Review

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Ultrasound in the comprehensive management of nodal lymphoma: from conventional B-mode to multimodal ultrasound and artificial intelligence

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Abstract

Nodal lymphoma requires precise diagnosis and longitudinal monitoring. Ultrasound is now established as a first-line tool for evaluating superficial lymphadenopathy, and the introduction of shear-wave elastography, contrast-enhanced ultrasound, super-resolution contrast-enhanced ultrasound, and artificial-intelligence-based decision support has expanded its role far beyond simple morphological assessment. This updated review outlines the evolving role of multimodal ultrasound and its advanced applications in the comprehensive management of nodal lymphoma, from initial diagnosis and biopsy guidance to treatment evaluation and prognosis stratification, highlighting current evidence, clinical utility, and future research directions.

Keywords: Lymphoma; Multimodal ultrasound; Elasticity imaging techniques; Contrast-enhanced ultrasonography; Artificial intelligence

Introduction

Lymphoma is a highly heterogeneous malignancy, including Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), in which 90% of cases are NHL. Lymphoma originating from B-cell, T-cell, or natural killer (NK)-cell subsets at different stages of development, and approximately 85-90% of NHL originates from B-cell subsets [1]. In high-income countries, the incidence of B-cell lymphoma is approximately 20 cases per 100,000 population [2]. Several factors, including immune disorders, medications, and infections, contribute to the development of NHL [3]. Lymphoma can be unifocal, multifocal, or diffuse, affecting isolated lymph nodes (LNs) or any organ system. When confined to LNs, it is referred to as nodal lymphoma, clinically presenting as painless lymphadenopathy [2,4].

In recent years, new diagnostic methods and treatment strategies have emerged, significantly improving the prognosis of NHL. However, challenges remain, such as treatment resistance, relapse, and therapy-related toxicity [5]. Although cross-sectional imaging modalities such as CT, MRI, and FDG PET/CT are currently recommended for staging and response assessment, ultrasound (US) has emerged as a valuable complementary tool, particularly for superficial nodal disease, owing to its high spatial resolution (up to 100 μm), real-time assessment, and ability to guide small-volume biopsies. Recent tech-

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nical developments now allow the simultaneous evaluation of nodal morphology, tissue stiffness, microvascular perfusion, and quantitative imaging features through AI-based radiomics. Together, these advances position US as a multiparametric imaging platform with growing relevance in the comprehensive management of nodal lymphoma [4,6] (fig 1).

This review provides a critical overview of established and emerging ultrasound techniques in nodal lymphoma, focusing on their clinical applications, current evidence, and practical limitations.

Ultrasound diagnosis and differential diagnosis in Nodal Lymphoma

Conventional US

Conventional US plays a fundamental role in evaluating superficial lymphadenopathy by assessing LN size, morphology, internal architecture, and vascular patterns. On grayscale imaging, malignant LNs typically exhibit a long-to-short axis (L/S) ratio of less than 2, loss of the echogenic hilum, and heterogeneous internal echotexture [7]. However, conventional US alone is often insufficient to differentiate lymphoma from metastatic lymphadenopathy. In a comparative study involving 62 malignant LNs (24 lymphomas and 38 metastatic nodes), the accuracy of differential diagnosis of conventional US (grayscale combined with color Doppler) were 67.74% to 72.58% in three independent readers [8]. Metastatic LNs more frequently present internal necrosis, appearing as hyperechoic foci, cystic regions, or hypoechoic areas, depending on the necrotic type, whereas lymphomas rarely show necrosis but often display intranodal reticulation. The identification of reticulated intranodal architecture strongly suggests lymphoma, while internal necrosis indicates metastasis (fig 2A,3A) [9]. Lymphomas typically present with smooth, well-defined nodal margins, and approximately half of metastatic LNs show irregular borders.

