Original Article

Comparative analysis of different biopsy techniques for pancreatic lesions in diagnostic value, safety, and cost-effectiveness

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Background: Pancreatic cancer is highly lethal and often diagnosed at an advanced stage, highlighting the need for early and accurate diagnosis. Although imaging plays a crucial role, definitive pathological confirmation requires biopsy. Percutaneous ultrasound-guided core needle biopsy (US-CNB), computed tomography-guided core needle biopsy (CT-CNB), and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) are the three main biopsy techniques, each differing in diagnostic accuracy, safety, and cost-effectiveness. The aim of this study was to compare the diagnostic value, safety, and cost-effectiveness of these three biopsy techniques for suspiciously malignant pancreatic lesions.

Methods: We retrospectively evaluated patients with suspicious malignant pancreatic lesions who underwent US-CNB, CT-CNB, or EUS-FNA from January 2018 to January 2023. We compared technical success rates, sample adequacy, diagnostic accuracy, sensitivity, specificity, and complication rates of three groups. Additionally, we calculated the cost/effectiveness ratio (C/E) and incremental cost-effectiveness ratio (ICER) for each method.

Results: A total of 399 patients were enrolled (US-CNB, n=86; CT-CNB, n=55; EUS-FNA, n=258), achieving 100% technical success. Sample adequacy satisfaction rates were 97.70% for US-CNB, 90.90% for CT-CNB, and 74.03% for EUS-FNA, with EUS-FNA significantly lower compared to the other two methods (P<0.001). Diagnostic accuracy was significantly higher for US-CNB (97.70%) and CT-CNB (90.90%) compared to EUS-FNA (69.80%) (P<0.001). Complication rates were 15.12% for US-CNB, 16.36% for CT-CNB, and 10.47% for EUS-FNA, with no significant differences (P=0.319). Compared to EUS-FNA, ICER for US-CNB was –14,367.7 yuan and for CT-CNB was –8,279.22 yuan per correct diagnosis, both below the willingness-to-pay threshold.

Conclusions: US-CNB and CT-CNB demonstrate superior diagnostic accuracy and specimen adequacy compared to EUS-FNA for suspected malignant pancreatic lesions. There are no significant differences in postoperative complication rates among three biopsy methods. In terms of cost-effectiveness, US-CNB and CT-CNB have lower costs and higher effectiveness than EUS-FNA, indicating greater economic efficiency.

Keywords: Pancreatic cancer; ultrasound-guided; fine needle aspiration (FNA); core needle biopsy (CNB); cost-effectiveness analysis

Submitted Nov 27, 2024. Accepted for publication Mar 03, 2025. Published online Apr 28, 2025.
doi: 10.21037/qims-2024-2670
View this article at: https://dx.doi.org/10.21037/qims-2024-2670

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Introduction

Pancreatic cancer is a common malignancy of the digestive system, with both incidence and mortality rates rising annually. Globally, it has become the seventh leading cause of cancer-related death (1,2). The disease is characterized by an insidious onset, with early symptoms typically being non-specific. Commonly, patients experience symptoms such as upper abdominal discomfort, back pain, indigestion, jaundice, and weight loss only when the disease has progressed to an advanced stage. Consequently, many patients are diagnosed at an advanced stage, often with metastasis, making them ineligible for surgery (3). In such cases, accurate pathological assessment is essential for guiding nonsurgical treatment; it is also necessary for defining the disease before neoadjuvant therapy in potentially resectable cases (4). Furthermore, conditions such as focal chronic pancreatitis can mimic malignancy, also requiring biopsy for accurate diagnosis (5).

Currently, pancreatic lesion biopsies can be guided by various imaging modalities, including ultrasound (US), computed tomography (CT), and endoscopic ultrasound (EUS) (6). Biopsies may also be performed through laparoscopic or open surgical approaches. Although surgical biopsy remains the most conclusive and reliable diagnostic approach, its high cost, invasiveness, and greater risk of complications make it a last resort. In contrast, imaging-guided fine needle aspiration or biopsy is minimally invasive, cost-effective, convenient, and safer, leading to its growing use in clinical practice.

Previous research has mainly compared the diagnostic efficacy or safety of two biopsy techniques for pancreatic lesions (7-9), with limited studies directly comparing three methods. Additionally, there is a significant gap in cost-effectiveness analysis for pancreatic biopsy techniques. Therefore, the objective of this study was to compare the diagnostic efficacy, postoperative complication rates, and cost-effectiveness of three methods: percutaneous ultrasound-guided core needle biopsy (US-CNB), percutaneous computed tomography-guided core needle biopsy (CT-CNB), and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). We present this article in accordance with the STARD reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-2024-2670/rc).

