Efficacy of contrast-enhanced ultrasound-guided percutaneous core needle biopsy in anterior mediastinal masses

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ABSTRACT

Objective: To evaluate the efficacy and safety of percutaneous core needle biopsy (PCNB) using ultrasound (US)-guided and contrast-enhanced ultrasound (CEUS)-guided procedures for anterior mediastinal masses (AMMs).
Methods: In total, 284 consecutive patients (166 men, 118 women; mean age, 43.0 ± 18.4 years) who underwent PCNB for AMMs were enrolled. Patients were divided into the US-guided group (n = 133) and the CEUS-guided group (n = 151). PCNB was performed using a core needle (16-gauge or 18-gauge). Internal necrosis, diagnostic yield, and diagnostic accuracy were compared between the two groups.
Results: The predominant final diagnosis of the cases in this study was thymoma (29.7%), lymphoma (20.5%), thymic carcinoma (13.3%), and germ cell tumour (13.3%), respectively. There was no significant difference in patient age, sex, number of percutaneous biopsies, or display rate of internal necrosis on conventional US between the two groups. The rate of internal necrosis of the lesions was significantly higher after contrast agent injection (72.2% vs. 41.7%; $P < 0.001$). The CEUS-guided group had a higher diagnostic yield than the US-guided group (100% vs. 89.5%, $P < 0.001$). There was no significant difference between the diagnostic accuracy of the CEUS-guided and US-guided groups (97.3% vs. 97.4%; $P = 1.000$). None of the patients experienced adverse reactions or complications after US-guided or CEUS-guided PCNB.
Conclusions: CEUS-guided PCNB can improve the diagnostic yield by optimizing the biopsy procedure.

1. Introduction

The mediastinum is the general name for the organs, structures, and connective tissue between the two pleural sacs, while the anterior mediastinum is defined as the narrow gap between the sternal body and the anterior wall of the pericardium. Anterior mediastinal masses (AMMs) are the most common group of mediastinal tumours (54%), and 25–50% of AMMs are malignant.[1] AMMs have a low incidence and high heterogeneity. Early accurate diagnosis is important for the selection of treatment strategies.[2] Although non-invasive imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and contrast-enhanced ultrasonography (CEUS), are widely used to distinguish AMMs and determine tumour extension,[3,4] such imaging is still not sufficient to make an accurate differential diagnosis. Treatment strategies are largely based on pathological results.

As early as 1992, ultrasound (US)-guided percutaneous core needle biopsy (PCNB) of AMMs had been reported to be a safe, cost-effective and reliable method and a good alternative to the traditional biopsy techniques via mediastinoscopy or thoracotomy.[5] The use of US-guided PCNB has several advantages, such as real-time imaging and dispensability of radiation exposure. First, continuous monitoring of the needle confirmed that the biopsy specimen was representative. Second, vascular structures (especially the internal thoracic artery) can be avoided more easily through the biopsy route. Furthermore, the rate of occurrence of lung injuries is very low. However, US-guided PCNB of AMMs also has disadvantages. Gas is a major barrier interfering with the ultrasonic imaging. Indeed, it is impossible to view the lesion when lung tissue is located between the US transducer and lesion. This limits US-guided PCNB of AMMs as only suitable for lesions directly contacting the thoracic wall or protruding into the thoracic outlet.

CT-guided PCNB is another common approach that is not restricted to lung tissues. The diagnostic yield of the US-guided approach is similar to that of the CT-guided approach, but it has fewer complications, including pneumomediastinum, pneumothorax, hemoptysis, hemothorax, and hematoma formation. In prior studies, the complication rate of the CT-guided approach ranged from 2% to 17%, while that of the US-guided approach was consistently close to zero.[6–9]

The main reason for the diagnostic failure of US-guided PCNB is insufficient sampling due to necrotic or fibrotic tissue, especially in large lesions. CEUS has obvious potential in US-guided interventional procedures. CEUS can accurately delineate tissue vascularization. Biopsy of necrotic tissue can be avoided by directing the biopsy needle toward the contrast-enhanced areas within the target lesion.[10]

Herein, we conducted a retrospective study to compare the diagnostic yield, diagnostic accuracy, and complication rate of CEUS-guided vs. US-guided PCNB for AMMs.

