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Differentiating benign and malignant superficial lymph nodes using super-resolution contrast enhanced ultrasound - a pilot study

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Abstract

Objective The study aimed to evaluate the feasibility and clinical value of super-resolution contrast enhanced ultrasound (SR CEUS) in the differential diagnosis of superficial lymph nodes (LNs) and to establish an appropriate imaging protocol.

Method Patients with enlarged superficial LNs from March to August 2024 were prospectively enrolled. SR CEUS were performed post bolus injection of 0.5 ml and 1.0 ml microbubble contrast agents for 6 s. Microvascular density (MVD), flow weighted density of the vessel (FWVD), perfusion index (PI), fractal dimension (FD), velocity variance (Vel var) and mean velocity (Vmean) were generated from SR CEUS images. The parameters were statistically analyzed to differentiate benign from malignant LNs. The dosage of contrast agent and the duration of image acquisition suitable for diagnosis were explored.

Results 34 malignant and 20 benign LNs were included. Post 0.5 ml injection, the benign LNs showed significantly higher MVD, FWVD, PI and lower Vel var compared with malignant LNs from the 1st to 6th second, and the gap of parameters between benign and malignant LNs increased over time; Post 1.0 ml injection, no significant difference existed between benign and malignant LNs in terms of all parameters.

Conclusions This study demonstrated the feasibility of using SR CEUS for the differential diagnosis of superficial LNs, with 0.5 ml bolus injection of contrast agent and 6 s acquisition time recommended for clinical practice. Parameters MVD, FWVD, PI & Vel var could serve as imaging markers for clinical evaluation of superficial LNs.

Clinical trial number Not applicable.

Highlights

- Injection dose affected MVD in malignant LNs, not in benign LNs.

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- 0.5 ml bolus injection and 6 s acquisition were recommended for SR CEUS.
- MVD, FWVD, PI, Vel var could be markers identifying malignant LNs.
- Malignant LNs showed sparser vessels, lower perfusion, greater flow heterogeneity.

Keywords Super-resolution contrast enhanced ultrasound, Superficial lymph nodes, Microvascular density, Differential diagnosis

Introduction

Superficial lymph node (LN) enlargement is a common clinical manifestation arising from various etiologies including infections, lymphomas, and metastasis, etc [1–3]. The accurate diagnosis of lymphadenopathy, especially the differentiation between benign and malignant, is crucial for determining appropriate treatment and predicting prognosis [1, 3, 4]. In clinic, the gold standard for LN diagnosis is biopsy (either through core-needle biopsy or surgical excision), which is an invasive procedure carrying risks such as bleeding, infection, and damage to surrounding tissues. Moreover, it may not be suitable for some patients, particularly those with comorbidities or in whom the interesting LN are difficult to access [5]. Therefore, non-invasive diagnostic methods for identifying benign and malignant lymphadenopathy possess immense clinical value.

Ultrasound is widely recognized as the primary imaging modality for evaluating superficial lymphadenopathy due to its non-invasiveness, real-time imaging capabilities, and cost effectiveness [6–8]. Although conventional ultrasound can provide valuable information for initial evaluation, it has limitations in accurately differentiating between benign and malignant LNs, as some features may overlap [1, 9].

It has been demonstrated that microvessel parameters, including microvascular density, distribution and perfusion characteristics, were significantly different between benign and malignant tissues [10, 11]. Nowadays, as an adjunct to conventional ultrasound, contrast-enhanced ultrasound (CEUS) is widely used in clinic to evaluate tissue perfusion [3, 12]. Benefiting from dynamic imaging of vascular & microvascular perfusion, CEUS provided better diagnostic accuracy in identifying benign and malignant LNs, mainly based on different vascularity and perfusion patterns within LNs [13–16]. Nevertheless, the interpretation of CEUS results is operator-dependent. Moreover, quantitative parameters derived from time-intensity cure (TIC) analysis of CEUS clips remain controversial in identifying malignant superficial LNs [1, 17, 18]. These drawbacks hindered the widespread application of CEUS in the assessment of superficial LNs.

Super-resolution contrast enhanced ultrasound (SR CEUS) emerged as a novel technique that offers high resolutions in visualizing microvascular structures (19, 20). It also has the ability to provide objective parameters regarding the morphology and hemodynamics of microvascular networks, which can overcome some of the limitations of CEUS and might be utilized for differentiating between benign and malignant lymphadenopathy [21]. In this study, we aimed to explore the feasibility of SR CEUS in the differential diagnosis of benign and malignant superficial lymphadenopathy, and to establish an appropriate imaging protocol.

Materials and methods

Study patients

This study was approved by the Ethics committee of Tongji Medical College of Huazhong University of Science and Technology (No: 2024-S213). A written consent was obtained from each participant.

This study prospectively enrolled patients who underwent percutaneous biopsy of enlarged superficial LNs at Tongji Hospital Affiliated to Tongji Medical College between March and August 2024 consecutively. The inclusion criteria were as follows: (1) age over 14 years old with stable vital signs; (2) patients without history of surgery around evaluated LNs (3). patients with no history of radiotherapy, chemotherapy, targeted drug therapy, or anti-tuberculosis treatment. The exclusion criteria were as follows: (1) poor ultrasound image quality resulting from inevitable LNs shaking caused by the pulsation of large blood vessels; (2) patients with side effects during contrast-enhanced ultrasound imaging; (3) patients with uncertain pathological diagnosis.

