

Thinprep® test versus conventional smear for the detection of pancreatic neoplasms after percutaneous ultrasound-guided fine-needle aspiration biopsy

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Abstract

Background

Few studies have defined the diagnostic value of ThinPrep pap test (a liquid-based cytology) for pancreatic samples obtained by percutaneous fine-needle aspiration (FNA). This study aimed to compare the efficacy of ThinPrep cytologic test (TCT) in screening pancreatic neoplasms to the conventional smear (CS), especially in the absence of rapid on-site evaluation (ROSE).

Methods

The study evaluated 78 patients with suspected pancreatic tumors who underwent percutaneous ultrasound-guided fine-needle aspiration (US-FNA) combined with CS and TCT. Final disease diagnosis was based on biopsy, surgery, or clinical progress.

Results

The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of TCT were 95.8%, 100%, 96.1%, 100%, 62.5%, whereas the values for CS were 90.1%, 100%, 90.8%, 100%, 41.7%, respectively. The combination of CS and TCT recorded 98.6%, 100%, 98.7%, 100%, 83.3%, respectively, for the parameters evaluated. None of the participants recorded serious complications.

Conclusions

This study shows that TCT is a more reliable tool in the detection of pancreatic neoplasms, especially for percutaneous US-FNA samples. Whereas TCT may be used as an alternative to CS in the absence of ROSE, the use of both methods in the screening process yields better results.

Background

There are different types of pathological solid pancreatic tumors, which inform clinical management, treatment strategies as well as disease prognosis. Due to the high malignancy and mortality rates associated with pancreatic ductal adenocarcinoma, it is important to differentiate it from other solid tumors. In some cases, other lesions such as focal pancreatitis can complicate proper diagnosis. Hence, pancreatic biopsy is often required as the ultimate option for the proper diagnosis of pancreatic lesions. Moreover, patients with locally advanced, unresectable pancreatic cancer or metastatic disease often undergo a biopsy to qualify for neoadjuvant therapy [1]. The use of FNA biopsy in the management of pancreatic tumors has been well established. Whereas pancreatic FNA routinely applies CS for diagnosis, previous studies have shown that the diagnostic performance of pancreatic FNA partly depends on the rapid assessment provided by cytologists [2–6]. ROSE ensures the effectiveness of biopsy and avoids inadequate sampling. However, many institutions have been reluctant to implement ROSE for FNA because of domestic problems such as staffing inadequacies, as well as the geographical location of the victims.

TCT has been used as an alternative to CS since 1996. Within the last 20 years, TCT has been widely used for processing gynecologic specimens because of its advantages in sampling, film making and programmed treatment. Despite the widespread use of TCT in the diagnosis of various organs and specimens as well as in cervical cytology,

few studies have documented the use of TCT for detection of pancreatic lesions. Besides, data comparing CS and TCT for percutaneous pancreatic FNA is scant.

On the other hand, although endoscopic ultrasound–guided biopsy has been widely recognized, many institutions still use ultrasound-guided procedures as the initial diagnostic tool for pancreatic tumors. Ultrasound-guided puncture has the advantages of both short operation time and low cost [7]. The diagnostic accuracy of US-FNA is comparable to endoscopic ultrasound–guided (EUS)-FNA [8]. In their studies, Mirko D'Onofrio summarized the incidence of complications associated with EUS or US guidance and showed that both ranged from 0–5% [9]. However, US-FNA was proved to be more cost-effective and safer.

In this study, we interrogated the diagnostic benefits of CS or TCT in the same group of patients to minimize bias. The ultimate goal of this study was to compare the value of using CS or/and TCT in screening pancreatic neoplasms after percutaneous US-FNA, especially in the absence of ROSE.

Methods

PATIENTS

This study retrospectively evaluated 78 patients who underwent US-FNA combined with CS and TCT for the detection of suspected solid pancreatic lesion. The study included patient files from January 2014 to February 2019. Data collection was approved by the Institutional Review Board of Peking Union Medical College Hospital. The patients underwent both imaging and blood biochemistry examination before biopsy. Biopsy indications include unresectable pancreatic tumors before neoadjuvant therapy, inconclusive imaging findings, and suspected tumors with poor prognosis or helpful treatment. The contraindication of biopsy was coagulation disorder (PT > 13 s). Anticoagulant was discontinued one week before biopsy. Written and informed consent was obtained from every patient.

US-FNA PROCEDURE

Prior to the biopsy procedures, all lesions were thoroughly reviewed by interventional (ultrasound) radiologists (K.L. and L.T., with 15 and 10 years of ultrasound interventional experience respectively). The size, location and composition of the lesions were evaluated. To choose the safest percutaneous route, color Doppler imaging was used to examine the vascularity of neoplasms and peripancreatic major blood vessels. Contrast-enhanced ultrasound (CEUS) was used to enhance precision in locating the lesions as well as to avoid possible necrotic areas. Thus, combined with CT and MR examinations, the best biopsy route was planned.

