

# EUS-guided fine-needle biopsy *versus* fine-needle aspiration for histopathological evidence for type 1 autoimmune pancreatitis: A single-center retrospective study in China

Yuyan Zhou<sup>1</sup>, Liqi Sun<sup>1</sup>, Xinyue Wang<sup>1</sup>, Dongling Wan<sup>1</sup>, Jiaheng Xu<sup>1</sup>, Mengruo Jiang<sup>1</sup>, Yue Liu<sup>1</sup>, Chao Liu<sup>1</sup>, Yatao Tu<sup>1</sup>, Haojie Huang<sup>1,\*</sup>, Zhendong Jin<sup>1,\*</sup>

## ABSTRACT

**Background and Objectives:** EUS is recommended for guiding pancreatic tissue acquisition in suspected autoimmune pancreatitis (AIP) cases. However, there is a lack of comparative research on the effectiveness between EUS-guided fine-needle aspiration (EUS-FNA) and EUS-guided fine-needle biopsy (EUS-FNB) for diagnosing AIP in China. This study aimed to evaluate the diagnostic accuracy of EUS-guided tissue acquisition (EUS-TA) specifically for type 1 AIP.

**Methods:** Between 2010 and 2023, individuals with AIP who received EUS-TA at Changhai Hospital were included in the study.

**Results:** A total of 173 patients diagnosed with AIP who underwent EUS-TA were included in the final analysis. Of these, 104 patients (60.1%) received EUS-FNA, and 69 patients (39.9%) underwent EUS-FNB. Sufficient pancreatic tissue samples (>5 cells/high-power field) were obtained in 164 of 173 patients (94.8%), with success rates of 94.2% for EUS-FNA and 95.7% for EUS-FNB ( $P > 0.05$ ). EUS-FNB exhibited higher rates of reliable level 1 histopathological findings (40.9% vs. 16.3%,  $P < 0.001$ ) and reliable level 2 histopathological findings (33.3% vs. 12.2%,  $P < 0.001$ ) compared with EUS-FNA. Furthermore, a higher occurrence of IgG4-positive plasma cell infiltration (>10 cells/high-power field) was observed with EUS-FNB compared with EUS-FNA (74.2% vs. 27.9%,  $P < 0.001$ ). The multivariate logistic analysis also revealed that EUS-FNA was less effective in obtaining reliable evidence compared with EUS-FNB, as evident in both level 2 ( $P = 0.002$ ; odds ratio, 0.21; 95% confidence interval, 0.08–0.56) and level 1 ( $P = 0.001$ ; odds ratio, 0.19; 95% confidence interval, 0.08–0.49) histopathological evidence.

**Conclusions:** EUS-FNB demonstrates higher rates of level 1 and level 2 histopathological findings, as well as more abundant IgG4-positive plasma cell infiltration, compared with EUS-FNA.

**Key words:** Type 1 autoimmune pancreatitis; EUS-guided tissue acquisition; EUS-guided fine-needle aspiration; EUS-guided fine-needle biopsy

## INTRODUCTION

Autoimmune pancreatitis (AIP), initially reported by Sarles et al. in 1961,<sup>[1]</sup> has gained increased attention over the past 2 decades. It represents a relatively uncommon form of pancreatic inflammation. AIP demonstrates a notable response to glucocorticoid treatment, distinguishing it from other pancreatic disorders.<sup>[2]</sup> However, comprehensive data on the incidence and prevalence rates of AIP in China are currently limited.

Diagnosing AIP typically involves a thorough evaluation that includes clinical symptoms, laboratory tests, imaging scans, and histopathological examinations. AIP can be divided into 2 subtypes based on histopathological findings: type 1 AIP, characterized by lymphoplasmacytic sclerosing pancreatitis and linked to IgG4-related autoimmune diseases, and type 2 AIP, characterized by idiopathic duct-centric chronic pancreatitis and associated with inflammatory bowel diseases.<sup>[3]</sup> In Asia, type 1 AIP is more common among Chinese patients, comprising more than 96% of AIP cases in the region.<sup>[4,5]</sup>