Methods

Patient selection

This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This retrospective study was approved by the Ethics Committee of West China Hospital, Sichuan University (No. 2023-329). The collection of informed consent from patients was deemed unnecessary and waived due to the retrospective nature of the study. This study was conducted at the Department of Medical Ultrasound, West China Hospital, Sichuan University. From January 2018 to January 2023, consecutive patients who underwent US-CNB, CT-CNB, or EUS-FNA for suspected malignant pancreatic lesions based on imaging procedure results from CT, magnetic resonance imaging (MRI), and/or EUS were included in this study. Patients with inadequate follow-up data were excluded. We calculated the power of the Wald tests for assessing whether the parameters are equal to zero (null hypothesis) at a 5% significance level (two-sided). The final sample size in this study ensures an adequate level of precision.

Data on lesion size, location, cytologic or histological report, histological diagnosis after surgical resection or clinical/radiological follow-up findings, and short-term complications after pancreatic biopsy (≤7 days after the procedure, or until discharge if this occurred before day 7). Lesion size was primarily determined using contrast-enhanced CT/MRI, as it was the standard imaging modality in all cases. The measurements were taken at the largest cross-sectional diameter of the lesion. Post-biopsy complications were categorized into minor and major according to the Society of Interventional Radiology's guidelines (10).

Sampling techniques

During the biopsy procedure, US systems with abdominal probes were utilized, including Hitachi HI VISION Preirus (Hitachi, Tokyo, Japan), the Philips IU-22 (Philips Healthcare, Chicago, IL, USA), and the Mindray Resona7 (Mindray, Shenzhen, China). Lesion size, location, echogenicity, shape, and depth were re-evaluated to ensure accurate biopsy planning. Color Doppler imaging was used to assess the vascular supply of the lesion and proximity to major vessels to minimize the risk of vascular injury. Depending on the lesion's location, patients were positioned supine or in the right lateral decubitus position, and the optimal puncture site was marked. Standard protocols for skin disinfection were followed, and local anesthesia with 1% lidocaine was administered. Under real-time ultrasound guidance, a 17G coaxial puncture needle (Bard Peripheral Vascular Inc., Tempe, AZ, USA) was advanced to the lesion's

periphery. The coaxial cannula was stabilized, the stylet was removed, and an 18G tissue biopsy needle (Bard Peripheral Vascular Inc.) was used to obtain 2–3 tissue samples, depending on the tissue quality and bleeding. Specimens were fixed in 10% formalin and sent for pathological analysis.

Before the biopsy, a CT scan (SOMATOM Definition AS+ 64; Siemens Healthineers, Erlangen, Germany) was performed to visualize the pancreatic lesion and assess blood flow, ensuring major vessels and necrotic areas were avoided. The biopsy site was marked on the skin, followed by standard disinfection and draping. After administering 1% lidocaine for local anesthesia, a small incision was made. A 17G coaxial puncture needle (Bard Peripheral Vascular Inc.) was positioned at the lesion's edge, and a CT scan confirmed its placement. After verifying the needle placement, the stylet was removed, and an 18G biopsy needle (Bard Peripheral Vascular Inc.) was advanced through the coaxial cannula to obtain a tissue. The specimen was then fixed in 10% formalin and sent for pathological analysis.

During the biopsy, the patient was typically positioned in the left lateral decubitus position under general anesthesia. An EUS (UM-G20-29R; Olympus, Tokyo, Japan) was inserted into the stomach or duodenal to assess the pancreatic lesion, including its location, size, pancreatic duct dilation, and surrounding structures. Based on this assessment, a 22G puncture needle (ECHO-3-22; COOK, Bloomington, IN, USA) was directed towards the lesion. A 5 mL syringe was used to create continuous suction, employing a negative pressure technique to collect the specimen. The specimen was sent to the pathology department for further processing.

Evaluation of FNA/CNB and follow-up findings

The successful acquisition of cytological or histological specimens was considered a technical success. Samples were considered 'diagnostic' when a formal pathological report was issued; they were considered 'non-diagnostic' if the collected sample was deemed inadequate for proper cytological analysis. Cytological/histological results of FNA/CNB were reviewed by experienced physicians blinded to the clinical and biologic data of patients. According to the Papanicolaou Society of Cytopathology (PSC) (11), FNA cytology diagnoses are categorized into six classes: nondiagnostic (I); benign (II); atypical (III); neoplastic, benign (IV A); neoplastic, other (IV B); suspicious (V); and malignant (VI). Cytologically negative cases were defined as categories II and IV A, representing specimens with no evidence of malignancy. Cytologically positive cases included categories IVB and VI, reflecting samples with malignant or high-risk neoplastic features. Categories III and V, associated with higher malignancy risk (9), were also considered positive, following D'Onofrio *et al.*'s (12) approach. CNB pathological diagnoses were classified into nondiagnostic, benign, atypical, and malignant. Benign was considered negative, whereas atypical and malignant were classified as positive, based on previously published medical literature standards (13).

