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Original article

Analysis on diagnostic failure of US-guided core needle biopsy for soft tissue tumors

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ABSTRACT

Purpose: To evaluate the diagnostic yield of ultrasonography (US)-guided core needle biopsy (CNB) in the diagnosis of soft tissue tumors (STTs) and to analyze the failure factors.
Methods: 139 patients with STTs that underwent both US-guided CNB and surgical resection were collected retrospectively. Compared with the histopathological results of surgical resection, the biopsy failure was defined as the following conditions: indefinitive diagnosis, including insufficient samples and unknown subtypes with correct biological potential classification; wrong diagnosis, including wrong biological potential classification and wrong subtypes with correct biological potential classification. Univariate and multivariate analyses from the perspectives of histopathological, demographic and US features together with biopsy procedures were performed to determine risk factors for diagnostic failure.
Results: The diagnostic yield of US-guided CNB for STTs in our study was 78.4%, but when only considering the correct biological potential classification of STTs, the diagnostic yield was 80.6%. The multivariate analysis showed that adipocytic tumors (odds ratio (OR) = 10.195, 95% confidence interval (CI): 1.062 - 97.861, $p = 0.044$), vascular tumors (OR = 41.710, 95% CI: 3.126 - 556.581, $p = 0.005$) and indeterminate US diagnosis (OR = 8.641, 95% CI: 1.852 - 40.303, $p = 0.006$) were correlated with the diagnostic failure. The grade III vascular density (OR = 0.019, 95% CI: 0.001 - 0.273, $p = 0.007$) enabled a higher diagnostic accuracy.
Conclusion: US-guided CNB can be an effective modality for the diagnosis of STTs. The diagnostic yield can be increased when the tumor vascular density was grade III in Color Doppler US, but can be decreased in adipocytic tumors, vascular tumors and masses with indeterminate US diagnosis.

1. Introduction

Soft tissue tumors (STTs) constitute a rare and heterogeneous group of mesenchymal neoplasms and represent clinical challenges [1]. Surgical resection remains critical for the treatment of STTs, but some histologic subtypes may require neoadjuvant therapies before surgery, such as Ewing sarcoma [2]. Since treatment of STTs can be handled differently, it is essential to make correct early diagnoses to avoid inappropriate therapeutic options [3–5]. The imaging modalities such as ultrasonography (US), magnetic resonance imaging (MRI) and computed tomography (CT) are commonly used for non-invasive preoperative evaluation of STTs [6]. Usually, US shows great advantage in the assessment of suspected cysts. CT or MRI allows the evaluation of other tumor features such as hemorrhage, necrosis, lesion margins and perilesional characteristics. CT is ideal for patients with contraindications to MRI and demonstrates great competence in identifying calcification [7]. However, the diagnostic efficiency of them may remain limited due to the diversity of STTs morphological characteristics [7]. To avoid a delayed or wrong diagnosis, more invasive procedures must be conducted when diagnoses cannot be made based on imaging [3,8,9].

Although open surgical resection remains the gold standard for diagnosing STTs, imaging-guided core needle biopsy (CNB) like US-guided or CT-guided CNB offers a cost-effective and safe alternative with diagnostic accuracy ranging from 66% to 98% [10–13]. Of these modalities, US-guided CNB has been performed as a regular procedure in our institution to obtain STTs specimens for the reason that it not only enables real-time visualization of biopsy needles without radiation exposure but also avoids vessel injury with the help of Doppler imaging [12]. The diagnostic accuracy of US-guided CNB

Abbreviations: STTs, soft tissue tumors; US, ultrasonography; MRI, magnetic resonance imaging; CT, computed tomography; CNB, core needle biopsy; IHC, immunohistochemical; BMI, body mass index; ICC, intraclass correlation coefficient; OR, odds ratio; CI, confidence interval; FISH, fluorescence in situ hybridization; MDM2, murine double minute 2

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ranged from 80% to 92.7% [14–16]. In order to improve diagnostic accuracy, it is important to identify failure factors, which can help avoid unnecessary biopsy, encourage the radiologists to use an alternative method for biopsy and reduce the complications. Potential causes of diagnostic failure may include operator skills, histopathological factors, technical aspects, demographic features and tumor intrinsic characteristics [13]. Kubo et al. [17] suggested that expert radiologists who were familiar with interventional radiology should be preferred to perform CNB. Regarding the histopathological factors, technical aspects and demographic features, limited studies indicated that adipocytic tumors, vascular tumors, short specimen length and insufficient specimens may be associated with diagnostic failure, but no consensus has been reached [13,18]. To the best of our knowledge, there is no study about the correlation between the US features of STTs and biopsy failure, while analogous studies have been performed on thyroid studies [19]. Then, we hypothesized that the US features of STTs that can show intrinsic characteristics of tumors may predict the likelihood of non-diagnostic results.

In short, our study was therefore dedicated to assessing the diagnostic yield of US-guided CNB conducted by radiologists as well as finding the failure factors from the perspectives of histopathological features, demographic features, biopsy procedures and US characteristics.