Common symptoms of AIP include painless obstructive jaundice, abdominal pain, indigestion, weight loss, and so on. AIP is often accompanied by pancreatic insufficiency and complications such as diabetes. Its symptoms can closely resemble those of pancreatic ductal adenocarcinoma (PDAC). However, whereas PDAC typically requires surgical intervention, AIP treatment mainly involves glucocorticoids and immune inhibitors. Therefore, it is crucial to accurately distinguish between AIP and PDAC using radiological imaging and histopathological evaluation. EUS is recommended for guiding pancreatic tissue acquisition (TA) in suspected AIP cases. On the one hand, although several studies worldwide have evaluated the utility of EUS-guided fine-needle aspiration (EUS-FNA) for AIP diagnosis,<sup>[6,7]</sup> data on its application in China are scarce. On the other hand, most prior research on EUS-guided fine-needle biopsy (EUS-FNB) has focused on malignant diseases,<sup>[8–10]</sup> with

<sup>1</sup>Department of Gastroenterology, National Clinical Research Center for Digestive Diseases, Changhai Hospital; and National Key Laboratory of Immunity and Inflammation, Naval Medical University, Shanghai, China.

\* **Address for Correspondence:** Department of Gastroenterology, National Clinical Research Center for Digestive Diseases, Changhai Hospital; National Key Laboratory of Immunity and Inflammation, Naval Medical University, Shanghai, China. E-mail: zhendongjin@163.com (Z. Jin), huanghaojie@smmu.edu.cn (H. Huang).

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Endoscopic Ultrasound (2024) 13:6

Received: 24 April 2024; Accepted: 27 October 2024.

Published online: 17 December 2024

<http://dx.doi.org/10.1097/eus.0000000000000095>

limited research on its use for AIP diagnosis. Additionally, few studies have compared the diagnostic efficacy of EUS-FNB and EUS-FNA for AIP.

To fill this knowledge gap, we conducted a retrospective study to evaluate the diagnostic accuracy of EUS-FNB and EUS-FNA specifically in the Chinese population with AIP. Additionally, the study aimed to examine the diagnostic efficiency of various types of EUS needles for AIP diagnosis.

**METHODS**

*Study design*

This study was conducted at Changhai Hospital in Shanghai, China. As a retrospective, single-center study, it received approval from the institutional review board. All participants provided written informed consent, and the study adhered to the ethical guidelines in accordance with the Declaration of Helsinki.

*Study population*

Individuals 18 years or older were considered for enrollment if they exhibited characteristics consistent with AIP, as defined by the International Consensus Diagnostic Criteria (ICDC). These criteria include (1) parenchymal imaging revealing diffuse or segmental/focal enlargement with delayed enhancement; (2) ductal imaging showing long (>1/3 length of the main pancreatic duct) or multiple strictures, or segmental/focal narrowing without significant upstream dilatation; (3) elevated serum IgG4 levels exceeding the upper normal limit; (4)

