



Utility of endoscopic ultrasound-guided fine-needle aspiration in pancreatic cancer patients who failed to obtain a pathological diagnosis in surgical exploration

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Background: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) allows for the analysis of diagnostic tissue specimens from various regions. For pancreatic tumors, especially un-resectable ones, how to obtain pathological confirmation is important for determining sub-sequent treatment. The purpose of this study is to investigate the clinical utility of EUS-FNA in patients who failed to obtain a pathological diagnosis in surgical exploration.

Methods: Patients who underwent EUS-FNA due to unsuccessful biopsy in surgical exploration in our center were retrospectively reviewed. All of the patients were diagnosed with resectable disease before surgery but were found to be unresectable during surgery. The positive rate of pathological diagnosis of EUS-FNA was analyzed.

Results: A total of 11 patients were included in this study, among which 8 were males and 3 were females. The median age of the patients was 55 years (range, 48 to 73 years). The median lesion size was 34 mm (range, 25 to 44 mm). The median number of needle passes was 3 (range, 1 to 3). Two patients underwent biliary stent implantation while 3 patients underwent gastrojejunostomy before EUS-FNA. The technical success rate of EUS-FNA was 100% (11/11); 10 (90.9%, 10/11) samples were positive and 1 was negative (being inadequate).

Conclusions: Intraoperative biopsy is the first choice diagnostic modality for unresectable pancreatic neoplasms. However, for patients who fail to obtain a pathological diagnosis in surgical exploration, EUS-FNA is still worth an attempt.

Keywords: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA); unresectable pancreatic cancer; surgical exploration

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Introduction

Pancreatic cancer is an aggressive malignancy with a poor prognosis, with an overall 5-year survival rate of 2–9% (1). Surgery remains the only potentially curative treatment for pancreatic cancer, but most patients are

diagnosed at an advanced stage and only 15% to 20% of patients are eligible for this procedure (2). Pancreatic cancer resectability is determined primarily by the degree of tumor-vascular contact, based on a routine pancreas CT. Although in recent decades emerging imaging

techniques have improved the predictive accuracy of resectability, unresectable lesions may still be encountered at surgery. Intraoperative pancreas biopsy or resection of suspicious metastatic lymph nodes is most widely used for pathological confirmation in these patients (3,4), though sometimes these techniques still cannot obtain pathological confirmation, which is important for the subsequent therapeutic regimen. Whether the utility of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) still benefit these patients who fail to obtain a pathological diagnosis in surgical exploration has not yet been reported. Anatomy change and tissue swelling sometimes happened after surgical exploration, whether these factors impact the utility of EUS-FNA in these patients remained unclear. The purpose of this study is to investigate the clinical utility of EUS-FNA in patients that fail to obtain a pathological diagnosis in surgical exploration. We present the following article in accordance with the STROBE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gS-21-913/rc>).

Methods

Patients

This is a single-center retrospective cohort study investigating the utility of EUS-FNA in patients that fail to obtain a pathological diagnosis in surgical exploration. With the approval of the institutional ethics board of Zhongshan Hospital (No. B2021-213R), all patients who underwent EUS-FNA for pancreatic disease from July 2017 to June 2020 at Zhongshan Hospital, Fudan University were screened retrospectively. The inclusion criteria were as follows: (I) patients were stratified as resectable before surgery but were found to be unresectable at surgery; (II) intraoperative biopsy and/or resection of suspicious metastatic lymph nodes was performed, but pathological assessment was negative for malignancy; (III) there was no previous pathological confirmation. Medical records were reviewed to obtain information regarding patient characteristics, lesion size and location, biliary stent prior to EUS, surgery performed, EUS results, clinical outcomes, and pathology. Informed consent was obtained before the EUS-FNA procedures. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

EUS-FNA procedures

EUS was performed using a convex linear-array endoscope (EG-580UT or 530UT; Fujifilm Corp, Tokyo, Japan) connected to an ultrasound device (SU-9000 or SU-8000 ultrasound processor; Fujifilm Corp). Before EUS-FNA, a systematic scan of the pancreatobiliary system was conducted. The location of the mass was defined as uncinata, head, neck, body, and tail. The maximum diameter of the mass was recorded as the size of the mass. EUS-FNA was performed with a 22 G needle (EchoTip, Cook Medical, Bloomington, IN, USA). EUS-FNA was repeated until sufficient macroscopic sampling (tiny white filiform tissue) had been acquired.

