—Original Article—

Accuracy and clinical outcomes of pancreatic EUS-guided fine-needle biopsy in a consecutive series of 852 specimens

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ABSTRACT

Background and Objectives: Pancreatic EUS-guided fine needle biopsy (EUS-FNB) is increasingly used. Accuracy of EUS-FNB, particularly for benign diseases, utility of additional EUS-FNB if malignancy is suspected but initial diagnosis is inconclusive, and complication rate are not fully elucidated. We evaluated operating characteristics of EUS-FNB overall and for different diagnostic categories, value of additional EUS-FNB if malignancy is suspected but initial diagnosis is inconclusive, and frequency and type of complications. **Methods:** A retrospective tertiary single-center study including 852 consecutive pancreatic SharkCore EUS-FNBs from 723 patients between 2015 and 2020. EUS-FNB diagnoses were applied according to Papanicolaou Society's system and each category was further subcategorized. **Results:** Sufficient tissue cylinders for a histologic diagnosis were obtained in 93.4% (796/852). Accuracy was overall, for malignant, and benign entities 85.6% (confidence interval [CI]: 83.2%–87.9%), 88.3% (CI: 85.9%–90.4%), and 94% (CI: 92.2%–95.5%). Sensitivity and accuracy of EUS-FNB for autoimmune pancreatitis (AIP) ($n = 15$) was 83.3% (CI: 58.6%–96.4%) and 99.2% (CI: 98.3%–99.7%). Of patients in whom malignancy was suspected but initial EUS-FNB diagnosis was inconclusive, 7.3% (53/723) underwent one or two additional EUS-FNBs, and in 54.7% (29/53) of these, a malignant diagnosis was established. The frequency of hospitalization following EUS-FNB was 4.7%, with 0.2% ($n = 2$) incidents needing active intervention. **Conclusions:** We found a high accuracy of pancreatic EUS-FNB across all diagnostic categories including rare entities, such as AIP. In patients with a clinical suspicion of malignancy, additional EUS-FNB resulted in a conclusive diagnosis in more than half of cases. Complications necessitate hospitalization in almost 5%, but the majority are self-limiting.

Key words: pancreas; EUS; fine needle biopsy; EUS-FNB; accuracy; complications; histology; pancreatic cancer; autoimmune pancreatitis; chronic pancreatitis; intraductal papillary mucinous neoplasm

INTRODUCTION

For many years, EUS and EUS-FNA cytology have been the standard procedures for evaluating pancreatic

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lesions.[1] Pancreatic EUS-guided fine needle biopsy (EUS-FNB) is increasingly used as an alternative to EUS-FNA. However, the precise accuracy of EUS-FNB for the diagnosis of the entire spectrum of pancreatic diseases has not been fully elucidated. Moreover, the value of additional EUS-FNB if malignancy is suspected but initial diagnosis is inconclusive is not known, and few data exist on the frequency and type of complications following EUS-FNB.

EUS-FNA has an accuracy of up to 92% for diagnosis of malignancy in the setting of solid pancreatic lesions.[2,3] Diagnostic accuracy of EUS-FNA is depending on the availability of rapid on-site evaluation (ROSE).[1] To overcome limitations of EUS-FNA, EUS-FNB producing histologic tissue cylinders and depending on ROSE to a lesser extent has emerged.[4-7] EUS-FNB tissue cylinders enable additional immunohistochemical stains, special stains and molecular analyses, potentially improving diagnostics of pancreatic lesions.[8-12] Using a fork-tip EUS-FNB needle, a diagnostic accuracy of 91%–92% was recently demonstrated.[13,14]

Most studies of pancreatic EUS-FNB had a limited sample size, included extra-pancreatic lesions, and focused mainly on diagnostic yield, predominantly in malignant lesions. Studies on the role of pancreatic EUS-FNB in benign pancreatic diseases such as chronic pancreatitis and autoimmune pancreatitis (AIP) are limited to selected series of patients. The utility of additional EUS-FNB in patients suspected of malignancy is currently not clear. Studies evaluating frequency and type of pancreatic EUS-FNB-related complications are sparse.[5,14]

In this retrospective tertiary single-center study of a consecutive series of 852 prospectively collected pancreatic EUS-FNBs, we evaluated operating characteristics of EUS-FNB overall and for different diagnostic categories, examined the value of additional EUS-FNB if malignancy is suspected but initial diagnosis is inconclusive, and report frequency and type of complications during the first 7 days following EUS-FNB.

METHODS

Patient population and EUS-FNB specimens

Inclusion criteria were: All pancreatic SharkCore (Medtronic Corp., Minneapolis, MN) EUS-FNBs performed at a single tertiary center in the period from January 01, 2015, to December 31, 2020 [Figure 1]. Consequently, exclusion criteria were: Biopsy not performed at the tertiary center (but submitted to the pathology department for consultation), biopsy performed laparoscopically or percutaneously, biopsy acquired using a different EUS-FNB needle than SharkCore, and biopsy from an extrapancreatic site (*e.g.,* duodenum). This study was approved by the Danish National Ethics Committee (case-ID: 2101718), Region of Southern Denmark's registry of research projects (journal-ID 21/9629), and by the Strategic Research Council of Region of Southern Denmark (journal-ID 21/13792).

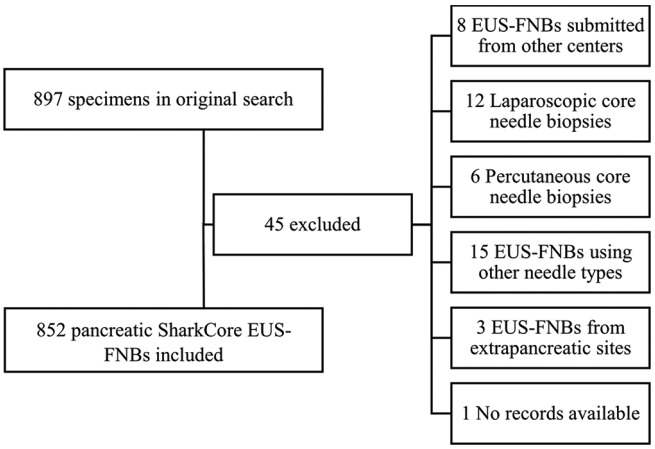

Figure 1. Study flowchart of our series of consecutive pancreatic EUS-FNBs. In the original search, 897 specimens were identified. Forty-five specimens were excluded, leaving 852 EUS-FNBs for inclusion

EUS-FNB procedure and specimen processing

EUS-FNB was only performed if it would make an impact on the patient management or treatment strategy. The EUS-FNB procedure was performed using curved array echo-endoscopes (Pentax Europe, Germany) connected to high-end ultrasound scanners (Hitachi EUB-7500/8000, Arietta V70, Hitachi Medical Systems Europe, Switzerland). All endoscopists (n = 7) were trained EUS experts having performed EUS for 5–30 years with an annual institution caseload of more than 1000 procedures. All punctures were made with the 22G SharkCore FNB needle utilizing a trans-gastric or trans-duodenal approach. As previously described, prior to puncturing the target, the stylet was retracted a few millimeters before the tip of the needle was advanced into the target tissue.[15] The stylet was then retracted while performing multiple movements of the needle within the lesion (slow pull technique).[15] The use of suction and fanning techniques were at the discretion of the endoscopist. If used, suction was released before removal of the needle from the target. A maximum of 3 passes were conducted. If macroscopically

sufficient material was obtained, no additional passes were performed. Contrast-enhanced EUS was not used.

