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Impact of pleural thickness on the sensitivity of computed tomography scan-guided cutting-needle pleural biopsy in diagnosing unexplained exudative pleural effusion

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Abstract

Background In most cases, patients with pleural effusion require a pleural biopsy to confirm the diagnosis, due to the low diagnostic sensitivity of thoracentesis. Among the different biopsy modalities, real time computed tomography scan-guided cutting-needle pleural biopsy (CT-CNPB) ensures high sensitivity and accessibility. However, there is no study investigating the difference in the diagnostic sensitivity of CT-CNPB for lesions with variable pleural thickness in effusions of different types.

Methods Of the 303 patients who underwent CT-CNPB, 218 met the eligibility criteria and were retrospectively analyzed from November 2021 to June 2024. Patients were divided into malignant pleural effusion (MPE), tuberculosis pleural effusion (TPE), and non-tuberculous benign pleural effusion (BPE) groups according to the diagnosis with a minimum follow-up of 6 months. Pleural thickness was defined as the length of the portion of the puncture needle that passes through the thickened parietal pleura or the pleural lesion (nodule/mass). In further analysis, we compare the differences in sensitivity between subgroups with different pleural thicknesses in each group.

Results The overall diagnostic sensitivity is 74.3%. The sensitivity in MPE, TPE, and BPE is 75.7%, 78.6%, and 67.8%, respectively. There was a significant difference in sensitivity between the < 5 mm and ≥ 5 mm groups in MPE and BPE groups but was not observed in the TPE group. In the further analysis, there was a significant difference in sensitivity between < 3 mm and 3–5 mm groups in TPE ($p = 0.046$) and a significant difference in sensitivity between 3 and 5 mm and 5–10 mm groups in MPE ($p = 0.017$), but a significant difference was not observed in BPE group.

Conclusion CT-CNPB may serve as a preferred diagnostic approach in suspected TPE with pleural thickening ≥ 3 mm and suspected MPE with thickening ≥ 5 mm on chest CT. Where MT is unavailable, CT-CNPB is a viable alternative for suspected MPE or TPE patients with pleural thickening, nodularity, or mass lesions observed on CT. However, in

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suspected BPE, CT-CNPB alone is often insufficient; integrated clinical, laboratory, and imaging evaluation remains essential.

Keywords Exudative pleural effusion, Real time computed tomography scan-guided cutting-needle pleural biopsy, Diagnosis

Introduction

Pleural effusions are often the presenting feature of pleural disease, including a wide spectrum of malignant and benign conditions [1, 2]. Although pleural fluid examination and imaging provide essential information, a definite diagnosis was only obtained in 18% of the patients after initial thoracentesis in the previous study [3]. The final characterization of disease relies on histologic findings obtained through pleural biopsy, in most cases. However, an algorithm based on imaging findings has not yet been developed for the invasive diagnosis of pleural diseases that suggests which method should be used for which patient to improve diagnostic accuracy, safety, and cost [4]. Medical thoracoscopy (MT) and real time computed tomography scan-guided cutting-needle pleural biopsy (CT-CNPB) are the preferred diagnostic modalities, as both are characterized by a greater diagnostic sensitivity compared with blind pleural biopsy [5, 6]. However, MT requires a degree of expertise and is not available in many parts of the world [7]. Recent studies have proposed that image guidance significantly increases the yield of such biopsies and also decreases the risk of complications. It's reported that the diagnostic sensitivity of CT-CNPB ranges from 75–87.5% [8, 9, 10, 11].

There have been no studies investigating the diagnostic sensitivity of CT-CNPB performed on different pleural thicknesses in the diagnosis of the different pleural diseases. Here we retrospectively analyse a large number of cases to determine the relationship between the pleural thickness of patients with pleural effusion and the diagnostic sensitivity of CT-CNPB.

Methods and materials

Study design

This is a retrospective analysis of 309 patients with pleural effusion who underwent CT-CNPB at West China Hospital of Sichuan University from November 2021 to June 2024. The study was approved by the Ethics Committee of West China Hospital, Sichuan University and the requirement for informed consent was waived due to the study's retrospective nature.

