Original Article

The value of sonographically guided fine-needle aspiration in the diagnosis of small lymph

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Background: To analyze the diagnostic value of ultrasound-guided fine-needle aspiration (FNA) biopsy for lymph nodes with short-axis diameters ≤1 cm and to investigate whether the short-axis diameter influences the results of FNA biopsy.

Methods: The cytological results of ultrasound-guided FNA lymph node biopsies in 1,242 cases treated at our hospital between December 2015 and June 2017 were retrospectively analyzed. The results were compared with the final diagnostic results of the cases (988 cases had core-needle biopsies, and 254 cases were followed-up for more than six months) to explore the diagnostic value of ultrasound-guided FNA for small lymph nodes.

Results: The sensitivities, specificities and accuracies of ultrasound-guided FNA were 99.6%, 99.5% and 99.5% for small lymph nodes with short-axis diameters ≤1 cm and 97.2%, 94.4% and 96.4% for lymph nodes with short-axis diameters >1 cm, respectively. No significant differences were detected between the two groups (P>0.05). Lymph nodes with short-axis diameters ≤1 cm were divided into three groups according to the following diameters: 0.7 cm ≤ short-axis diameter ≤1 cm, 0.5 cm ≤ short-axis diameter <0.7 cm, and short-axis diameter <0.5 cm. The sensitivities of ultrasound-guided FNA for these three groups were 99.6%, 99.5% and 98.0% respectively; the specificities were 99.5%, 99.0% and 98.0%, respectively; and the accuracies were 99.8%, 99.3% and 99.0%, respectively. The differences in accuracy between the three groups were significant (P<0.05), while the differences in sensitivity and specificity were not significant (P>0.05).

Conclusions: The diagnostic results of ultrasound-guided FNA for small lymph nodes are not affected by the short-axis diameter. For lymph nodes with short-axis diameters ≤1 cm, the accuracy decreases as the short-axis diameter decreases, but FNA still has a high diagnostic accuracy for these small lymph nodes.

Keywords: Lymph node; core-needle; fine-needle aspiration (FNA); ultrasound examination

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Introduction

The lesions of superficial lymphadenopathies are complicated and can be divided into two categories: neoplastic and non-neoplastic (1). Thapa *et al.* (1) found that 25.4% of lymph node lesions were neoplastic and that 74.6% were non-neoplastic. In addition, 70% of lymph node lesions were located in the neck. Plukker *et al.* believed that lymph nodes with short-axis diameters less than 1 cm, clear boundaries, uniform internal echogenicity and normal lymphatic portals are largely benign (2). Another

Table 1 Lymph node distribution of the 1,242 cases undergoing ultrasound-guided FNA biopsy

Area	Number of cases
Neck	
Level II	35
Level III	32
Level IV	25
Level V	954
Level VI	15
Subclavian area	2
Armpit	161
Groin area	18
Total	1,242

FNA, fine-needle aspiration.

Table 2 Primary tumors in the 1,242 cases undergoing ultrasound-guided FNA lymph node biopsy

Primary site	Number of cases
Head and neck	325
Breast	320
Chest	445
Abdomen	53
Pelvic	65
Blood system	23
Unexplained lymphadenopathy	11
Total	1,242

FNA, fine-needle aspiration.

study, however, indicated that lymph nodes with short-axis diameters less than 1 cm that contain micrometastases and without abnormal imaging findings are difficult to distinguish from nonmetastatic lymph nodes (3). Ultrasound-guided lymph node core-needle biopsy (CNB) and fine-needle aspiration (FNA) are widely applied in the diagnosis of superficial lymphadenopathies. CNB can retrieve more tissue but is not suitable for some elderly patients in poor health and with poor coagulation function. CNB cannot effectively retrieve small lymph node samples. Ultrasound-guided FNA cytology examination is minimally invasive, simple and fast (4), rarely causes complications and is associated with very good patient compliance. However, due to the limited number of cells retrieved and the high false-negative rate associated with FNA of lymph nodes with smaller short-axis diameters, Ewing *et al.* suggested that the size of lymph nodes affects FNA biopsies and that the corresponding results therefore have limited significance (5). This study aimed to investigate the diagnostic sensitivity, specificity and accuracy of ultrasound-guided FNA for lymph nodes with different short-axis diameters, analyze the diagnostic value of ultrasound-guided FNA, and determine whether a short-axis diameter ≤1 cm influences FNA results.