The final diagnosis was confirmed by histopathology of resected specimens (surgical pathology) or by clinical and radiological follow-up of at least six months. Criteria for a positive result included the following: (I) malignancy confirmed by postoperative pathology; (II) significant lesion reduction after anti-tumor therapy; or (III) over 50% lesion enlargement or new metastases during follow-up. Negative results were determined by the following: (I) benign pathology after surgery; (II) lesion reduction or disappearance without anti-tumor therapy; (III) spontaneous resolution of pancreatic abnormalities during follow-up; or (IV) no lesion growth over at least six months without anti-tumor treatment. Intraductal papillary mucinous neoplasms (IPMN) encompasses both benign and malignant neoplasms. The final diagnosis of IPMN was based on postoperative pathological findings in patients who had undergone surgery. For non-surgical cases, assessment followed the 2017 International IPMN Guidelines (Fukuoka Consensus) (14), with particular attention to High-Risk Stigmata. Additionally, during follow-up, the development of Worrisome Features was closely monitored.

Cost-effectiveness analysis

This study focused on direct medical costs, including biopsy procedures, pathology diagnostics, and post-biopsy complication management, excluding indirect costs such as productivity loss and travel (15). Pathology costs encompass routine microscopy diagnosis and immunohistochemistry (IHC) tests for certain patients. IHC staining helps identify specific protein expressions, aiding diagnosis in selected cases. Diagnostic accuracy is used as the effectiveness metric to calculate the cost/effectiveness ratio (C/E) and incremental cost-effectiveness ratio (ICER). According to World Health Organization (WHO) guidelines, willingness-to-pay (WTP) threshold for cost-effectiveness analysis in China is set at 196,500 yuan (three times the per capita

GDP in 2018), and a method is cost-effective if its ICER is below this threshold (16,17). A one-way sensitivity analysis, adjusting biopsy costs by ±10%, ensures robust conclusions.

Statistical analysis

Statistical analysis was conducted using SPSS 20.0 (IBM Corp., Armonk, NY, USA). Quantitative data were presented as mean ± standard deviation, with differences in age and lesion size compared using analysis of variance (ANOVA). Categorical variables were expressed as frequencies and percentages. The chi-square test or Fisher's exact test was used to compare the technical success rates, sample adequacy, diagnostic accuracy, sensitivity, specificity, and complication rates among the three groups. Subgroup analyses based on lesion size and location were performed using Fisher's exact test to compare diagnostic accuracy, sample adequacy, and complication rates. Statistical significance was determined using Bonferroni correction, with a P<0.0167 considered statistically significant.

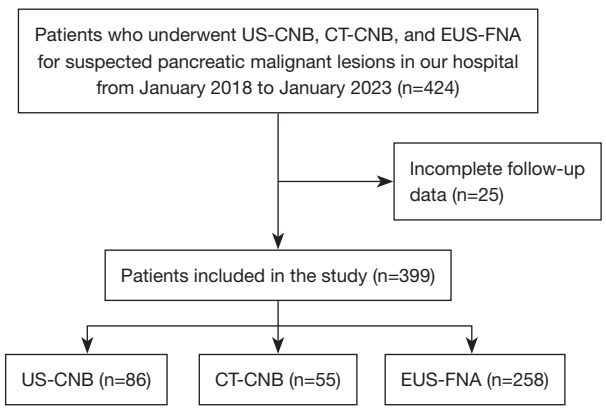

Figure 1 The flow chart of patient inclusion process. CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; US-CNB, ultrasound-guided core needle biopsy.

Results

Participant characteristics

Between January 2018 and January 2023, 424 patients underwent biopsy for suspected malignant pancreatic lesions using US-CNB, CT-CNB, or EUS-FNA. After excluding 25 patients due to insufficient follow-up data, 399 patients (mean age, 58.27±13.32 years) were analyzed (*Figure 1*). Of these, 258 underwent EUS-FNA, 86 underwent US-CNB, and 55 underwent CT-CNB. Lesion sizes in the EUS-FNA group (3.32±1.32 cm) were significantly smaller compared to those in the US-CNB (4.80±2.25 cm) and CT-CNB (4.37±1.74 cm) groups (P<0.001). Additionally, lesions in the EUS-FNA group (78.70%) were more frequently located in the pancreatic head or neck compared to the US-CNB (44.19%) or CT-CNB group (47.27%) (P<0.001) (*Table 1*).