Exclusion criteria: (1) who reach a diagnosis based on clinical, radiological findings, and thoracentesis results; (2) who did not have a definite diagnosis as of six months after CT-CNPB; (3) who lacked the CT imaging of the puncture procedure; (4) who had a transudate pleural effusion; (5) who lacked complete clinical or histologic data. A total of 218 patients were enrolled in the study, as shown in Fig. 1.

Procedure of CT-CNPB

CT-CNPB was performed in the pulmonary intervention room. The entry site was identified as the most appropriate and accessible position by reviewing the chest CT scans on the computer by two experienced pulmonologists while the patients were in the intervention room. The distance between the entry site and the target point was measured two dimensionally on CT. The entry site for the cutting needle was marked on the patient's chest wall immediately before biopsy. We used a 16 G automated cutting needle with a specimen notch of 20 mm (MC1816, Bard Max. Core, Bard Inc., USA) to perform the biopsy with the patient under local anaesthesia with 2% lidocaine. The tip of the cutting needle was inserted through the guide channel into the pleural superstratum. Four to six biopsy specimens were obtained from the parietal pleura using the distal tip of the needle at different angles. If only pleural effusion was detected on the CT scan, biopsies were performed at the mid-scapular line near the diaphragm.

Pleural thickness (x, mm) was defined as the length of the portion of the puncture needle that passes through the thickened parietal pleura or the pleural lesion (nodule/mass), which was measured jointly by the two experienced pulmonologists on CT images, as shown in Fig. 2.

Standardized diagnostic criteria for MPE, TPE, and BPE

Malignant pleural effusion (MPE) was diagnosed based on: (1) the combination of cytology, biopsies, and imaging studies confirmed malignant tumour with a minimum follow-up of 6 months; (2) pleural effusion cytology or pleural biopsy was positive for malignant cells.

Tuberculosis pleural effusion (TPE) was diagnosed based on: (1) the culture of spectrum, pleural effusion grew *Mycobacterium tuberculosis*; (2) *Mycobacterium tuberculosis* has been isolated from the granulomatous inflammation in pleural biopsy histology; (3) granulomatous inflamed tissue in the pleural biopsy coexisting with clinical response to antituberculosis therapy.

Non-tuberculous benign pleural effusion (BPE) was diagnosed based on: (1) the combination of cytology, biopsies, imaging and clinical data confirmed a diagnosis of a benign condition, with a minimum follow-up of 6 months; (2) the culture of spectrum, pleural effusion did not grow *Mycobacterium tuberculosis*; (3) pleural effusion