US-FNA was performed using the Esaote MyLab70 ultrasound unit (Esaote Biomedica, Genova, Italy) and a 20-gauge FNA needle. While lying in supine position, lidocaine was used to locally anesthetize all the patients. When the patients held their breath, the operator aligned the guide line with the lesion site, then inserted the needle along the guide line under the guidance of ultrasound. Throughout the US-FNA procedure, real-time imaging was done to ensure continuous visualization of the needle tip. On every pass, 20 to-and-fro movements within the lesion were performed with negative pressure created by a 10-ml syringe. Following excision of the samples, thin smears were made on glass slides and immediately fixed in 95% alcohol solution. Additional samples were deposited in preservative solutions for ThinPrep® (Hologic Inc., Marlborough, Mass., USA) cytologic test. Two or three passes per FNA session were standard in our department, and the number of passes was at the discretion of the operator until sufficient materials were visually confirmed. At the end of each pass, the needle was rinsed within this preservative solution. There was no on-site cytopathological assessment in the operating room. Color Doppler ultrasound was used to carefully assess whether there was significant bleeding.

The samples were then transferred to the pathology department for cytological evaluation. Both CS and TCT smears were stained using the Papanicolaou procedure and interpreted by experienced pathologists. Patients were monitored for four hours after biopsy to assess vital signs and any other complications.

CYTOLOGY ANALYSIS

FNA cytologic diagnoses were classified into six categories using the pancreaticobiliary cytology guidelines from the Papanicolaou Society of Cytopathology (PSC): I. Non-diagnostic, II. Negative (for malignancy), III. Atypical, IV. Neoplastic, V. Suspicious (for malignancy), and VI. Positive or malignant [10]. “Neoplastic: other” and “Positive or malignant” are assumed as pathologically positive. Considering the high risk of malignancy for atypical and suspicious categories that were reported to be approximately 74% and 82% respectively [10, 11], we classified them as positive diagnoses in Best-Case. However, many previous literatures classify atypical as negative while suspicious as positive malignancy [12, 13, 14]. To avoid overestimating true diagnostic performance, the Average-Case as well as the Worst-Case were also taken into account. In this study, the Average-Case refers to the classifying of Atypical as negative cases and Suspicious as positive cases, while the Worst-Case refers to classify Atypical or Suspicious as negative cases.

FOLLOW-UP

Final diagnoses were determined based on biopsy (repeated biopsy or core needle biopsy), surgery, or clinical progress. Follow-up was done for a minimum of 6 months. Clinical records, imaging and laboratory results were reviewed to evaluate short-term and long-term complications after biopsy.

STATISTICAL ANALYSIS

Continuous data were expressed as mean \pm standard deviation (range), while categorical variables were presented as frequencies and percentages. Student's t test and Mann Whitney U test were used to compare means between two groups having continuous variables. The comparison of categorical variables and rates was performed using χ^2 analysis with Yate's correction (or Fisher's exact test, when appropriate). GraphPad Prism Version 6.07 (GraphPad Software, La Jolla, CA) was used for statistical analyses and graphical presentation. The P-value was set at 0.05 ($p < 0.05$).

Results

PATIENTS The basic characteristics of the patients are summarized in Table 1. A total of 78 patients (47 males and 31 females) were enrolled in this study. The mean (\pm SD) age was 58.5 ± 12.0 years (range, 23–81 years). The mean (\pm SD) of the anteroposterior and largest diameters of neoplasms were 3.5 ± 1.2 cm (range, 1.4–8.0 cm) and 5.2 ± 1.7 cm (range, 1.7–12.5 cm), respectively. 41.0% of the mass was located in the head and uncinate, 56.4% in the body and tail, while 2.6% of the mass could not be accurately localized. There were no complications reported in the study.

Table 1
Baseline Characteristics of Patients

	Patients (N = 78)
Sex (Male/female)	47/31
Age(year)*	58.5 ± 12.0 (23–81)
Lesion size (cm)*	3.5 ± 1.2 (1.4-8.0)
Anteroposterior diameter	5.2 ± 1.7 (1.7–12.5)
Largest diameter	
Lesion location	32 (41.0%)
Head/uncinate	44 (56.4%)
Body/tail	2 (2.6%)
Not specified	
No. of slides*	3.7 ± 2.0 (1–11)
*Values are presented as mean ± SD (range).	

CYTOLOGICAL RESULTS AND FINAL DIAGNOSIS

Table 2 and Fig. 1 summarize the cytologic diagnoses based on different methods and the follow-up results. The study obtained adequate specimens from all the 78 patients for both CS and TCT. Two patients were lost to follow-up. Conventional smears found 38 patients to be malignant, 7 neoplastic, 14 suspicious, 5 atypical while 12 were negative. On the other hand, TCT showed that 42 cases were malignant, 7 neoplastic, 12 suspicious, 7 atypical while 8 were negative. Using both the CS and TCT defined 48 patients to be malignant, 7 neoplastic, 9 suspicious, while atypical and negative categories had 6 cases each.

Table 2
Cytological diagnosis and Final Diagnosis in 71 confirmed malignant cases

Final diagnosis and diagnostic method	Cytological diagnosis					Total
	Malignant	Neoplastic	Suspicious	Atypical	Negative	
PDAC CNB 4 CB + IHC 13 Re-biopsy 1	S11, T14, ST15		S4, T3, ST2	S1	S2, T1, ST1	18
PanNEN CNB + IHC 3 Surgery 1 PanNEC CB + IHC 1	S1, T1, ST1	S3, T3, ST3		T1, ST1	S1	4 1
IPMN Re-biopsy 1 Surgery 1	S1, T1, ST1			S1, T1, ST1		2
SPN CB + IHC 1 Surgery 1 CCA Surgery 1 NS Clinical progress	S25, T26, ST31	S2, T2, ST2	S1, ST1	S3, T5, ST4	T1	2 1 43
		S2, T2, ST2	S9, T9, ST6		S4, T1	1
Total	S38, T42, ST48	S7, T7, ST7	S14, T12, ST9	S5, T7, ST6	S7, T3, ST1	71
S = CS, T = TCT, ST = CS + TCT.						
PDAC: Pancreatic ductal adenocarcinoma; PanNEN: Pancreatic neuroendocrine tumor; PanNEC: Pancreatic neuroendocrine carcinoma; IPMN: Intraductal papillary mucinous neoplasm; SPN: Solid-pseudopapillary neoplasm; CCA: Cholangiocarcinoma; NS: Not specific; CNB: Core needle biopsy; IHC: Immunohistochemistry; CB: Cell block.						
Values represent the number of cases.						