Table 1 Clinical information of patients with suspected malignant pancreatic lesion under different biopsy methods

Variable	US-CNB	CT-CNB	EUS-FNA	P value*
Age (years)	59.70±12.35	60.71±9.21	58.52±10.89	0.132
Gender				
Male	44 (51.16)	32 (58.20)	155 (60.08)	0.349
Female	42 (48.84)	23 (41.80)	103 (39.92)	
Lesion location				
Head/neck	38 (44.19)	26 (47.27)	203 (78.70)	<0.001†
Body/tail	47 (55.81)	29 (52.73)	55 (21.30)	
Lesion size (cm)	4.80±2.25	4.37±1.74	3.32±1.32	<0.001†
<2	5 (5.80)	4 (7.27)	45 (17.40)	0.014†
≥2	81 (94.20)	51 (92.73)	213 (82.60)	

Data are presented as mean ± standard deviation or number (percentage, %); *, P value <0.0167, the difference is statistically significant; †, there is a statistical difference in US-CNB *vs.* EUS-FNA group, CT-CNB *vs.* EUS-FNA group. CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; US-CNB, ultrasound-guided core needle biopsy.

Table 2 Final diagnosis of patients with suspected malignant pancreatic lesions under different biopsy methods

Final diagnosis	US-CNB	CT-CNB	EUS-FNA
Malignant, n (%)	84 (97.67)	49 (89.10)	196 (75.97)
Adenocarcinoma	71	44	159
NETs	3	2	21
G1	1	0	9
G2	1	2	9
G3	1	0	3
NECs	3	1	0
Adenosquamous carcinoma	1	0	2
Lymphoma	2	0	3
Metastasis	3	1	7
Malignant IPMN*	0	0	1
Other malignant[&]	1	1	3
Benign, n (%)	2 (2.33)	6 (10.90)	62 (24.03)
Benign IPMN*	0	2	3
SPN	0	1	1
Serous cystadenoma	0	0	1
Chronic pancreatitis	0	0	5
Autoimmune pancreatitis	1	2	9
Tuberculosis	0	0	1
Other benign	1	1	42

*, IPMN encompasses both benign and malignant neoplasms. [&], this category refers to cases where pathological examination failed to provide a definitive malignant diagnosis, but follow-up imaging results or clinical progression indicated features suggestive of malignancy. CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; IPMN, intraductal papillary mucinous neoplasms; NETs, neuroendocrine tumor; NECs, neuroendocrine carcinomas; SPN, solid pseudopapillary neoplasm; US-CNB, ultrasound-guided core needle biopsy.

Sample analysis

All 399 cases had a 100% sample acquisition rate. The satisfaction rates for sample adequacy were 97.70% for US-CNB, 90.90% for CT-CNB, and 74.03% for EUS-FNA. Notably, the satisfaction rate for EUS-FNA was significantly lower compared to the other two methods (P<0.001).

In the US-CNB group, 83 cases were diagnosed as malignant, all of which were confirmed as malignant through surgery or follow-up. One initially negative case was later confirmed as benign during follow-up. In the CT-CNB group, 43 cases were identified as malignant and confirmed through surgery or follow-up. Four atypical cases were classified as malignant per the study's criteria and later confirmed during follow-up, whereas three initially benign cases were confirmed as benign during follow-up (Table S1). In the EUS-FNA group, cytology identified 112 malignant, 22 neoplastic, 22 suspicious, and nine atypical specimens, all classified as positive for malignancy. Surgery or follow-up confirmed all but one case as malignant. Of 26 negative FNA cases, 10 were later diagnosed as malignant, with the rest confirmed as benign (Table S2). The final diagnoses of all patients are listed in *Table 2*.

Diagnostic value analysis

The analysis demonstrated that the diagnostic accuracy of the US-CNB (97.70%) and CT-CNB (90.90%) groups was significantly higher than that of the EUS-FNA group (69.80%), with a statistically significant difference (P<0.001). However, there were no statistically significant differences in sensitivity or specificity among the US-CNB, CT-CNB, and EUS-FNA groups (*Table 3*).

Procedure-related complication rates

The overall complication rates following biopsy procedures were 15.12% for US-CNB, 16.36% for CT-CNB, and 10.47% for EUS-FNA, with no statistically significant differences among these groups (P=0.319), as detailed in *Table 4*.

Pain was the most common complication: 13 cases in the US-CNB group, eight in CT-CNB, and 26 in EUS-FNA. Except for one major bleeding case in the EUS-FNA group, all were minor and managed with observation or symptomatic treatment. Each group had one case of bleeding. In the US-CNB group, one patient experienced hemorrhagic fluid from an abdominal drain (placed pre-procedure due to significant ascites) the day after the biopsy. This patient's hemoglobin dropped from 124 g/L to 115 g/L, but the bleeding was controlled with tranexamic acid and aprotinin finally (*Figure 2*). In CT-CNB, one patient's hemoglobin dropped from 120 to 97 g/L post-procedure. A follow up abdominal CT revealed a new 10.6 cm × 7.8 cm hematoma in the left upper abdomen, not present before. This patient was treated with tranexamic acid and aprotinin.