On color Doppler flow imaging (CDFI), lymphomas exhibit nonspecific vascular patterns, including hilar, peripheral, or mixed (hilar and peripheral) vascularity (fig 2B,C) [10]. The diagnostic value of resistive index (RI) and pulsatility index (PI) remains controversial, with varying cutoff values reported. These discrepancies likely reflect differences in tumor histology and degrees of nodal infiltration. Reported RI and PI values for lymphomatous nodes range from 0.64 to 0.84 and 1.2 to 2.2, respectively, and RI and PI values in lymphomatous nodes are considered higher than in benign reactive nodes, but lower than in metastatic nodes [11,12]. Although one study suggested that RI>0.595 may help distinguish aggressive from indolent lymphomas, the clinical utility of Doppler indices remains limited when used in isolation [13].

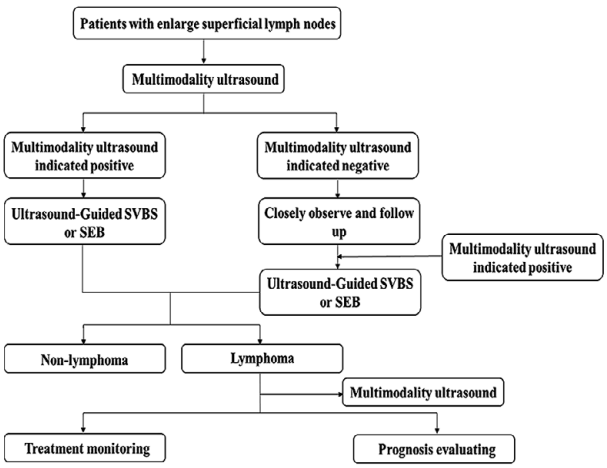


Fig 1. The flowchart of ultrasound in the comprehensive management of nodal lymphoma. SVBS, small volume biopsies; SEB, surgical excisional biopsy.

Shear-wave elastography (SWE)

SWE is an advanced US technique that quantitatively assesses tissue stiffness by measuring the velocity of shear wave propagation. Unlike conventional B-mode US, which relies on differences in acoustic impedance, SWE provides additional diagnostic value by offering quantitative parameters such as shear wave velocity (Vs, m/s) and Young's modulus (E, kPa), calculated as $E=3\rho Vs^2$, where ρ represents tissue density [14]. Among these metrics, mean elasticity (Emean) and maximum elasticity (Emax) have shown the best reproducibility.

In lymphoma, the proliferation of undifferentiated lymphocytes within the nodal capsule increases overall nodal stiffness and contributes to heterogeneous elasticity distributions [14]. A recent meta-analysis by Gao et al, encompassing 16 studies with 1,276 patients and 1,479 LNs, demonstrated that SWE exhibits moderate-to-high diagnostic performance in differentiating malignant from benign lymphadenopathy. Reported cutoff values varied widely (Emax: 15.2–57 kPa; Emean: 18.4–30.6 kPa), likely reflecting differences in US machines, histopathological heterogeneity, and study design. Despite these discrepancies, Emax demonstrated the highest pooled sensitivity at 0.78 (95% CI: 0.69–0.87), while Emean achieved the highest specificity at 0.93 (95% CI: 0.88–0.98), with AUC values of 0.88 and 0.89, respectively [15]. To distinguish metastatic carcinoma from lymphoma within malignant LNs, Chae et al reported that metastatic LNs exhibited an Emean and Vs of 94.87 kPa and 5.63 m/s, while lymphoma nodes measured 42.75 kPa and 3.49 m/s [8]. Another study reported Emax values of 34.18±7.02 kPa and 25.92±4.18 kPa for metastatic and lymphomatous nodes ($F=33.751$; $p<0.001$) [16]. These results show that lymphomatous nodes are generally

