasound characteristics, and Doppler indices to enhance the diagnostic accuracy of lymph node malignancies. While ultrasound proved to be an effective initial screening tool with high sensitivity, its limitations in distinguishing benign from malignant cases highlight the necessity of supplementary diagnostic techniques such as fine-needle aspiration cytology or histopathology. The study reaffirmed the diagnostic value of lymph node shape and Doppler indices, particularly the Resistive Index, as significant predictors of malignancy. These findings emphasize the need for a multimodal approach that combines imaging, clinical assessment, and cytological evaluation to reduce diagnostic errors and improve patient outcomes. By refining diagnostic protocols, this research contributes to more precise and early detection of malignancies, ultimately leading to better-informed clinical decision-making and enhanced patient care.

AUTHOR CONTRIBUTIONS

Author	Contribution
Rimsha Iftikhar	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Saima Haider	Methodology, Investigation, Data Curation, Writing - Review & Editing
Awais Ur Rehman Qaiser	Investigation, Data Curation, Formal Analysis, Software

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