Ultrasound imaging protocol

The Mindray Resona A20 Ultrasound system (Mindray Biomedical Electronics Co., Ltd., Shenzhen, China), equipped with a SL10-3U linear array transducer (frequency 2.5–11.0 MHz) was used for detailed ultrasound scanning and SR CEUS of superficial LNs prior to ultrasound-guided percutaneous biopsy. All ultrasound data acquisition were performed with the same settings. The ultrasound scanning and subsequent ultrasound guidance provided for biopsy were completed by three board-certified radiologists (W.Z., DC.T. and HM.Y., with 15, 12, and 15 years of experience, respectively).

All patients were positioned in a proper posture breathing naturally. The transducer was fixed on a section allowing for clear visualization of enlarged superficial LNs after systematic ultrasound scanning. Each vial of SonoVue (Barcco, Milan, Italy) was reconstituted by adding 5 mL of saline (0.9% NaCl) solution and shaken

evenly according to the manufacturer's recommendations. A bolus of 0.5 ml reconstituted suspension was injected via an indwelling catheter in the upper limb vein, followed by flushing with 5 mL of saline. While the ultrasound microbubbles reached the LNs, SR CEUS data of the whole field of view or a selected square field of view including the interested LN were acquired for 6 s at a frame rate of 500 fps. Subsequently, the microvascular images of the field of view including LNs were automatically depicted in real time. 10 min later, while ultrasound confirmed the absence of circulating microbubbles, another bolus of 1.0 ml Sonovue suspension was injected, then the image acquisition procedure was the same as that aforementioned.

Quantification parameters

Quantitative parameters including microvascular density (MVD), flow weighted density of the vessel (FWVD), fractal dimension (FD), perfusion index (PI), mean Velocity (Vmean) and velocity variance (Vel var), were generated offline by using SR CEUS processing software (SR CEUS Platform, Mindray Biomedical Electronics Co., Ltd., Shenzhen, China). Based on B-mode images and the corresponding SR CEUS microvascular images, the ROIs were set manually to cover the interesting LNs while avoiding surrounding large blood vessels in the SR CEUS Platform following the consensus reached by three radiologists (JW.H., XF.Z. and HM.Y., with 3, 6, and 15 years of experience, respectively).

The formulations of each parameter were as follows:

MVD was defined as the ratio of the number of microvessel pixels to the total number of pixels in the ROI, measuring the abundance of microvessels within the ROI.

$$MVD = \frac{Microvessel\ Pixels}{OverallPixels} \tag{1}$$

FWVD was defined as the ratio of the sum of the vessel pixel values (densities) to the total number of pixels in the ROI, measuring the volume of blood flow within the ROI.

$$FWVD = \frac{\sum Microvessel\ Pixels}{Overall\ Pixels} \tag{2}$$

FD was defined as the ratio of graphical detail changes to measurement scale changes, describing the complexity of microvessel morphology within the ROI.

$$FD = \lim_{S \to 0} \frac{\log N\,(s)}{\log 1/s} \tag{3}$$

PI was defined as the product of mean blood flow velocity and microvascular density in the ROI, describing the perfusion level within the ROI.

$$PI = \bar{V} \times MVD \tag{4}$$

Vel var was used to measure the degree of dispersion of velocity within the ROI.

$$Vel\ Var = \frac{1}{N-1} \sum_{i=1}^{N} |v_i - \bar{v}| \tag{5}$$

Statistical analysis

All data were statistically analyzed using SPSS 27.0 software (*SPSS Inc.*, *Chicago*, *Illinois*, *USA*). Quantitative data are expressed as the mean ± standard deviation (SD). Non-parametric tests were used due to the small sample size involved in this study. All LNs were grouped according to their benign or malignant diagnoses as well as the injection dose. Then the average values of each parameter were calculated and the parameter-time curves were plotted. The comparisons of parameters between 0.5 ml and 1.0 ml bolus injections in both benign and malignant lymph nodes were conducted using Wilcoxon tests. Mann-Whitney tests were used to compared the parameters between benign and malignant LNs post 0.5 ml bolus injection as well as 1.0 ml bolus injection. $p < 0.05$ were considered statistically significant among all tests.

Results

Patient characteristics

54 patients with age of 48.74 ± 8.95 (mean ± SD) were enrolled in this study. Among them, 34 patients suffered from malignant superficial LNs and 20 patients had benign superficial LNs. According to pathology, this study comprised 54 enlarged superficial LNs (22 metastatic LNs, 12 lymphomas, 16 reactive LNs and 4 tuberculous). Detailed enrollment process was shown in Fig. 1. The clinical characteristics of patients included were shown in Table 1.

Ultrasound imaging

All patients underwent SR CEUS successfully without any side effects. Compared with conventional ultrasound, SR CEUS provided a detailed visualization of the internal microvascular structure of LNs and their blood flow maps. At each time point, SR CEUS images can be switched among four modes, including vascular density, flow, direction & velocity modes as needed (Fig. 2).

The vessels inside the LNs and surrounding tissues gradually increased over time within 6 s. By using offline processing software, ROIs were set to cover interested LNs, and parameters MVD, FWVD, FD, PI, Vel var and