2. Materials and methods

2.1. Patients

From February 2015 to July 2022, a total of 958 patients underwent US-guided CNB of soft-tissue lesions and 153 of them were pathologically confirmed with STTs via US-guided CNB and surgical resection at the first affiliated Hospital of Nanjing Medical University. Fourteen patients were excluded according to the following criteria: (1) patients with no completely visible region of interest in the US images or images with unsatisfactory quality (n = 9); (2) incomplete clinical data (n = 4); (3) the interval between surgery resection and US examination exceeding 60 days (n = 1). Finally, 139 patients (mean age = 47.89 ± 17.42 years, range 11 - 88 years, male/female ratio 1:1.14) were enrolled in this study (Fig. 1). This study attained the approval of the institutional review board of our hospital and the informed consent was waived due to the retrospective nature of the study.

2.2. US-guided CNB procedures

Prior to US-guided CNB, patients were asked to maintain in the proper position to fully expose the lesions. An ultrasound scanner (LOGIQ E9, GE Healthcare, Milwaukee, WI, USA) with a 6–15 MHz linear transducer and a 2–6 MHz convex transducer was employed to perform conventional US examination. Radiologists flexibly adjusted probes in attempt to catch the optimum US images. The US features of the lesions including the depth, maximum diameter, echogenicity, internal content, echotexture, shape, boundary, margin, calcification, vascular type, vascular density and US diagnosis were routinely documented.

Then, after the conventional US examination, all the biopsy procedures were performed under the guidance of US appropriately by two radiologists specialized in musculoskeletal imaging. At least two specimens were acquired safely in sterile conditions at different puncture sites where the solid component could be targeted as much as possible and fixed in 10% formaldehyde. A 14-, 16- or 18-gage semiautomatic biopsy instrument (BardMagnum Biopsy System, Becton, Dickinson and Company, Franklin Lakes, NJ, USA) equipped with a coaxial introducer needle could be chosen depending on the mass size, location and vascular distribution. The immunohistochemical (IHC) evaluation was conducted for biopsy in accordance with patients' preferences and clinical demands. Patients were monitored for at least 30 min after the US-guided CNB, followed by the examination of complications.

2.3. Histopathological evaluation and diagnostic yield of US-guided CNB results

Histopathological results of surgical excision served as the reference standard. According to WHO classification 2020 [1], STTs of the musculoskeletal system can be differentiated based on the histogenesis (adipocytic tumors, fibroblastic and myofibroblastic tumors, so-called fibrohistiocytic tumors, vascular tumors, chondro-osseous tumors, peripheral nerve sheath tumors, tumors of uncertain differentiation and undifferentiated small round cell sarcomas). All findings were categorized into benign, intermediate (locally aggressive), intermediate (rarely metastasizing), or malignant subtypes according to potential malignancy aggressivity. To evaluate the diagnostic yield of US-guided CNB in STTs, the enrolled patients were sorted into the success and failure groups. The former group consisted of patients who gained definitive subtype diagnoses. By contrast, biopsy results of patients in the failure group consisted of 2 conditions: 1. indefinitive histopathological diagnosis: insufficient samples and unknown subtypes with correct biological potential classification; 2. wrong histopathological diagnosis: erroneous biological potential classification and erroneous subtypes with correct biological potential classification [14].

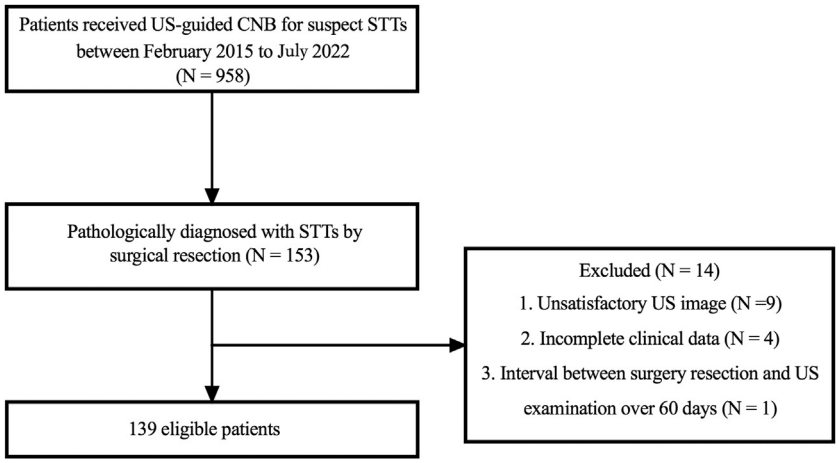

Fig. 1. A flowchart indicating inclusion and exclusion criteria. Note: US, ultrasonography; CNB, core needle biopsy; STTs, soft tissue tumors.