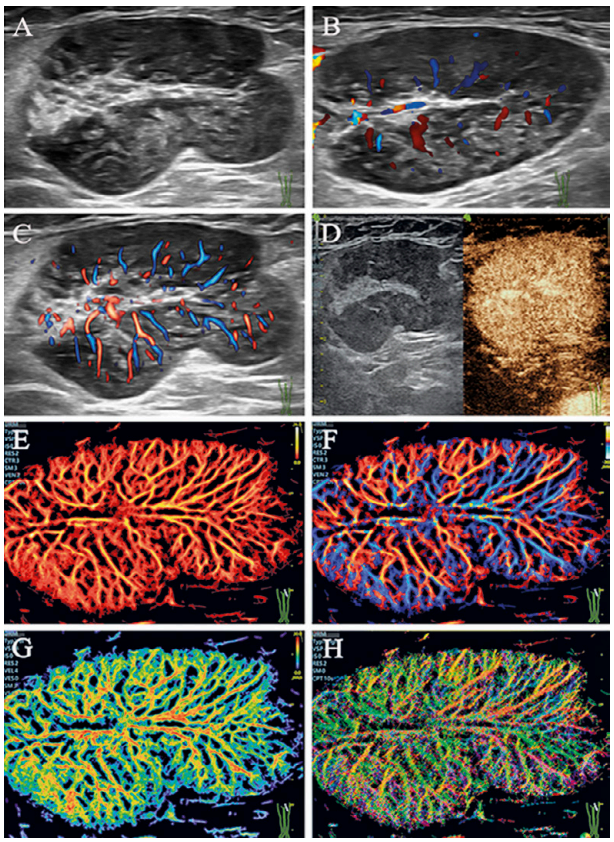


Fig 2. An 80-year-old man with a lymphoma in the left groin: A) Grey-scale ultrasound image; B) Color Doppler image; C) Superb microvascular image; D) CEUS image; E, F, G and H) SR-CEUS images in vascular density mode, direction mode, velocity mode, and angle mode, respectively.

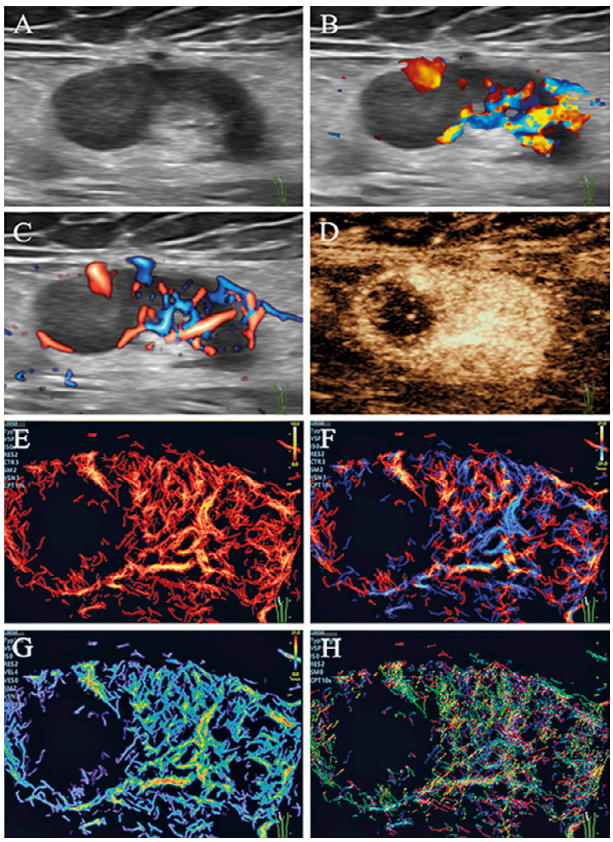


Fig 3. A 71-year-old man with a metastatic node in the right groin: A) Grey-scale ultrasound image; B) Color Doppler image; C) Superb microvascular image; D) CEUS image; E, F, G and H) SR-CEUS images in vascular density mode, direction mode, velocity mode, and angle mode, respectively.

softer than metastatic nodes. Clinically, SWE should be regarded as a complementary tool that enhances lymph-node characterization and assists in biopsy targeting, rather than a standalone diagnostic method.