Methods

Subjects

Ultrasound-guided FNA examinations of 1,725 patients showing abnormal lymph nodes during routine sonographic examination were performed in our hospital from December 2015 to June 2017. Abnormal ultrasound findings include an irregular lymph node morphology, an unclear boundary, a ratio of long-axis diameter to short-axis diameter >2, eccentric or absent lymphatic portals, thickening of cortical bands, and abnormal blood flow. Among the cases, 483 were excluded from the study due to missed follow-ups and lack of a final diagnosis, and 1,242 cases were enrolled, including 662 males and 580 females aged 13–92 years, with an average age of 56.22±12.7 years. Among these, 1,061 cases of cervical and supraclavicular lymph nodes, 2 cases of subclavian bone, 161 cases of axillary lymph nodes, and 18 cases of inguinal lymph nodes were included. The distribution of the 1,242 cases is shown in *Table 1*. The primary tumors in patients with enlarged lymph nodes are shown in *Table 2*. All patients signed an informed consent form before undergoing ultrasound-guided biopsy, and coagulation function was examined.

Apparatus, biopsy procedure and final diagnostic results

Apparatus

The real-time color ultrasound scanner used for ultrasound-guided biopsy was the ALOKA 10 diagnostic ultrasonic system (Aloka Co., Ltd., Japan), and the probe used was a 5- to 12-MHz linear array Transducer. For CNB, 18-G biopsy needles with lengths of 6 or 10 cm by C. R. Bard, Ltd., USA were used. For FNA biopsy, Sonopsy-C1 vacuum aspiration biopsy needles (21 G) produced by Hakko Co., Ltd., Japan were used.

Biopsy method

The patient was placed in the supine or lateral position to fully expose the location of the lymph node to be punctured. General ultrasound scanning was performed, the optimal puncture position was selected, the depth of needle insertion was measured, and the puncture site on the body surface was located. The puncture site was wiped with a general disinfectant and injected with 2% lidocaine for local anesthesia.

FNA

A 5-mL syringe with a 21-G needle was manually inserted until the needle tip reached the edge of the lymph node while avoiding important tissues and organs, such as large blood vessels, nerves and the trachea, under color Doppler ultrasound guidance. After confirming the target, the needle was inserted into the lymph node cortex, and then the needle was set at a 2-mL scale to maintain negative pressure in the syringe. After rotating and aspirating the syringe 3–5 times, the direction of the needle was changed such that aspiration was performed in a fan shape at different trajectories in the lymph node. The needle was withdrawn once tissue was present in the syringe. The puncture site was covered with sterile gauze and pressure was applied with appropriate force for 10 min. Patients who showed no adverse reactions after 20 min of observation were released.

CNB

The skin of the puncture site was first pierced by a thick, 12-G needle tip, and then, the surgeon inserted the needle into the puncture point while avoiding large blood vessels, nerves and the trachea under ultrasound guidance. The biopsy gun was quickly pressed and the needle was withdrawn to complete the biopsy. After confirming that a sufficient sample was obtained, the collected specimen was quickly fixed with formaldehyde solution and sent for histological examination. The puncture site was covered with sterile gauze, and pressure was applied with appropriate force for 10 min. Patients who showed no adverse reactions after 30 min of observation were released.