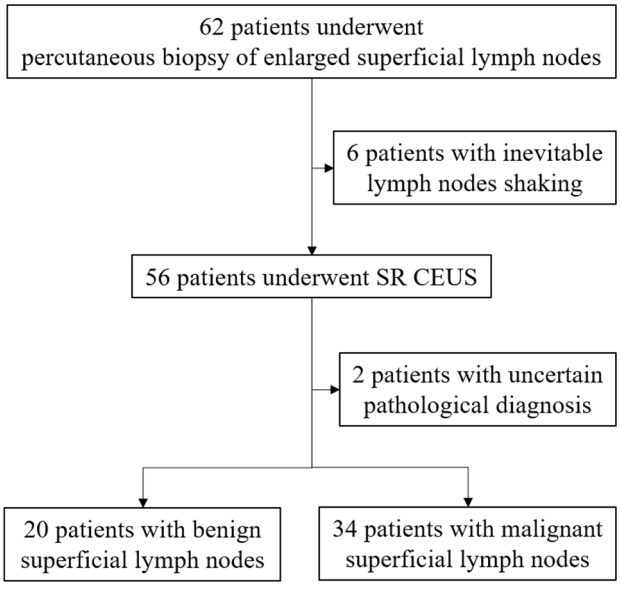

Fig. 1 Flowchart of participants enrolled in this study. 8 of 62 patients with enlarged superficial LNs were excluded due to LN shaking and uncertain pathological diagnosis. 54 participants (20 with benign LNs and 34 with malignant LNs) were included in the statistical analyses. SR CEUS = super-resolution contrast enhanced ultrasound, LN = lymph node

Table 1 Clinical characteristics of participants included in this study

	Benign ($n=20$)	Malignant ($n=34$)
Age (year)	36 ± 11.29	58.35 ± 11.13
Gender		
Female	$n=16$ (80.0%)	$n=4$ (11.7%)
Male	$n=4$ (20.0%)	$n=30$ (88.3%)
Diameter (cm)		
Long-axis	2.7 ± 0.72	3.2 ± 0.79
Short-axis	1.2 ± 0.61	2.1 ± 0.57
Location		
Neck	18(90.0)	28(82.3)
Axilla	2(10.0)	4(11.7)
Groin	0(0)	2(6.0)

Vmean generated from SR CEUS images at each second were collected for subsequent analyses (Fig. 3).

Quantitative parameters of SR CEUS between 0.5 ml and 1.0 ml bolus injection

It was found that MVD, FWVD, PI, and FD increased over time, while Vel var decreased over time, and Vmean did not show significant changes. In addition, the features of the changes in these parameters over time were consistent in both benign and malignant LNs, regardless of whether the injection dose was 0.5 ml or 1.0 ml. (Fig. 4)

In malignant LNs group, when compared with 0.5 ml bolus injection, 1.0 ml bolus injection can achieve significantly higher MVD and FWVD, while PI, FD, Vel var and Vmean didn't show significant difference at 6th second. (Figures 4 and 5) (Table 2).

In contrast, in benign LNs group, no significant differences exited in terms of all parameters between 0.5 ml and 1.0 ml bolus injection (Figs. 4 and 5).

Quantitative parameters of SR CEUS between benign and malignant lymph nodes

After 0.5 ml bolus injection, from 1st to 6th second, the parameters MVD, FWVD & PI of benign LNs were all significantly higher than those of malignant LNs, while Vel var of malignant LNs was significantly greater than that of benign LNs. No significant difference existed regarding FD & Vmean between benign and malignant LNs (Table 3). Moreover, the gap between benign and malignant LNs increased over time in terms of average values of MVD, FWVD, PI & Vel var (Fig. 4).

Specifically, SR CEUS images at the 6th second showed that benign superficial LNs had higher MVD (0.50 ± 0.21 vs. 0.24 ± 0.17), FWVD (2.20 ± 1.24 vs. 0.90 ± 0.85), PI (11.74 ± 6.72 vs. 6.49 ± 4.57) and lower Vel var (122.35 ± 32.65 vs. 180.40 ± 43.70), and similar FD (1.64 ± 0.10 vs. 1.58 ± 0.18) & Vmean (22.74 ± 5.83 vs. 25.21 ± 4.30) as compared with malignant LNs. (Fig. 6). Nevertheless, subgroup analyses revealed that no significant difference existed between lymphomas & metastatic LNs in terms of MVD (0.30 ± 0.12 vs. 0.21 ± 0.19, $p=0.37$), FWVD (1.01 ± 0.53 vs. 0.81 ± 1.06, $p=0.46$), FD (1.64 ± 0.13 vs. 1.53 ± 0.21, $p=0.37$), PI (7.98 ± 3.67 vs. 5.42 ± 5.12, $p=0.29$), Vel var (172.26 ± 28.63 vs. 186.21 ± 53.49, $p=0.94$) and Vmean (26.60 ± 3.81 vs. 24.22 ± 4.64, $p=0.46$).

Unfortunately, after 1.0 ml bolus injection, SR CEUS images showed that all parameters were not significantly different between benign and malignant LNs all the time.

Discussion

In this study, microvessels within superficial LNs were depicted rapidly and efficiently by using a clinical ultrasound apparatus through SR CEUS approach. Previously, ultrasound microvascular imaging was generally achieved by ultrasound microbubble data acquisition and subsequent post-processing computation, which were indeed time-consuming and primarily conducted by engineers [19–23]. In contrast, the protocol of this study was concise enough to be accomplished by radiologists and physicians independently without the need for algorithm assistant. Therefore, SR CEUS maintained some of the core merits of ultrasound examination, which were real-time, convenient and user-friendly.