EUS-FNB specimens were processed as described previously.[15] In short, specimens were fixed in formalin (6–24 h) end embedded in paraffin. Thirteen serial sections were cut from the paraffin blocks. Section no. 1 and 13 were stained with hematoxylin and eosin (HE) and section no. 2 with Alcian blue periodic acid-Schiff (AbPAS pH 2.7). Sections 3–12 were initially left unstained. If found necessary by the pathologist, additional HE, immunohistochemical or histochemical stains were performed. All pathologists (n = 7) were board-certified and had a special interest in gastrointestinal pathology.

EUS-FNB diagnosis

EUS-FNB pathology reports were reviewed and the following data were extracted: Date of biopsy, gender, age, and histologic diagnosis including macroscopic and microscopic findings. Each specimen was classified using Papanicolaou's Society of Cytopathology Terminology System as either malignant, suspicious of malignancy, neoplastic: Benign, neoplastic: Other, atypical, benign, or nondiagnostic.[16] EUS-FNB diagnoses were further subcategorized as follows:

"Malignant" EUS-FNBs: Adenocarcinoma incl. subtypes, acinic cell carcinoma, metastasis, lymphoma, neuroendocrine carcinoma, or undifferentiated carcinoma.[17]

"Neoplastic: Other" EUS-FNBs: Intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN), neuroendocrine tumor (NET) Grade 1 or 2, paraganglioma, or solid-pseudopapillary neoplasm (SPN).[17]

"Neoplastic: Benign" EUS-FNBs: Serous cystadenoma or Schwannoma.

"Atypical" EUS-FNBs: Atypical cells, dysplasia, mucin, or "atypical histologic lesion" with observer caution in diagnosis, as described by Papanicolaou Society.[16]

"Benign" EUS-FNBs: Normal pancreas, unspecific fibrosis, acute pancreatitis, chronic pancreatitis, AIP, or pseudocyst. Chronic pancreatitis was defined as interlobular fibrosis (with or without intralobular fibrosis), mixed inflammatory infiltrate (macrophages, lymphocytes, neutrophilic granulocytes), fat tissue necrosis, pseudocyst(s), and/or hemorrhage.[18] Unspecific fibrosis was defined as fibrosis with no or only limited, unspecific inflammation.

"Nondiagnostic" EUS-FNBs: Nonpancreatic tissue or too sparse tissue for diagnosis.

EUS-FNB diagnosis of autoimmune pancreatitis

EUS-FNB diagnosis of AIP was based on the histologic International Consensus Diagnostic Criteria (ICDC) level 1 and 2 for diagnosis of type 1 and type 2 AIP.[19] ICDC for type 1 AIP were slightly modified: As a periductal lymphoplasmacytic infiltrate was rarely seen, possibly due to the small diameter (around 0.4 mm) of most SharkCore EUS-FNBs, the criterion "periductal lymphoplasmacytic infiltration" was modified to "periductal and/or diffuse lymphoplasmacytic infiltration."

The final AIP diagnosis was based on the ICDC.[19] Parenchymal imaging with diffuse, voluminous enlargement of the pancreas on computed tomography (CT) or ductal imaging with focal or multiple narrowing(s) of the main pancreatic duct (MPD) without marked upstream dilatation (<5 mm) corresponding to at least level 2 ICDC were recorded for each AIP patient.[19] Other organ involvement (OOI) was recorded as described previously.[20]

Follow-up and accuracy

The reference standard diagnosis was defined as the diagnosis based on a pancreatic resection specimen. If no such was available within 6 months after EUS-FNB, the final diagnosis was based on best clinical evidence within 6 months of EUS-FNB, in accord with Fitzpatrick *et al.* and others.[6,17,21-23] This clinical evidence was based on histologic diagnosis from metachronous EUS-FNBs, histologic diagnosis based on specimens from other organs (*i.e.,* biopsies from liver, lymph nodes, etc.), and/or comprehensive clinical follow-up, including imaging results.

For the overall accuracy, EUS-FNB diagnoses "malignant" or "suspicious of malignancy" were considered true positive if the final diagnosis was malignant and false-positive if the final diagnosis was benign, in accord with previous studies.[17,22,24,25] EUS-FNB diagnoses "neoplastic: Other"

were considered true positive if the final diagnosis was malignant or neoplastic: Other, as described previously. EUS-FNB diagnoses "atypical," "benign," "neoplastic: Benign." and "nondiagnostic" were considered true negative if the final diagnosis was benign (including neoplastic: Benign), and false negative if the final diagnosis was malignant or neoplastic: Other.[23]

For the accuracy of "malignant," "neoplastic" (including "neoplastic: Other" and "neoplastic: Benign"), and "benign" categories, a positive or negative interpretation was related to the final diagnosis of the category in question. In the benign category, a "benign," "atypical" or "nondiagnostic" EUS-FNB with final benign diagnosis was considered true positive. In the malignant category, a "malignant," "suspicious of malignancy," or "neoplastic: Other" EUS-FNB with final malignant diagnosis was considered true positive. A "neoplastic: Other" EUS-FNB with final neoplastic: Other or malignant diagnosis, and a "neoplastic: Benign" EUS-FNB with a final benign diagnosis, was considered true positive.[22]

For the accuracy of "AIP," the definition of a true positive EUS-FNB diagnosis was either histologic level 1 or level 2 ICDC. EUS-FNB diagnosis of "chronic pancreatitis" was interpreted as "false negative" if the final diagnosis was AIP.[26,27]

Electronic health records were reviewed for early EUS-FNB-related complications prior to discharge and for late complications including hospitalizations within 7 days of procedure. The total number of days hospitalized and any admission to the intensive care unit (ICU) was recorded. Type of complication and intervention were graded using the Clavien–Dindo (CD) Classification.[28]

Statistical analysis

To determine diagnostic accuracy of SharkCore EUS-FNB, we calculated operating characteristics (sensitivity, specificity, positive predictive value, negative predictive value, and accuracy) with 95% confidence interval (CI). These calculations were performed overall and for the categories "malignant," "neoplastic" (including "neoplastic: Other" and "neoplastic: Benign"), "benign", and "AIP." In the calculations for each category, all EUS-FNBs (n = 852) were included. Statistical analyses were performed using SPSS version 26 (IBM, NY, USA).