2.4. Factors related to non-diagnostic outcomes

Various parameters were investigated from histopathological, demographic, technical and US viewpoints. Firstly, histopathological factors comprised tumor histogenesis and biological potentials. Secondly, demographic factors including the age, sex, body mass index (BMI), history of STT and tumor location (head or neck, trunk, limbs) were all considered. Thirdly, technical factors documented the biopsy needle gage (14 −16 or 18), the quantity of specimens (< 3 or 3 and more), MRI (enhanced MRI, non-enhanced MRI and absent), immunohistochemistry of biopsy specimens and operators' difference. Lastly, the US features were evaluated. Sufferers' information and histopathological diagnosis were kept confidential, and all recorded images were respectively evaluated by two radiologists with at least 5 years of experience in the musculoskeletal US. Inconsistent evaluation would be reanalyzed by another senior radiologist with over 10 years of experience to make a review decision. The image parameters were as follow [18,20,21]: (1) maximum diameter: divided into 3 grades (≤ 2 cm, 2–5 cm, ≥ 5 cm) for the reason that some masses were too enormous to measure; (2) depth: superficial or deep fascia layers and length from the epidermis to the tumors margin; (3) shape: regular, lobulated and irregular; (4) boundary: well-defined: less than 10% vague and ambiguous boundary, partially defined: 10% - 50% vague and ambiguous, ill-defined: > 50% vague and ambiguous; (5) margin: smooth: an even curving interface with < 10% irregular curving interface, spiculated: 10% - 50% irregular curving interface, rough: over 50% irregular curving interface; (6) echogenicity: predominantly hypo- / iso / hyper- echoic in contrast to adjacent tissue; (7) internal content: mainly solid (cystic content ≤ 10%), mixed (cystic content >10% but ≤ 50%) and predominantly cystic (cystic content > 50%); (8) echotexture: homogeneous and heterogeneous; (9) calcification: absent and present; (10) vascular type: none, peripheral, internal and mixed; (11) vascular density: grade 0: no obvious blood flow signal, grade I: less than 2 punctate or rod-shaped blood flow, grade II: moderate blood flow (3 - 4 punctate vessels or an great perforator vessel), grade III: multiple blood flow. (12) US diagnosis: probably benign; suspicious for malignancy and indeterminate (biologic potential of the tumor could not be determined from US findings); (13) histogenesis assessment.

2.5. Statistical analysis

Data management and analysis were performed using SPSS 26.0 software (IBM, Ehningen, Germany). Before analysis, continuous variables were expressed as mean ± standard deviation while categorical variables were expressed as numbers. To compare the differences between success and failure groups, the χ^2 or Fisher's exact test was applied for the comparison of categorical variables, and independent-samples t tests (for normally distributed data) and Mann-Whitney U tests (for data with non-normal distribution) were employed for the comparison of continuous variables. A two-sided p value < 0.05 indicated a statistically significant difference. Logistic regression analysis was performed to ascertain the independent factors for diagnostic failure. All parameters with $p < 0.05$ at univariate analysis were included in the multivariate analysis. Intraclass correlation coefficient (ICC) and kappa were employed to assess the US evaluation consistency between observers and ICC/kappa values ranging from 0 to 1. When the ICC/kappa was > 0.80, > 0.60 but ≤ 0.80, > 0.40 but ≤ 0.60 and ≤ 0.40, the consistency between observers was supposed to be excellent, good, general, and poor, respectively [22].

3. Results

3.1. Histopathological findings and diagnostic yield

In total, 139 patients who underwent both US-guided CNB and surgical resection were identified. The detailed histopathological results of all cases and diagnostic failure entities were summarized in Supplementary material 1 and 2. 139 STTs included 37 cases of fibroblastic and myofibroblastic tumors (26.6%), 31 cases of adipocytic tumors (22.3%), 7 cases of so-called fibrohistiocytic tumors (5.0%), 11 cases of vascular tumors (7.9%), 24 cases of peripheral nerve sheath tumors (17.3%), 25 cases of tumors of uncertain differentiation (18.0%), 2 cases of undifferentiated small round cell (1.4%), one chondro-osseous tumor (0.7%) and one smooth muscle tumor (0.7%). A Definitive subtype diagnosis was obtained in 78.4% of all cases while the correct biological potential classification was obtained 80.6% of all enrolled patients. As shown in Fig. 2, adipocytic tumors accounted for 56.7% of all non-diagnostic cases, followed by vascular tumors

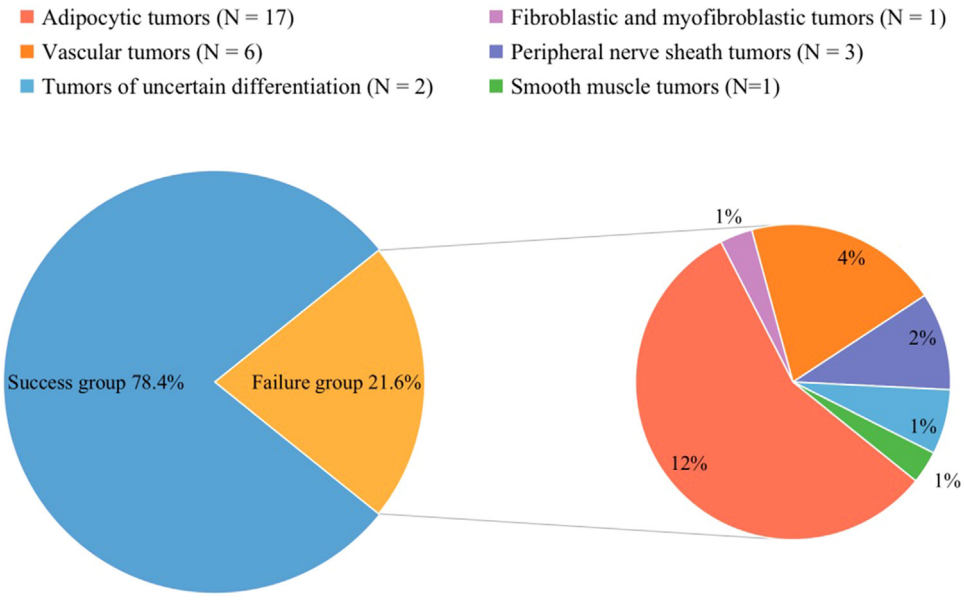

Fig. 2. Diagnostic yield of US-guided CNB and histopathological results of non-diagnosed tumors. Note: US, ultrasonography; CNB, core needle biopsy; N, number.