When differentiating benign and malignant LNs, the sensitivity, specificity and accuracy of conventional ultrasound were 51%, 47% and 55%, respectively, while the sensitivity, specificity and accuracy of contrast-enhanced

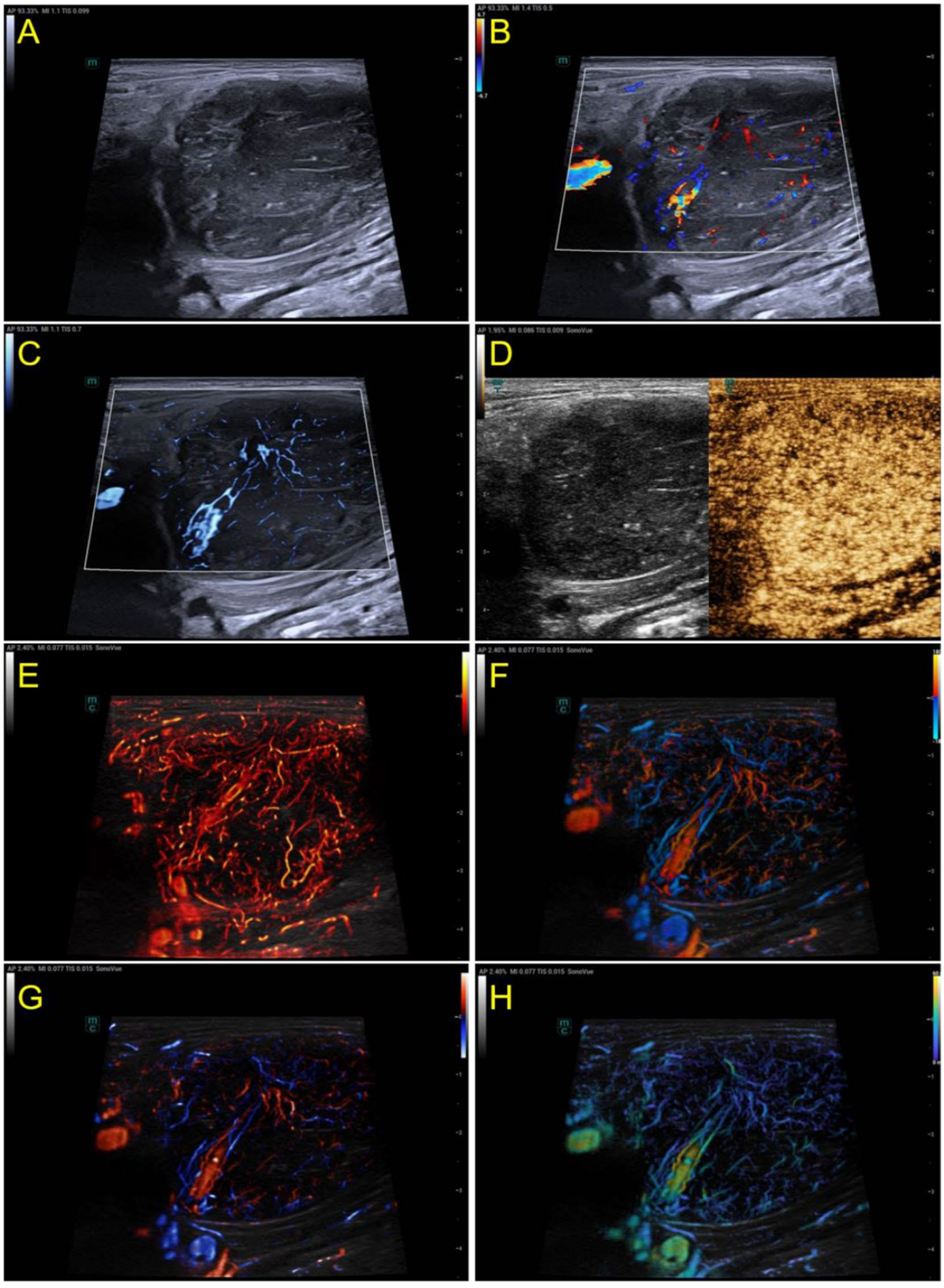

Fig. 2 Ultrasound images at the same section in a patient with lymphoma in the right neck. (**A**) Grey-scale ultrasound image of the enlarged lymph node, (**B**) Color Doppler image of the lymph node, (**C**) Ultra-sensitive microvascular image of the lymph node, (**D**) CEUS image of the lymph node, (**E, F, G & H**) Super-resolution contrast enhanced ultrasound images of the lymph node post 0.5 ml bolus injection of contrast agent in vascular density mode, flow mode, direction mode & velocity mode, respectively

ultrasound (CEUS) reached 84%, 79% and 80%, respectively. Moreover, the efficacy of ultrasound ultra-sensitive microvascular imaging lies between that of Doppler ultrasound and CEUS [1, 6, 9, 17, 24]. These results suggested that more detailed vascular and perfusion information could be more beneficial for distinguishing between benign and malignant LNs [25]. Since ultrasound microbubbles can gradually fill all vessels