RESULTS

Study cohort

The original search included 897 specimens. Forty-five did not fulfill the inclusion criteria resulting in the inclusion of 852 pancreatic EUS-FNBs from 723 patients [Figure 1]. Of these, 55% (n = 398) were males, and mean age was 67 years (SD: 12.0). Patient and EUS-FNB characteristics are shown in Table 1. Lesion site was the pancreatic head in 52% (n = 445), body in 26% (n = 220), tail in 17% (n = 142), and uncinate process in 5% (n = 45). Overall, 103 patients underwent at least one additional EUS-FNB amounting to 129 additional EUS-FNBs in total. In 53 of these 103 patients, the reason for additional biopsy was clinical suspicion of malignancy but initial inconclusive EUS-FNB diagnosis. Data on the number of passes were available for 35.4% (n = 302) EUS-FNBs. Of these, 5% (n = 15) had one pass, 41% (n = 124) had two passes, and 54% (n = 163) had three passes. The average was 2.5 passes (SD: 0.6). No statistically significant difference in diagnostic accuracy was found in relation to number of passes. The technical success rate was 100%, meaning that sufficient tissue, as judged by the endoscopist, was obtained in all EUS-FNBs (n = 852). During microscopic (and/or macroscopic) evaluation at the pathology department, however, the relative frequency of nondiagnostic EUS-FNB, containing only blood or too sparse tissue for diagnosis, was 6.6% (n = 56), meaning that material sufficient for a histologic diagnosis was yielded in 93.4% (796/852). The diagnostic yield for mucinous pancreatic cysts was 84.6% (data not shown). Selected microscopic images of EUS-FNBs are shown in Figure 2. The most frequent EUS-FNB diagnosis was pancreatic ductal adenocarcinoma (PDAC) incl. subtypes (43%, 364/852), while all malignant EUS-FNB diagnoses accounted for 46.7% (398/852). Of the remaining EUS-FNB diagnoses, 5.3% (45/852) were suspicious of malignancy, 9.1% (78/852) neoplastic, 7.3% (62/852) atypical, 25% (213/852) benign, and 6.6% (56/852) nondiagnostic [Table 1].

Diagnostic accuracy of SharkCore EUS-FNB

The operating characteristics of pancreatic EUS-FNB are presented in Table 2 and Supplementary Table 1. Overall accuracy was 85.6% (CI: 83%–87.9%), and accuracy for the categories "malignant," "neoplastic," "benign," and "AIP" was 88.3% (CI: 85.9%–90.4%), 95.5% (CI: 93.9%–96.8%), 94% (CI: 92.2%–95.5%), and 99.2% (CI: 98.3%–99.7%). All patients with EUS-FNB

diagnosis "suspicious of malignancy" (*n* = 45) had a final malignant diagnosis. The final diagnosis in these was PDAC, malignancy not otherwise specified, cholangiocarcinoma, and metastasis in 84.5% (*n* = 38), 6.7% (*n* = 3), 4.4% (*n* = 2), and 4.4% (*n* = 2). Metastases to the pancreas were most frequently from the lungs (36%, *n* = 9), kidneys (20%, *n* = 5), and breast (12%, *n* = 3). Overall, there were no EUS-FNBs false positive for malignancy. However, the false-negative rate was 14.4% (*n* = 123) [Table 3]. Of the patients with false-negative EUS-FNB diagnosis, 67% (*n* = 83) had a final diagnosis of PDAC. The highest fraction (79%, n = 97) of false-negative EUS-FNB diagnoses were "unspecific fibrosis" (*n* = 38, 31%), "atypical" (*n* = 32, 26%), and "nondiagnostic" (*n* = 27, 22%).

Table 1. Demographics of 723 patients who underwent pancreatic EUS-FNB. Absolute and relative frequencies of EUS-FNB diagnoses, with further subcategorization, are given

Patients/diagnosis	Mean (SD), number (%)
All patients (*n*=723): Mean age (SD)	67.0 (12.0)
All patients (*n*=723): Female, *n* (%)	325 (45)
EUS-FNB diagnosis (*n*=852)	
Malignant	398 (46.7)
Adenocarcinoma (incl. subtypes)	364 (92)
Metastasis	25 (6)
Lymphoma, NEC, ACC or undifferentiated carcinoma*	9 (2)
Suspicious of malignancy, *n* (%)	45 (5.3)
Neoplastic: benign, *n* (%)	9 (1)
Serous cystadenoma	9 (100)
Neoplastic: other, *n* (%)	69 (8.1)
MCN or mucinous cyst, NOS	7 (10)
IPMN	15 (21)
NET	45 (66)
SPN	2 (3)
Atypical, *n* (%)†	62 (7.3)
Benign, *n* (%)	213 (25)
Normal pancreas	28 (13)
Chronic pancreatitis	74 (34)
Acute pancreatitis	4 (2)
Unspecific fibrosis	75 (35)
AIP‡	19 (9)
Pseudocyst	12 (6)
GPA	1 (1)
Nondiagnostic, *n* (%)	56 (6.6)

*Lymphoma (*n*=4), neuroendocrine carcinoma (NEC) (*n*=3), acinic cell carcinoma (ACC) (*n*=1), and undifferentiated carcinoma (n=1); †Atypical cells or atypical histologic lesion (*n*=44), dysplasia (*n*=17), mucus (*n*=1); ‡Eleven EUS-FNBs with type 1 AIP (seven ICDC level 1, four ICDC level 2), eight EUS-FNBs with type 2 AIP (four ICDC level 1, four ICDC level 2). ICDC: International Consensus Diagnostic Criteria; AIP: Autoimmune pancreatitis; MCN: Mucinous cystic neoplasm; NOS: Not otherwise specified; IPMN: Intraductal papillary mucinous neoplasm; NET: Neuroendocrine tumor; SPN: Solid-pseudopapillary neoplasm; GPA: Granulomatosis with polyangiitis

Patients suspected of malignancy and undergoing more than one EUS-FNB for a final malignant diagnosis

Of 723 patients, 7.3% (*n* = 53) underwent at least one additional pancreatic EUS-FNB procedure due to suspicion of malignancy [Supplementary Table 2]. In these patients, the most frequent initial EUS-FNB diagnoses were "unspecific fibrosis" (*n* = 14, 26%), "suspicious of malignancy" (*n* = 10, 19%), "atypical" (*n* = 9, 17%), and "nondiagnostic" (*n* = 8, 15%), in total accounting for 77% (*n* = 41). In all patients with false negative results, a lesion suspicious of malignancy was visualized.

Forty-eight and five patients underwent one and two additional EUS-FNBs. In 54.7% (*n* = 29) patients, the additional EUS-FNBs were able to classify the pancreatic lesion as malignant. Of these, 93.1% (*n* = 27) patients needed just one additional EUS-FNB, while 6.9% (*n* = 2) patients needed two additional EUS-FNBs. The patients not reaching final malignant diagnosis at EUS-FNB had a final diagnosis based on histologic pancreatic specimens other than EUS-FNB (58%, *n* = 14), histologic nonpancreatic specimens (25%, *n* = 6), and clinical evaluation with imaging revealing tumor in the pancreas (17%, *n* = 4).

Final diagnosis in patients with a benign or nondiagnostic EUS-FNB

In 25% (*n* = 213) of the EUS-FNBs, the diagnosis was "benign," and in 7% (*n* = 56) "nondiagnostic." The final diagnosis regarding these patients for each of the EUS-FNB subcategories is shown in Table 4.