Interpretation of ultrasound-guided lymph node FNA results and the final diagnostic criteria

For ultrasound-guided FNA cytological diagnosis, the presence of cancer cells and atypical cells was regarded as a positive result; otherwise, the result was considered negative. Among the 1,725 patients who underwent ultrasound-guided FNA biopsy, 988 also underwent CNB, and the CNB results were regarded as the final diagnosis. The 737 patients who did not undergo CNB were followed-up. The follow-up duration was between 6 and 22 months. The criteria for the diagnosis of lymph nodes were no significant changes in lymph node size and a benign internal structure (n=200). If lymph nodes were enlarged or the internal structure was changed during the follow-up, patients were subjected to additional CNB or FNA, and the results were used as the final diagnosis. Among the cases that underwent a second FNA biopsy, cancer cells in the lymph nodes accompanied by lymph node enlargement were identified in 2 cases, and the results of the second FNA biopsy were used as the final diagnosis. Negative results were found in the lymph nodes by a second ultrasound-guided FNA biopsy in 137 cases. Due to the presence of enlarged lymph nodes, these patients were followed-up again and eventually excluded from the study. Additionally, another 346 cases were excluded due to loss to follow-up or the presence of enlarged lymph nodes but no pathological data. Ultimately, 1,242 patients were included in this study.

Lymph node grouping

The 1,242 cases of biopsied lymph nodes were divided into two groups according to the length of the short-axis diameters (short-axis diameters ≤1 cm and >1 cm) to investigate the diagnostic value of FNA biopsy.

The 883 cases of lymph nodes with short-axis diameters ≤1 cm were divided into three groups according to the following diameters to investigate the diagnostic value of FNA biopsy: 0.7 cm ≤ short-axis diameter ≤1 cm, 0.5 cm ≤ short-axis diameter <0.7 cm, and short-axis diameter <0.5 cm.

Statistical analysis

SPSS24 statistical software was used for the statistical analysis. The Chi-square test was performed to assess the diagnostic value of ultrasound-guided FNA in the different groups. $P<0.05$ was used to define statistically significant differences.

Results

Lymph node size

The short-axis diameters of the lymph nodes in the study ranged from 0.3 to 5.7 cm, with an average diameter of 0.93±0.52 cm. The average short-axis diameter of each group is shown in *Table 3*.

Table 3 Average short-axis diameter of each lymph node group

Short-axis diameter of the lymph node (cm)	Average (cm)
>1	1.56±0.58
≤1	0.69±0.18
0.7–1	0.82±0.11
0.5–0.7	0.55±0.51
<0.5	0.39±0.04

Table 4 Cytological results of the 1,242 cases of lymph nodes undergoing ultrasound-guided FNA biopsy

Pathological results	Number
Spindle cell hyperplasia	15
Inflammation	22
Tuberculosis	7
Lymphatic tissue	498
Mild atypia	25
Metastasis	675
Total	1,242

FNA, fine-needle aspiration.

FNA diagnosis and final diagnosis

The results for the FNA cytology diagnosis of 1,242 lymph nodes are shown in *Table 4*. Based on the cytological diagnosis, 700 cases were positive, and 542 cases were negative. In addition, 988 cases underwent CNB, among which 699 cases were positive and 289 cases were negative, based on histological diagnosis. Among the 254 cases without CNB, 2 cases were positive (*Figure 1*) and 252 cases were negative (*Figure 2*) according to follow-up and second biopsy or final diagnosis results. The final diagnosis results corresponded to 700 positive cases and 542 negative cases. Among the 1,242 cases, FNA examinations revealed 692 true-positive cases (*Figure 3*), 533 true-negative cases (*Figure 4*), 8 false-negative cases (*Figure 5*) and 9 false-positive cases (*Figure 6*) according to the final diagnosis criteria.

Diagnostic results of ultrasound-guided FNA for lymph nodes with short-axis diameters ≤1 and >1 cm

The diagnostic results of the lymph nodes with short-axis diameters ≤1 and >1 cm by ultrasound-guided FNA are shown in *Table 5*. The diagnostic efficacy is shown in *Table 6*. No significant differences in sensitivity, specificity and accuracy were observed between the two groups (P>0.05).

Diagnoses of different groups of lymph nodes with a short-axis diameter <1 cm by ultrasound-guided FNA

The diagnostic efficacy in the three groups of lymph nodes (0.7 cm ≤ short-axis diameter ≤1 cm, 0.5 cm ≤ short-axis diameter <0.7 cm and short-axis diameter <0.5 cm) by ultrasound-guided FNA is shown in *Table 7*. A significant difference in accuracy was found among the three groups (P<0.05), but no significant differences in diagnostic sensitivity and specificity were observed (P>0.05).