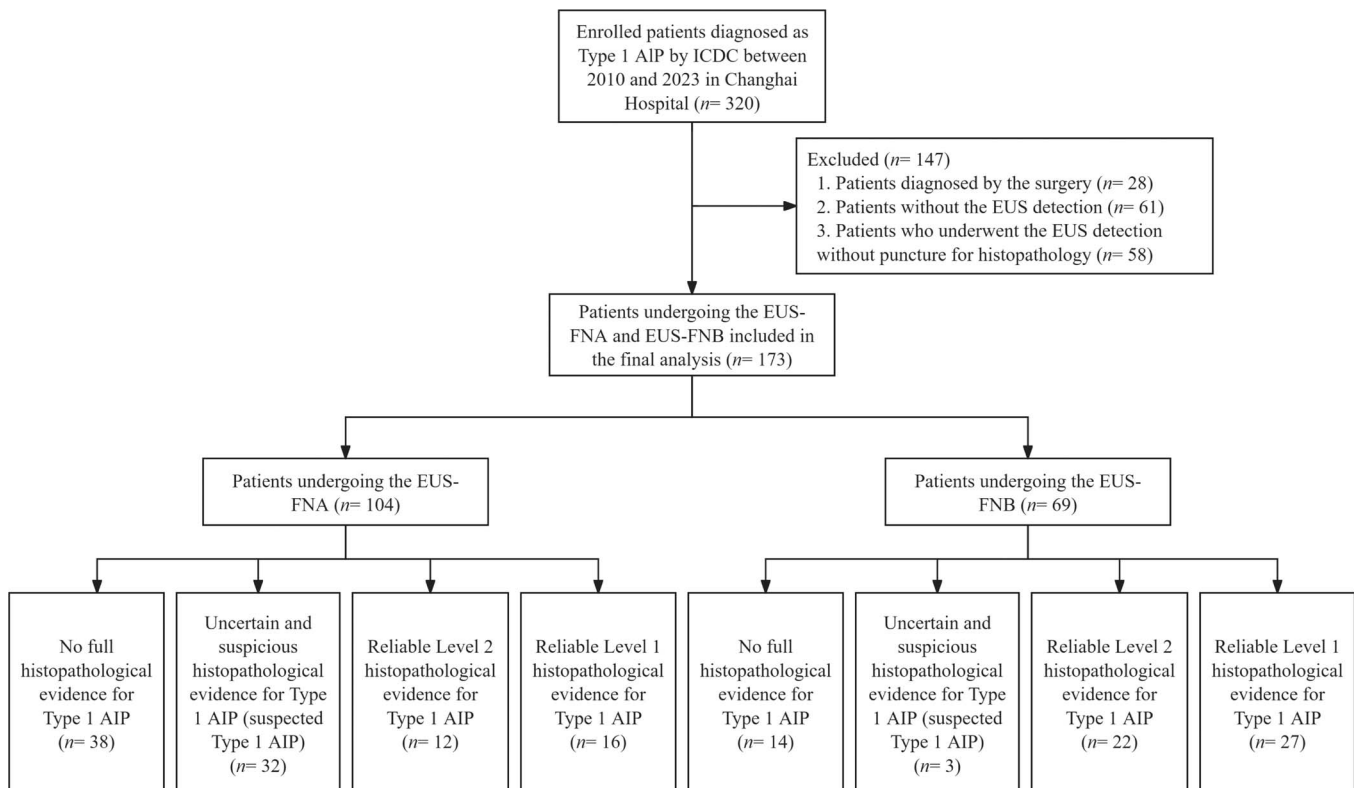
evidence of involvement of other organs; and (5) positive responses to steroid treatment, characterized by swift (<2 weeks) radiologically observable resolution or notable improvement in pancreatic and extrapancreatic symptoms. The above standards are divided into different levels of evidence according to the degree.<sup>[11]</sup>

Criteria for exclusion included refusal or inability to undergo EUS detection, a willingness to undergo surgery, recent acute pancreatitis within the past 4 weeks, and conditions that would make EUS-TA procedures unsafe, such as cardiorespiratory issues, mental health disorders, blood clotting problems, or substance abuse.

Between 2010 and 2023, 320 patients were diagnosed with AIP at Changhai Hospital. Of these, 147 patients were excluded based on specific criteria [Figure 1]. The final study cohort thus comprised 173 patients, including 104 patients who underwent EUS-FNA and 69 patients who received EUS-FNB.

*EUS-FNA*

All endoscopists who participated in the research were highly skilled, with 5–30 years of experience and an annual performance of more than 1000 EUS procedures. The EUS-TA procedure utilized puncture needles from various manufacturers, primarily Wilson-Cook (85%) (Wilson-Cook Medical, Inc., Winston-Salem, NC, USA), followed by Boston Scientific (Boston Scientific, Marlborough, MA, USA) (8.7%), Medi-Globe GmbH (Medi-Globe GmbH, Achenmühle, Germany) (5.2%), and Olympus (Olympus Corporation, Tokyo, Japan) (1.2%). Ultrasound



**Figure 1.** Study flowchart of enrollment of patients who underwent EUS-TA. EUS-TA: EUS-guided tissue acquisition; ICDC: International Consensus Diagnostic Criteria; EUS-FNA: EUS-guided fine-needle aspiration; EUS-FNB: EUS-guided fine-needle biopsy.

equipment from Olympus and Aloka, including the EU-ME1, EU-ME2, and Aloka Alpha-5 models, were used. Echoendoscopists selected the most direct path to the lesion, carefully avoiding blood vessels. The needle was inserted into the lesion with EUS guidance, followed by 10–20 back-and-forth movements using either suction or slow-pull techniques. A maximum of 3 passes were made at each puncture site. Tissue samples were embedded in paraffin, fixed in formalin, thinly sliced into serial sections, and then subjected to hematoxylin-eosin staining. If necessary, pathologists specialized in histology performed immunohistochemical staining with anti-IgG4 antibodies.