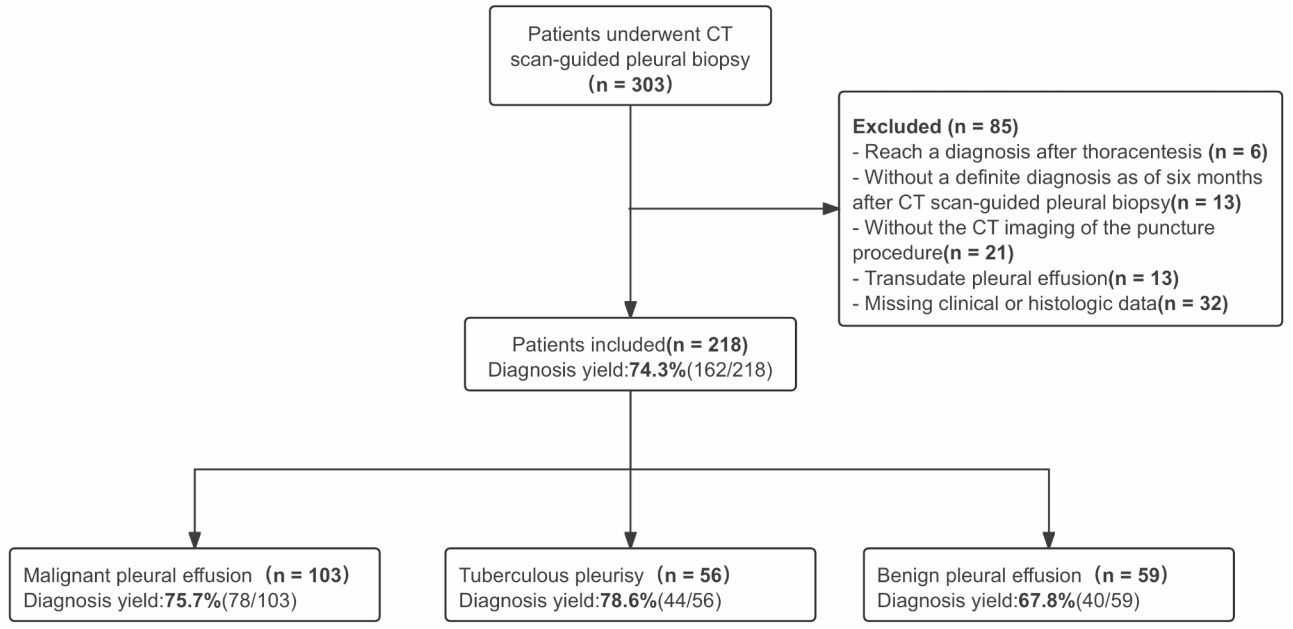

Fig. 1 Flowchart of the study screening and grouping

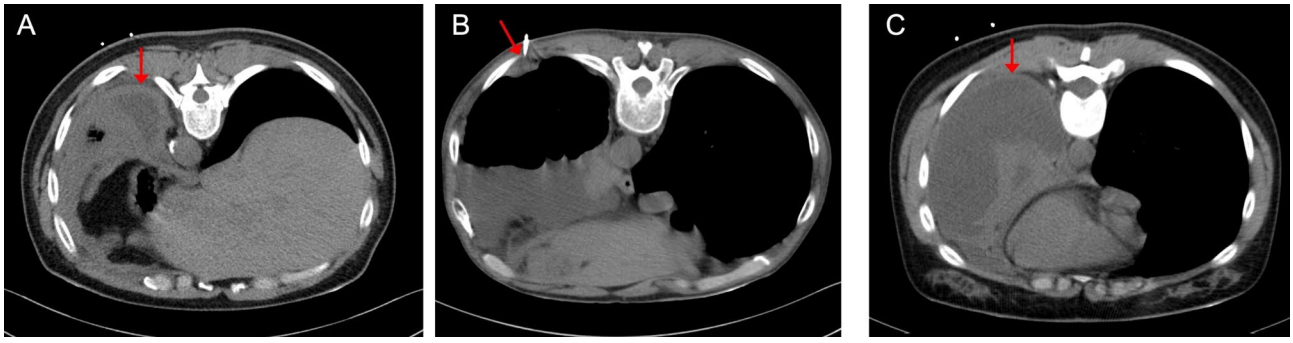

Fig. 2 Real time computed tomography scan-guided cutting-needle pleural biopsy imaging, the red arrows indicate the entry sites. **A**, CT imaging of a patient who was subsequently confirmed tuberculosis pleural effusion, with a pleural thickness of 7 mm. **B**, CT imaging of a patient who was subsequently confirmed malignant pleural effusion, with a pleural mass of 10 mm. **C**, CT imaging of a patient who was subsequently confirmed tuberculosis pleural effusion, with a pleural thickness of 2 mm

cytology or pleural biopsy was negative for malignant cells or *Mycobacterium tuberculosis*; (4) the pathological manifestations of inflammatory pleuritis, pleural fibrosis, plaques, or chronic empyema disappeared after anti-inflammatory treatment.

Statistical analysis

Parametric data are presented as the median (interquartile range). Comparisons of diagnostic sensitivity across different pleural thickness subgroups were performed using the Chi-squared test (with Yates correction) or Fisher's exact test, depending on sample size. All statistical analyses were performed with GraphPad Prism 10 (GraphPad Software, San Diego, CA, USA) and SPSS version 25 (SPSS Inc., Chicago, IL, USA). $P<0.05$ was considered statistically significant.