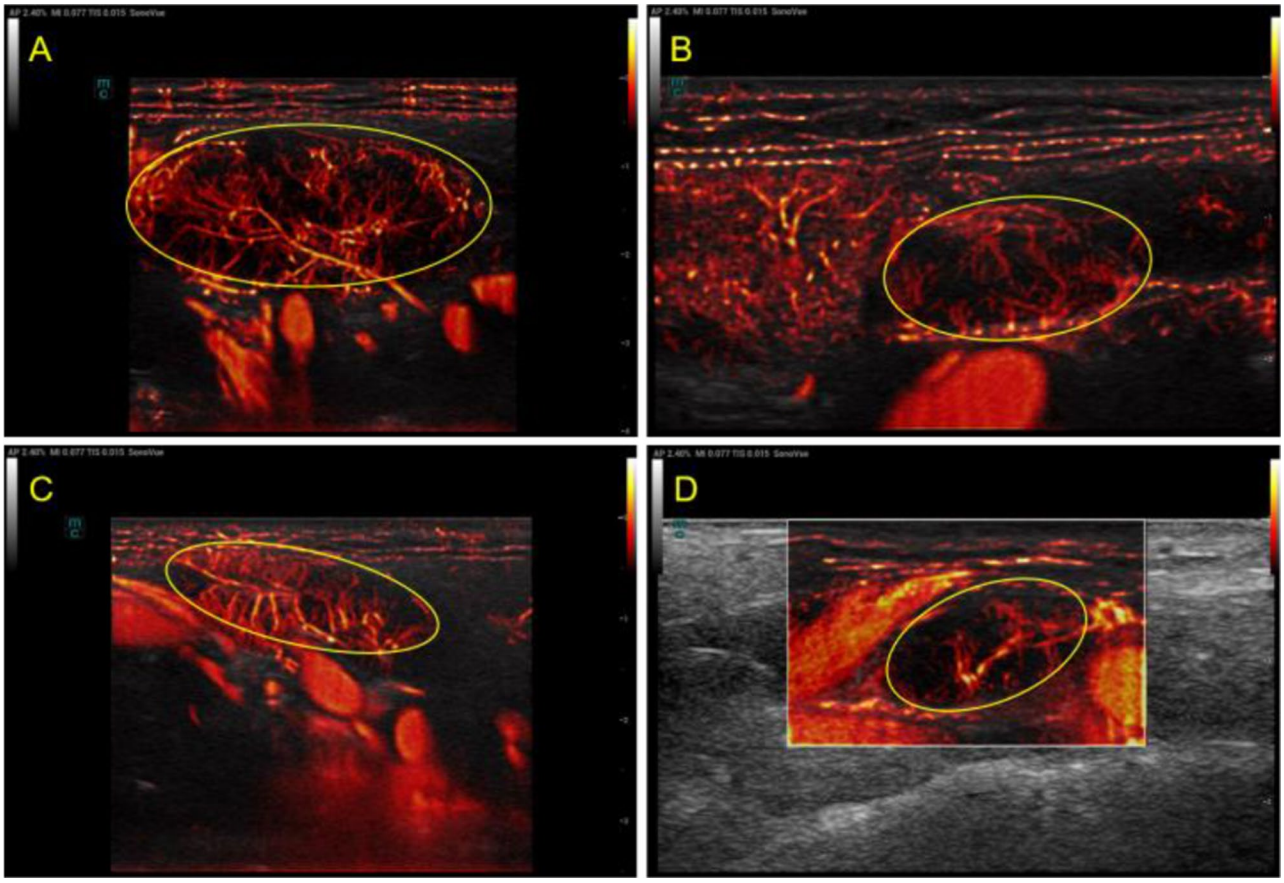

Fig. 3 The ROI setting on SR CEUS images for quantitative analyses. An ellipse ROI was placed to cover the interested lymph node and avoid surrounding larger vessels in each image. (**A**) SR CEUS of the whole field of view in a patient with metastatic carcinoma of lymph node in the left neck post 0.5 ml bolus injection of contrast agent, (**B**) SR CEUS of the whole field of view in a patient with lymphoma in the left neck post 0.5 ml bolus injection of contrast agent, (**C**) SR CEUS of the whole field of view in a patient with reactive lymphadenitis in the right neck post 0.5 ml bolus injection of contrast agent, (**D**) SR CEUS of a selected square field of view in a patient with lymph node tuberculosis in the left neck post 0.5 ml bolus injection of contrast agent

including capillaries, CEUS has the potential to provide integrate information of the whole microvascular networks [12, 16]. In order to avoid inter-operator variability in the interpretation of results, quantitative analysis of CEUS had developed for several year, and time-intensity curve (TIC) fitting of dynamic CEUS was established to provide perfusion parameters [26–28]. However, this was a semi-quantitative analysis and its parameter values were vulnerable to various factors, leading to the reproducibility been compromised [29]. In addition, due to the limitation of spatial resolution, visualization and analysis of microvascular network was not available in CEUS images. These shortcomings had partly resulted in the ongoing controversy regarding CEUS quantitative analysis in distinguishing between benign and malignant LNs [1, 17, 26]. Accordingly, to obtain microvascular network images and the objective values of their hemodynamic parameters, the present study employed SR CEUS in patients with enlarged superficial LNs and demonstrated the feasibility of using SR CEUS for the visualization of microvessels within human superficial LNs in routine clinic.

This study found that both 0.5 ml and 1.0 ml of Sonovue bolus injection can lead to SR CEUS imaging successfully, and quantitative analyses through multiple microvascular parameters demonstrated that the vessels within LNs were depicted and increased gradually over time. In addition, some parameters derived from 0.5 ml bolus injection showed significant difference between benign and malignant superficial LNs, while 1.0 ml bolus injection failed to do so.

Specifically, after 0.5 ml bolus injection, benign LNs had significantly higer MVD, FWVD & PI, and significantly lower Vel var, and similar Vmean compared with malignant LNs. These results indicated that malignant LNs had sparser vessels and lower perfusion compared to benign LNs, which were consistent with previous studies [21, 26, 30]. The Vel var of the malignant LNs was significantly higher than that of the benign LNs. This result suggested that the distribution of blood flow velocity in malignant LNs is more chaotic. Previous CEUS study has