All of adverse reaction was recorded if happened. Once perforation or uncontrolled bleeding happened and observed under scope during EUS-FNA procedure, the operation was ceased and turned for surgical intervention. All the patients were closely monitored for vital signs and fasting for 1 day after EUS-FNA, fluid infusion treatment was supplied to the patients. Once patients showed with persistent fever, unstable blood pressure, or chest and abdominal pain, blood test and CT scan were applied to help judging whether happening of minor perforation, delayed bleeding, pancreatitis or infection.

Pathological evaluation

All the aspirated tissue was directly embedded in gel and sent for paraffin fixation. Slices were subjected to hematoxylin-eosin staining and immunohistochemical staining. The definitive pathological diagnosis was made by 2 pathologists. The final results were classified into positive (atypical cells or malignancy) or negative (no malignancy or being inadequate) according to the pathological diagnosis.

Statistical analysis

Normally distributed data were expressed as mean and standard deviation (SD), whereas non-normally distributed data were expressed as median and range.

Results

Patient characteristics, lesion features, and clinical outcomes are summarized in *Table 1*. A total of 11 patients were included in this study, among which 8 were males

Table 1 Characteristics, lesion features, and clinical outcomes of the patients

Case no.	Age (years)	Gender	Location	Size (mm)	Stent	No. of passes	Pathological result of FNA	Anatomy change
1	48	F	Neck	30	No	3	Inadequate	None
2	56	F	Neck	30	No	3	PDAC	None
3	55	M	Uncinate	36	No	2	PDAC	Gastrojejunostomy
4	55	M	Neck	25	No	3	PDAC	None
5	49	M	Head	44	No	2	IPMN malignant progression	Choledochojejunostomy
6	59	M	Head	35	No	2	PDAC	None
7	73	M	Uncinate	27	Yes	3	PDAC	None
8	53	M	Head	40	No	2	IPMN malignant progression	Choledochojejunostomy
9	65	F	Head	25	No	1	PDAC	None
10	53	M	Head	34	Yes	3	PDAC	None
11	68	M	Head	35	No	3	PDAC	Gastrojejunostomy, choledochojejunostomy

FNA, fine-needle aspiration; PDAC, pancreatic ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasm.

and 3 were females. The median age of the patients was 57.6 ± 7.55 years (range, 48 to 73 years). The technical success rate of EUS-FNA was 100% (11/11). Eleven lesions were detected at the pancreas neck (n=3), head (n=6), and uncinate process (n=3). The average lesion size was 35 ± 3.16 mm (range, 25 to 44 mm). The median number of needle passes was 3 (range, 1 to 3). Five patients suffered from biliary obstruction, among which 2 patients underwent percutaneous transhepatic cholangiodrainage (PTCD) before surgical exploration and switched to biliary stent implantation afterwards [1 endoscopic retrograde biliary drainage (ERBD), 1 self-expanding metal stent (SEMS) under PTCD], while the other 3 patients had choledochojejunostomy during surgery. Furthermore, prophylactic gastrojejunostomy was performed in 2 patients.

According to the pathological results, 10 (90.9%, 10/11) samples were positive and 1 was negative (being inadequate). Of these 10 positive samples, 8 were pancreatic ductal adenocarcinoma and 2 were intraductal papillary mucinous neoplasm with malignant progression. No EUS-FNA-related complications occurred.