Results

Overall study population

Baseline clinical characteristics are summarized in Table 1. Patients' median age was 59 (47.8–70) years, and 50.9% (137/218) of the patients were male. The overall diagnostic sensitivity is 74.3% (162/218). Diagnostic distribution of pleural disease and respective diagnostic sensitivity is given in Table 2. Among these 218 patients, 47.2% (103/218) patients were diagnosed with MPE, 25.7% (56/218) patients were diagnosed with TPE, and 27.1% (59/218) patients were diagnosed with BPE after a minimum follow-up of 6 months. Diagnostic sensitivity in the three groups is 75.7% (78/103), 78.6% (44/56), and 67.8% (40/59), respectively. The histopathological features of the 162 patients confirmed by results of CT-CNPB is given in Table S3. In this study, pleural thickness

Table 1 General clinical characteristics of the study population

Characteristics	MPE ($n=103$)	TPE ($n=56$)	BPE ($n=59$)	Overall ($N=218$)
Age	65 (55–72)	48.5 (32.8–67)	57 (47.5–69.5)	59 (47.8–70)
Sex (male)	61 (59.2%)	34 (60.7%)	42 (71.2%)	137 (62.8%)
Puncture position (right)	54 (52.4%)	21 (37.5%)	36 (61.0%)	111 (50.9%)
Pleural Pathologies Observed on CT				
Only pleural effusion	3 (3.0%)	1 (1.8%)	6 (10.2%)	10 (4.6%)
Pleural based nodule or mass	31 (30.1%)	3 (5.4%)	7 (11.9%)	41 (18.8%)
Pleural thickening	69 (67.0%)	52 (92.9%)	46 (78.0%)	167 (76.6%)

Table 2 Sensitivity of CT-CNPB in diagnosing different pleural disease

Diagnosis	Sensitivity
MPE	75.7% (78/103)
Malignant pleural effusions caused by Lung cancer	76.3% (61/80)
Pleural metastasis due to other organ carcinomatosis	70% (7/10)
Malignant mesothelioma	88.9% (8/9)
Malignant pleural effusion secondary to Hematologic malignancies	50% (2/4)
TPE	78.6% (44/56)
BPE	67.8 (40/59)
Empyema and parapneumonic effusion	75% (36/48)
Benign peripheral nerve sheath tumors	75% (3/4)
Autoimmune-related pleural effusion	0 (0/3)
Nontuberculous Mycobacteria infection	0 (0/1)
Chylothorax	0 (0/1)
Hypereosinophilic syndrome	100% (1/1)
Yellow nail syndrome	0 (0/1)
Total number of cases	74.3% (162/218)

was less than 5 mm in 61.7% (71/115) of patients. Based on pleural thickness (x), we divided the patients into two groups ($0 \le x < 5$ mm, $x \ge 5$ mm). The group ($0 \le x < 5$ mm) was subdivided into three groups (0, $0 < x < 3$ mm and $3 \le x < 5$ mm) and the group ($x \ge 5$ mm) was subdivided into two groups ($5 \le x < 10$ mm and $x \ge 10$ mm). The sensitivity for each subgroup is shown in Table 3. The incidence of post-operative complications was 16.1%. The complications are summarized in Table S1 and biochemical and cellular characteristics of serum and pleural effusion analysis is shown in Table S2.

Malignant pleural effusion

The diagnostic sensitivity in MPE is 75.7% (78/103). The sensitivity increased with pleural thickness: 59.1% (26/44) for $0 \le x < 5$, including 33.3% (1/3) for 0 mm, 58.8% (10/17) for $0 < x < 3$, and 62.5% (15/24) for $3 \le x < 5$. The sensitivity further increased to 84.4% (27/32) for $5 \le x < 10$ and reached 92.6% (25/27) for $x \ge 10$. There was a significant difference in sensitivity between the $0 \le x < 5$ and $x \ge 5$ groups ($p = 0.003$). In the further analysis, there was no significant difference in sensitivity between $0 \le x < 3$ and $3 \le x < 5$ groups but there was a significant difference in sensitivity between the $3 \le x < 5$ and $x \ge 5$ groups ($p = 0.017$), which is shown in Fig. 3.

Tuberculosis pleural effusion

The diagnostic sensitivity in TPE is 78.6% (44/56). The sensitivity increased with pleural thickness: 70.6% (24/34) for $0 \le x < 5$, including 0 (0/1) for 0 mm, 58.8% (10/18) for $0 < x < 3$, and 87.5% (14/16) for $3 \le x < 5$. The sensitivity further increased to 91.7% (11/12) for $5 \le x < 10$ and reached 90% (9/10) for $x \ge 10$. There was no significant difference in sensitivity between the $0 \le x < 5$ and $x \ge 5$ groups. In the further analysis, there was a significant difference in sensitivity between $0 \le x < 3$ and $3 \le x < 5$ groups ($p = 0.046$) but there was no significant difference in sensitivity between the $3 \le x < 5$ and $x \ge 5$ groups, which is shown in Fig. 3.