Contrast-enhanced US (CEUS)

CEUS enhances the real-time visualization of LN microvascular architecture through the intravenous administration of microbubble contrast agents. This technique enables the detection of microvessels with diameters of 100 μm and low-flow vessels, surpassing the sensitivity of CDFI [17]. Common US contrast agents such as SonoVue and Sonazoid provide harmonic imaging under low mechanical index conditions, with SonoVue being a blood-pool agent and Sonazoid also phagocytosed by the reticuloendothelial system, enabling post-vascular imaging [18].

CEUS facilitates both qualitative and quantitative assessment of LNs. Qualitative CEUS includes enhancement intensity, degree, pattern (centripetal, centrifugal, and mixed), presence of perfusion defects, and peripheral ring-like enhancement. The vascular characteristics of lymphomatous nodes vary according to disease stage. In early-stage lymphoma, the lesion typically originates in the parenchyma while sparing the subcapsular region, preserving the hilar vasculature and allowing visualization of central perfusion. As the disease progresses, neovascularization emerges, the hilum becomes obscured, and peripheral or mixed perfusion patterns dominate [19]. Most lymphomas demonstrate rapid, homogeneous hyperenhancement with centripetal or mixed perfusion, as shown in our case (fig 2D), and rarely present with perfusion defects or ring-like peripheral enhancement, which are typical findings of metastatic LNs (fig 3D) [20,21]. A minority of B-cell lymphomas have been reported to exhibit heterogeneous enhancement patterns [22].

Quantitative CEUS provides valuable metrics for hemodynamic characterization and staging lymphomas. These parameters mainly include - Blood volume-related: Peak Intensity (PI), Time-related: Arrival Time (AT), Time to Peak (TP), and enhancement duration (ΔT = TP – AT), Composite: Area Under the Curve (AUC),

integrating both time and intensity characteristics [23]. In 2022, a meta-analysis reported pooled sensitivity and specificity values of 76% (95% CI: 66–83%) and 80% (95% CI: 45–95%) for conventional US in characterizing malignant cervical LNs and the integration of CEUS increased these values to 92% (95% CI: 89–95%) and 91% (95% CI: 87–94%), respectively [24]. Focusing on lymphoma, Deng et al [20] and Nie et al [21] reported that the PI and AUC of lymphomatous LNs are generally higher than those observed in benign lymphadenopathy but lower than those of metastatic LNs. Furthermore, Jiang et al demonstrated that quantitative parameters could assist in staging and subtyping of nodal lymphoma. In staging analysis, a ΔT value < 5.5 s or an ascending slope (AS) >2.58 has been associated with advanced-stage lymphoma, reflecting more robust perfusion kinetics. In pathologic patterns analysis, NHL was characterized by longer AT and TP values (>11.5 s and >18.5 s, respectively) than HL, suggesting a slower contrast uptake pattern in NHL [13]. Despite these advances, the role of quantitative parameters in differentiating malignant superficial LNs remains a subject of debate. TIC parameters are semi-quantitative and sensitive to various physiological and technical factors [25]. Moreover, inconsistencies in data acquisition protocols and analytical methodologies contribute to inter-study variability [26]. Consequently, the standardization of imaging protocols and parameter collection is essential for future research.

Super-resolution contrast-enhanced US (SR-CEUS)

SR-CEUS is developed based on CEUS. It was originally proposed by Mickael Tanter in 2011 and has emerged as a transformative imaging modality over the past decade [27]. Conventional US resolution is constrained by the diffraction limit, typically ranging from 200 μm to 1 mm in clinical practice. Although CEUS can detect vessels smaller than 100μm using intravenously administered microbubbles, it remains insufficient for visualizing capillary-level structures. SR-CEUS circumvents this limitation by employing ultrafast imaging – acquiring thousands of frames per second – to localize and track individual microbubbles with high precision. The accumulated microbubble trajectories are then reconstructed into super-resolution images, achieving spatial resolution as fine as 10-50 μm. In addition to structural visualization, SR-CEUS enables direct measurement of microbubble motion, offering angle-independent, quantitative assessment of blood flow velocity [28]. Representative SR-CEUS images depicting vascular density, direction, velocity, and angularity are shown in figures 2E–H (an 80-year-old male with lymphoma in the left groin) and figures 3E–H (a 71-year-old male with metastatic lymphadenopathy in the right groin).