Final diagnosis in patients fulfilling level 1 or level 2 International Consensus Diagnostic Criteria criteria for autoimmune pancreatitis

In the present series of 852 consecutive pancreatic EUS-FNBs, EUS-FNB diagnosis was AIP in 2.2% (*n* = 19). Of these 19 EUS-FNBs, the final diagnosis was AIP, chronic pancreatitis, and granulomatosis with polyangiitis (GPA) in 79% (*n* = 15), 16% (*n* = 3), and 5% (*n* = 1). In total, 2.1% (*n* = 15) of 723 patients had a final diagnosis of AIP, three of which underwent one additional EUS-FNB. Ten of 15 AIP patients were male and median age was 61 years (range: 24–81). Of the included AIP patients, 86.7% (13/15) were correctly diagnosed at EUS-FNB, one of which had to undergo two EUS-FNB procedures to reach final AIP diagnosis. Patient information and histologic findings according to the histologic ICDC criteria are shown in

Table 2. Operating characteristics of 852 pancreatic EUS-FNBs obtained from 723 patients

	Overall	Malignant	Neoplastic	Benign	AIP
Sensitivity	80.6 (77.3-83.6)	81.9 (78.4-85)	67.2 (57.9-75.7)	100 (98.1-100)	83.3 (58.6-96.4)
Specificity	100 (98.3-100)	100 (98.7-100)	100 (99.5-100)	92.3 (90-94.2)	99.5 (98.8-99.9)
PPV	100 (99-100)	100	100	79.1 (74.4-83.1)	79 (58-91.1)
NPV	63.8 (60.1-67.4)	75.1 (71.6-78.2)	95.1 (93.7-96.2)	100	99.6 (99-99.6)
Accuracy	85.6 (83-87.9)	88.3 (85.9-90.4)	95.54 (93.9-96.8)	94 (92.2-95.5)	99.2 (98.3-99.7)

Data are given as percentages (95% CI) overall and for the categories "malignant," "neoplastic" (including "neoplastic: Other" and "neoplastic: Benign"), "benign," and "AIP". PPV: Positive predictive value; NPV: Negative predictive value; AIP: Autoimmune pancreatitis; CI: Confidence interval

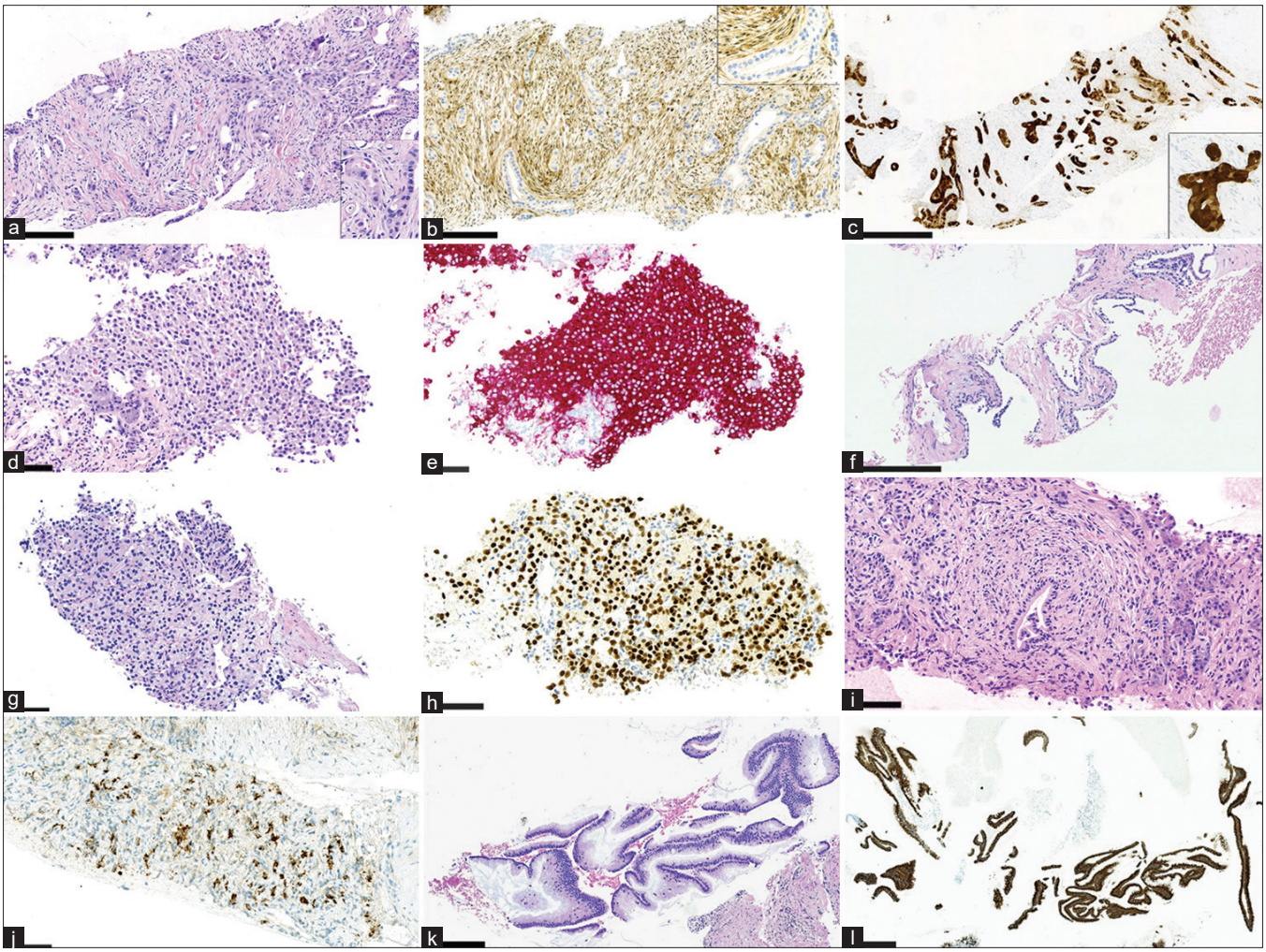

Figure 2. Selected microscopic images from pancreatic EUS-FNBs. Size of scale bars in brackets. (a) Pancreatic ductal adenocarcinoma (PDAC) (HE, 250 µm); (b) PDAC with loss of SMAD4 (250 µm); (c) Expression of maspin in PDAC (500 µm); (d) Neuroendocrine tumor (NET) (HE, 100 µm); (e) Synaptophysin-positivity (red) and Ki67-negativity (brown) in NET (100 µm); (f) Serous cystadenoma (HE, 250 µm); (g) Metastasis from renal clear cell carcinoma (RCC) (HE, 100 µm); (h) Pax8-positivity in metastatic RCC (100 µm); (i) Type 1 autoimmune pancreatitis (AIP) (HE, 100 µm); (j) Increased IgG4-positive cells in type 1 AIP (100 µm); (k) Intraductal papillary mucinous neoplasm (IPMN) (HE, 250 µm); (l) MUC2-positivity in IPMN (500 µm)

Table 5. In the EUS-FNBs that were false negative for AIP (n = 3), the diagnosis was "normal pancreas" in a scant biopsy material in all cases. All (n = 3) patients with EUS-FNB diagnosis AIP and chronic pancreatitis as final diagnosis had histologic ICDC level 2 criteria for type 2 AIP at EUS-FNB. The EUS-FNB diagnosis in the patient with a final GPA diagnosis was level 1 type 1 AIP. Operating characteristics of pancreatic EUS-FNB for the diagnosis of AIP are shown in Table 2. Accuracy and sensitivity of EUS-FNB for the diagnosis AIP were 99.2% (CI: 98.3%–99.7%) and 83.3% (CI: 58.6%–96.4%).