Table 1
Postoperative histopathological results of patients in the success and failure groups.

Postoperative pathological results	Success group	Failure group	Diagnostic yield (%)	p value
Histogenesis				<0.001
Fibroblastic and myofibroblastic tumors	36 (33.0%)	1 (3.3%)	97.3	
Adipocytic tumors	14 (12.8%)	17 (56.7%)	45.2	
So-called fibrohistiocytic tumors	7 (6.4%)	0 (0.0%)	100.0	
Vascular tumors	5 (4.6%)	6 (20.0%)	45.5	
Chondro-osseous tumors	1 (0.9%)	0 (0.0%)	100.0	
Peripheral nerve sheath tumors	21 (19.3%)	3 (10.0%)	87.5	
Tumors of uncertain differentiation	23 (21.2%)	2 (6.7%)	92.0	
Undifferentiated small round cell sarcomas	2 (1.8%)	0 (0.0%)	100.0	
Smooth muscle tumors	0 (0.0%)	1 (3.3%)	0.0	
Biological potential classification				0.359
Benign	56 (51.4%)	14 (46.7%)	80.0	
Intermediate (locally aggressive)	14 (12.8%)	8 (26.7%)	63.6	
Intermediate (rarely metastasizing)	5 (4.6%)	1 (3.3%)	83.3	
Malignant	34 (31.2%)	7 (23.3%)	82.9	

(20.0%). A statistically significant relationship between histogenesis and diagnostic failure was found ($p < 0.001$, Table 1).

3.2. Demographic and technical factors

There were no significant differences between two groups in terms of age ($p = 0.525$), gender ($p = 0.688$), BMI ($p = 0.629$), STTs history ($p = 0.420$) and tumor location ($p = 0.057$) (shown in Supplementary material 3). Most specimens were obtained by using 14- or 16-gage needles in this study. In 92.1% of all cases, three or more specimens were obtained in each case. The technical factors did not differ significantly including the biopsy needle gage ($p = 0.976$), the number of specimens ($p = 0.923$), MRI ($p = 0.517$) and operators' difference ($p = 0.867$). Noteworthy, the IHC tests were performed in 34.5% of biopsy specimens and 50.2% of surgical specimens. Patients who accepted IHC tests were more likely to be successfully diagnosed ($p = 0.006$) as shown in Table 2.

3.3. US characteristics

The consistency of the interpretation and classification of US images between observers was excellent (ICC/kappa was over 0.80). Univariate comparisons of detailed US parameters between the success group and the failure group were displayed in Table 3. Only the echogenicity ($p = 0.001$), vascular type ($p < 0.001$) and vascular density ($p < 0.001$) were linked to diagnostic failure. 79.1% of all cases were got the US diagnosis of biological potential classification or specific entities, 16 cases of which were proved as misdiagnosed. What's more, US was capable of identifying the histogenesis of 75.0% adipocytic tumors and 63.6% vascular tumors.

3.4. Multivariate analysis

On the ground of multivariate analysis (Table 4 and Fig. 3), adipocytic tumors (odd ratio (OR) = 10.195, 95% confidence interval (CI): 1.062 - 97.861, $p = 0.044$), vascular tumors (OR = 41.710, 95% CI: 3.126 - 556.581, $p = 0.005$) and indeterminate US diagnosis (OR = 8.641, 95% CI: 1.852 - 40.303, $p = 0.006$) were independent factors for biopsy diagnostic failure. The grade III vascular density (OR = 0.019, 95% CI: 0.001 - 0.273, $p = 0.007$) was the only significant independent protective predictor of diagnostic failure. Figs. 4 and 5 showed US images of representative cases of diagnostic success and failure.

4. Discussion

Preoperative identification of patients with STTs allows surgeons to tailor their perioperative management. Widely reported in the literature, US-guided CNB is one of the mainstream biopsy methods for preoperative diagnosis, but its accuracy is not 100%. Finding out causes of biopsy failure is very important to avoid unnecessary biopsy and reduce complications. It was shown in previous studies that inherent tumor heterogeneity as well as inadequate biopsy samples may be the reasons for CNB diagnostic failure [23,24]. In this study, we defined successful diagnosis as recognition of detailed subtypes of STTs, since the accurate histological subtypes were paramount for

Table 2
Technical characteristics of patients in the success and failure groups.