Zhu et al pioneered the clinical application of SR-CEUS, revealing significantly elevated local flow direction irregularity (LFDI) in metastatic nodes, although differences in microvascular density (MVD) remained insignificant due to limited sample sizes [29]. Subsequent studies have consistently demonstrated the aberrant microarchitecture of malignant lymphadenopathy, yet findings on vascular density remain heterogeneous. He et al reported higher perfusion in benign nodes, attributing malignant hypoperfusion to structural destruction [30]; conversely, Zhang et al observed increased density and fractal dimension in metastases, reflecting vigorous tumor angiogenesis [31]. Despite these discrepancies, a consensus exists regarding the "hemodynamic chaos" of malignancy, characterized by elevated velocity variance and directional disorder. Specifically, regarding lymphoma, Wang et al distinguished the regular, centrifugal "firework-like" enhancement of indolent subtypes from the distorted "starry-sky" patterns of aggressive forms [32]. Collectively, these SR-CEUS features reflect the chaotic neoangiogenesis of neoplastic infiltration, providing a robust basis for differential diagnosis. Future endeavors should prioritize large-scale, standardized multi-center studies to validate these specific imaging signatures, particularly within lymphoma subtypes. Overcoming the statistical limitations inherent in current small-cohort designs is imperative to bridge the gap between experimental exploration and widespread clinical implementation.

Multimodal US

Numerous studies have demonstrated that the combination of conventional US with SWE or CEUS markedly enhances diagnostic accuracy (table I). For instance, Chae et al reported that the addition of SWE to conventional US increased diagnostic accuracy in differentiating cervical metastatic lymphadenopathy and lymphoma from 67.7-72.6% to 80.7-83.9% across three independent readers in a cohort of 62 malignant cervical LNs (24 lymphomas and 38 metastases) [8]. Similarly, in a study differentiating 63 head and neck lymphomas from 80 metastatic nodes, the combination of conventional US and CEUS achieved a high sensitivity, specificity, and accuracy of 85.0%, 81.0%, and 89.9%, respectively [22]. Three-modal US, which combines conventional US + SWE + CEUS, significantly raises the AUC from 0.74 to 0.93 in a retrospective cohort of 170 patients (136 lymphomas and 34 benign cases) with cervical lymphadenopathy, with sensitivity, specificity, and accuracy of 95.6%, 87.5%, and 93.5%, respectively – significantly surpassing the performance of any single modality [20]. By synthesizing morphological features, tissue stiffness, and microvascular perfusion data, multimodal US provides a non-invasive, multifaceted diagnostic platform.

Looking forward, incorporating the capillary-level structural detail provided by SR-CEUS into these multimodal protocols is expected to further refine the precision of lymphoma characterization and longitudinal monitoring.

Artificial intelligence in US imaging

Artificial intelligence (AI), particularly machine learning (ML) and deep learning (DL), has revolutionized medical imaging. ML algorithms are trained to recognize and classify features within images, while DL leverages multilayer neural networks to extract high-level features from complex data automatically [33]. In LN imaging, AI-augmented US has shown significant promise for enhancing diagnostic precision.