Type 1 AIP was the final diagnosis in 66.7% (10/15) of all AIP patients. The median age was 66 years (range: 24–81), and 80% (8/10) were male. Among type 1 AIP patients, 80% (8/10) responded

Table 3. EUS-FNB diagnosis and final diagnosis for all false-negative EUS-FNBs (*n*=123)

False-negative EUS-FNBs (*n*=123)	
EUS-FNB diagnosis number (%)	**Final diagnosis number (%)**
Unspecific fibrosis 38 (30)	PDAC 27 (71) NET 4 (11) Metastasis Pancreatic cancer, NOS 2 (5) IPMN 2 (5)
Atypical histologic lesion 32 (26)	PDAC 23 (72) Pancreatic cancer, NOS 2 (6) IPMN 3 (10) MCN 1 (3) NET 1 (3) Cholangiocarcinoma 1 (3) Paraganglioma 1 (3)
Nondiagnostic 27 (22)	PDAC 11 (41) Pancreatic cancer, NOS 6 (22) NET 5 (18) IPMN 3 (11) MCN 1 (4) Metastasis 1 (4)
Dysplasia 13 (11)	PDAC 11 (85) IPMN 2 (15)
Chronic pancreatitis 8 (7)	PDAC 6 (75) Pancreatic cancer, NOS 2 (25)
Normal pancreas 4 (3)	PDAC 4 (100)
Acute pancreatitis 1 (1)	PDAC 1 (100)

IPMN: Intraductal papillary mucinous neoplasm; MCN: Mucinous cystic neoplasm; NET: Neuroendocrine tumor; NOS: Not otherwise specified; PDAC: Pancreatic ductal adenocarcinoma including its subtypes

to steroid therapy, and 70% (7/10) had elevated serum IgG4 levels (cut-off 1.35 g/L) with a median of 2.76 g/L (range: 0.4–15.7 g/L). Both nonresponders (n = 2) had spontaneous remission and did not have elevated serum-IgG4, but IgG4-positivity (20 and 32 IgG4-positive cells per HPF) and level 1 histologic ICDC at EUS-FNB. OOI was observed in 50% (5/10). None of the type 1 AIP patients had inflammatory bowel disease (IBD). Parenchymal imaging and ductal imaging corresponding to at least ICDC level 2 were observed in 40% (4/10) and 50% (5/10).

Type 2 AIP was the final diagnosis in 33.3% (5/15) of all AIP patients. The median age was 52 years (range: 38–70), and 40% (2/5) were male. No type 2 AIP patients had elevated serum IgG4 level, and 60% (3/5) responded to steroid therapy. IBD was observed in 60% (3/5). Parenchymal and ductal imaging corresponding to at least ICDC level 2 were observed in 60% (3/5) and 20% (1/5).

EUS-FNB-related complications

In 5.4% (n = 46) of the EUS-FNB procedures, the patient experienced immediate complications during the procedure, prior to discharge or within 7 days.

The complications prior to discharge were all graded as CD-I, needing conservative treatment only (analgesics). One patient developed acute pancreatitis 3 h after EUS-FNB and was discharged two days later. The remaining 3.3% (n = 28) had self-limiting local bleeding during the procedure, while 2% (n = 17) complained of abdominal pain and were all discharged the same day as the EUS-FNB procedure.

In 4.7% (n = 40) of the EUS-FNB procedures, the patient was admitted to a hospital within 7 days after the EUS-FNB procedure (late complications). Of these patients, 25% (n = 10) also had immediate complications. The average time admitted was 7.9 days (median: 3). This included one patient admitted for 114 days, suffering from severe necrotic pancreatitis with abscess undergoing necrosectomy, and admission to the ICU for a total of 40 days (CD-IV). One patient was hospitalized for 25 days with bleeding and underwent gastroduodenoscopy in general anesthesia, showing duodenal bleeding, most likely caused by the trans-duodenal EUS-FNB procedure (CD-IIIb), and was treated by endoscopic therapy only.

Thus, 0.2% (n = 2) of EUS-FNB procedures needed intervention. The remaining 4.5% (n = 38) patients were hospitalized for an average of 4.6 days, all type CD-I, requiring only conservative treatment. These included 2.3% (n = 20) cases of acute pancreatitis, 1.5% (n = 13) of abdominal pain, 0.2% (n = 2) of self-limiting bleeding, and 0.1% (n = 1) each of infection, sepsis, and fever.

DISCUSSION

In this large single-center study based on 852 specimens from 723 patients, we examined the utility of pancreatic EUS-FNB. A specimen sufficient for histologic diagnosis was obtained in 93.4% (796/852). Accuracy was overall, for malignant, and benign entities 85.6%, 88.3%, and 94%. Due to suspicion of malignancy, 7.3% of patients (53/723) underwent one or two additional EUS-FNBs, and in 54.7% (n = 29) of these, the correct malignant diagnosis was established. For diagnosis of AIP, sensitivity and accuracy of EUS-FNB were 83.3% and 99.2%, respectively. Finally, we found that

Table 4. Final diagnosis in patients with a benign (*n*=213) or nondiagnostic (*n*=56) pancreatic EUS-FNB

EUS-FNB diagnosis	Nondiagnostic EUS-FNB diagnosis (*n*=56)	Benign EUS-FNB diagnosis (*n*=213)						
		Normal pancreas (*n*=28; 13.1%)	Unspecific fibrosis (*n*=75; 35.3%)	Acute pancreatitis (*n*=4; 1.9%)	Chronic pancreatitis (*n*=74; 34.7%)	AIP (*n*=19; 8.9%)	Pseudocyst (*n*=12; 5.6%)	GPA (*n*=1; 0.5%)
Final diagnosis	Chronic pancreatitis (*n*=15; 26.8%) Idiopathic (*n*=10) Alcohol-induced (*n*=5) PDAC (*n*=11; 19.6%) Serous cystadenoma (*n*=8; 14.3%) Pancreatic cancer, NOS (*n*=6; 10.7%) NET G1 (*n*=5; 8.9%) Normal pancreas (*n*=4; 7.1%) IPMN (*n*=3; 5.4%) Benign cyst (*n*=2; 3.6%) MCN (*n*=1; 1.8%) Metastasis (*n*=1, 1.8%)	Normal pancreas (*n*=14; 50%) Chronic pancreatitis (*n*=6; 21.4%) AIP* (*n*=3) Alcohol-induced (*n*=1) Idiopathic (*n*=1) Hereditary (*n*=1) PDAC (*n*=4; 14.3%) Serous cystadenoma (*n*=2; 7.1%) Schwannoma (*n*=1; 3.6%) Benign cyst (*n*=1; 3.6%)	PDAC (*n*=27; 36%) Chronic pancreatitis (*n*=16; 21.3%) Idiopathic (*n*=10) Alcohol-induced (*n*=6) Normal pancreas (*n*=10; 13.3%) Unspecific fibrosis (*n*=4; 5.3%) NET G1 (*n*=4; 5.3%) Benign cyst (*n*=4; 5.3%) Metastasis (*n*=3; 4%) Pancreatic cancer, NOS (*n*=2; 2.7%) IPMN (*n*=2; 2.7%) Serous cystadenoma (*n*=2; 2.7%)† PanIN-2 (*n*=1; 1.3%)	Chronic pancreatitis (*n*=2; 50%) Alcohol-induced (*n*=1) Idiopathic (*n*=1) PDAC (*n*=1; 25%) Abscess (*n*=1; 25%)	Chronic pancreatitis (*n*=61; 82.4%) Idiopathic (*n*=34) Alcohol-induced (*n*=24) Hereditary (*n*=3) PDAC (*n*=6; 8.1%) Pancreatic cancer, NOS (*n*=2; 2.7%) Serous cystadenoma (*n*=1; 1.4%) GPA (*n*=1; 1.4%) Pseudocyst (*n*=1; 1.4%) Fibrosis following abscess (*n*=1; 1.4%) Benign cyst (*n*=1; 1.4%)	AIP (*n*=15; 78.9%) Type 1 (*n*=10) Type 2 (*n*=5) Chronic pancreatitis (*n*=3; 15.8%)‡ Idiopathic (*n*=2) Alcohol-induced (*n*=1) GPA (*n*=1; 5.3%)§	Pseudocyst (*n*=12; 100%)	GPA (*n*=1; 100%)