Discussion

Pancreatic cancer is one of the most challenging tumors due to its delayed detection and poor prognosis. Surgical resection remains the most potentially curative intervention. Imaging has a crucial role in helping to stratify patients to

stage-appropriate therapies. The characteristics used to define resectable, borderline resectable, and unresectable disease are based on the use of cross-sectional imaging. After ruling out distant metastasis, local resectability is mainly determined by the degree of circumferential involvement of regional arteries and veins surrounding the tumor and the narrowing of veins. The accuracy of evaluation for resectability of pancreatic cancer was shown to be 60–83% (5). In our study, all the ruled-in lesions (unresectable at surgery) were on the right side of the superior mesenteric vein (SMV) (neck, head, and uncinate process; *Figure 1A*). For the special anatomical characteristics of the pancreas, sometimes it is difficult to precisely predict the resectability, especially when the lesion is close to important vessels (6).

Intraoperative pancreas core biopsy is a suitable method for intrasurgical confirmation of pancreatic carcinoma. The level of sensitivity was shown to be 93.1%, specificity was 99.1%, the predictive value of positive results was 99.2%, and the predictive value of negative results was 92.1% (7). For patients who fail to obtain a pathological diagnosis in surgical exploration (*Figure 1B*), how to obtain pathological confirmation before initiating chemoradiotherapy becomes crucial.

EUS-FNA plays an important role in pancreatic cancer management due to its ability to obtain pathological confirmation. The sensitivities and specificities of EUS-FNA for the diagnosis of pancreatic cancer were 85–92% and 96–98%, respectively. EUS-FNA is helpful in N-staging