A comprehensive meta-analysis of 19 studies, including 2,354 patients, evaluated the US-based AI systems in differentiating benign from malignant LNs. The pooled sensitivity and specificity were 83.6% and 85.0%, respectively, with a diagnostic odds ratio (DOR) of 33.33 [34]. Specific to lymphoma, Liu et al. developed a composite AI model integrating features derived from conventional US and CEUS to distinguish cervical tuberculous lymphadenitis (CTL) from primary lymphoma. Among 155 enrolled patients, three models (conventional US, CEUS, and conventional US plus CEUS) were constructed using the least absolute shrinkage and selection operator (LASSO) regression and logistic regression algorithms. The combined model outperformed both single-modality approaches, achieving AUCs of 0.958 and 0.946 in the training and validation sets, respectively, with corresponding accuracies of 91.7% and 87.2% [35]. Building on this, Jiang et al proposed a radiomics-based AI model leveraging multi-phase CEUS images to classify superficial LNs in 426 patients. In their study, multi-phase CEUS radiomics models, which integrated features across all imaging phases (the prevascular phase, vascular phase, and postvascular phase), demonstrated a good performance with AUCs of 0.838 (training set), 0.739 (internal validation set), and 0.733 (external validation set). Model 3 (multi-phase CEUS radiomics + conventional US) achieved the best performance, with AUCs of 0.943 (training set), 0.823 (internal validation set), and 0.785 (external validation set) [36].

Beyond diagnosis, AI-assisted US has also been explored for lymphoma risk stratification. Weng et al developed a predictive model incorporating both clinical indicators (e.g, LDH levels, extranodal involvement) and US features (e.g, L/S ratio, enhancement intensity, perfusion defects) to differentiate aggressive from indolent lymphomas in 236 patients [37]. This integrated model demonstrated superior diagnostic efficacy (AUC=0.87) compared to the clinical model alone (AUC=0.78; $p<0.001$). Aggressive lymphomas exhibited significantly higher enhancement intensity (OR=7.91–10.43, $p<0.01$) and more perfusion defects (19.0%) than indolent types (2.6%), consistent with their greater angiogenesis and vascular heterogeneity due to rapid proliferation and immature neovascularization.

Despite encouraging outcomes, the current reliance on retrospective, single-center data with limited external validation remains a challenge. Due to potential intersystem variability, AI currently serves as a decision-support. Establishing standardized image acquisition protocols and multi-center datasets is crucial for the future implementation of AI in routine lymphoma management.

Table I. Multimodal ultrasound characteristics of nodal lymphoma vs. metastatic lymphadenopathy

Ultrasound modality	Feature category	Feature	Lymphoma	Metastatic lymph nodes	Reference
Conventional US	Echogenicity	Internal echo pattern	Reticular or homogeneous hypoechoic pattern; necrosis uncommon	Internal necrosis (hyperechoic foci, cystic or heterogeneous hypoechoic areas)	[7,9]
	Morphology	Margins	Smooth, well-defined	Often irregular or ill-defined	[9]
CDFI	Vascular distribution	Blood flow pattern	Hilar, peripheral, or mixed (hilar and peripheral)	Predominantly peripheral or mixed vascularity	[10]
SWE	Tissue stiffness	Elasticity	Lower stiffness values	Higher stiffness values	[8,16]
CEUS	Enhancement pattern	Temporal characteristics	Rapid, homogeneous hyperenhancement	Heterogeneous enhancement with perfusion defects	[20,21]
		Spatial distribution	Centripetal or mixed enhancement	Ring-like peripheral enhancement	[20,21]
SR-CEUS	Microvascular architecture	Microvascular pattern	Centrifugal “firework-like” enhancement in indolent subtypes; distorted “starry-sky” pattern in aggressive forms	Chaotic microvascular flow with increased velocity variance and directional disorder	[29-32]

US, ultrasound; CDFI, color Doppler flow imaging; SWE, shear wave elastography; CEUS, contrast-enhanced ultrasound; SR-CEUS, super-resolution CEUS.