Table 3 Diagnostic efficacy, sampling satisfaction rate and technical success rate of different biopsy methods in patients with suspected malignant pancreatic lesions

Variable	US-CNB	CT-CNB	EUS-FNA	P value*
Accuracy, %	97.70	90.90	69.80	<0.001†
Sensitivity, %	100	100	94.30	0.02
Specificity, %	100	100	94.10	0.88
Satisfactory rate, %	97.70	90.90	74.03	<0.001†
Technical success, %	100	100	100	>0.999

*, P value <0.0167 is considered statistically significant; †, there is a statistical difference in US-CNB *vs.* EUS-FNA group, CT-CNB *vs.* EUS-FNA group. CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; US-CNB, ultrasound-guided core needle biopsy.

Table 4 Complications of patients with suspected malignant pancreatic lesions under different biopsy methods

Variable	US-CNB	CT-CNB	EUS-FNA	P value*
Complication rate, n (%)	13 (15.12)	9 (16.36)	27 (10.47)	0.319
Pain	12	8	26	
Bleeding	1	1	1	

*, P value <0.0167 is considered statistically significant. CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; US-CNB, ultrasound-guided core needle biopsy.

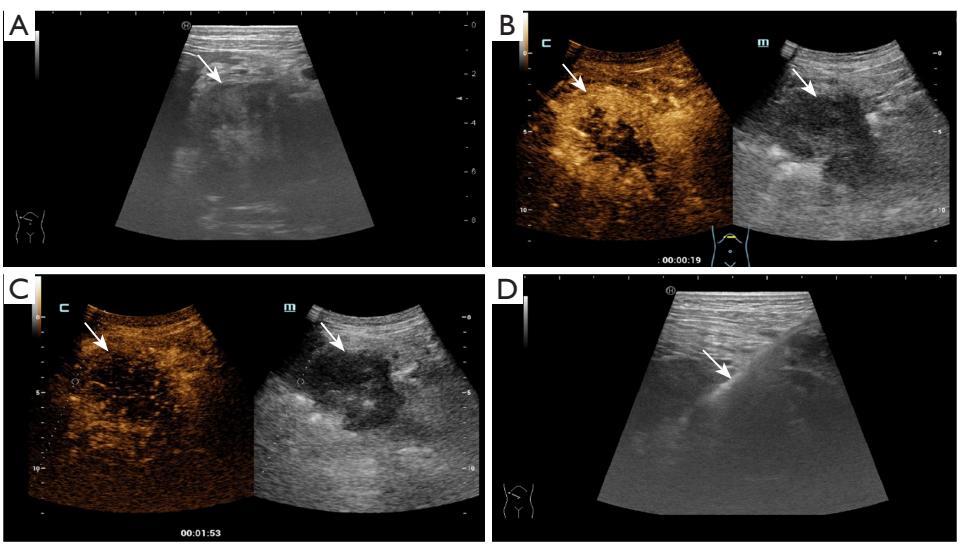

Figure 2 A 69-year-old male patient underwent US-CNB for pancreatic head lesion. (A) On gray-scale ultrasound, a hypoechoic lesion demonstrated unclear boundaries and an irregular shape, measuring 6.8 cm × 5.2 cm (arrow indicates the lesion). (B,C) Contrast-enhanced ultrasound revealed slight peripheral hyper-enhancement during the arterial phase (19 s) and hypo-enhancement within the lesion followed by overall hypo-enhancement during the venous phase (113 s) (arrow indicates the lesion). (D) A core needle biopsy of the pancreatic head was performed under percutaneous ultrasound guidance (arrow indicates the puncture needle). On the second day post-procedure, the abdominal drainage tube (initially placed due to massive ascites, which was drained before the ultrasound-guided biopsy) discharged bloody fluid, and the patient's hemoglobin level dropped from 124 g/L pre-procedure to 115 g/L post-procedure. Hemostasis was achieved with sodium carbazochrome sulfonate and batroxobin. US-CNB, ultrasound-guided percutaneous core needle biopsy.