Discussion

Accurate cancer staging is key to determining an individualized treatment plan and to predict prognosis, while lymph node evaluation is key to cancer staging. Clearly determining whether lymph node metastasis is present has guiding significance for surgical resection and selection of radiotherapy and chemotherapy regimens. The short-axis diameters of metastatic lymph nodes are often considered to be greater than 1 cm (3), but for some sites, especially the head and neck, only 8% to 37.5% of metastatic lymph nodes have a short-axis diameter greater than 1 cm. Therefore, increasing the detection rate of metastatic lymph nodes with short-axis diameters ≤1 cm is important for selecting treatment plans and predicting a patient's prognosis. However, diagnosing the nature of suspected lymph nodes by relying solely on clinical manifestations, imaging studies and laboratory tests is often difficult. Pathological examination is the gold standard for the diagnosis of such diseases. Currently, surgical resection, histological analysis based on ultrasound-guided core-needle puncture or cytological analysis based on FNA are used to obtain lymph node tissue (5). The advantage of surgical biopsy is that the materials are complete and easily meet the needs of pathological examination. However, the trauma caused by this type of surgical biopsy is relatively extensive, the procedure is very costly, and patients' compliance is poor. Ultrasound-guided CNB can generally obtain a sufficient specimen and preserve the surrounding tissue structure, allowing immunohistochemistry analysis based on histomorphological examination, resulting in high diagnostic efficiency (6-9). However, for lymph nodes with small short-axis diameters, the application of CNB is very limited and is associated with complications such as hemorrhage and nerve injuries (10,11).