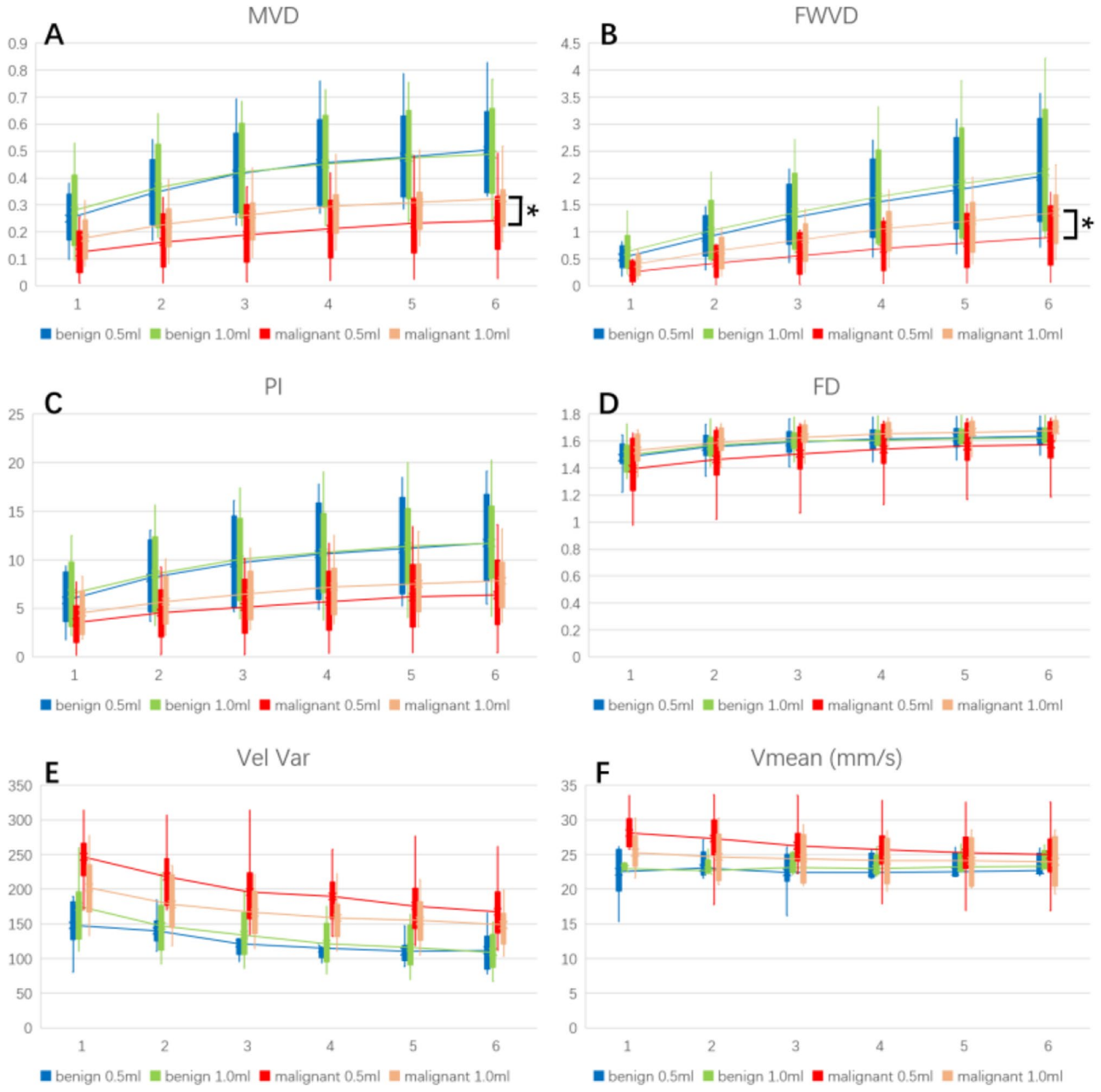

Fig. 4 Parameter-time curves derived from SR CEUS images of benign and malignant superficial LNs post 0.5ml & 1.0 ml bolus injection of Sonovue. (**A-D**) MVD, FWVD, PI and FD increased over time, (**E**) Vel Var decreased over time, (**F**) Vmean did not show significant changes. *$p < 0.05$ showing that in malignant LNs, a 1.0 ml injection dose resulted in significantly higher MVD and FWVD compared to a 0.5 ml injection dose by SR CEUS images at 6th second

indicated that in the high-perfusion areas of both benign and malignant LNs, the perfusion volume is similar, while in the low-perfusion areas, the perfusion is higher in the benign group, resulting in worse overall perfusion and greater flow heterogeneity in the malignant LNs [31]. No significant difference existed between benign and malignant LNs regarding FD, which demonstrated similar complexity of blood vessels between benign and malignant LNs. Overall, these results suggested that malignant LNs were mainly characterized by sparser blood vessels, lower perfusion and greater blood flow heterogeneity. Therefore, as for superficial LNs, in the areas invaded by malignancy, blood vessels might decrease and blood flow might slow down, and angiogenesis should not be a main feature. The LN vasculature comprises arteries, capillaries, high endothelial venules (HEVs) and veins. Previous studies demonstrated that different etiologies such as inflammation, lymphoma and metastasis induced different alterations in the lymph node microenvironment, which in turn caused varied angiogenesis and vascular