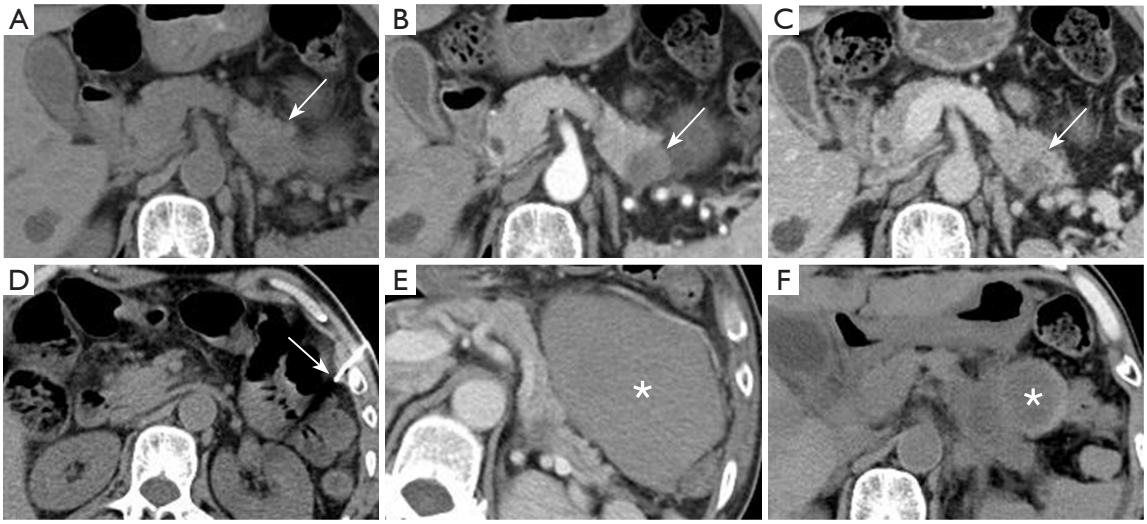

Figure 3 A 68-year-old male individual underwent CT-guided percutaneous core needle biopsy for pancreatic lesion. (A) On non-contrast CT, a low-density lesion shows in the pancreatic body and tail (arrow indicates the lesion). (B,C) The lesion exhibited unclear boundaries and an irregular shape. Post-contrast imaging revealed hypo-enhancement of the lesion (arrow indicates the lesion). (D) A core needle biopsy of the pancreatic lesion was performed under CT guidance (arrow indicates the puncture needle). (E) On the second day post-procedure, an abdominal CT scan revealed a mixed, slightly high-density mass measuring approximately 10.6 cm × 7.8 cm in the left upper abdomen, without enhancement, suggesting a possible hematoma (* indicates the bleeding site). Hemostasis was managed with carbazochrome sodium sulfonate and batroxobin. (F) A follow-up CT scan 4 weeks later showed a reduction in the size of the hematoma to approximately 2.4 cm × 1.8 cm (* indicates the bleeding site). CT, computed tomography.

Four weeks later, the second CT-scan showed that the hematoma had reduced to 2.4 cm × 1.8 cm (*Figure 3*). In EUS-FNA, one patient developed intermittent hematemesis and melena the day after the procedure, with hemoglobin dropping from 118 to 92 g/L. The patient was treated with pharmacological hemostatics and a red blood cell transfusion, leading to resolution of the bleeding (*Figure 4*).

Subgroup analysis

In both lesions <2 and ≥2 cm, diagnostic accuracy and sampling satisfaction rates were significantly higher in the US-CNB and CT-CNB groups compared to EUS-FNA. Subgroup analyses by lesion location similarly showed that the US-CNB and CT-CNB groups had superior diagnostic accuracy and sampling satisfaction rates compared to EUS-FNA, with statistically significant differences. Further details are presented in Table S3.

Cost-effectiveness analysis

Table 5 shows the costs, C/Es, and ICERs for each biopsy technique. The per capita costs were 2,510.71 yuan for US-CNB, 4,772.38 yuan for CT-CNB, and 6,519.30 yuan for EUS-FNA. Compared to EUS-FNA, the ICER for US-CNB was –14,367.7 yuan, and for CT-CNB was –8,279.22 yuan per correct diagnosis, both below the WTP threshold. Since needle biopsy costs have the greatest impact on the overall total, we adjusted this variable by 10% in our sensitivity analysis. As the cost of biopsy fluctuates within a certain range, the ICERs remains at a level below the established threshold standard (Tables S4,S5).

Discussion

This study evaluated the diagnostic efficacy, safety, and cost-effectiveness of US-CNB, CT-CNB, and EUS-FNA for pancreatic suspicious malignant lesions. The results demonstrated that US-CNB and CT-CNB had superior diagnostic accuracy (97.70% *vs.* 90.90% *vs.* 69.80%, P<0.001) and sampling satisfaction (97.70% *vs.* 90.90% *vs.* 74.03%, P<0.001) compared to EUS-FNA, with no significant difference in postoperative complications among groups. Moreover, cost-effectiveness analysis showed that