2. Material and methods

2.1. Patients

This retrospective study was approved by the ethics committee of our institution. Written informed consent was obtained from each patient before the CEUS and biopsy procedures. We reviewed the data from an institutional biopsy database and patients' medical records between January 2015 and December 2021 in a single center. Three hundred and one consecutive patients with AMMs detected on chest CT were admitted to our department for a pre-biopsy US examination. Sixteen patients cancelled their original biopsy plans because the lesions were not visualized via the intercostal space by conventional US, or were smaller than 2.5 cm. One patient was cancelled because the lesion was completely cystic, as examined by CEUS. Finally, 284 patients (166 men, 118 women; mean age, 43.0 ± 18.4 years; age range, 13–82 years) were included in our study. According to the actual situation of the retrospective data, all the patients were divided into two groups: US-guided and CEUS-guided groups.

2.2. Pre-biopsy US examination

Before biopsies, patients were examined in the supine position. Conventional US scanning (Philips HD15, USA; Medison Acuvix V10, Korea; Mindary DC-8, China) or CEUS (Philips HD15, USA; Mindary DC-8, China) was performed with a low-frequency convex array probe in all lesions.

Conventional US examination was performed to observe the lesion's location, size, internal echo, and adjacent relationship with the heart and the large vessels. Color Doppler flow imaging was performed to observe the intralesional and surrounding vascularity of the lesions. The parenchyma of the lesion with relatively abundant blood supply was selected for biopsy. In this procedure, it is important to pay attention to the large vessels on the biopsy route, such as the internal mammary and intercostal arteries. "Internal necrosis" on conventional US was defined as a hypoechoic or anechoic area with a clear boundary from the surrounding tissue without a blood flow signal.

CEUS was performed after a bolus injection of 2.0 mL SonoVue® via a 20-gauge intravenous catheter in the cubital vein. Enhanced areas and necrosis (areas without enhancement) of the lesion were identified, and the enhanced areas were selected for biopsy.

2.3. Biopsy technique

PCNB was performed or supervised by a trained interventional ultrasound doctor with 3–20 years of experience. The biopsy route and device were selected at the discretion of the doctor. After the skin was sterilized, local anesthesia in the form of 2% lidocaine was administered. PCNB was performed with a 16-gauge/18-gauge fully automatic (Bard

Medical, USA) or semi-automatic (CareFusion, USA) core needle device (Max cutter length 22 mm). The complete biopsy procedure was monitored under real-time US guidance to adjust the route. In the CEUS-guided group, the target area for biopsy was the enhanced area selected from the previous CEUS examination. Two core specimens were obtained for each patient. If the parenchyma of the core specimens was too small, an additional one or two core specimens were obtained. Biopsy specimens were placed on a small piece of filter paper and stored in a specimen bottle containing 10% formalin for further histological diagnosis. Post-biopsy, the patients were observed for a minimum of 2 h in bed.

2.4. Diagnosis yield and accuracy

Pathological classification of the anterior mediastinal lesions was performed based on the World Health Organization tumour classification (2015 version).[11] Each biopsy was classified according to the following diagnostic results: malignancy, benignity, indeterminate result, or non-diagnostic result, based on the diagnosis of two trained pathologists with 5–20 years of experience. Non-diagnostic results were defined when an insufficient tissue sample was obtained via PCNB for a specific diagnosis. For example, the pathological examination revealed only blood or coagulative necrosis. Precise diagnosis of malignancy or benignity was considered the histologic result of PCNB in accordance with surgical pathology or clinicoradiologic diagnosis. Indeterminate results were defined as cases where the mediastinal lesion was not clear, whether benign or malignant, despite sufficient tissue sample.[12]

$$Diagnostic\ yield = \frac{diagnostic\quad results}{diagnostic\ \ results + non-diagnostic\ \ results}$$

$$Diagnostic\ accuracy = \frac{precise\ \ diagnosis\ \ of\ \ the\ \ malignancy\ \ or\ \ benignity}{all\ \ determinate\ \ results}$$

2.5. Statistical analysis

All data are expressed as mean ± standard deviation (SD). The difference between the two groups was analyzed using the independent samples *t-test* and the chi-square test. All statistical analyses were performed using the SPSS software (version 20.0; SPSS Inc.). Statistical significance was set at $P < 0.05$.

3. Results

Ultimately, 284 patients who underwent 285 biopsy procedures were enrolled, comprising 133 in the US-guided group and 151 in the CEUS-guided group. In the US-guided group, one patient underwent two biopsy procedures (one US-guided and one CEUS-guided). Two hundred and sixty-three cases had a definite pathological diagnosis (114 cases confirmed by surgical pathological diagnosis and 149 cases confirmed by clinicoradiological diagnosis) (Fig. 1). The predominant final diagnoses in this study were thymoma (29.7%, 78/263), lymphoma (20.5%, 54/263), thymic carcinoma (13.3%, 35/263), and germ cell tumours (13.3%, 35/263) (Table 1).