Technical characteristics	Success group	Failure group	Diagnostic yield (%)	p value
Biopsy needle gauges				0.976
14 - 16	99 (90.8%)	27 (90.0%)	78.6	
18	10 (9.2%)	3 (10.0%)	76.9	
Number of specimens				0.923
< 3	8 (7.3%)	3 (10.0%)	72.7	
3 and more	101 (92.7%)	27 (90.0%)	78.9	
Immunohistochemistry of biopsy specimens				0.006
Yes	44 (40.4%)	4 (13.3%)	91.7	
No	65 (59.6%)	26 (86.7%)	71.4	
MRI				0.517
Enhanced MRI	35 (32.1%)	12 (40.0%)	74.5	
Non-enhanced MRI	25 (22.9%)	8 (26.75%)	75.7	
Absent	49 (45.0%)	10 (33.3%)	83.1	
Operators				0.867
Radiologist 1	78 (71.6%)	21 (70.0%)	78.8	
Radiologist 2	31 (28.4%)	9 (30.0%)	77.5	

Note: MRI, magnetic resonance imaging.

Table 3
US patterns of patients in success and failure groups.

US patterns	Success group	Failure group	Diagnostic yield (%)	p value
Maximum diameter(cm)				0.052
≤ 2	6 (5.5%)	0 (0.0%)	100.0	
2–5	56 (51.4%)	11 (36.7%)	83.6	
≥5	47 (43.6%)	19 (63.6%)	71.2	
Depth				0.797
Superficial fascia	19 (17.4%)	4 (13.3%)	82.6	
Deep fascia	90 (82.6%)	26 (86.7%)	77.6	
Depth(mm)				0.106
	7.97 ± 6.55	9.95 ± 5.65	78.4	
Shape				0.109
Regular	31 (28.4%)	6 (20.0%)	83.8	
Lobulated	29 (26.6%)	14 (46.7%)	67.4	
Irregular	49 (45.0%)	10 (33.3%)	83.1	
Boundary				0.189
Well-defined	64 (58.7%)	12 (40.0%)	84.2	
Partially-defined	38 (34.9%)	15 (50.0%)	71.7	
Ill-defined	7 (6.4%)	3 (10.0%)	70.0	
Margin				0.505
Smooth	23 (21.1%)	4 (13.3%)	85.2	
Spiculated	50 (45.9%)	17 (56.7%)	74.6	
Rough	36 (33.05%)	9 (30.0%)	80.0	
Echogenicity				0.001
Hypoechoic	96 (88.1%)	18 (60.0%)	84.2	
Isoechoic	3 (2.8%)	1 (3.3%)	75.0	
Hyperechoic	10(9.2%)	11 (36.7%)	47.6	
Inner content				0.158
Mainly solid	100 (91.7%)	29 (96.7%)	77.5	
Mixed	7 (6.4%)	0 (0.0%)	100.0	
Mainly cystic	2 (1.8%)	1 (3.3%)	66.7	
Echotexture				0.999
Homogeneous	13 (11.9%)	3 (10.0%)	81.3	
Heterogeneous	96 (88.1%)	27 (90.0%)	78.0	
Calcification				0.640
Absent	103 (94.5%)	27 (90.0%)	79.2	
Present	6 (5.5%)	3 (10.0%)	66.7	
Vascular type				<0.001
None	13 (11.9%)	15 (50.0%)	46.4	
Internal	75 (68.8%)	13 (43.3%)	85.2	
Peripheral	6 (5.5%)	2 (6.7%)	75.0	
Mixed	15 (13.8%)	0 (0.0%)	100.0	
Vascular density				<0.001
0	13 (11.9%)	15 (50.0%)	46.4	
I	22 (20.2%)	6 (20.0%)	78.6	
II	27 (24.8%)	6 (20.0%)	81.8	
III	47 (43.1%)	3 (10.0%)	94.0	
US diagnosis				<0.001
Probably benign	59 (54.1%)	8 (26.7%)	88.1	
Suspicious for malignancy	37 (33.9%)	6 (20.0%)	86.0	
Indeterminate	13 (11.9%)	16 (53.8%)	44.8	

Note: US, ultrasonography.

the treatment of each STT. Unhesitatingly, surgery remains the mainstay of treatment for most STTs, but different subtypes of STTs require different safety margins [25,26]. In addition, neoadjuvant therapy is currently gaining attention, but responses to therapies differ. For instance, the standard treatment for Ewing sarcoma is surgical resection associated with local radiotherapy and chemotherapy, but dedifferentiated liposarcoma is comparatively chemo-resistant which may lead to different treatment protocols [27,28].

The diagnostic yield of our study was 78.4% which was lower than the previous findings of 80% to 92.7% [14–16]. Except for criteria discrepancies of diagnostic failure, other studies always included soft tissue lymphoma and soft tissue metastasis whereas we merely focused on the primary STTs of the musculoskeletal system. Besides, our study showed that the diagnosis failure rate of benign tumors was higher than that of malignant tumors, which was in accordance with the previous studies [29], but the difference in our study was not statistically significant. Therefore, the tiny disparity in the diagnostic yield among different studies may be associated with the diversity of tumor subtypes in different study sets.