Ultrasound in treatment monitoring and prognosis assessment

Accurate evaluation of treatment response and prognosis is crucial for individualized lymphoma management. Microvascular architecture and hemodynamic patterns serve as critical biomarkers for therapeutic monitoring in hematologic malignancies [38]. Since angiogenesis is integral to lymphoma progression and represents a key therapeutic target, multimodal US – particularly CEUS – offers a noninvasive, radiation-free alternative for the real-time, dynamic assessment of morphological and perfusion changes [39,40].

Prognostic stratification

Initial sonographic features provide significant prognostic insights. In a study of 111 DLBCL patients, Lu et al found that absence of the lymphatic hilum before chemotherapy was significantly associated with poorer overall survival (OS; HR=5.241, p=0.007) and progression-free survival (PFS; HR=3.31, p=0.002). A novel prognostic model incorporating hilum status and treatment response into the International Prognostic Index (IPI) significantly outperformed the IPI alone, achieving higher AUCs for 5-year PFS (0.82 vs. 0.68) and OS (0.86 vs. 0.76) [41]. Similarly, Duan et al retrospectively analysed 186 DLBCL patients with cervical lymphadenopathy and identified TP and PI on CEUS as independent prognostic factors ($p<0.05$). Notably, patients with hyper-enhancement on CEUS had significantly shorter PFS compared to those with non-hyper-enhancement ($p<0.001$) [42].

Therapeutic monitoring and interim assessment

In a study of 56 NHL patients undergoing R-CHOP or CHOP regimens, Lu et al utilized CEUS to monitor therapeutic response across three treatment cycles. Their results showed significant reductions in the short-to-long (S/L) axis ratio, peak intensity (PI), gradient, and perfusion area (all $p<0.05$). Notably, the non-complete response (non-CR) group exhibited a significantly longer pre-treatment arrival time (AT) (p=0.024), suggesting that delayed contrast kinetics may correlate with a higher tumor burden and unfavorable outcomes. Furthermore, a strong positive correlation was observed between baseline PI and its subsequent percentage reduction post-treatment ($r=0.736$, $p<0.001$). An early reduction in CEUS-derived PI≥60 % after two cycles served as a robust predictor of complete metabolic response on interim PET/CT. These findings suggest that higher baseline PI may predict a better mid-treatment response and could be used to tailor treatment intensity to minimize toxicity in responsive patients [40].

US, particularly CEUS, holds substantial promise in prognostic stratification and early therapeutic monitoring in lymphoma (Table II). Ongoing prospective trials (NCT05584234, NCT05723117) are validating CEUS-based response criteria against Lugano classification endpoints. Future multicenter trials and standardization of CEUS protocols are warranted for its broad clinical implementation.

Ultrasound-guided small volume biopsies (SVBs)

US-guided small volume biopsies (SVBs), including fine needle aspiration (FNA) and core needle biopsy (CNB), have become increasingly prevalent in the diagnostic workup of lymphoma due to their minimally invasive nature and high diagnostic yield. While US-guided FNA facilitates cytological assessment, it is inherently limited by its inability to evaluate tissue architecture, leading to variable sensitivity [43,44]. However, diagnostic performance has improved through the integration of ancillary techniques-including flow cytometry, cytogenetics, and molecular diagnostics-alongside advancements in cell block preparation and real-time US guidance [45]. FNA is currently most effective in detect-

Table II. Clinical value of quantitative CEUS parameters in lymphoma assessment

	Key parameters	Main findings and diagnostic criteria	References
Differential Diagnosis	PI, AUC	Lymphoma vs Benign: PI/AUC significantly higher in lymphoma. Lymphoma vs Metastasis: PI/AUC generally lower than in metastatic LNs.	[20,21]
Staging	ΔT, AS	Advanced Stage: Associated with hyperperfusion. Cut-off: ΔT<5.5 s or AS>2.58 indicates a higher stage.	[13]
Histological subtyping	AT, TP	NHL vs HL: NHL shows slower uptake kinetics. Criteria: AT>11.5 s and TP>18.5 s suggest NHL.	[13]
Prognostic stratification	TP, PI	DLBCL: Hyper-enhancement correlates with shorter PFS. TP and PI were identified as independent prognostic factors.	[42]
Therapeutic monitoring	PI, AT	Prediction: Longer baseline AT correlates with non-CR. Response: Early reduction in PI (≥ 60%) after 2 cycles predicts a complete response.	[40]