There was no significant difference in patient age, sex, number of percutaneous biopsies, or display rate of internal necrosis on conventional US between the US-guided and CEUS-guided groups. In the CEUS-guided group, internal necrosis was observed in 72.2% (109/151) of the lesions after contrast agent injection, which was significantly higher than that before injection (41.7%, 63/151; $P < 0.001$) (Table 2). In the CEUS-guided group, the display rate of internal necrosis was significantly lower in thymomas (40.5%, 17/42) than in lymphomas (63.9%, 23/36; $P = 0.039$) and thymic carcinoma (95.2%, 20/21; $P < 0.001$) (Fig. 2). The use ratio of the 18-gauge core needle was significantly lower in the CEUS-guided group than in the US-guided group (3.3%, 5/151 vs. 21.8%, 29/133; $P < 0.001$) (Table 2). All tissue samples obtained using 18-gauge
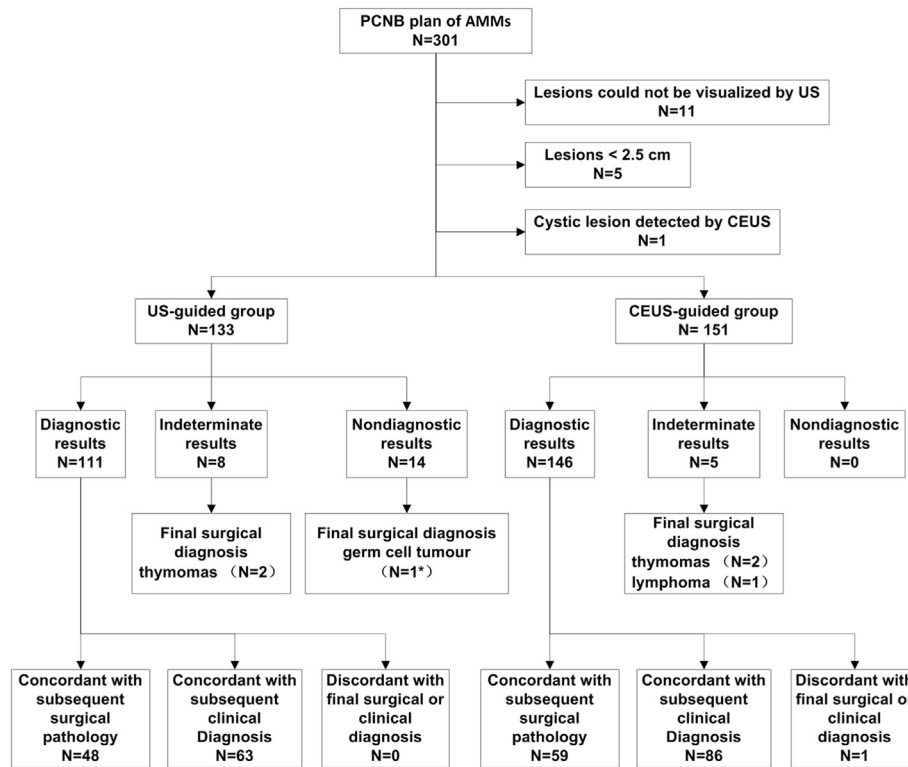
Fig. 1. Flow diagram shows the algorithm for the final diagnostic results of 284 patients with US-/CEUS- guided percutaneous core needle biopsy of AMMs. PCNB: percutaneous core needle biopsy. US: ultrasound. CEUS: contrast-enhanced ultrasound. *One case underwent re-PCNB by CEUS-guided.

Table 1
Final diagnosis confirmed by surgical pathology or clinic-radiologic diagnosis of the US-guided and the CEUS-guided groups.

Final diagnosis[a]	US-guided group (n = 114)	CEUS-guided group (n = 149)	All cases[b] (n = 263)
Thymomas	36	42	78 (29.7%)
Thymic carcinoma	14	21	35 (13.3%)
Neuroendocrine tumours	15	9	24 (9.1%)
Germ cell tumours	13	22	35 (13.3%)
Lymphomas	18	36	54 (20.5%)
Soft tissue tumours			
Liposarcoma	3	2	5 (1.9%)
Synovial sarcoma	2	5	7 (2.7%)
Neurogenic tumours	2	2	4 (1.5%)
Solitary fibrous tumour	2	2	4 (1.5%)
Malignant mesothelioma	1	1	2 (0.8%)
Metastases	4	6	10 (3.8%)
Tuberculous granuloma	1	1	2 (0.8%)
Ecropic thyroid tumours	1	0	1 (0.4%)
Hyperplasia of thymus gland	2	0	2 (0.8%)

[a] Pathological classification referred to the World Health Organization classification of tumours (2015 version).
[b] The remaining 21 cases had no definitely pathological diagnosis.