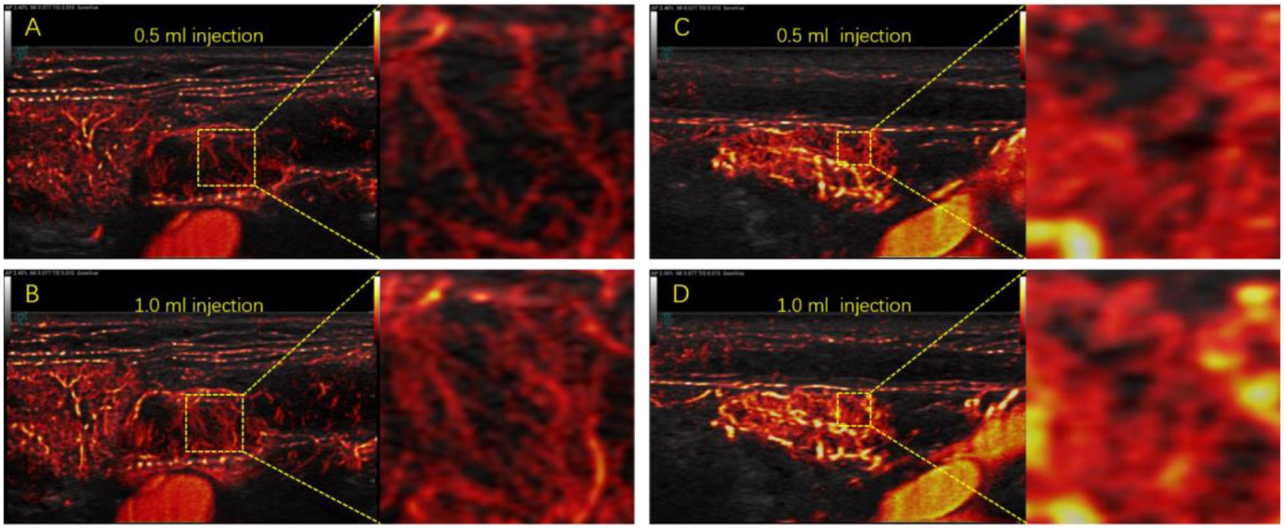

Fig. 5 SR CEUS images of benign and malignant superficial LNs post 0.5 ml & 1.0 ml bolus injection of Sonovue. (**A-B**) In a malignant LN, a 1.0 ml bolus injection can delineate more microvessels than a 0.5 ml bolus injection. (**C-D**) In a benign LN, a 1.0 ml bolus injection didn't not reveal significantly more microvessels compared with a 0.5 ml bolus injection

Table 2 The p values of the statistical analysis regarding injection doses (0.5 ml vs. 1.0 ml) on SR CEUS parameters in malignant lymph nodes

Parameter	1s	2s	3s	4s	5s	6s
VD	0.005*	0.005*	0.005*	0.005*	0.005*	0.005*
FWVD	0.005*	0.005*	0.005*	0.005*	0.005*	0.005*
PI	0.03*	0.03*	0.03*	0.047*	0.14	0.09
FD	0.03*	0.05	0.06	0.05	0.07	0.06
Vel var	0.007*	0.01*	0.047*	0.03*	0.07	0.14
Vmean	0.047*	0.04*	0.09	0.11	0.24	0.24

Table 3 The p values of statistical analysis of SR CEUS parameters between benign and malignant lymph nodes post 0.5 ml bolus injection of sonovue

Parameter	1s	2s	3s	4s	5s	6s
MVD	0.007*	0.006*	0.007*	0.01*	0.005*	0.004*
FWVD	0.02*	0.02*	0.01*	0.01*	0.01*	0.01*
PI	0.03*	0.01*	0.01*	0.02*	0.02*	0.01*
FD	0.19	0.19	0.21	0.26	0.26	0.26
Vel var	0.006*	0.001*	0.003*	0.001*	0.002*	0.012*
Velocity	0.24	0.39	0.51	0.60	0.74	0.90

remodeling processes. Numerous immune cells, cytokines and chemokines were involved in the microenvironment changes. However, the precise mechanisms still need further investigation [25].

Moreover, this study showed that a 1.0 ml bolus injection resulted in significant higher MVD & FWVD than a 0.5 ml bolus injection in malignant LNs. However, 0.5 ml and 1.0 ml injection doses didn't lead to significant difference in benign LNs. SR CEUS was based on microbubble identification and reconstruction, and local microbubble concentration significantly affects this process. As mentioned above, benign LNs had more abundant blood vessels, which could lead to greater microbubble overlap and make microbubble identifying difficult. Therefore, a higher dose of contrast agent might not increase microvessel visualization in benign LNs due to the enhanced overlapping effect and the underestimation of microvessel numbers. Conversely, malignant LNs had sparser blood vessels, which allowed microbubbles to separate individually and more easily to be identified [19, 20]. Therefore, a larger dose of contrast agent could depict more microvessels in malignant LNs. Accordingly, when compared with a 0.5 ml injection dose, a 1.0 ml injection dose depicted more blood vessels in malignant LNs, but not in benign LNs. As a result, SR CEUS post 1.0 ml injection reduced the difference between benign and malignant LNs, and failed to demonstrate significant difference in terms of SR CEUS quantitative parameters.