After all the diagnostic evaluations, 93.4% (71 patients) showed evidence of malignancy while 6.6% (5 patients) were diagnosed with a benign tumors. Malignant tumors included 18 cases of ductal adenocarcinomas (4 confirmed by core needle biopsy, 13 by both cell block and immunohistochemistry, 1 by US repeat biopsies), 4 cases of neuroendocrine tumors (1 case confirmed by surgery, the others confirmed by both core needle biopsy and immunohistochemistry), 1 case of neuroendocrine carcinoma (confirmed by both cell block and immunohistochemistry), 2 cases of Intraductal papillary mucinous neoplasms (1 case confirmed by surgery, the other by surgical biopsy), 2 cases of solid-pseudopapillary neoplasms (1 confirmed by surgery, the other by both cell block

and immunohistochemistry), 1 case of cholangiocarcinoma which was confirmed by surgery as well as 43 malignant lesions confirmed by follow-up clinical progress. Benign tumors included 2 cases of focal chronic pancreatitis and 3 cases of autoimmune pancreatitis (confirmed by both CT and EUS repeat biopsies, as well as clinical progress).

Specimens classified as malignant/neoplastic/atypical/suspicious were all followed up as malignant on CS or TCT as well as on both CS and TCT. Benign lesions were correctly classified as negative by any of these three methods. There were 9.2% (7 cases) false negative cases reported by CS while TCT showed 3.9% false negative cases. Dual diagnosis with both CS and TCT had only 1 false negative case, representing 1.3%.

DIAGNOSTIC YIELD OF US-FNA

The diagnostic yields of CS, TCT or both CS and TCT are shown in Table 3 and Fig. 2. Cytological analysis showed that the sensitivity, accuracy and negative predictive value were significantly higher on TCT, but the combination of both CS and TCT had even better performance. All the three diagnostic methods showed no difference in specificity and positive predictive value.

Table 3
Diagnostic performance analysis, including Best-Case, Average-Case, and Worst-Case, to assess the impact of different Atypical/Suspicious classifications on results.

	SEN, %	SPE, %	PPV, %	NPV, %	ACC, %
<i>Best-Case</i>					
CS	90.1 (81.0-95.1)	100 (56.6-100)	100 (94.3-100)	41.7 (19.3-68.1)	90.8 (82.2-95.5)
TCT	95.8 (88.3-98.9)	100 (56.6-100)	100 (94.7-100)	62.5 (30.6-86.3)	96.1 (89.0-98.9)
CS + TCT	98.6 (92.4-99.9)	100 (56.6-100)	100 (94.8-100)	83.3 (43.7-99.2)	98.7 (92.9-99.9)
<i>Average-Case</i>					
CS	83.1 (72.7-90.0)	100 (56.6-100)	100 (93.9-100)	29.4 (13.3-53.1)	84.2 (74.4-90.7)
TCT	85.9 (76.0-92.2)	100 (56.6-100)	100 (94.1-100)	33.3 (15.2-58.3)	86.8 (77.5-92.7)
CS + TCT	90.1 (81.0-95.1)	100 (56.6-100)	100 (94.3-100)	41.7 (19.3-68.1)	90.8 (82.2-95.5)
<i>Worst-Case</i>					
CS	63.4 (51.8-73.6)	100 (56.6-100)	100 (92.1-100)	16.1 (7.1-32.6)	65.8 (55.5-75.5)
TCT	69.0 (57.5-78.6)	100 (56.6-100)	100 (92.7-100)	18.5 (8.2-36.7)	71.1 (60.0-80.0)
CS + TCT	77.5 (66.5-85.6)	100 (56.6-100)	100 (93.5-100)	23.8 (10.6-45.1)	79.0 (68.5-86.6)
Best-Case: "Atypical" and "Suspicious" were both classified as positive. Average-Case: "Atypical" was classified as negative while "Suspicious" was classified as positive. Worst-Case: "Atypical" and "Suspicious" were both classified as negative.					
The sensitivity and accuracy of TCT was significantly greater than those of CS ($P < 0.0001$), and the sensitivity and accuracy of both CS and TCT were significantly greater than those of TCT or CS based on the three cases ($P < 0.0001$).					
Data in parentheses are 95% confidence intervals.					
CS: Conventional smear, TCT: ThinPrep® cytologic test, SEN: Sensitivity, SPE: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, ACC: Accuracy.					