Our findings indicated that the diagnostic failure was more likely to occur with vascular or adipocytic tumors which was consistent with a previous study by Yoon et al. [18]. Reported in literature, the first-time diagnostic success rate by core needle biopsy of vascular tumors was 60% [18], which was 45.5% in our study. We speculated that one of the contributory failure causes was that specimens of biopsy failed to reveal the entire tumor composition. Most biopsy samples were reported as blood clots or some blood vessels which were insufficient for the diagnosis of vascular tumors in our diagnostic failure cases. In terms of adipocytic tumors, the diagnostic accuracy was as low as 45.2% in our study, compared with 87.4% to 95% reported in the literature [18,30]. Reasons of twofold can be raised, and one of which was lack of IHC staining or fluorescence in situ hybridization (FISH) gene detection for biopsy samples. In our investigation, diagnostic failure mainly occurred in the differential diagnosis between lipomas and atypical lipomatous. Indeed, it would be hard to distinguish atypical lipomatous tumors from lipomas morphologically if atypical hyperchromatic stromal cells and lipoblasts cannot be identified [31]. Applications of IHC staining of the resultant

Table 4
Multivariate logistic regression analysis of factors associated with significant diagnostic failure.

Characteristics	B	SE	OR	Lower Limit of 95% CI	Upper Limit of 95% CI	P
Vascular density						
0			1 (reference)			
I	−1.512	0.795	0.221	0.046	1.048	0.057
II	−1.467	0.847	0.231	0.044	1.213	0.083
III	−3.981	1.368	0.019	0.001	0.273	0.007
Histogenesis						
Fibroblastic and myofibroblastic tumors			1 (reference)			
Adipocytic tumors	2.322	1.154	10.195	1.062	97.861	0.044
So-called fibrohistiocytic tumors	−17.070	14,205.987	0.000	0.000	-	0.999
Vascular tumors	3.731	1.322	41.710	3.126	556.581	0.005
Chondro-osseous tumors	−18.416	40,192.970	0.000	0.000	-	0.999
Peripheral nerve sheath tumors	1.855	1.251	6.391	0.550	74.230	0.113
Tumors of uncertain differentiation	1.670	1.387	5.312	0.350	80.574	0.138
Undifferentiated small round cell sarcomas	−17.750	26,589.794	0.000	0.000	-	0.999
Smooth muscle tumors	−26.504	40,192.969	0.000	0.000	-	0.999
US diagnosis						
Probably benign			1 (reference)			
Suspicious for malignancy	1.396	0.884	4.038	0.714	22.821	0.114
Indeterminate	2.156	0.786	8.641	1.852	40.303	0.006

Note: US, ultrasonography; OR, odds ratio; CI, confidence interval.

murine double minute (MDM2) and MDM2 FISH gene detection can remedy this shortcoming [31,32]. The other one was that complicated internal components of some subtypes of malignant adipocytic tumors made biopsy samples insufficient for diagnosis. One dedifferentiated liposarcoma in our study was regarded as proliferative myositis because part of tumor cells showed the characteristics of proliferative myositis revealed by the surgical resection. As a result, this case was diagnostically refuted despite the use of IHC detection. On top of that, the previous studies demonstrated that US was effective in the diagnosis of adipocytic tumors and vascular tumors [33,34]. In our study, a large fraction of tumors originating from adipose tissue can be distinguished (75.0%), and the correct identification of tissue origin can also appear in vascular tumors. In a word, we believed that US-CNB procedures can be alternative when US indicated that the STTs originated from adipose and vascular tissues. Once US-CNB had been selected, it was vital to gain ample biopsy tissues and make good use of IHC staining and FISH gene detection. Further research should be conducted on how to improve the diagnostic accuracy of US-guided CNB with the help of new detection methods.

In addition, US features was proved to be useful for the differential diagnosis of benign and malignant STTs [35–37]. Nevertheless, the impact of US characteristics and diagnosis on the biopsy diagnostic yield was barely discussed. In our study, through the univariate analysis, there was no statistical differences in the majority of US features in the discussion of diagnostic failure, while vascular density, US diagnosis for possible biological potential, vascular types and echogenicity were different between failure and success groups. The vascular density was the only protective US characteristic included in the multivariate logistic regression equation. It is accepted that the vascularity of tumors relying on the degree of neoangiogenesis and the hypervascularity is a hallmark of malignancy in STTs [38]. Color Doppler imaging can do a good favor to avoid hemorrhagic or necrotic zones as well as vital blood vessels and nerves by showing blood flow signal [39]. Contrary to the thyroid-based studies [40], the higher the vascular density in STTs, the higher the success rate of the biopsy diagnosis. We inferred that the identification of the representative parts for sampling can be realized after displaying vascular distribution and density [41]. In addition, in conjunction with US characteristics of STTs such as lesion sizes, depth, margin and vascularity [42], US diagnosis of possible biological potential or specific entities can be made. Consequently, we figured out that indeterminate US diagnosis can be used as an independent risk factor for biopsy diagnostic failure because imaging impression had the potential to effect pathological diagnosis [18]. Besides, our study implied that the vascular distribution was considered to be relevant to non-diagnostic outcomes but cannot be the independent predictor. What's more, the isoechoic and hyperechoic tumors owned lower diagnostic yield than hypoechoic ones, but the echogenicity cannot be used as an independent indicator of diagnostic failure. We deemed that the echogenicity was correlated to the discrepancy in acoustic impedance among the composition of the tumors which included tumor cells, fatty tissue, vascular, fibers, collagen, and cartilage [43]. The inflammatory cell infiltration, hemorrhage and fatty tissues in the tumors with isoechoic and hyperechoic may hinder the