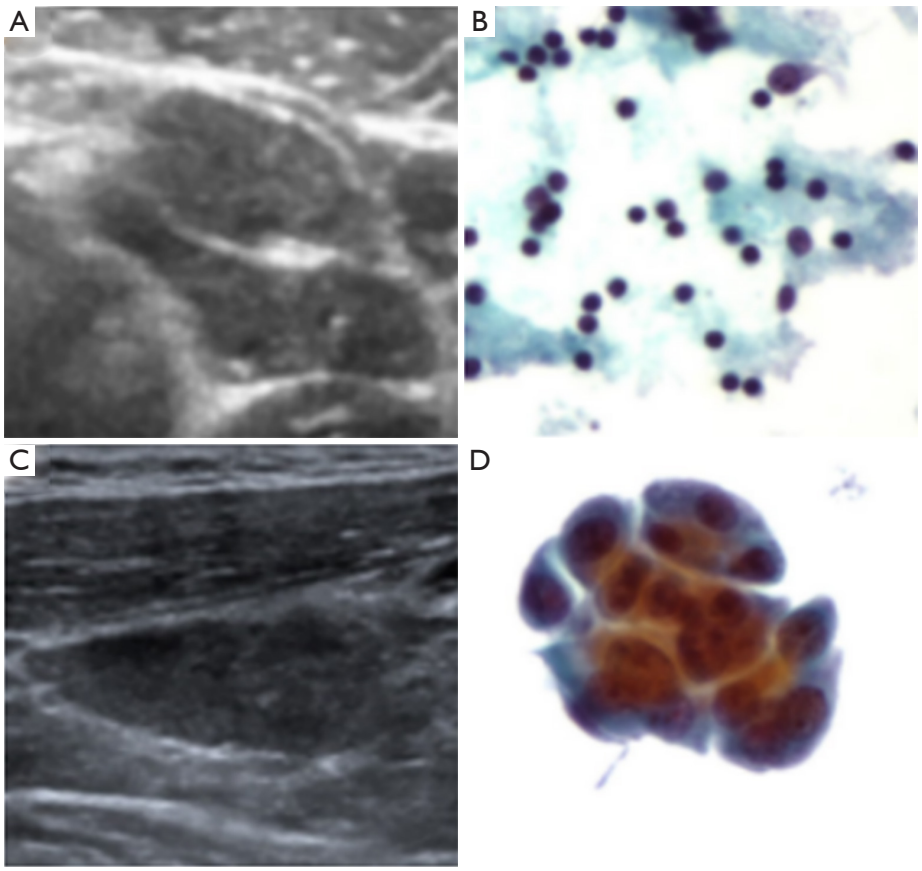

Figure 1 False-negative result of a 69-year-old female patient with breast cancer undergoing FNA biopsy of a lymph node of left neck at level III. (A) The lymphatic portal was absent in the first two-dimensional ultrasound image of the lymph node. (B) FNA biopsy cytologic smear showing no tumor cells (Papanicolaou stain, original magnification ×40). (C) After 7 months of follow-up, a second FNA biopsy cytologic smear was performed due to an increased mass of the targeted lymph node. (D) The second FNA biopsy cytologic smear showing tumor cells (Papanicolaou stain, original magnification ×40). FNA, fine-needle aspiration.

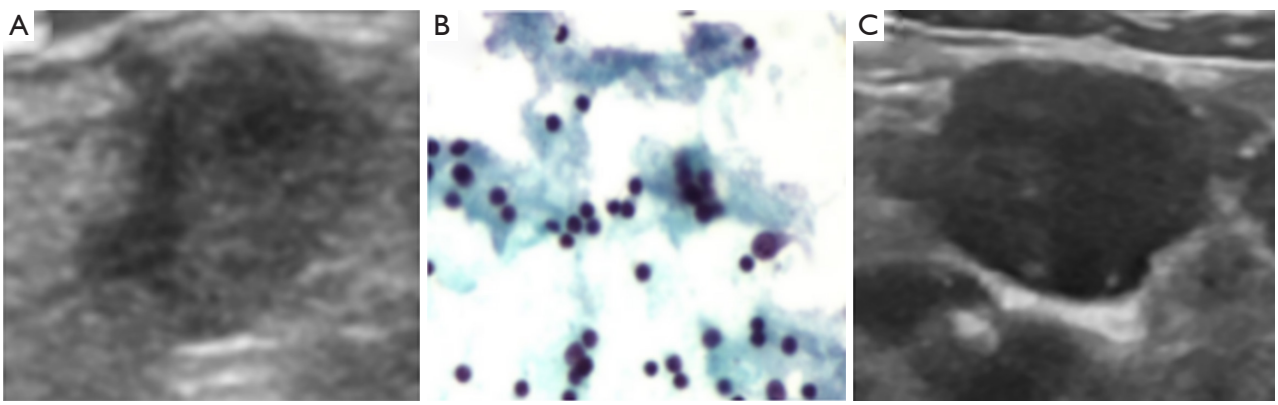

Figure 2 True-negative result of a 78-year-old female patient with breast cancer undergoing FNA biopsy of a lymph node in the left armpit. (A) The lymphatic portal was absent in the first two-dimensional ultrasound image of the lymph node. (B) FNA biopsy cytologic smear showing no tumor cells (Papanicolaou stain, original magnification ×40). (C) A second FNA biopsy was not performed because of the mass of the targeted lymph node was essentially unchanged. FNA, fine-needle aspiration.