In the Best-Case category, the sensitivity, negative predictive value and accuracy were 95.8%, 62.5%, 96.1% and 90.1%, 41.7%, 90.8% for TCT and CS respectively. The above diagnostic values for the combination of both CS and TCT were 98.6%, 83.3% and 98.7%, respectively. On the other hand, in the Average-Case category, the sensitivity, negative predictive value and accuracy were 85.9%, 33.3%, 86.8% and 83.1%, 29.4%, 84.2%, for TCT and CS respectively. In contrast the use of both techniques recorded 90.1%, 41.7% and 90.8% for sensitivity, negative predictive value and accuracy, respectively. Even after taking into account the impossible Worst-Case, TCT had higher diagnostic sensitivity, negative predictive value and accuracy than CS (69.0% vs. 63.4%, 18.5% vs. 16.1% and 71.1% vs. 65.8%), and the values for both CS combined with TCT were 77.5%, 23.8% and 79.0%. The sensitivity and accuracy of TCT was significantly greater than those of CS ($P < 0.0001$), and the sensitivity and accuracy of both CS and TCT were significantly greater than those of TCT or CS based on the three cases ($P < 0.0001$).

Discussion

Our findings demonstrate that TCT was superior to CS in diagnostic sensitivity, negative predictive value and accuracy (95.8% vs. 90.1%, 62.5% vs. 41.7%, 96.1% vs. 90.8%, respectively). However, dual diagnosis by the use of both methods improve the performance of FNA. With the use of both tools, the sensitivity, negative predictive value and accuracy reached 98.6%, 83.3% and 98.7%, respectively. A patient example, demonstrating the value of US-FNA combined with TCT in the diagnosis of pancreatic neoplasm, is presented in Fig. 3, 4 and Video S1.

CS is a traditional and standard method for diagnosing FNA samples of pancreatic lesions. Due to the manual preparation, the sample collected is not evenly distributed on the slide or may span the entire surface area of the slide. Moreover, background elements such as necrosis, blood, inflammation and mucin may obscure diagnostic cells and lead to diagnostic problems. Such issues could be easily overcome by the use of ROSE. ROSE helps to evaluate on-site sampling, decrease inadequate samples and improve the diagnostic rate by 10–30% [2–6]. However, due to labor and time requirements, ROSE is hardly used. By comparison, Liquid-based cytology (LBC) is a thin layer slide preparation procedure that was developed to overcome challenges related to CS such as cell crowding and blood pollution. LBC uses standardized processing techniques to obtain samples with uniform cell distribution and in a monolayer to avoid cell overlap. Samples produced with LBC also show a cleaner background [15, 16]. In LBC, the cytological features of malignancy are retained and enhanced in a smaller screening area, which enhances accuracy in detection of malignant cells. Moreover, samples prepared from LBC can be saved for later cytological analysis, immunocytochemistry, special staining, and molecular based tests [17, 18]. However, due to changes in background and cytological characteristics, pathologists need to be familiar with the morphology of LBC to avoid misdiagnosis [18]. Therefore, the diagnostic performance of LBC is closely related to the pathologist's preference and experience.

Unlike the 22G–25G needle for EUS-FNA, this study used 20G needle for percutaneous puncture. Therefore, the risk of both bleeding and blood contamination was relatively higher. This risk makes it difficult to prepare for CS and reduces the success rate of CS preparation without ROSE. The technical features of LBC help solve this problem. LBC is more suitable in these cases as it lyses any blood-contaminated specimens during preparation. This partly explains our results that show such a satisfactory diagnostic performance of TCT. We observe that in the absence of ROSE, TCT can be used as an alternative to CS for percutaneous FNA, especially for hypervascular lesions.

To the best of our knowledge, this is the first comparative report revealing the diagnostic efficacy of TCT against that of CS utilizing percutaneous FNA for pancreatic lesions. There are few recent studies available comparing liquid-based cytology of pancreatic fine needle aspiration with smear and most findings remain controversial, as summarized in Table 4. Unlike EUS-FNA, none of the recent studies evaluate percutaneous biopsy. Five studies showed that CS had better diagnostic performance compared to LBC [13, 14, 19, 20, 21], which was inconsistent with our findings. The poor

performance of LBC may be due to several limitations highlighted in these studies. The most remarkable could be low sample concentration for LBC. In all the five studies, the inadequate sampling rate in LBC was significantly higher than that in CS. This may be attributed to the biases in the study design that favored CS. Besides, the impact of technical biasness on the results could not be ignored. For instances, the 2018 study [13] used CellPrepPlus (CP; Biotdyne, Seongnam, Korea) as the LBC method, a method that filters cells using a vacuum filter system. The vacuum filter system may reduce cell counts resulting in inadequate samples for LBC. In addition, whereas ROSE could not be performed with TCT preparation in some studies, the same studies used ROSE prior to CS [14, 21]. On the other hand, and in line with our findings, seven studies recognized the value of LBC of pancreatic FNA. A study from Masahiro Itonaga et al [18] indicated that CS combined with TCT improved the diagnostic efficacy compared to CS alone, even with the help of ROSE. The study of Shinichi Hashimoto et al [22], the retrospective study of Wei Zhou in 2019 and the prospective study of Priscilla in 2020 found LBC had higher diagnostic sensitivity and accuracy than CS without ROSE. The first two studies used BD SurePath™ (BD Diagnostics, Burlington, N.C., USA), a different system from ThinPrep® in cell collection and specimen preparation. In addition, both the prospective study from Shan-yu Qin et al [23] and Jund Won Chun reported the diagnostic efficacy of TCT to be relatively higher than that of CS, though there was no significant difference. In 2005, Momin T. Siddiqui et al [24] revealed that, with the help of Endoscopic retrograde cholangio-pancreatography (ERCP), TCT was more sensitive in detection of malignancy compared to CS (with ROSE). ERCP is attributed to superior cytological features of TCT slides.