Non-tuberculous benign pleural effusion

The diagnostic sensitivity in BPE is 67.8% (40/59). The sensitivity for pleural thickness $0 \le x < 5$ was 56.8% (21/37), including 66.7% (4/6) for 0 mm, 42.9% (6/14)

Table 3 Diagnostic sensitivity in different pleural thickness groups

Diagnostic sensitivity	MPE ($n=103$)	TPE ($n=56$)	BPE ($n=59$)	Overall ($N=218$)
$0 \le x < 5$	59.1% (26/44)	70.6% (24/34)	56.8% (21/37)	61.7% (71/115)
$0 \le x < 3$	55.0% (11/20)	55.6% (10/18)	50% (10/20)	53.4% (31/58)
0	33.3% (1/3)	0 (0/1)	66.7% (4/6)	50% (5/10)
$0 < x < 3$	58.8% (10/17)	58.8% (10/17)	42.9% (6/14)	54.2% (26/48)
$3 \le x < 5$	62.5% (15/24)	87.5% (14/16)	64.7% (11/17)	70.2% (40/57)
$x \ge 5$	88.1% (52/59)	90.9% (20/22)	86.4% (19/22)	88.3% (91/103)
$5 \le x < 10$	84.4% (27/32)	91.7% (11/12)	76.9% (10/13)	84.2% (48/57)
$x \ge 10$	92.6% (25/27)	90% (9/10)	100% (9/9)	93.5% (43/46)
Total	75.7% (78/103)	78.6% (44/56)	67.8% (40/59)	74.3% (162/218)

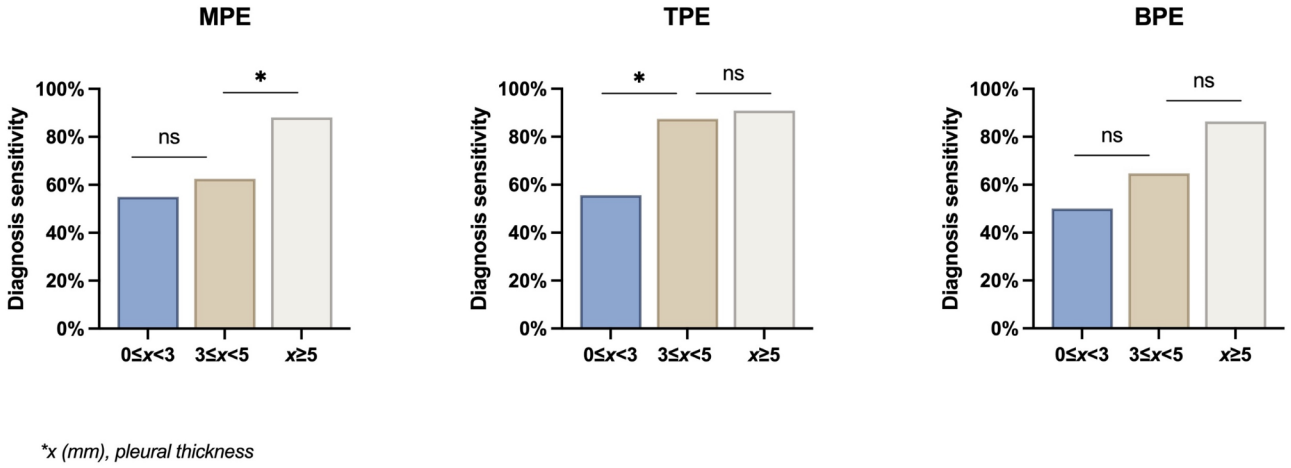

Fig. 3 Diagnostic sensitivity of different pleural thickness subgroups in different types of pleural effusion

for $0 < x < 3$, and 64.7% (11/17) for $3 \le x < 5$. For greater thickness, the sensitivity was 76.9% (10/13) for $5 \le x < 10$ and 100% (9/9) for $x \ge 10$. There was a significant difference in sensitivity between the $0 \le x < 5$ and $x \ge 5$ groups ($p = 0.006$). In the further analysis, there was no significant difference in sensitivity between $0 \le x < 3$ and $3 \le x < 5$ groups and between the $3 \le x < 5$ and $x \ge 5$ groups, which is shown in Fig. 3.