Table 2
Patient characteristics, biopsy technique, lesion characteristics: comparison of US-guided group versus CEUS-guided group.

	US-guided group (n = 133)	CEUS-guided group (n = 151)	P value
Age (range), years	43.9 ± 19.5 (13–82)	42.6 ± 17.7 (14–80)	0.680
Male/female	78/55	88/63	0.950
Number of percutaneous biopsy	2.1 ± 0.4 (2–4)	2.1 ± 0.3 (2–3)	0.401
16-gauge/18-gauge core needle	104/29	146/5	<0.001*
Internal necrosis (conventional US/CEUS)	50/-	63/109	0.478/-

Values shown are number or mean ± SD (range) as appropriate.
*$p < 0.05$.

= 1.000). In the CEUS-guided group, one case was initially diagnosed as hyperplasia of the thymus gland by biopsy pathology, but was finally diagnosed as a seminoma with a large necrotic area by subsequent surgical pathology. In the US-guided group, one case underwent re-PCNB with CEUS guidance 5 days later. The result of the specimen first obtained by US-guided PCNB was non-diagnostic because of only coagulative necrosis in the pathological examination. The second result of the specimen obtained by CEUS-guided PCNB was diagnosed as a germ cell tumor confirmed by surgical pathology (Fig. 3).

CEUS examination was performed in 151 patients, and no adverse reactions to SonoVue® were observed. None of the patients experienced adverse reactions or complications after US-guided or CEUS-guided PCNBs.

4. Discussion

The histological types of mediastinal lesions are complex, and their clinical and imaging manifestations of mediastinal lesions usually lack
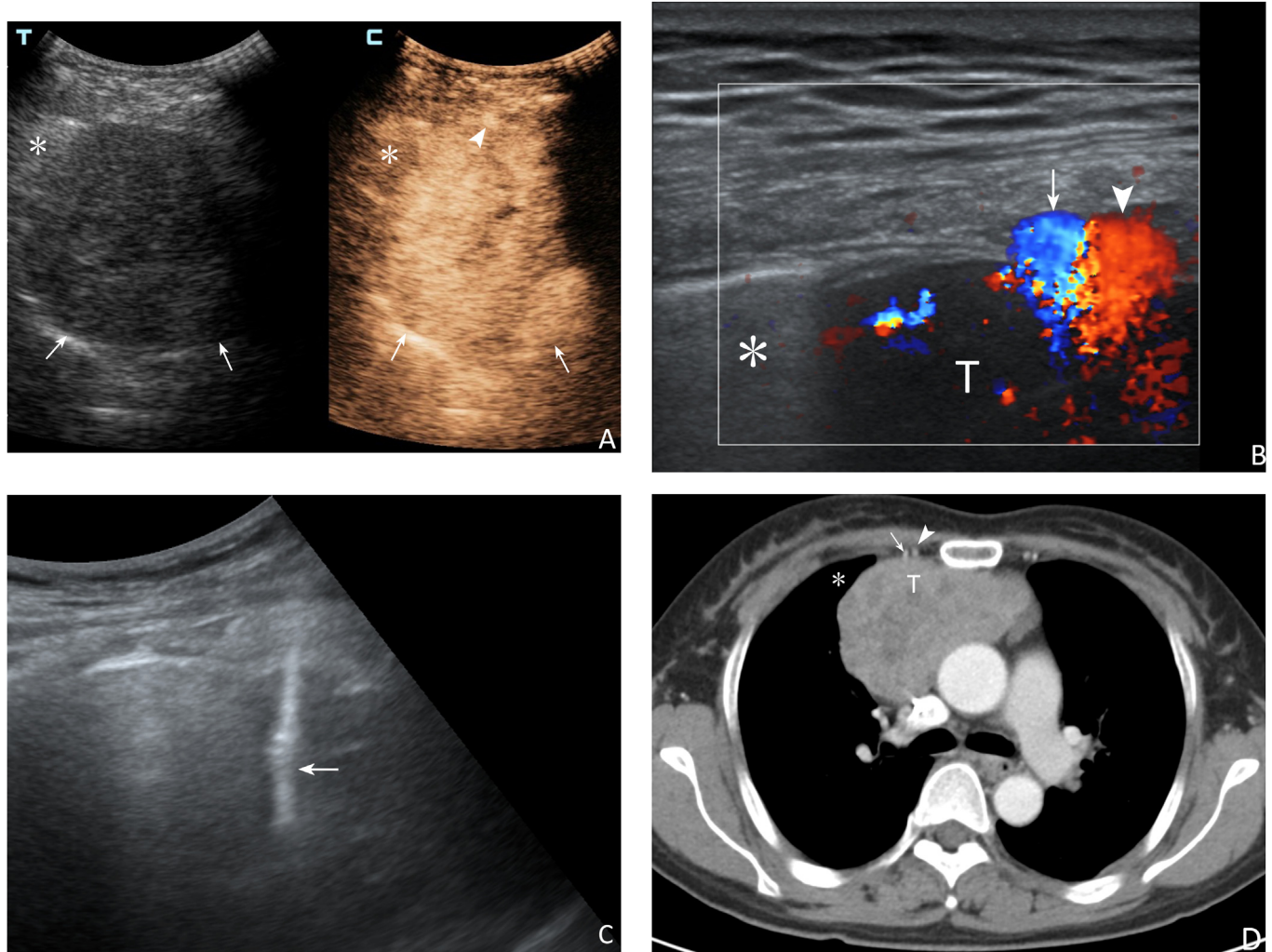
core needles provided a precise diagnosis. The diagnostic yield of the CEUS-guided group was significantly higher than that of the US-guided group (100% [151/151] vs. 89.5% [119/133]; P < 0.001). There was no significant difference in diagnostic accuracy between the CEUS-guided and US-guided groups (97.3%, 145/149 vs. 97.4%, 111/114; P