Table 4
Comparative Literature Review of Pancreatic Cytology by FNA

First author	Year	LBC vs. CS	Study design	Patients	Imaging modalities	Needle passes	ROSE	LBC method	Inadequate sample rate (CS vs. LBC)
Yeon Myeong [13]	2018	LBC < CS	PS	43	EUS	≥ 5	No	CellPrepPlus	12.5% vs. 41.7%
Kyong Joo Lee [19]	2016	LBC < CS	RS	48	EUS	4	No	Thinprep	0.0% vs. 14.6%
Jun Kyu Lee [20]	2011	LBC < CS	PS	58	EUS	3.8 (2–8)	No	Thinprep	13.8% vs. 34.5%
J. K. LeBlanc [14]	2010	LBC < CS	PS	50	EUS	> 3	Yes	Thinprep	0.0% vs. 12.0%
Regina de Luna [21]	2004	LBC < CS	RS	62	EUS	NR	Yes	Thinprep	7.5% vs. 23.9%
Priscilla A. van Riet [17]	2020	LBC > CS	PS	71	EUS	3(2–3)	No	Thinprep	NR
Jung Won Chun [15]	2019	LBC ≠ CS	PS	170	EUS	3	No	BD SurePath	5.33% vs. 1.78%
Masahiro Itonaga [18]	2019	LBC + CS > CS	RS	204	EUS	2.8(1–7)	Yes	Thinprep	0.98% vs. 0.0%
Wei Zhou [16]	2019	LBC > CS	RS	514	EUS	NR	No	BD SurePath	4.28% vs. 2.33%
Shinichi Hashimoto [22]	2017	LBC > CS	RS	126	EUS	3.1(1–6)	No	BD SurePath	NR [†]
Shan-yu Qin [23]	2014	LBC > CS *	PS	72	EUS	3	No	Thinprep	NR [‡]
Momin T. Siddiqui [24]	2005	LBC > CS	PS	51	ERCP	NR	Yes	Thinprep	25.0% vs. 12.0%
*In this literature, although the data showed that LBC had higher diagnostic performance than CS, the results were not statistically significant.									
†This study mentioned that the inadequacy sample rates of CS and TCT samples were similar.									
‡This study excluded inadequate cases.									
CS: Conventional smear, LBC: Liquid-based cytology, PS: Prospective, RS: Retrospective, NR: Not reported, ROSE: Rapid on-site evaluation.									

In the absence of ROSE, more needles are needed for effective sampling. However, our findings revealed that the needle passes for TCT and CS didn't exceed three times, compared to the 5 to 6 passes required for EUS-FNA (without ROSE) as reported in the previous studies. We observe that, besides the US puncture needle having a larger suction range within the lesion, a single injection can obtain maximum sampling of the tumor samples within the safe range, unlike EUS guidance. In addition, the lifting range of EUS puncture is limited by the gastrointestinal tract, which affects the sampling to some extent. Therefore, we deduce that in the absence of ROSE, percutaneous puncture may reduce the number of needles required.

Based on Best-case, the clinical impact of false-negative biopsy results (NPV) associated 62.5% and 41.7% to TCT and CS respectively, as showed in Table 3. This finding is not sufficient to reliably exclude the presence of pancreatic malignancy. When CS was combined with TCT, a single false negative case was reported, which improved the reliability of the negative results. The causes of false-negative results include extremely desmoplastic reaction induced by the pancreatic adenocarcinoma that limit the pathological interpretation. Sampling errors, blood contamination, paucicellular lesions, needle deviation, and small-size lesions were also cited as reasons for the false-negative results [25, 26]. Many studies have recommended that caution should be taken when viewing negative results of biopsy [27–29], and radiological and clinical findings should always be considered during pathology examination.

Whereas the study findings reveal important information, this research is retrospective in nature and was carried out at a single unit. Therefore, distribution of smears and TCT samples were not even and were not standardized. ThinPrep technology is a routine clinical practice for pancreatic neoplasms in our institution. We reviewed the group that underwent both CS and TCT. Samples obtained by US-FNA were highly adequate for cytological analysis (either for CS or TCT). Due to the fact that our study involved a small sample size, future studies with a large number of subjects are warranted. In addition, follow-ups for complications were not regular, thus inconsistency in data. Fourthly, although final diagnoses were made according to the clinical course for at least 6 months in the patients, only four patients (5.1%) underwent surgery. Finally, we did not correct for possible learning curve effects during the 5-year period of this study, as the aim of our study was to examine the effect of using TCT in routine practice. This observation also includes a possible learning effect of pathologists on TCT preparation technology.

Conclusion

In summary, our results revealed that LBC using TCT technique might provide better diagnostic sensitivity and accuracy compared to CS, especially for percutaneous pancreatic US-FNA and in cases where ROSE is not available. Indeed, we have demonstrated that a combination of TCT and CS, produces superior diagnostic performance of FNA, and is worthy of clinical promotion.

Abbreviations

US-FNA

Ultrasound-guided fine-needle aspiration

TCT

ThinPrep cytologic test

CS

Conventional smear

ROSE

Rapid on-site evaluation

PPV

Positive predictive value
NPV
Negative predictive value

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Peking Union Medical College Hospital (Protocol number: S-K1112).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. The image depicted in figure X is our own.