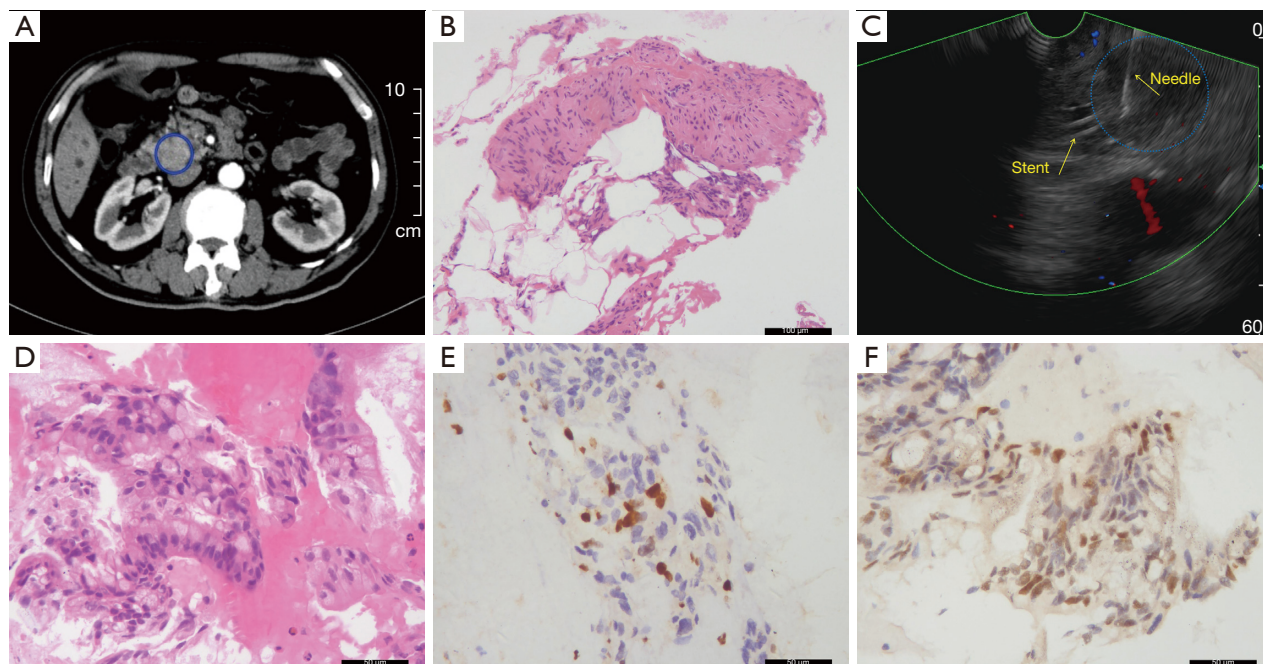


Figure 1 EUS-FNA for a patient who failed to obtain a pathological diagnosis in surgical exploration. (A) A mass (blue circle) was found at the pancreas head under abdominal CT with contrast; (B) intraoperative pancreas core biopsy during surgical exploration revealed normal pancreas tissue (HE staining); (C) EUS-FNA. The mass was at the pancreas head (blue dotted circle). The plastic stent was observed under EUS: (D) tissues obtained by EUS-FNA diagnosed as pancreatic ductal adenocarcinoma (HE staining); (E) immunohistochemical staining for Ki-67; (F) immunohistochemical staining for p53. EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration; CT, computed tomography.

and M-staging for its ability of pathological confirmation of lymph node metastasis, malignant ascites or liver metastases (8). For borderline resectable, unresectable, and metastatic stage patients, EUS-FNA is especially important for it can help to obtain a tissue diagnosis before initiating chemotherapy or radiation.

However, for the resectable pancreatic mass, whether to proceed with FNA before surgery remains a dilemma (9-12). The benefits and risks of FNA should be well balanced. In our hospital, based on the National Comprehensive Cancer Network Guidelines for Pancreatic Adenocarcinoma, pathological diagnosis is not mandatory before surgery for resectable cases if malignancy is highly suspected (13). It was reported that repeat EUS-FNA of pancreatic lesions is necessary in patients with a negative first EUS-FNA due to its improvement of the diagnostic yield (14,15). Whether EUS-FNA plays the same role in patients who fail to obtain a pathological diagnosis in surgical exploration has not yet been reported. In our study, all the ruled-in patients achieved technical success in EUS-FNA. Ten patients (90.9%) obtained pathological confirmation after EUS-FNA.

Obstructive jaundice is a common symptom complex in pancreatic cancer. In addition to choledochojejunostomy, it can also be managed by placement of a plastic or metal biliary stent. The biliary endoprosthesis, particularly SEMS, can cast an acoustic shadow and make EUS visualization of a pancreatic mass more difficult. Furthermore, the inflammatory reaction induced by a stent may have a negative impact on the diagnostic yield of FNA (16,17). Bekkali *et al.* reported that SEMS use had a negative impact on tissue diagnosis in pancreatic head masses (18), while Ranney *et al.* reported that the presence or absence of a biliary stent, whether plastic or metal, does not have an impact on the diagnostic yield or technical difficulty of EUS-FNA (19). In our study, 2 patients underwent biliary stent implantation, in whom EUS-FNA was not affected and positive pathological diagnosis was achieved (*Figure 1C-1F*).

Surgically altered anatomy sometimes limits EUS imaging. In our study, 2 patients underwent choledochojejunostomy to relieve jaundice, 1 patient underwent prophylactic gastrojejunostomy to prevent digestive tract obstruction caused by subsequent tumor progression, and 1 patient

underwent both choledochojejunostomy and prophylactic gastrojejunostomy. In these situations, the surgical anatomy did not significantly alter the standard endoscopic relationship or the orientation to the extraluminal organs. As a result, the standard imaging planes were not affected, and EUS-FNA was successful (20).

Intraoperative biopsy is the first choice diagnostic modality for unresectable pancreatic neoplasms at surgery, while our experience suggests that for patients who fail to obtain a pathological diagnosis in surgical exploration, EUS-FNA is still worth an attempt. However, this study had several limitations. First, this was a cohort with a limited sample size. Second, all the patients were selected in a single tertiary hospital retrospectively. Thus, further multi-center large-scale prospective studies are required to fully evaluate the efficacy and safety.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-21-913/rc>

Data Sharing Statement: Available at <https://gs.amegroups.com/article/view/10.21037/gc-21-913/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gc-21-913/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. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board

of Zhongshan Hospital (No. B2021-213R) and informed consent was taken from all the patients.

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