Discussion

For patients whose diagnosis cannot be confirmed by thoracocentesis, further biopsies are essential to obtain histopathological evidence [12]. It would be advantageous to suggest the preference of needle biopsy or MT according to the patients' pleural pathologies observed on CT scans. In this study, we aimed to investigate whether CT-CNPB can achieve comparable sensitivity to MT in the diagnosis of specific pleural disease even when pleural thickness is not overly significant.

The overall diagnostic sensitivity in our study is 74.3%, which is relatively lower than the previous studies. We consider this a result of differences in the study populations, with fewer of our population having a significant pleural thickness. It was reported that the sensitivity of MT for the diagnosis of exudative pleural effusion was 91% [13]. However, MT requires a degree of expertise and is not available in many parts of the world [14]. Based on our results, we consider 5 mm can be the threshold for performing CT-CNPB in suspected MPE cases, with a sensitivity of at least 84.4%; and 3 mm can be considered the threshold for performing CT-CNPB in suspected TPE cases, reaching a sensitivity of at least 87.5%. Moreover, in cases where MT is not available, whenever pleural thickening, nodule or mass is present on chest CT of suspected MPE or TPE patients, we can still consider CT-CNPB, as the sensitivity reaches a sensitivity of at least 58.8% both in MPE and TPE.

The sensitivity of CT-CNPB in BPE does not exactly increase incrementally with pleural thickness. We consider that the first reason is the uneven disease distribution of BPE in the subgroups, and the second reason is that in practice, the diagnosis of BPE depends on a combination of clinical information, rather than on a single CT-CNPB [15]. For benign pleural thickness less than 10 mm, the sensitivity of CT-CNPB is only 62%. Therefore, we suggest that the diagnosis of BPE should be based on a combination of clinical, imaging, pathological and laboratory tests.

Strengths of our study include a relatively large sample size with follow-up for more than 6 months to ensure a final diagnosis to validate the sensitivity of CT-CNPB, and this is the first study to specifically investigate the impact of pleural thickness on the sensitivity of CT-CNPB in diagnosing different types of exudative pleural effusion. Our study has several limitations. First, it is a retrospective study with known inherent bias. Second, CT scans at our center were performed with a slice thickness of 3 mm, which may not be consistent with protocols used at other institutions. Differences in CT slice thickness across centers may affect the generalizability of our findings. Third, all clinical parameters were not available for every case, which is caused by the retrospective study design. We are planning a prospective study to compare the diagnostic performance of CT-CNPB and MT in patients with pleural effusion, across subgroups of patients with varying pleural thickness on imaging.

Conclusion

Our study suggests that CT-CNPB may serve as a preferred diagnostic approach in suspected TPE cases with pleural thickening ≥ 3 mm and suspected MPE cases with pleural thickening ≥ 5 mm, as identified on CT imaging. In settings where MT is unavailable, CT-CNPB can be considered for patients with suspected MPE or TPE,

provided that pleural thickening, nodularity, or mass lesions are observed. However, in patients with suspected BPE, CT-CNPB alone appears insufficient for definitive diagnosis; comprehensive clinical, laboratory and radiological correlation is essential in such cases.

Abbreviations

BPE	Non-tuberculous benign pleural effusion
CT	Computed tomography
CT-CNPB	Real time computed tomography scan-guided cutting-needle pleural biopsy
MPE	Malignant pleural effusion
TPE	Tuberculosis pleural effusion

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03229-2.

Supplementary Material 1

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Author contributions
Dan Liu and Kaige Wang designed the study. Rui Xu, Ling Zuo and Kaige Wang collected clinical data, created the figure, and wrote the manuscript. Kaige Wang, Ying Liu, Chiyong Yang and Li Jiang performed real time computed tomography scan-guided cutting-needle pleural biopsy on patients. Ping Fan managed the biopsy tissue of patients. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was performed in accordance with the declaration of Helsinki and was approved by the ethic committee of the West China Hospital of Sichuan University (No. 2024 – 1582). Written informed consent was waived approved by the ethic committee of the West China Hospital of Sichuan University due to the retrospective noninterventional design.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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