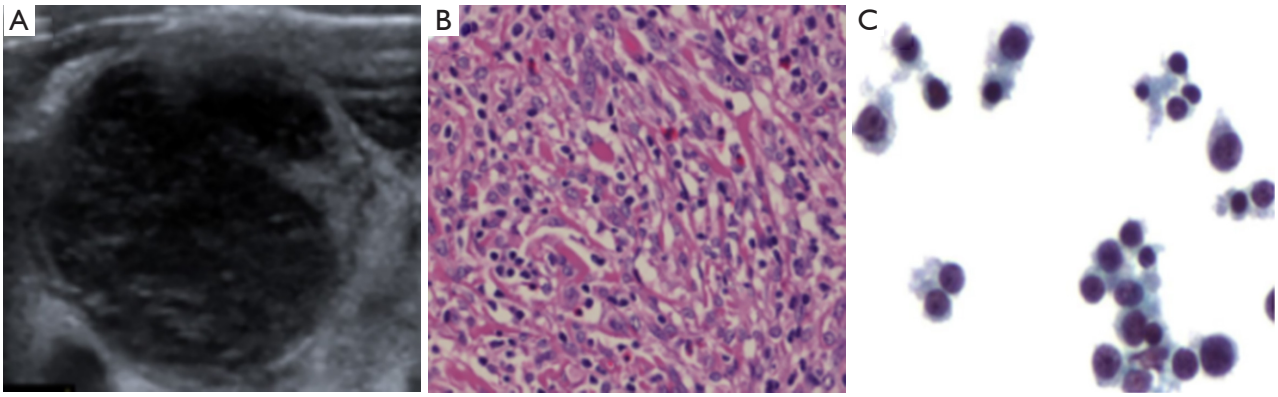

Figure 3 True-positive result of a 56-year-old female patient with Hodgkin's lymphoma undergoing FNA biopsy of a lymph node in the left armpit. (A) An eccentric lymphatic portal was detected in the two-dimensional ultrasound image of the lymph node. (B) Core-needle specimen showing tumor cells (hematoxylin-eosin stain, original magnification ×200). (C) FNA biopsy cytologic smear showing tumor cells (Papanicolaou stain, original magnification ×40). FNA, fine-needle aspiration.

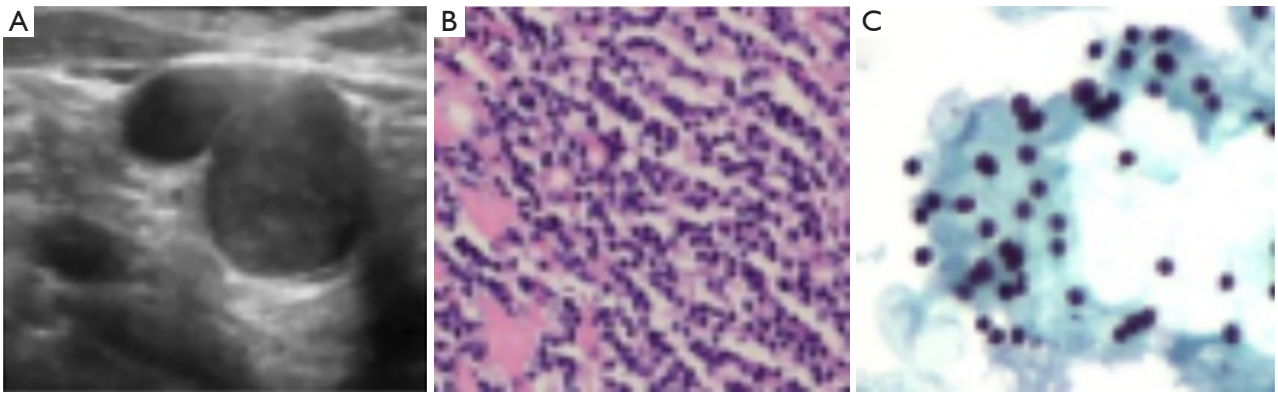

Figure 4 True-negative result of a 39-year-old female patient with cervical cancer undergoing FNA biopsy of a lymph node at level IV of the right neck. (A) The lymphatic portal was absent in the two-dimensional ultrasound image of the lymph node. (B) Core-needle specimen showing lymph node tissue without tumor cells (hematoxylin-eosin stain, original magnification ×200). (C) FNA biopsy cytologic smear showing no tumor cells (Papanicolaou stain, original magnification ×40). FNA, fine-needle aspiration.

Cytological examination via ultrasound-guided FNA has the advantages of producing minimal trauma, simple and rapid execution (12), very good patient compliance and a low incidence of serious complications. Additionally, ultrasound-guided FNA allows biopsy of suspicious lymph nodes in complicated structures such as posterior pharyngeal space under endoscopic ultrasound guidance. Lymphadenopathy can be identified by observing cell morphological abnormalities such as the nuclear membrane, nucleolus and nuclear-cytoplasm ratio (4,9,13,14).

Most existing studies of lymph nodes with short diameters ≤1 cm have indicated that FNA can be performed in cases with absent lymphatic portals, local cortical thickening and changes in the blood supply pattern in the primary lymph node drainage area (15,16). However, Plukker *et al.* believe that the results of FNA are limited due to the limited number of cells obtained by FNA (2). Furthermore, Ewing *et al.* believe that FNA is not suitable for lymph nodes with short-axis diameters ≤1.2 cm due to relatively high false-negative rates (5).