CEUS, contrast-enhanced ultrasound; PI, Peak Intensity; AUC, Area Under the Curve; ΔT, enhancement duration; AS, Ascending Slope; AT, Arrival Time; TP, Time to Peak; NHL, Non-Hodgkin Lymphoma; HL, Hodgkin Lymphoma; DLBCL, Diffuse Large B-Cell Lymphoma; PFS, Progression-Free Survival; CR, Complete Response

ing disease recurrence or transformation to high-grade lymphoma [46]. Retrospective multicenter studies have shown that FNA more frequently requires multiple attempts in primary diagnosis compared to recurrence or transformation assessment, underscoring its greater utility in the latter context [43,46]. Notably, in relapsed/refractory diffuse large B-cell lymphoma (DLBCL), US-guided FNA combined with flow cytometry achieved a sensitivity of 94.7% [47].

In contrast, CNB provides histological samples suitable for immunohistochemical and molecular analyses. A meta-analysis by Kwon et al demonstrated that US-guided CNB achieves a sensitivity of 94% (95% CI: 89%–96%) and a specificity of 100% (95% CI: 94%–100%) for lymphoma diagnosis, with a low complication rate of 1% (95% CI: 0%–3%) [48]. The addition of CEUS to guide CNB further improves diagnostic precision by enabling targeted sampling of viable tumor regions [49]. CNB has thus emerged as a practical alternative to surgical excisional biopsy (SEB), particularly in patients unfit for surgery or with suspected relapse. However, several factors influence the diagnostic efficacy of CNB. Needle gauge significantly impacts performance; larger-bore needles (<18 G) yielded higher pooled sensitivity (97% vs. 94%, $p<0.001$) and specificity (100% vs. 95%, $p<0.001$) than smaller-bore needles (≥18 G) [45]. Moreover, diagnostic yield differs by histological subtype: CNB demonstrates superior sensitivity in NHL (96.7%) but is less effective for HL (66.0%), likely due to the latter's complex tissue architecture and the sparse distribution of diagnostic Reed–Sternberg cells [50,51]. In HL cases, repeat CNB or SEB is often warranted to achieve a definitive diagnosis.

The choice between CNB, FNA, and SEB should be tailored to patient-specific factors, suspected pathology, and institutional expertise. While less invasive modalities show strong potential, SEB remains indispensable in diagnostically challenging or inconclusive cases. Continued comparative studies and integration of multimodal approaches are essential for optimizing biopsy strategies in lymphoma.

Conclusion and future perspectives

In conclusion, multimodal US has evolved from a basic morphological tool into a sophisticated multiparametric platform – integrating tissue stiffness (SWE), microvascular kinetics (CEUS), capillary-level architecture (SR-CEUS), and AI-driven radiomics – that profoundly enhances the management of nodal lymphoma. However, several challenges must be addressed before its full clinical potential can be realized.

Technical standardization remains the primary hurdle. Future efforts must prioritize the development of system-independent protocols to mitigate variability in stiffness cut-offs and perfusion metrics across different manufacturers. While SR-CEUS and AI offer unprecedented diagnostic depth, their transition from the laboratory to the bedside requires optimizations in imaging depth, motion compensation, and validation through robust multicenter datasets. Furthermore, future research should account for biological and anatomical heterogeneity, ensuring that diagnostic strategies are tailored to specific nodal stations and histological subtypes.

Ultimately, shifting the focus from retrospective diagnostic studies to prospective prognostic modeling is essential. By integrating standardized sonographic biomarkers with histopathological and molecular data, multimodal US is poised to become an indispensable pillar in the personalized, precision-guided management of nodal lymphoma.

Conflict of interest: none

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