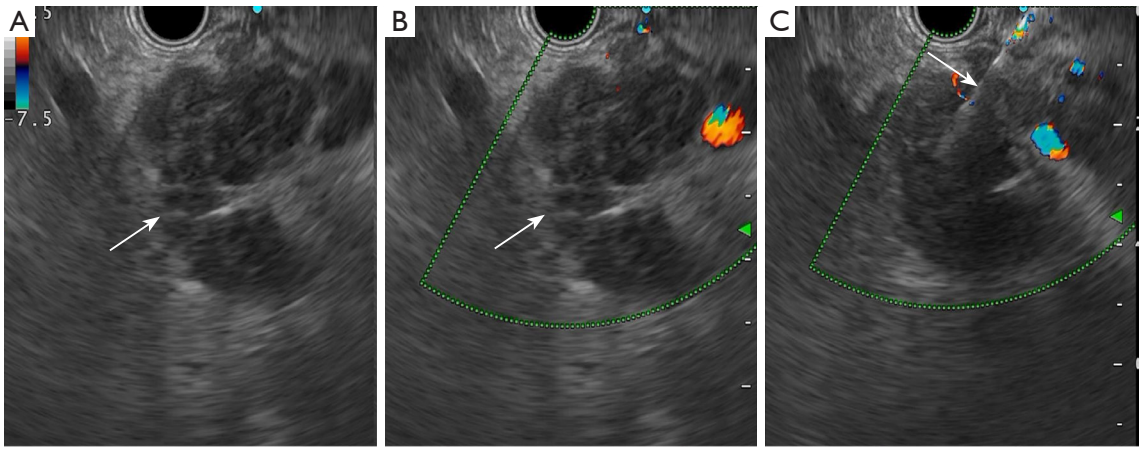

Figure 4 A 49-year-old male patient underwent endoscopic ultrasound-guided fine needle aspiration. (A) A hypoechoic lesion with unclear boundaries was identified in the pancreatic head by endoscopic ultrasound (arrow indicates the lesion). (B) Doppler imaging showed no blood flow signals around or within the pancreatic lesion (arrow indicates the lesion). (C) Under endoscopic ultrasound guidance, fine needle aspiration of the pancreatic head lesion was performed (arrow indicates the puncture needle). The day after the procedure, the patient experienced intermittent hematemesis and black stools, accompanied by a drop of hemoglobin levels (from 118 g/L pre-procedure to 92 g/L post-procedure). In addition to pharmacological hemostasis, the patient received a transfusion of red blood cell suspension, which successfully resolved the bleeding.

Table 5 Cost-effectiveness analysis of different biopsy methods

Group	Cost/person (yuan)	Accuracy	C/E	ICER
US-CNB	2,510.71	97.70%	2,569.81	–14,367.7
CT-CNB	4,772.38	90.90%	5,250.15	–8,279.22
EUS-FNA	6,519.30	69.80%	9,339.97	–

C/E, cost/effectiveness ratio; CT-CNB, computed tomography-guided core needle biopsy; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; ICER, incremental cost-effectiveness ratio; US-CNB, ultrasound-guided core needle biopsy.

US-CNB and CT-CNB were more cost-effective and economically advantageous than EUS-FNA.

Currently, several methods exist for obtaining pancreatic tissue samples. EUS-FNA is commonly the first choice for diagnosing pancreatic lesions, combining endoscopy and ultrasound to provide clear images by bypassing interference from gastrointestinal gas or fat (18). FNA samples are limited by providing predominantly cytological material with minimal tissue architecture, which is crucial for diagnosing conditions such as lymphoma, neuroendocrine tumors, and autoimmune pancreatitis (19). This limitation may hinder identifying key features such as lymphoplasmacytic infiltrates, angioinvasion, or stromal patterns necessary for accurate diagnosis, staging, and treatment planning. Combining FNA with core needle biopsy or IHC is essential to ensure comprehensive pathological evaluation and guide optimal therapeutic strategies. Rapid onsite evaluation (ROSE) helps ensure sample adequacy by allowing real-time assessment by a cytopathologist. Previous research has indicated that the presence of ROSE during EUS-FNA of pancreatic lesions is a factor that affects diagnostic outcomes (20). Ecka *et al.* reported that ROSE significantly reduces unsatisfactory samples (5.6% *vs.* 29.3%, P=0.001) (21). Without ROSE, this study found sample adequacy and diagnostic accuracy rates of 71.1% and 67.6%, respectively. In cases where pathology results conflict with clinical suspicion of malignancy, a second biopsy or further investigation is necessary, despite the increased risk of complications and psychological or financial burden on patients (22). CNB samples are of higher quality than FNA, providing more tissue for comprehensive histological and IHC analysis (13). Studies confirm that CNB yields

sufficient tissue for accurate diagnosis, with superior accuracy compared to FNA for pancreatic diseases (23-25). This study also found significantly higher diagnostic accuracy in the US-CNB and CT-CNB groups compared to EUS-FNA. Similar results were reported by Sur *et al.* (25), with CT-guided pancreatic biopsy showing over 90% accuracy, consistent with our findings.

To assess if pancreatic lesion size and location affect the diagnostic efficacy and safety, we categorized based on lesion location and size, and compared diagnostic accuracy, sample adequacy, and complication rates within subgroups. The results showed US/CT-CNB had higher accuracy and sample adequacy than EUS-FNA, regardless of lesion size or location. In clinical practice, EUS-guided biopsy is preferred for small lesions due to the challenges percutaneous biopsy faces, particularly with lesion localization and guidance. The higher resolution of EUS enables more precise localization, providing clear advantages for targeting small lesions. In contrast to our findings, the study by van Riet *et al.* (26) indicated that there was no significant difference in diagnostic accuracy between US-CNB and EUS-FNA, regardless of lesion size or location.