In the current study, we found that the sensitivities, specificities and accuracies of ultrasound-guided FNA were 99.6%, 99.5% and 99.5% for lymph nodes with short-axis diameters ≤1 cm and 97.2%, 94.4% and 96.4% for lymph nodes with short-axis diameters >1 cm, respectively. No significant differences were observed between the two

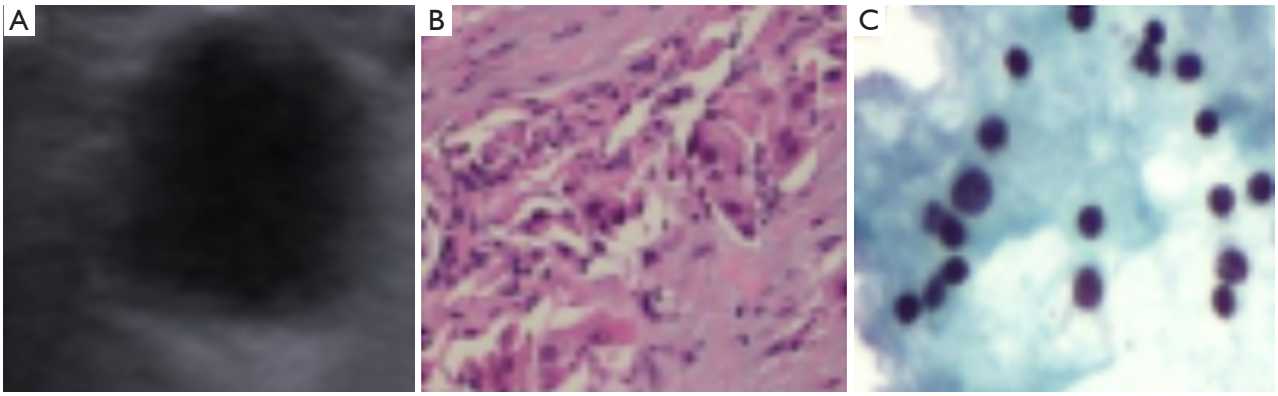

Figure 5 False-negative result of a 55-year-old male patient with lung adenocarcinoma undergoing FNA biopsy of a lymph node at level IV of the left neck. (A) The lymphatic portal was absent and the lymph node boundary was unclear in the two-dimensional ultrasound image of the lymph node. (B) Core-needle specimen showing tumor cells and residual lymph node tissue (hematoxylin-eosin stain, original magnification ×200). (C) FNA biopsy cytologic smear showing no tumor cells (Papanicolaou stain, original magnification ×40). FNA, fine-needle aspiration.