Fig. 2. The case in a 46-year female by CEUS-guided PCNBs. The anterior mediastinum lesion was confirmed as thymoma by subsequent surgical pathology. Before the biopsies, CEUS showed the lesion was heterogeneous hyper-enhancement without obvious necrosis (A, arrows; * lung), and the internal thoracic artery in front of the lesion was visible (A, arrowhead). High-frequency ultrasound could see the internal thoracic artery (B, arrow) and vein (B, arrowhead; T: lesion; * lung) more clearly. Biopsy route was adjusted to avoid blood vessel damage, and real-time US showed the transpleural pathway of the biopsy needle (C, arrow). Contrast-enhanced chest computed tomography showed the heterogeneous enhanced lesion and the internal thoracic artery (D, arrow) and vein (D, arrowhead; T: lesion; * lung) in the soft tissue window.

specificity. More than 50% of mediastinal lesions seen in adults are observed in the anterior mediastinum.[2] An accurate pathological diagnosis is crucial to decide on the most effective therapeutic strategy. In the past, the diagnosis was mainly based on thoracotomy or mediastinoscopy, both of which were associated with invasive damage and even morbidity.[13] Currently, image-guided PCNB of AMMs, including US, CT and MRI, has been verified to be a minimally invasive and relatively safe procedure.[9,14–18]

AMMs directly contacting the thoracic wall or with the soft tissues of the jugular fossa can be visualized by US scan through the parasternal intercostal space. CDFI can distinguish the relationship between lesions and the surrounding large vessels and the heart. Therefore, US-guided PCNB has become a cost-effective, time-saving, and feasible method to obtain pathological specimens of AMMs.[8] The diagnostic yield of US-guided PCNB of AMMs ranged from 79% to 100%.[5,8,15,19,20] The pathological tissue obtained by PCNB represents only a small part of the lesion, and the tissue composition in different parts of the same lesion may vary greatly. Obtaining adequate tissue specimens representing the essential characteristics of the lesion is essential to improve the diagnostic yield and accuracy of PCNB. Conventional US-guided percutaneous biopsies can usually be used to obtain adequate tissue specimens.

Nevertheless, necrosis or liquefaction caused by insufficient blood supply often occurs during tumour growth. Conventional US cannot accurately distinguish the active area from necrosis; therefore, the diagnostic yield of US-guided percutaneous biopsy may be unsatisfactory in these circumstances. Combined with CDFI, necrosis of the lesion may be avoided by experienced operators. However, AMMs are adjacent to the heart and large blood vessels, and their pulsation may affect the presentation of low-velocity blood flow on CDFI. CEUS can accurately display the blood flow perfusion of different tissue structures in the lesion and is not disturbed by the pulsation of large cardiac vessels. In our study, the CEUS-guided group showed a higher rate of internal necrosis of the lesions. CEUS can accurately distinguish the active area and necrosis of the lesion to allow an optimal route to guide PCNB and improve diagnostic yield. Our study showed that the diagnostic yield of CEUS-guided PCNB for AMMs was significantly higher than that of US-guided PCNB (100% vs. 89.5%).