Competing interests

The authors declare no competing interests.

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Author Contributions

KL and LT participated in the design of this study. KL, GY and GZ carried out the concepts, design, definition of intellectual content, literature search, data acquisition, data analysis and manuscript preparation. LT wrote the main manuscript text. GY, GZ and ZM provided assistance for data acquisition, data analysis and statistical analysis. XC, JZ, TZ and XC carried out literature search, data acquisition and manuscript editing. MX, QZ, GZ and YJ performed manuscript review. All authors have read and approved the content of the manuscript.

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Figures

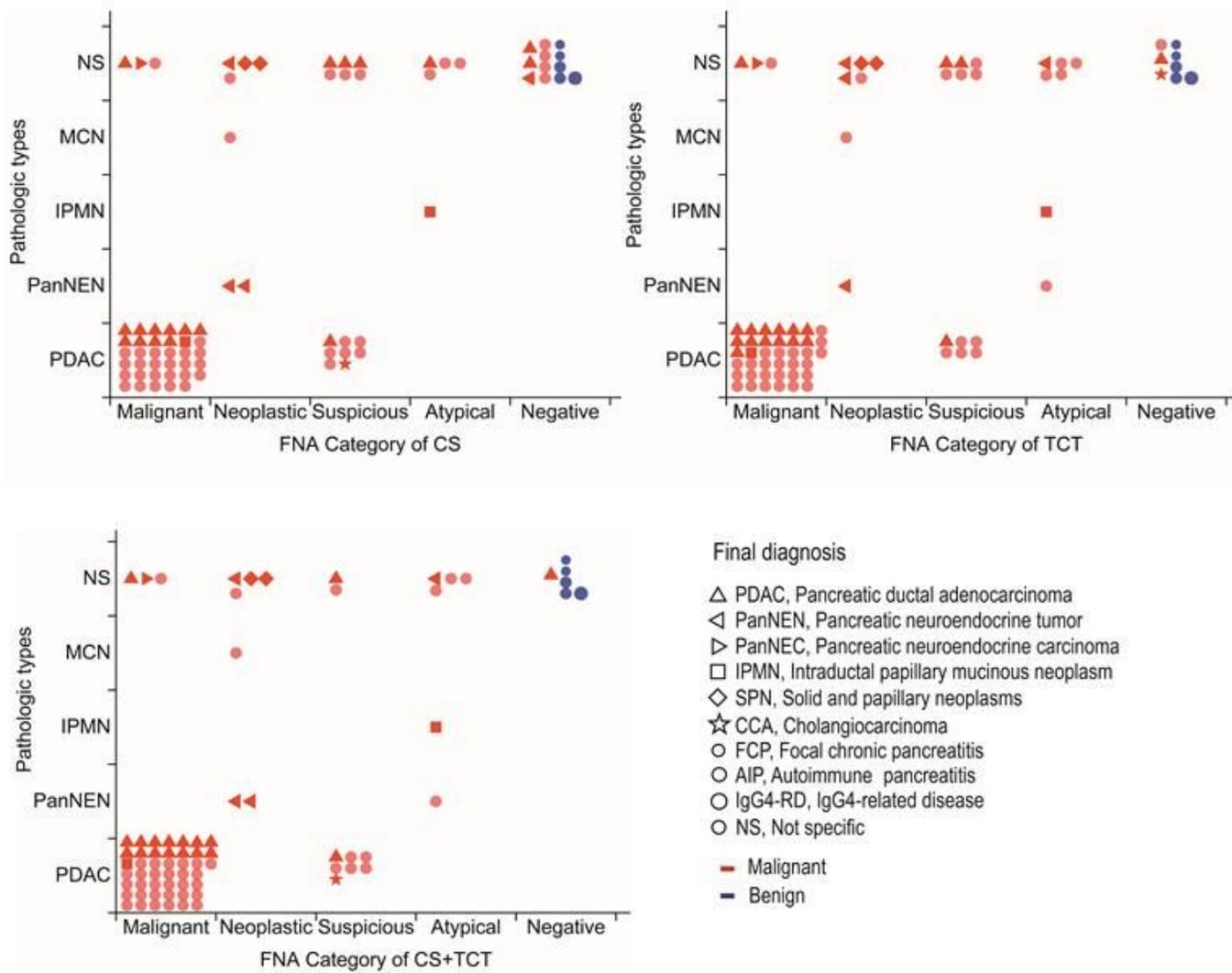


Figure 1

FNA cytologic diagnoses and follow-up final diagnoses based on CS, TCT and CS+TCT method. CS: Conventional smear, TCT: ThinPrep® cytologic test.