*Two type 1, one type 2 AIP; †One of these presenting as multiple pancreatic cysts, suspected of representing serous cystadenoma, also because the patient had von Hippel-Lindau syndrome; ‡All (*n*=3) EUS-FNBs with type 2 AIP, ICDC level 2; §EUS-FNB with type 1 AIP, ICDC level 1. ICDC: International consensus diagnostic criteria; IPMN: Intraductal papillary mucinous neoplasm; MCN: Mucinous cystic neoplasm; NOS: Not otherwise specified; NET: Neuroendocrine tumor; PanIN: Pancreatic intraepithelial neoplasia; PDAC: Pancreatic ductal adenocarcinoma including its subtypes; AIP: Autoimmune pancreatitis; GPA: Granulomatosis with polyangiitis

Table 5. Histologic findings and diagnosis in 22 EUS-FNBs from patients with an EUS-FNB diagnosis and/or final diagnosis of autoimmune pancreatitis (*n*=19)

Patient	Sex/age	EUS-FNB diagnosis	Final diagnosis	Periductal and/or diffuse lymphoplasmacytic infiltration	Granulocytic and lympho-plasmacytic acinar infiltrate	Granulo-cytic epithelial lesion	>10 IgG4-positive cells/HPF	Storiform fibrosis	Obliterative phlebitis
1	Female/42	AIP type 2 level 2	CP	+	+	–	–	–	–
2	Female/38	AIP type 2 level 2	AIP type 2	+	+	–	–	–	–
3	Male/53	AIP type 1 level 1	GPA	+	+	+	+	+	+
4	Male/65	AIP type 1 level 2	AIP type 1	+	–	–	+	–*	–
5	Female/52	AIP type 1 level 1	AIP type 1	+	–	–	+	+	–
6	Male/46	AIP type 1 level 2	AIP type 1	+	+	–	+	–	–†
7	Female/53	AIP type 2 level 1	AIP type 2	+	+	+	–	–*	–
8	Male/72	AIP type 1 level 1	AIP type 1	+	–	–	+	–*	+
9	Male/47	AIP type 2 level 1	AIP type 2	+	+	+	–	–*	+
10	Male/81	AIP type 1 level 1	AIP type 1	+	–	–	+	+	+
11	Female/61	AIP type 2 level 1	AIP type 2	+	+	+	–	–	–
12	Female/62	AIP type 2 level 2	CP	+	+	–	–	–	–
13A	Male/69	Normal pancreas‡	AIP type 2	–	–	–	–	–	–
13B	Male/70	AIP type 2 level 1	AIP type 2	+	+	+	–	+	+
14	Female/60	AIP type 2 level 2	CP	+	+	–	–	–	–
15A	Male/67	AIP type 1 level 2	AIP type 1	+	–	–	+	–*	–†
15B	Male/67	AIP type 1 level 1	AIP type 1	+	–	–	+	+	+
16	Male/64	AIP type 1 level 1	AIP type 1	+	–	–	+	+	–
17A	Male/73	AIP type 1 level 2	AIP type 1	+	–	–	+	–	–
17B	Male/73	AIP type 1 level 1	AIP type 1	+	–	–	+	+	–
18	Female/24	Normal pancreas‡	AIP type 1	+	–	–	–	–	–
19	Male/45	Normal pancreas‡	AIP type 1	–	–	–	–	–	–

*Cell-rich fibrosis that was not felt to entirely correspond to storiform fibrosis; †Stenosing phlebitis that was not felt to entirely correspond to obliterative phlebitis; ‡All (*n*=3) normal pancreas EUS-FNB with scant material. CP: Chronic pancreatitis; GPA: Granulomatosis with polyangiitis; HPF: High power field; –: Criterion not fulfilled; +: Criterion fulfilled; AIP: Autoimmune pancreatitis; IgG4: Immunoglobulin G4

EUS-FNB resulted in 4.7% (n = 40) hospitalizations with 0.2% EUS-FNBs (n = 2) needing intervention other than conservative treatment (CD-I).

This study represents the largest study on the utility of pancreatic EUS-FNB. Examining the utility of SharkCore EUS-FNB for diagnosis of pancreatic lesions in 313 patients, of which 282 EUS-FNBs had sufficient follow-up data available for analysis, Fitzpatrick *et al.* found an accuracy of 94.0%.[17] They previously reported an almost identical accuracy of 94.1% in a smaller study, in which 136 EUS-FNBs had sufficient follow-up data for analysis, however, only 49% of these were pancreatic lesions.[22] A crucial point to note, when comparing our results with these, is that we did not use ROSE (based on a synchronous cytologic smear). When ROSE was not utilized for EUS-FNB, the accuracy reported by Fitzpatrick *et al.* was significantly lower and very similar to our findings (88.6%).[17] Sweeney *et al.* found a significant odds ratio of 2.49 for a diagnostic specimen in the presence of ROSE with EUS-FNB compared to not using ROSE.[23] Only a relatively small number of our EUS-FNBs were nondiagnostic (6.6%). Similar rates of nondiagnostic specimens have been reported, ranging from 4.6% to 6%.[17,22,25]

Recent studies, mainly those focusing on solid pancreatic masses only, achieved a diagnostic accuracy of 86%–96.5%.[6,14,15,21,25,31,32] The present study was not limited to solid pancreatic masses but included all patients referred for pancreatic EUS-FNB including cystic and benign lesions, where a precise diagnosis was needed for optimal patient management. As cystic lesions tend to offer less opportunity to obtain an adequate biopsy as there often only are limited solid areas such as thickened cyst wall or mural nodules suitable for biopsy compared to solid pancreatic masses, the higher proportion of cystic compared to only including solid lesions may, at least in part, explain the slightly lower accuracy in the present study (85.6%).