There was no significant difference between the diagnostic accuracies of the CEUS-guided and US-guided groups. Although the 18-gauge core needle was used more frequently in the US-guided group than in the CEUS-guided group, all tissue samples obtained using 18-gauge core needles had a precise diagnosis in our study. For safety purposes, 18-gauge core needles were used for small AMMs in our study. Some
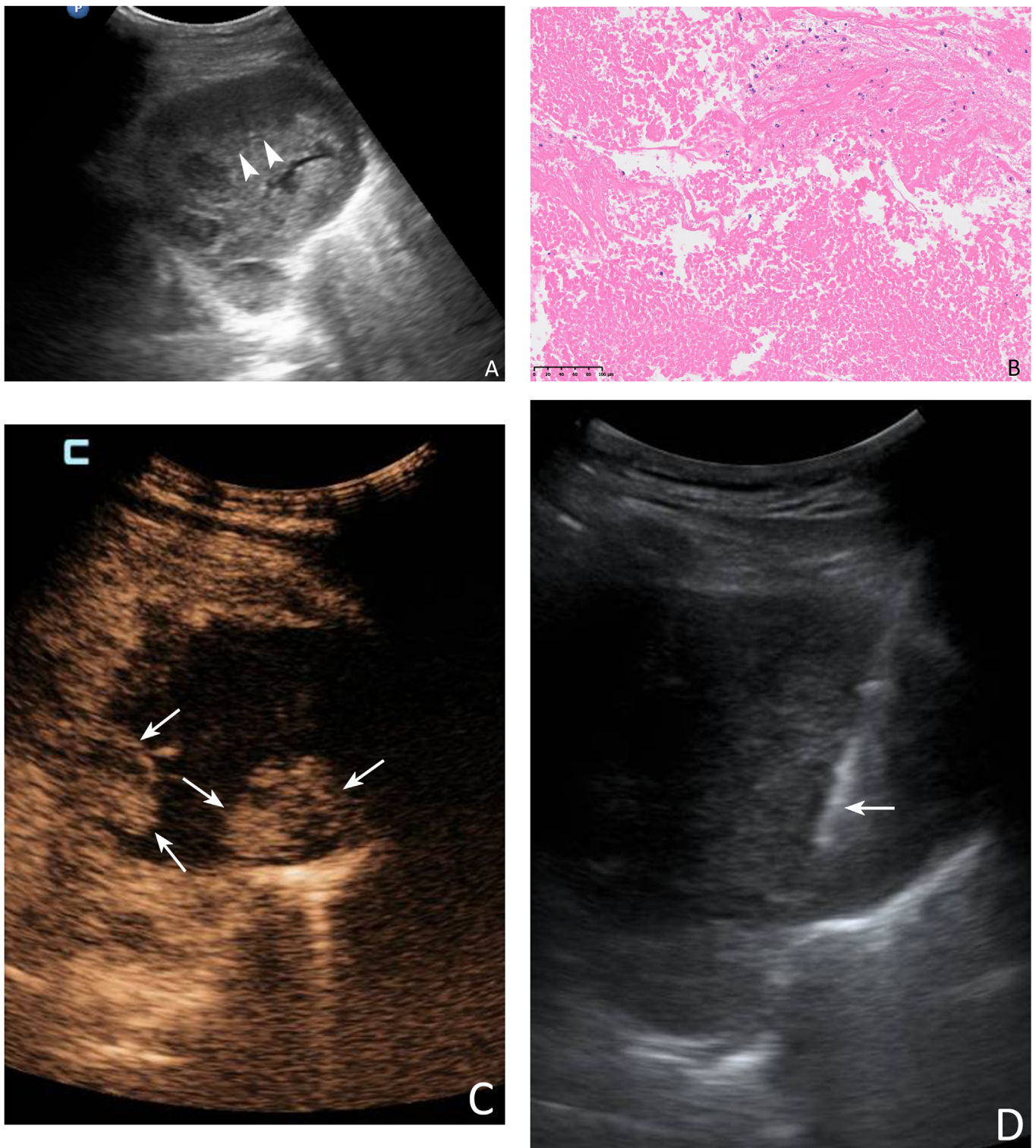
Fig. 3. A 52-year male underwent two PCNBs. The first time, US showed a heterogeneous hypoechoic anterior mediastinum lesion and selected a common target area for biopsy (A, arrowheads). The result of the specimen by US-guided PCNB was nondiagnostic due to only coagulative necrosis seen microscopically (B). Five days later, CEUS showed the deep area of the lesion was obviously enhanced (C, arrows), and the area of the first biopsy was unenhanced massively. PCNB was performed successfully in the active area of the lesion subsequently, and real-time US showed the transpleural pathway of the biopsy needle (D, arrow). Microscopically, atypical epithelioid cells could be seen (E), and the specimen of CEUS-guided PCNB was diagnosed as a germ cell tumour confirmed by surgical pathology.