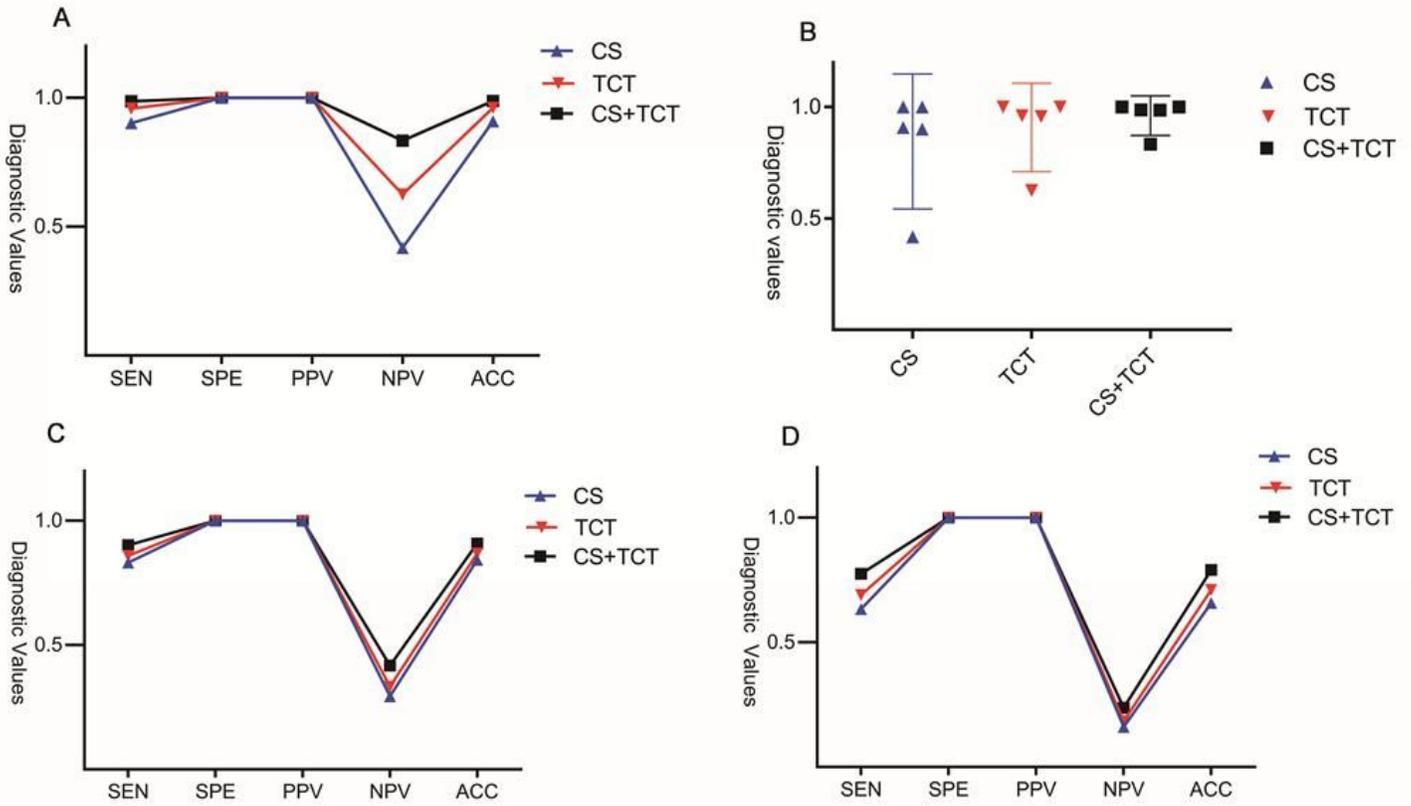


Figure 2

Diagnostic yield of US-FNA A, C, D represent Best-Case, Average-Case and Worst-Case respectively, while B represents the distribution of diagnostic indices in Best-Case. CS: Conventional smear, TCT: ThinPrep® cytologic test, SEN: Sensitivity, SPE: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, ACC: Accuracy.