The widely accepted method for evaluating pancreatic cystic lesions (PCLs) without a solid mass is currently EUS-FNA with cyst fluid analysis.[33,34] However, EUS-FNB might be of diagnostic value for PCLs using cyst wall histology for subtyping and grading of dysplasia, thereby potentially preventing further work-up for patients with nonmalignant serous cystadenoma. In the present study, 43 PCLs were evaluated using EUS-FNB. Only one previously published study has investigated the role of EUS-FNB in PCL, with a diagnostic yield of 87.2% in 47 pancreatic mucinous cysts.[35] Recently, the utility of EUS-guided through-the-needle biopsy (TTNB) for PCLs >15 mm has also been investigated.[36] The diagnostic yield was higher, compared to EUS-FNA cytology (69.3% *vs.* 20.8%). However, TTNB lead to a change in clinical management in 11.9%. Complications occurred in 9.9%, with four severe complications including one fatal outcome.[36] In the present study, we found a high diagnostic yield (84.6%) of EUS-FNB in mucinous PCLs with a lower number of complications, none of which were severe.

The "atypical" category included atypical cells, dysplastic lesions, and other types of histologically atypical lesions, in line with previous EUS-FNB studies.[17,23,25] We used the latter category when the histologic specimen was to be interpreted with caution, *i.e.,* a specimen not corresponding to "suspicious of malignancy", but with worrisome features. Therefore, in our study, the relatively high rate of false-negative EUS-FNBs may in part be due to the atypical category. Importantly, in Fitzpatrick *et al.*, 31% of false-negative EUS-FNBs (5/16) were atypical, while Jovani *et al.* interpreted "atypical" EUS-FNBs with a final malignant diagnosis as true positives, highlighting the malignant potential of a subset of these.[14,17]

A previous study found that repeated EUS-FNA holds substantial clinical impact for the patients, preventing further diagnostic work-up for 73%.[37] Moreover, the correct final diagnosis was not always achieved even though repeated EUS-FNA was performed.[37] We examined the clinical impact of performing one or two additional EUS-FNB procedures in patients in whom malignancy was suspected but initial diagnosis was inconclusive. In 54.7% of these patients (n = 29), a correct final diagnosis of malignancy was established. As 93.1% (n = 27) needed only one additional EUS-FNB, additional EUS-FNB may be a viable method for re-evaluating nonconclusive EUS-FNBs. We found no previous data on this topic in the English-language literature.

The accuracy for benign diagnosis was 94% in the present study, indicating that EUS-FNB is useful also in a nonmalignant setting. We found that only 12.2% (9/74) of "chronic pancreatitis" EUS-FNBs had a final neoplastic or malignant diagnosis. A previous study suggested that the risk of EUS-FNB being false negative for malignancy might be relatively high (28.6%, 4/14) in the setting of chronic pancreatitis.[22] This

most likely arises from their low sample size and the fact that we further subcategorized benign EUS-FNBs. Highlighting the latter, 53.3% (40/75) of our "unspecific fibrosis" EUS-FNBs had a final neoplastic or malignant diagnosis, suggesting that EUS-FNBs showing these features should be interpreted with caution. We found no previous studies on the utility of EUS-FNB specifically in chronic pancreatitis.

The histologic criteria for the diagnosis of AIP were initially based on pancreatic resection specimens and, a few years later, also tested on pancreatic core needle biopsies, initially obtained mainly by transabdominal ultrasound.[19,29,38,39] A recent systematic review assessed diagnostic yield of EUS-FNA (n = 321) and EUS-FNB (n = 310) in patients with AIP.[29,30] The pooled diagnostic accuracy of EUS-FNB was significantly higher than of EUS-FNA (63% *vs.* 45.7%), and sensitivity of EUS-FNB was 82.7%. The present study showed a highly similar sensitivity of 83.3%, and, in contrast, a higher accuracy of 99.2%. While most previous studies examining accuracy of EUS-FNB in AIP were mainly based on a subset of patients suspected of having AIP, our data stem from a "real-life" setting, including 852 consecutive specimens. A recent study of patients with suspicion of type 1 AIP demonstrated an accuracy of 78% (39/51) using EUS-FNB.[26] The higher accuracy found in the present study is plausibly caused by our large overall sample size (n = 852). Our findings highlight the potential advantage of utilizing EUS-FNB for diagnosis of AIP, in agreement with others.[40,41] However, as 16% (n = 3) of AIP EUS-FNBs were ICDC AIP type 2 level 2 in patients with a final diagnosis of chronic pancreatitis, the distinction between AIP type 2 level 2 and chronic pancreatitis on EUS-FNB remains a challenge.

We systematically recorded complications related to pancreatic EUS-FNB for 723 patients in the 7-day period following EUS-FNB. Only 0.2% (n = 2) incidents needing intervention occurred. These included one case each of duodenal bleeding (CD-IIIb) and acute necrotizing pancreatitis (CD-IV). The latter patient had neither pathologic findings in the pancreas on CT prior to nor during the EUS procedure, but due to clinical suspicion of AIP by the referring unit, a biopsy was taken. A similar case of acute necrotizing pancreatitis was observed by Jovani *et al.*, also necessitating admission to ICU.[14] The remaining complications were all graded as CD-I, needing only conservative treatment with a limited number of hospitalizations (4.7%), consistent with previous studies including 51–168 patients, reporting complication rates of 3.7%–6%.[5,14,22,32] We also confirmed that the risk of infectious complications following EUS-FNB is close to zero. Overall complication and incident rates of acute pancreatitis following EUS-FNA are between 2.5% and 0.3%–0.9%.[1] We demonstrated an incidence rate of acute pancreatitis of 2.3% (n = 20). Hence, compared to ERCP with a risk of acute pancreatitis of 9.7%, the risk was lower.[42] However, our data support that EUS-FNB requires careful consideration of indication criteria by the clinician and careful information of the patient prior to consenting. As only 2 (0.2%) procedures were associated with complications needing intervention, our data indicate that pancreatic EUS-FNB is a relatively safe method.

A recent survey among 35 endoscopic experts showed that for routine EUS-guided sampling of solid pancreatic masses and PCLs without a solid component, the preferred needle gauge was 22G.[43] In concordance with this, at our tertiary center, the 22G needle was used by default.

A major strength of our study is its large sample size, also allowing analysis of the utility of EUS-FNB for the diagnosis of relatively rare entities, such as AIP (n = 15), or even rarer diagnoses, such as GPA (n = 3), one of which was diagnosed initially on EUS-FNB, or SPN (n = 2). While most studies have focused on lesions suspicious of malignancy, our cohort includes a large proportion (25%) of benign EUS-FNBs that were systemically subcategorized, adding to the strength of our study.