researchers have reported that using a thinner needle (i.e., a 20-gauge needle) is the sole significant risk factor for diagnostic failure. As such, both 16-gauge and 18-gauge core needles are safe and effective for PCNB

of AMMs, and tissue specimens obtained by PCNB were adequate for pathological examination, although care should be taken regarding necrosis.
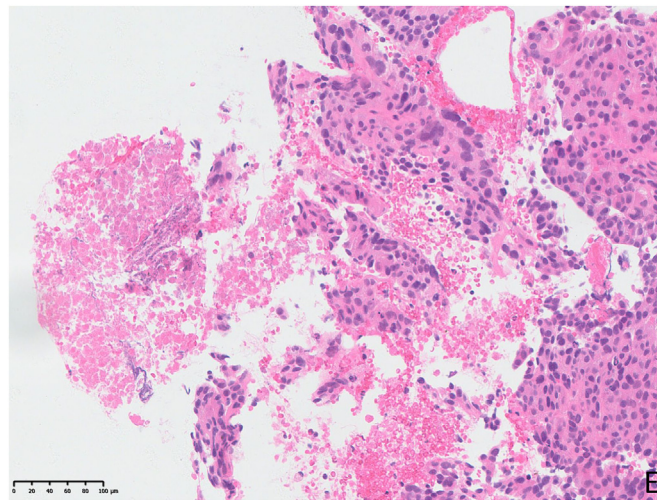
Fig. 3. (*continued*).

CT is the most commonly used modality for the localization of mediastinal lesions and to guide biopsy. The diagnostic yield of CT-guided PCNB ranged from 74% to 97%.[7,14,18,21–23] The pooled proportions of the diagnostic yield and accuracy of CT-guided PCNB for mediastinal masses were 92% and 94%, respectively, in a meta-analysis from 18 eligible studies.[12] The US-guided approach had a similar diagnostic yield to the CT-guided approach. No complications were reported in prior studies assessing the US-guided approach Conventional US, CDFI, and CEUS can be used to visualize vessels and guide the percutaneous biopsy process in real time to avoid important structures. Complication rates in CT-guided procedures range from 4% to 17%.[6] A transpleural route was reported as the only variable associated with an increased complication rate by CT-guided approaches.[6] It is impossible to view the lesion when the lung tissue is between the US transducer and the lesion; therefore, US-guided procedures usually avoid this route. This may be another reason for the fewer complications associated with the US-guided procedures.

The current study had several limitations. First, the retrospective design will have resulted in the introduction of selection bias. Second, only patients deemed suitable to undergo US-guided or CEUS-guided PCNB underwent this procedure. Third, the technique (including the approach, route, and biopsy gauge) was chosen by a trained and experienced interventional ultrasound doctor based on the case study.

5. Conclusions

Our study shows that US-guided and CEUS-guided PCNBs for AMMs are safe methods with high diagnostic yield and diagnostic accuracy. CEUS-guided PCNB can improve the diagnostic yield by allowing optimization of the biopsy procedure.

Author contributions

Peili Fan: Data curation, Formal analysis, Writing - original draft, **Jiaying Cao:** Writing - review & editing, **Yunjie Jin:** Investigation, **Hong Han:** Investigation, **Wenping Wang:** Funding acquisition, Validation, Supervision, **Huixiong Xu:** Validation, Supervision, **Zhengbiao Ji:** Conceptualization, Investigation, Methodology,

Declaration of competing interest

The authors declare no conflict of interest.