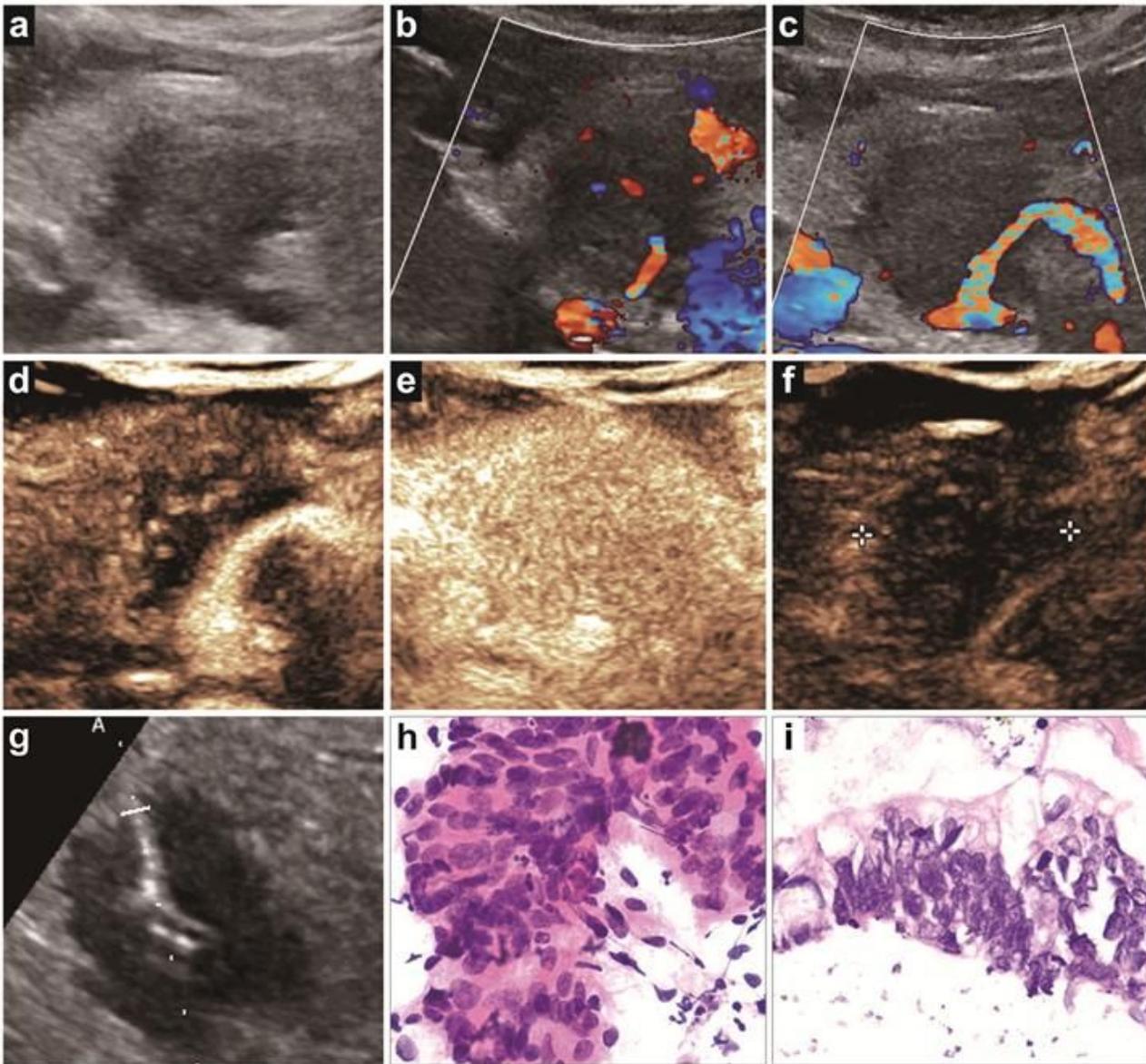


Figure 3

Ultrasound-guided FNA of pancreatic neoplasm in a 63-year-old woman (example case) a Gray-scale image showed a hypoechoic mass (arrowheads) with irregular margins in the pancreatic neck (arrows: the dilated pancreatic duct). b Color Doppler showed abundant color signals inside the mass. c Pre-contrast Color Doppler revealed splenic artery partially wrapped by the mass (triangles), with the bifurcation of the celiac artery involved. d-f Contrast-enhanced ultrasound (CEUS) of the lesion. d Mild enhancement was shown in the mass at 12th second in early arterial phase, with the splenic artery wrapped in it (triangles). e At 28th second in arterial phase, homogeneous and slightly low enhancement was revealed in the mass (arrowheads). f At 222th second in venous phase, clear hypoenhancement and washout of the mass was shown (crosses). g US-guided biopsy using a 20-gauge needle was aimed off splenic vessel, with the needle tip and the needle track clearly visible inside the targeted lesion (arrow). h-i Pathology confirmed the presence of pancreatic ductal adenocarcinomas. h CS, i TCT.

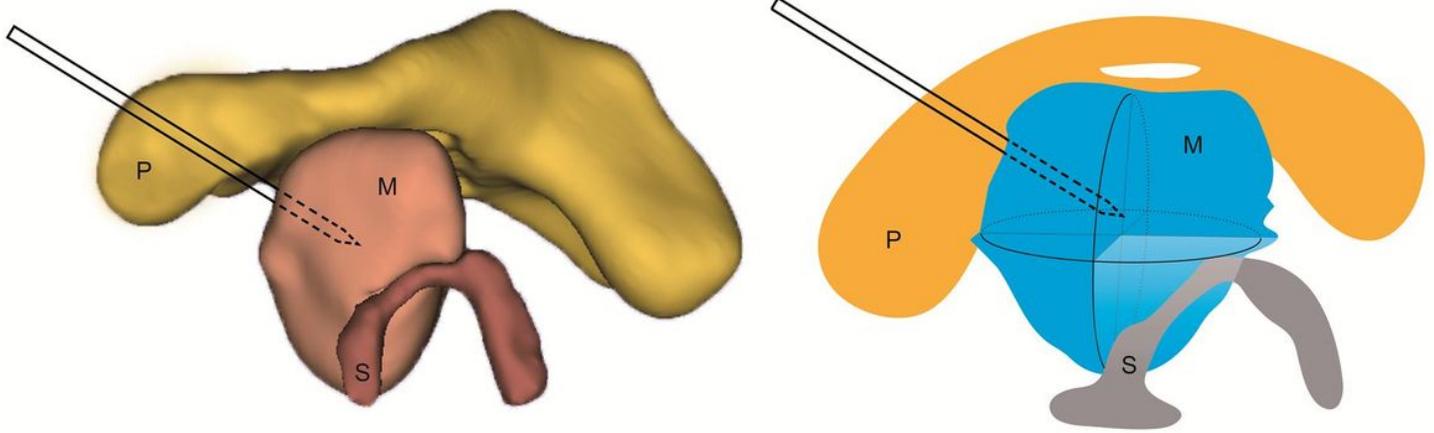


Figure 4

An illustration of ultrasound-guided FNA Pre-biopsy color Doppler and CEUS help to choose the safest percutaneous route by avoiding major blood vessel. P: pancreas, M: mass, S: splenic artery.

Supplementary Files

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- [SupplementaryVideoS1.avi](#)