Considering the relatively high diagnostic accuracy across all included pancreatic lesions (85.6%), we demonstrate that EUS-FNB is a valuable tool not only in distinguishing malignant *versus* nonmalignant entities, but also for diagnosis of specific lesions that previously have not been possible using EUS-FNA or even reverse-bevel EUS-FNB. EUS-FNBs were only performed if a positive finding would change the clinical approach to the patient, indicating that the results are representative for daily clinical practice, thus supporting the generalizability of our findings. However, as mentioned above, the utility of EUS-FNB in mucinous pancreatic cysts requires further study, particularly in comparison with TTNB.[35,36] Hence, the generalizability of our findings on this specific sub-topic is at present unclear. Future studies

should also evaluate whether molecular techniques such as next-generation sequencing can improve the utility of EUS-FNB for the classification of pancreatic mucinous cysts further, as it has been shown for EUS-FNA.[44]

CONCLUSIONS

Our data indicate that EUS-FNB is a feasible method not only for obtaining histologic specimens but also in evaluating pancreatic lesions of all types with a high overall diagnostic accuracy of 85.6% in a large cohort of patients. In patients suspected of malignancy, one or two additional EUS-FNBs seem to be justified. Overall, EUS-FNB is a relatively safe procedure while contributing to the diagnosis of a wide range of malignant, neoplastic as well as benign conditions, including important differential diagnoses of PDAC, such as AIP.

Supplementary materials

Supplementary information is linked to the online version of the paper on the Endoscopic Ultrasound website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Operating characteristics of pancreatic EUS-guided fine-needle biopsy (EUS-FNB) in cystic pancreatic lesions

	IPMN	MCN/Mucinous cyst, NOS	SCA	Pseudocyst
Sensitivity	66.7% (48.2%-82%)	87.5% (47.4%-99.7%)	100% (85.8%-100%)	100% (73.5%-100%)
Specificity	100% (99.5%-100%)	100% (99.6%-100%)	100% (99.6%-100%)	100% (99.6%-100%)
PPV	100%	100%	100%	100%
NPV	98.7% (97.9%-99.2%)	99.9% (99.3%-100%)	100%	100%
Accuracy	98.7% (97.7%-99.4%)	99.9% (99.4%-100%)	100% (99.6%-100%)	100% (99.6%-100%)

Data are given as percentages (95% confidence intervals) for the diagnostic categories intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN)/Mucinous cyst not otherwise specified (NOS), serous cystadenoma (SCA), and pseudocyst. NPV: negative predictive value. PPV: positive predictive value.

Supplementary Table 2: Patients suspected of malignancy who had to undergo more than one pancreatic EUS-guided fine-needle biopsy (EUS-FNB) procedure until establishment of the suspected diagnosis (*n*=53)

Patient ID	Additional EUS-procedures (*n*)	EUS procedure no. 1 (*n*=53)	EUS procedure no. 2 (*n*=48)	EUS procedure no. 3 (*n*=5)	Final diagnosis	Modality of final diagnosis			
						Pancreatic EUS-FNB	Pancreatic specimen other than EUS-FNB	Non-pancreatic specimen	Clinical evaluation including imaging
7	1	Unspecific fibrosis	PDAC		-	X			
18	2	Unspecific fibrosis	Unspecific fibrosis	Atypical	PDAC			X	
19	1	Suspicious of malignancy	PDAC		-	X			
41	1	Non-diagnostic	PDAC		-	X			
51	1	IPMN	PDAC		-	X			
61	1	Atypical	Atypical		PDAC		X		
77	1	Suspicious of malignancy	Suspicious of malignancy		PDAC		X		
89	1	Non-diagnostic	Atypical		Pancreatic tumor				X
113	1	Atypical	NET G1		-	X			
130	1	Suspicious of malignancy	PDAC		-	X			
144	1	Suspicious of malignancy	PDAC		-	X			
149	1	Unspecific fibrosis	PDAC		-	X			
163	1	Suspicious of malignancy	PDAC		-	X			
176	1	Unspecific fibrosis	Non-diagnostic		PDAC			X	
186	1	Suspicious of malignancy	Suspicious of malignancy		PDAC			X	
194	1	Atypical	Suspicious of malignancy		PDAC		X		
195	2	Unspecific fibrosis	Unspecific fibrosis	PDAC	-	X			
204	1	Suspicious of malignancy	NET G1		PDAC			X	
207	2	Dysplasia	Fibrosis, unspecified		PDAC			X	
208	1	Unspecific fibrosis	Dysplasia		PDAC		X		
210	1	Unspecific fibrosis	NET G1		-	X			
244	1	Atypical	NET G1		-	X			
245	1	Dysplasia	Suspicious of malignancy		PDAC		X		
258	1	Suspicious of malignancy	PDAC		-	X			
264	1	Atypical	Unspecific fibrosis		BD-IPMN				X
267	1	Non-diagnostic	BD-IPMN, lgd		-	X			
278	1	Unspecific fibrosis	PDAC		-	X			
283	1	Dysplasia	Suspicious of malignancy		PDAC		X		
292	1	Unspecific fibrosis	PDAC		-	X			
299	1	Chronic pancreatitis	Unspecific fibrosis		PDAC		X		
327	2	Dysplasia	Non-diagnostic	MD-IPMN, lgd	-	X			
366	1	Unspecific fibrosis	NET G1		-	X			
407	1	Atypical	Non-diagnostic		Pancreatic tumor				X

Contd...

Supplementary Table 2: Contd...

Patient ID	Additional EUS-procedures (*n*)	EUS procedure no. 1 (*n*=53)	EUS procedure no. 2 (*n*=48)	EUS procedure no. 3 (*n*=5)	Final diagnosis	Modality of final diagnosis			
						Pancreatic EUS-FNB	Pancreatic specimen other than EUS-FNB	Non-pancreatic specimen	Clinical evaluation including imaging
412	1	Unspecific fibrosis	Unspecific fibrosis		Metastasis (RCC)		X		
416	1	Atypical	Atypical		PDAC			X	
421	1	Suspicious of malignancy	PDAC		-	X			
430	1	Unspecific fibrosis	PDAC		-	X			
440	1	Atypical	Suspicious of malignancy		PDAC		X		
471	1	MCN	PDAC		-	X			
544	2	IPMN	IPMN	Non-diagnostic	PDAC		X		
565	1	Normal pancreas	PDAC		-	X			
570	1	Non-diagnostic	PDAC		-	X			
572	1	Atypical	PDAC		-	X			
584	1	Non-diagnostic	Unspecific fibrosis		PDAC		X		
615	1	Unspecific fibrosis	PDAC		-	X			
617	1	Normal pancreas	PDAC		-	X			
622	1	Non-diagnostic	Unspecific fibrosis		NET G1		X		
644	1	Mucinous cyst	PDAC		-	X			
645	1	Non-diagnostic	Suspicious of malignancy		PDAC		X		
698	1	Suspicious of malignancy	PDAC		-	X			
708	1	Non-diagnostic	PDAC		-	X			
730	1	Chronic pancreatitis	Dysplasia		PDAC		X		
736	1	Unspecific fibrosis	Unspecific fibrosis		Pancreatic tumor				X

EUS-FNB diagnosis, number of EUS-FNB procedures, final diagnosis ("-" indicates final diagnosis was established on additional EUS-FNB), and modality on which the final diagnosis was established, are shown. In 54.7% (n=29) of these patients, the correct malignant diagnosis was established on additional EUS-FNB. BD-IPMN: branch duct intraductal papillary mucinous neoplasm. lgd: low-grade dysplasia. MD-IPMN: main duct IPMN. NET: neuroendocrine tumor. PDAC: pancreatic ductal adenocarcinoma incl. subtypes. RCC: renal clear cell adenocarcinoma.