References

1. Hakiri S, Kawaguchi K, Fukui T, et al. Verification of the diagnostic strategy for anterior mediastinal tumors. *Int J Clin Oncol.* 2019;24:385–393.
2. Gonzalez M, Ris HB, Krueger T, et al. Quelle attitude face à une masse médiastinale antérieure chez l'adulte ? [Management of anterior mediastinal masses in adults]. *Rev Mal Respir.* 2012;29:138–148. French.
3. Nakazono T, Yamaguchi K, Egashira R, et al. Anterior mediastinal lesions: CT and MRI features and differential diagnosis. *Jpn J Radiol.* 2021;39:101–117.
4. Garrana SH, Rosado-de-Christenson ML. Imaging of the anterior/prevascular mediastinum. *Radiol Clin North Am.* 2021;59:155–168.
5. Andersson T, Lindgren PG, Elvin A. Ultrasound guided tumour biopsy in the anterior mediastinum. An alternative to thoracotomy and mediastinoscopy. *Acta Radiol.* 1992;33:423–426.
6. Navin PJ, Eickstaedt NL, Atwell TD, et al. Safety and efficacy of percutaneous image-guided mediastinal mass core-needle biopsy. *Mayo Clin Proc Innov Qual Outcomes.* 2021;5:1100–1108.
7. Rabbani M, Sarrami AH. Computed tomography-guided percutaneous core needle biopsy for diagnosis of mediastinal mass lesions: experience with 110 cases in two university hospitals in Isfahan, Iran. *Adv Biomed Res.* 2016;5:152.
8. Yi D, Feng M, Wen Ping W, et al. Contrast-enhanced US-guided percutaneous biopsy of anterior mediastinal lesions. *Diagn Interv Radiol.* 2017;23:43–48.
9. Petranovic M, Gilman MD, Muniappan A, et al. Diagnostic yield of CT-guided percutaneous transthoracic needle biopsy for diagnosis of anterior mediastinal masses. *AJR Am J Roentgenol.* 2015;205:774–779.
10. Sidhu PS, Cantisani V, Dietrich CF, et al. The EFSUMB guidelines and recommendations for the clinical practice of contrast-enhanced ultrasound (CEUS) in non-hepatic applications: update 2017 (Long Version). *Ultraschall Med.* 2018;39:e2–e44.
11. Travis WD, Brambilla E, Burke AP, et al. *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours Lung, Pleura, Thymoma and Heart.* Lyon: LARC Press; 2015.
12. Lee HN, Yun SJ, Kim JI, et al. Diagnostic outcome and safety of CT-guided core needle biopsy for mediastinal masses: a systematic review and meta-analysis. *Eur Radiol.* 2020;30:588–599.
13. Gossot D, Toledo L, Fritsch S, et al. Mediastinoscopy vs thoracoscopy for mediastinal biopsy. Results of a prospective nonrandomized study. *Chest.* 1996;110:1328–1331.
14. Burgard C, Stahl R, de Figueiredo GN, et al. Percutaneous CT fluoroscopy-guided core needle biopsy of mediastinal masses: technical outcome and complications of 155 procedures during a 10-year period. *Diagnostics (Basel).* 2021;11:781.
15. Shazlee MK, Ali M, Ahmed MS, et al. Ultrasound-guided transthoracic mediastinal biopsy: a safe technique for tissue diagnosis in middle- and low-income countries. *Cureus.* 2021;13, e13914.
16. Garnon J, Ramamurthy N, Caudrelier JJ, et al. MRI-guided percutaneous biopsy of mediastinal masses using a large bore magnet: technical feasibility. *Cardiovasc Intervent Radiol.* 2016;39:761–767.

17. Lü Y, Fritz J, Li C, et al. Magnetic resonance imaging-guided percutaneous biopsy of mediastinal masses: diagnostic performance and safety. *Invest Radiol.* 2013;48: 452–457.

18. Iguchi T, Hiraki T, Matsui Y, et al. CT fluoroscopy-guided core needle biopsy of anterior mediastinal masses. *Diagn Interv Imaging.* 2018;99:91–97.

19. Petkov R, Minchev T, Yamakova Y, et al. Diagnostic value and complication rate of ultrasound-guided transthoracic core needle biopsy in mediastinal lesions. *PLoS One.* 2020;15, e0231523.

20. Han J, Feng XL, Xu TY, et al. Clinical value of contrast-enhanced ultrasound in transthoracic biopsy of malignant anterior mediastinal masses. *J Thorac Dis.* 2019;11: 5290–5299.

21. Floridi C, Reginelli A, Capasso R, et al. Percutaneous needle biopsy of mediastinal masses under C-arm conebeam CT guidance: diagnostic performance and safety. *Med Oncol.* 2017;34:67.

22. Neyaz Z, Lal H, Thakral A, et al. Percutaneous computed tomography-guided aspiration and biopsy of intrathoracic lesions: results of 265 procedures. *Lung India.* 2016;33:620–625.

23. de Margerie-Mellon C, de Bazelaire C, Amorim S, et al. Diagnostic yield and safety of computed tomography-guided mediastinal core needle biopsies. *J Thorac Imag.* 2015; 30:319–327.