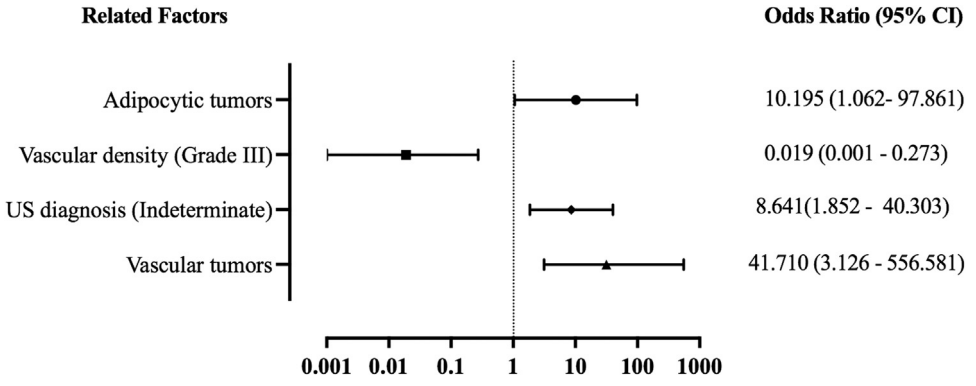

Fig. 3. Multivariate logistic regression analysis of factors associated with significant diagnostic failure. Note: US, ultrasonography; CI, confidence interval.

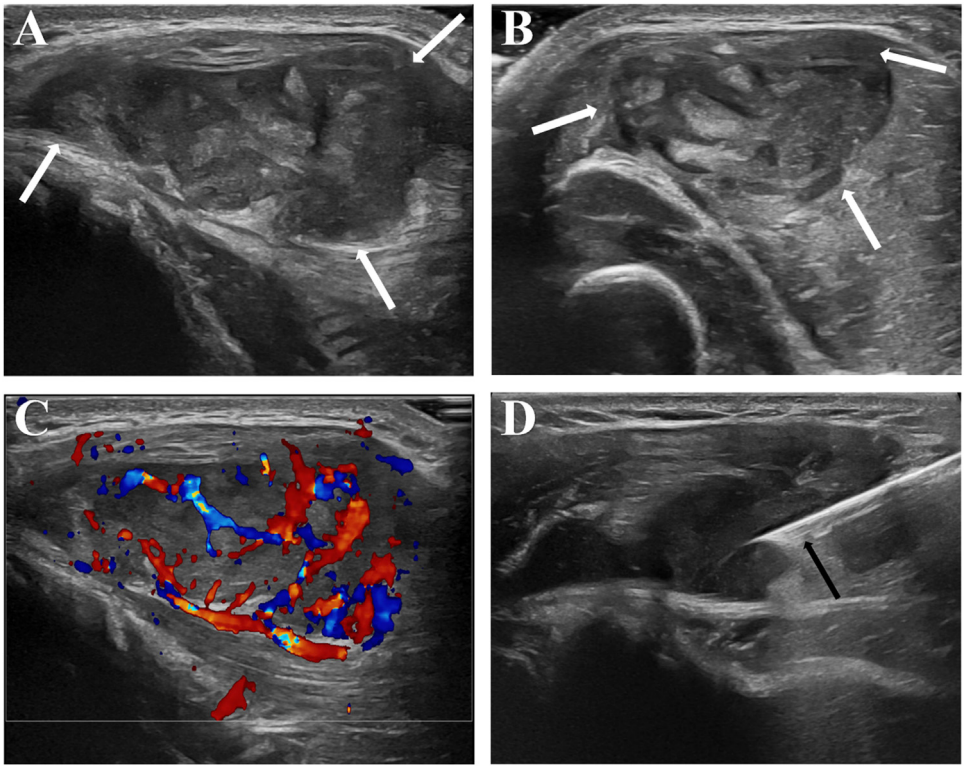

Fig. 4. US images of a representative case of diagnostic success. A 25-year-old male presenting with a painful synovial sarcoma in the right arm. (A), (B) and (C) Conventional US images showed a 44×16 mm mass located in the deep fascia with irregular shape, well-defined boundary, spiculate margin, hypoechoic pattern, mainly solid inner content, heterogeneous echotexture, no calcifications, and grade III internal blood flow. US diagnosis was suspicious for malignancy (white arrows pointed towards the mass). (D) The image showed the performance of US-guided CNB with a 16-gage core needle (the black arrow pointed towards the biopsy needle). Note: US, ultrasonography; CNB, core needle biopsy.