Ultrasound-guided percutaneous biopsy is portable, cost-effective, and avoids ionizing radiation (27,28). In contrast, EUS-FNA time-consuming, more expensive, and requires moderate sedation (29). CT-guided biopsy, though widely used, is reserved for cases where US- or EUS-guided biopsies fail or when lesions are inaccessible by these two methods (30). Although CT provides clear cross-sectional views and accurate distance measurements (24), its use is limited by radiation exposure to both the patient and the operator. In contrast, US-guided biopsy avoids ionizing radiation, making it safer and more acceptable. Furthermore, US-guided biopsy, with real-time monitoring and enhanced safety via color Doppler, avoids this risk (13). Although CEUS-CNB was not used in this study, it is widely used for abdominal organs, especially in liver biopsy (31,32). Further research is needed on its use for pancreatic lesions.

Although imaging-guided pancreatic biopsy is generally safe, complications still occur. Studies have shown that complication rates for percutaneous biopsy range from 0% to 21.4% (33,34), whereas those for EUS-guided biopsy range from 3.6% to 22% (35). This study found that the postoperative complication rates for US-CNB, CT-CNB, and EUS-FNA are 15.12%, 16.36%, and 10.47% respectively, with no significant differences (P=0.319). Previous reports on complications related to pancreatic biopsy have shown a wide range of incidence rates, which may stem from differing definitions. In Ross *et al.*'s study (36), performing EUS-FNA alongside retrograde cholangiopancreatography contributed to higher complication rates. Although our study was retrospective, all biopsy patients in our study were hospitalized, closely monitored, and underwent tests and imaging if complications were suspected. The entire process was carefully documented in the patients' hospital records to ensure accuracy. Previous studies have reported severe complications from US- or CT-guided CNB (12,30,34). However, in this study, only mild complications were observed in the US/CT-CNB group. The most common issue was postoperative pain, lasting less than 24 hours and relieved by analgesics. Two patients experienced bleeding, resolved with hemostatic medication. The absence of severe complications may be due to the coaxial technique, which minimizes tissue damage and bleeding. Additionally, injecting embolic agents through the coaxial cannula helps prevent potential postoperative bleeding (37,38). A prospective study involving 355 patients reported that the incidence of severe complications related to pancreatic lesions after EUS-FNA was 2.54% (39). In this study, the EUS-FNA group had 26 patients with mild complications and one with severe complication, lower than previously reported rates.

US-CNB, CT-CNB, and EUS-FNA each have advantages and disadvantages. When selecting a biopsy method, diagnostic accuracy, safety, and cost-effectiveness are key considerations. This study assessed biopsy cost-effectiveness and found US/CT-CNB to be more economical. However, EUS-FNA is often preferred due to ease of use, physician familiarity, and patient preference. EUS-FNA's high-resolution imaging and less invasive nature make it more acceptable, despite the cost advantage of US/CT-guided biopsies.

This retrospective study compared US-CNB, CT-CNB, and EUS-FNA for diagnosing suspected pancreatic malignant lesions, considering diagnostic efficacy, safety, and cost-effectiveness. However, it had several limitations. First, the retrospective design limited standardized long-term follow-up, with incomplete radiographic and clinical data. Additionally, the retrospective design of this study inherently restricted our ability to standardize the selection of biopsy methods, which would have contributed a certain degree of selection bias. Furthermore, the follow-up period was short, potentially hindering a full assessment of long-term effects. In addition, the cost-effectiveness analysis may

have lacked certain factors, with results varying by region and healthcare system.

Conclusions

Imaging-guided biopsy is a reliable and effective method for obtaining pancreatic tissue samples. For suspected malignant pancreatic lesions, US-CNB and CT-CNB provide superior sample adequacy and diagnostic accuracy compared to EUS-FNA. Additionally, US-CNB and CT-CNB are more cost-effective than EUS-FNA in diagnosing these lesions.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-2024-2670/rc

Funding: This work was supported by the National Natural Science Foundation of China (No. 82171952).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-2024-2670/coif). 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 study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Ethics Committee of West China Hospital, Sichuan University (No. 2023-329) and the requirement for individual consent was waived due to the retrospective nature of the study.

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Cite this article as: Bao W, Zeng K, Huang J, Yu B, Gou Z, Lu Q. Comparative analysis of different biopsy techniques for pancreatic lesions in diagnostic value, safety, and cost-effectiveness. Quant Imaging Med Surg 2025;15(5):4375-4386. doi: 10.21037/qims-2024-2670