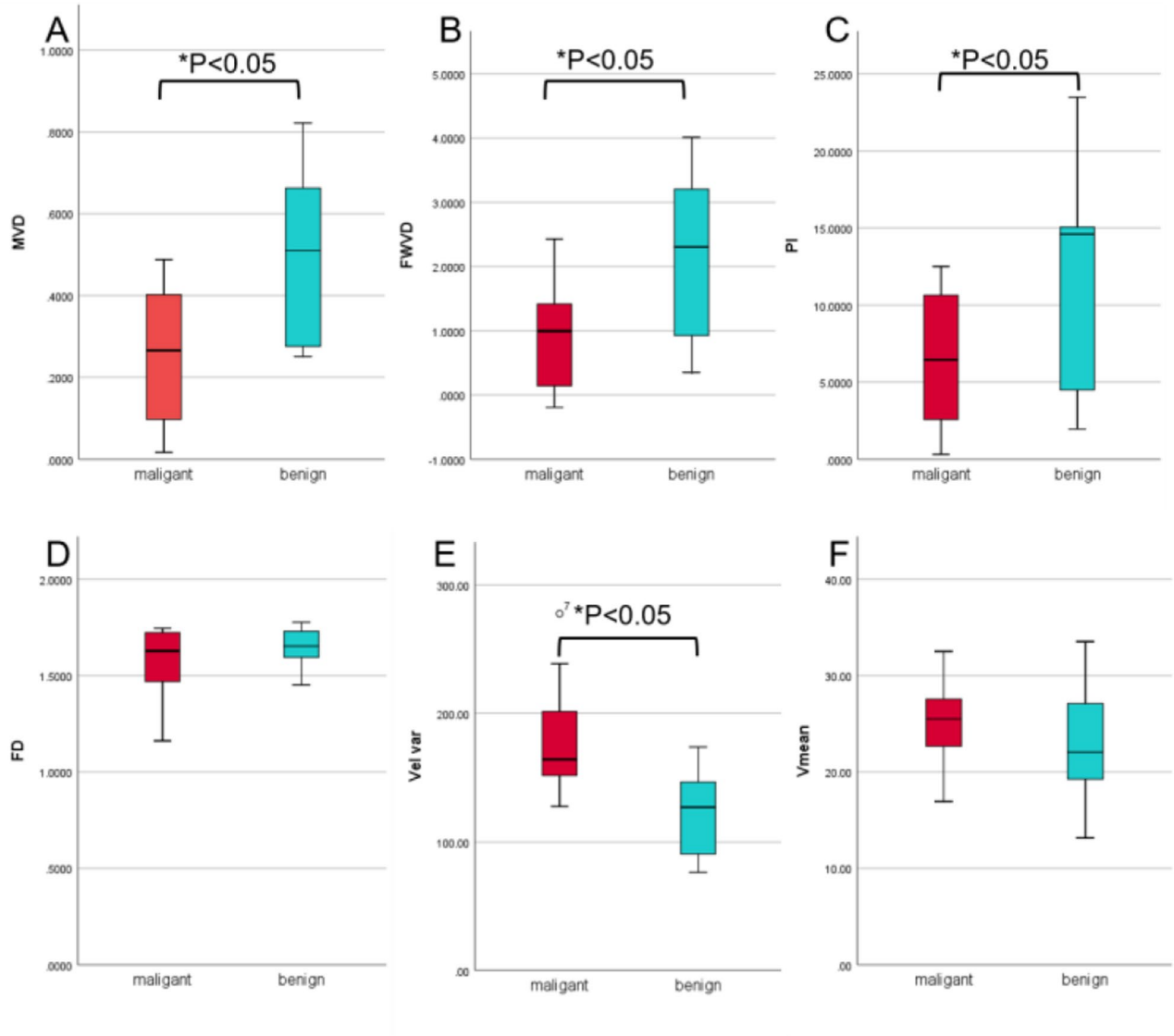

Fig. 6 Differentiation between benign and malignant superficial lymph nodes by SR CEUS images at the 6th second post 0.5 ml bolus injection of Sonovue. (**A, B, C & E**) Compared with benign lymph nodes, malignant lymph nodes showed significantly lower MVD, FWVD, PI & higher Vel var. (**D&F**) FD & Vmean were not found significantly different between benign and malignant lymph nodes

Based on these results, to establish a unified protocol for routine clinical practice, a 0.5 ml injection dose should be recommended for SR CEUS in the diagnosis of enlarged superficial LNs.

In addition, as illustrated in Fig. 4, after 0.5 ml bolus injection, although 1st – 6th second all demonstrated significant difference between benign and malignant LNs in terms of MVD, FWVD & PI, the gap of parameters between benign and malignant LNs increased over time, and p values at 6th second were minimum ones. Therefore, this study suggested that SR CEUS images at 6th second should be used for LN diagnosis in clinic.

Limitations

This study was subject to several limitations. Firstly, since parameters derived from smaller samples are more susceptible to bias due to random variation, a larger sample size might be required to obtain more reliable results. Secondly, due to the small sample size, this study was unable to distinguish metastatic LNs from lymphomas. In addition, although the diagnostic efficacy was not involved in the current study, it will be analyzed in further research with a large sample size. Thirdly, this is an initial study in which a commercially available SR CEUS apparatus was used for the differential diagnosis of superficial LNs. Since there is no guideline recommending the appropriate dose of contrast agent, the injection dose of 0.5 ml and 1.0 ml was tested in this study. Although we

recommended a 0.5 ml injection dose and 6 s acquisition time, further optimization of the imaging protocol is still needed.

Conclusions

This study demonstrated the feasibility of using SR CEUS for the differential diagnosis of superficial LNs, with a 0.5 ml bolus injection of contrast agent and 6-second acquisition time. In addition, parameters MVD, FWVD, PI & Vel var generated from SR CEUS could serve as imaging markers for clinical evaluation of superficial LNs.

Abbreviations

SR CEUS	Super-resolution contrast enhanced ultrasound
LN	Lymph node
MVD	Microvascular density;
FWVD	Flow weighted density of the vessel
PI	Perfusion index
FD	Fractal dimension
Vel var	Velocity variance
Vmean	Mean velocity

Author contributions

X.C. and W.Z. contributed to conception, design, funding acquisition, analysis and interpretation of data, and revised the manuscript drafting the work. J.H. and H.Y. contributed to conception, data acquisition, data analysis and drafting the work. D.T. and X.Z. contributed to data acquisition and data analysis. All authors read and approved the final manuscript.

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Data availability

Data generated or analyzed during this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics committee of Tongji Medical College of Huazhong University of Science and Technology (No: 2024-S213) and was performed in compliance with the principles of the World Medical Association Declaration of Helsinki for Biomedical Research involving Human Subjects. A written consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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