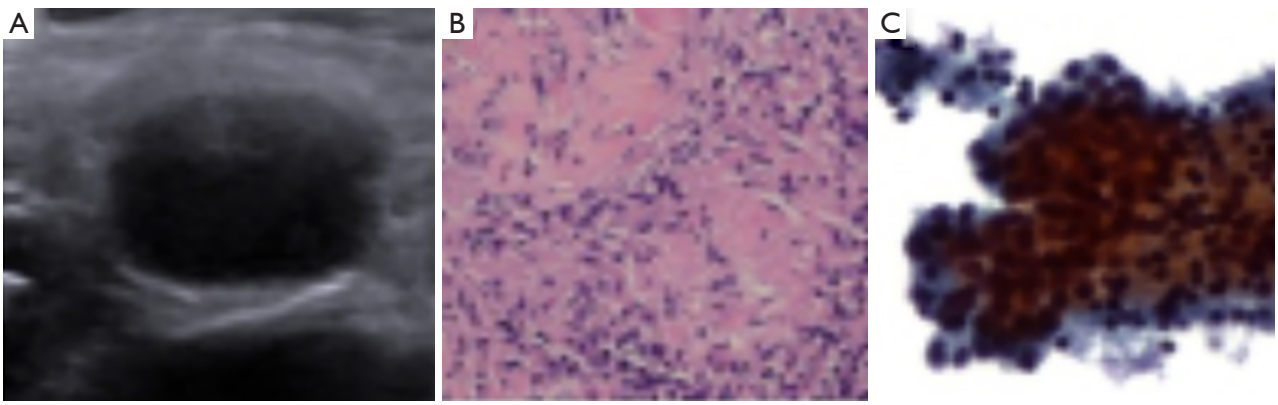

Figure 6 False-negative result of a 68-year-old male patient with lung adenocarcinoma undergoing FNA biopsy of a lymph node at level III of the left neck. (A) The lymphatic portal was absent in the two-dimensional ultrasound image of the lymph node. (B) Core-needle specimen showing lymph node tissue (hematoxylin-eosin stain, original magnification ×200). (C) FNA biopsy cytologic smear showing suspected tumor cells (Papanicolaou stain, original magnification ×40). FNA, fine-needle aspiration.

Table 5 Diagnoses of the two groups of lymph nodes with short-axis diameters ≤1 cm and >1 cm by ultrasound-guided FNA (cases)

Final diagnosis	Short-axis diameter ≤1 cm		Short-axis diameter >1 cm	
	Positive	Negative	Positive	Negative
Positive	448	2	244	6
Negative	2	431	7	102
Total	450	433	251	108

FNA, fine-needle aspiration.

Table 6 Diagnostic efficacy in the two groups of lymph nodes with short-axis diameters ≤1 cm and >1 cm by ultrasound-guided FNA

Parameter	Short-axis diameter of the lymph node		P
	>1 cm	≤1 cm	
Sensitivity	97.2% (244/251)	99.6% (448/450)	0.851
Specificity	94.4% (102/108)	99.5% (431/433)	0.343
Accuracy	96.4% (346/359)	99.5% (879/883)	0.818

FNA, fine-needle aspiration.

Table 7 Diagnostic efficacy for lymph nodes with different short-axis diameters (short-axis diameter <1 cm) by ultrasound-guided FNA

Parameter	Short-axis diameter of the lymph node			P
	0.7–1 cm	0.5–0.7 cm	<0.5 cm	
Sensitivity	99.6% (233/234)	99.5% (184/185)	98.0% (48/49)	0.142
Specificity	99.5% (213/214)	99.0% (104/105)	98.0% (50/51)	0.071
Accuracy	99.8% (447/448)	99.3% (288/290)	99.0% (99/100)	0.038

FNA, fine-needle aspiration.

groups (P>0.05). The sensitivities of ultrasound-guided FNA for the three groups of lymph nodes with short-axis diameters ≤1 cm were 99.6%, 99.5% and 98.0%, respectively. The specificities were 99.5%, 99.0% and 98.0%, respectively. The accuracies were 99.8%, 99.3% and 99.0%, respectively, with significant differences detected among the three groups (P<0.05). No significant differences in sensitivity and specificity were observed among the three groups (P>0.05). Our findings suggest that for lymph nodes with short-axis diameters ≤1 cm, the accuracy decreases as the short-axis diameter decreases, but FNA still has high diagnostic accuracy.

A limitation of this study is that all lymph nodes that underwent FNA were identified by routine ultrasound examination, and the results of routine ultrasound examination were affected by the expertise of the sonographers. Additionally, not all of the lymph nodes were diagnosed by CNB histological examination, and some cases of enlarged lymph nodes identified at the follow-ups were excluded due to a lack of second biopsy results, which may have affected our findings.

Conclusions

Ultrasound-guided FNA has high diagnostic value for metastatic lymph nodes. In particular, ultrasound-guided FNA has high accuracy for diagnosing small lymph nodes and can achieve an accurate diagnosis for lymph nodes that cannot be accessed by CNB.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/cco.2019.08.18). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This is a retrospective study, we collected all cases in hospital computer system (or called PACS), so we do not have ethics committee information. And this study have no conflict with anybody and do not broke any human ethics. All patients signed an informed consent form before undergoing ultrasound-guided biopsy, and coagulation function was examined.

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