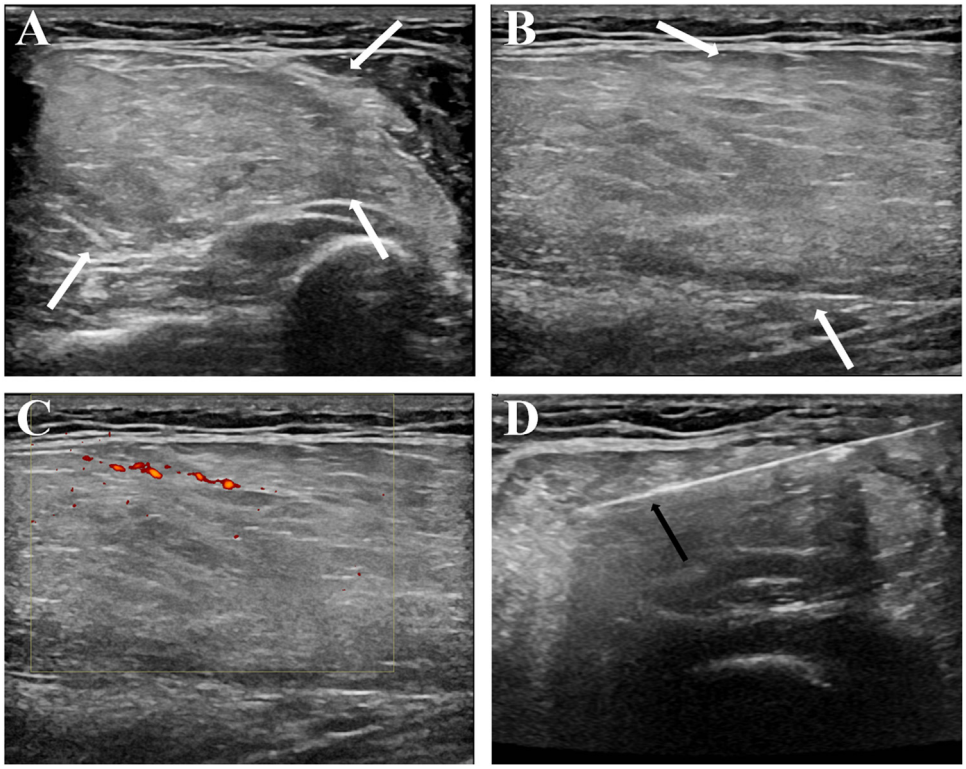

Fig. 5. US images of a representative case of diagnostic failure. A 54-year-old female presenting with a painless atypical lipomatous tumor in the right arm. (A), (B) and (C) Conventional US images showed a 104×22 mm located in the deep fascia with lobulated shape, partially-defined boundary, spiculate margin, hyperechoic pattern, mainly solid inner content, heterogeneous echotexture, no calcifications and grade II internal blood flow. US diagnosis was indeterminate (white arrows pointed towards the mass). (D) The image showed the performance of US-guided CNB with a 16-gage core needle (the black arrow pointed towards the biopsy needle). Note: US, ultrasonography; CNB, core needle biopsy.

acquisition of tumor cells during the biopsy [44]. However, our results may also be affected by the insufficient cases of isoechoic and hyperechoic tumors. Taken together, we could suggest that US-CNB can be highly recommended when US indicated enriched blood supply. If it was hard to discriminate biological potential by US, other examination methods such as CT or MRI and other biopsy technologies should be taken into account to minimize the biopsy diagnostic failure.

Furthermore, it was reasonable to assume that increasing biopsy specimens can promise a higher diagnostic yield. However, our results showed no statistical differences of the diagnostic yield among the different amount of specimens and among the varied types of biopsy needle gauges, which was in line with previous studies [13,18], Kim et al. [45] recommended to employ an 18-gage core needle and obtain a minimum of 4 biopsy specimens. In our institution, in order to reduce the pain of patients and avoid under- or over-collecting specimens, the operators usually determined the type of biopsy needle gauges and the number of specimens according to the US features of the tumors (such as the size and the vascular density). Most of our specimens were collected by using 14- or 16-gage core needles and 3 or more specimens were acquired from a single biopsy. In our opinion, proper biopsy procedures guaranteed successful diagnosis.

There were some limitations should be mentioned in our study. To begin with, as a single-center retrospective study, the sample size was far from enough with a certain degree of selection bias. Further prospective multicenter trials with a large population are needed to validate our results. Secondly, the interpretation and classification of US images by radiologists were subjective, although the consistency between observers was excellent. Lastly, we only evaluated the conventional US features, while other US parameters, such as US elastography and contrast-enhanced US parameters that may also affect the accuracy of CNB will be further investigated in future studies.

In conclusion, US-guided CNB can be an effective modality for the diagnosis of STTs. The diagnostic yield can be increased in the tumors with grade III vascular density whereas adipocytic tumors lack of IHC staining or FISH detection, vascular tumors and the indeterminate US diagnosis may be significant factors leading to the diagnostic failure. US-guided CNB should not be recommended if the risk factors mentioned above are identified.

Declaration of Competing Interests

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

CRediT authorship contribution statement

Ying-Lun Zhang: Data curation, Methodology, Writing – original draft. **Qian Ma:** Data curation, Methodology. **Yu Hu:** Data curation, Formal analysis, Software. **Meng-Jie Wu:** Data curation, Formal analysis. **Zong-Kai Wei:** Data curation, Formal analysis. **Qi-Yu Yao:** Data curation, Formal analysis. **Ju-Ming Li:** Investigation, Resources, Supervision. **Ao Li:** Conceptualization, Methodology, Writing – review & editing.

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Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.redii.2023.100023.

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