**EUS-FNB**

All punctures were performed using either an antegrade core trap (ProCore; Cook Medical) or a Franseen-type needle (Acquire; Boston Scientific), accessed via a transgastric or transduodenal approach. Before piercing the target, the stylet was slightly retracted, allowing the needle tip to be carefully advanced into the tissue. The needle was then carefully maneuvered within the lesion using a series of slow-pull movements. As required, the endoscopist applied suction and fanning techniques. A maximum of 3 passes was made at each puncture site. The EUS-FNB samples were preserved in formalin for 6–24 hours, subsequently fixed in paraffin, and subjected to further histopathological, immunohistochemical, or histochemical staining.

**Histopathological diagnosis of type 1 AIP**

The diagnosis of type 1 AIP was based on the ICDC criteria, which encompassed the evaluation of radiological features, laboratory tests, and histopathological findings. The level 1 histopathological criteria for type 1 AIP required the presence of at least 3 of the following 4 characteristics: (1) periductal lymphoplasmacytic infiltrate without granulocytic infiltration, (2) obliterative phlebitis, (3) storiform fibrosis, and (4) an abundance of IgG4-positive cells (>10 cells/high-power field [HPF]). For level 2 histopathological criteria, at least 2 of the aforementioned elements were necessary.

**Statistical analysis**

Categorical data were summarized as counts and percentages and were analyzed using the  $\chi^2$  test, Fisher exact test, or the Kruskal-Wallis *H* test, as appropriate. Continuous variables were expressed as mean  $\pm$  standard deviation and were analyzed using *t* tests, Mann-Whitney *U* test, analysis of variance, or Kruskal-Wallis *H* test, depending on the data distribution. Additionally, multivariate logistic regression was used to assess the effects of various variables. Significance levels were adjusted using the Bonferroni method. All statistical analyses were conducted using SPSS software (version 27.0.1.0, SPSS Statistics for Macintosh; IBM Corp, Armonk, NY) with a 2-tailed significance level of less than 0.05 considered statistically significant.

**RESULTS**

**Baseline characteristics**

Table 1 displays the baseline characteristics of the study cohort, which included 148 male (85.5%) and 25 female patients (14.5%), with an average age of 58.69  $\pm$  11.64 years (range, 30–82 years). Regarding medical history, 2 individuals (1.2%) had a family history of pancreatic diseases, 64 (37.0%) were smokers, and 41 (23.7%) had a history of alcohol consumption. Additionally, 41

**Table 1**  
**Clinical characteristics of the study patients (n = 173)**

Characteristics	Values
Time for hospital admission, n (%)	
2010–2016	53 (30.6)
2017–2023	120 (69.4)
Sex, n (%)	
Male	148 (85.5)
Female	25 (14.5)
Age, mean $\pm$ SD (range), y	58.69 $\pm$ 11.64 (30–82)
Family history of pancreatic disease, n (%)	2 (1.2)
Smoking history, n (%)	64 (37.0)
Drinking alcohol history, n (%)	41 (23.7)
Accompanied by diabetes, n (%)	41 (23.7)
Accompanied by hypertension, n (%)	27 (15.6)
Initial diagnosis upon hospital admission, n (%)	
Suspected as AIP	104 (60.1)
Nonspecified diagnosis	53 (30.6)
Chronic pancreatitis	4 (2.3)
Pancreatic cancer	12 (6.9)
Final diagnosis, n (%)	
Suspected as type 1 AIP without full histopathological evidence	75 (43.4)
Definitive type 1 AIP supported by full histopathological evidence	98 (56.6)
type of AIP	
Type 1 AIP	145 (83.8)
Type 2 AIP	28 (16.2)
Serum IgG4 expression level, n (%)	
<1 $\times$ upper limit of the normal value	32 (18.5)
Level 2, 1–2 $\times$ upper limit of the normal value	32 (18.5)
Level 1, >2 $\times$ upper limit of the normal value	103 (59.5)
Other organ involvement, n (%)	
Level 1, sclerosing cholangitis	34 (19.7)
Level 1, retroperitoneal fibrosis	4 (2.3)
Level 2, interstitial nephritis	5 (2.9)
Level 2, sialadenitis	2 (1.2)
Parenchymal imaging by EUS, n (%)	
Level 1, diffuse enlargement	83 (48.0)
Level 2, segmental/focal enlargement	80 (46.2)
Ductal imaging by EUS, n (%)	
Level 1, long or multiple strictures	1 (0.6)
Level 2, segmental/focal narrowing	35 (20.2)
Puncture type, n (%)	
EUS-FNA	104 (60.1)
EUS-FNB	69 (39.9)
Diameter size of puncture needles, n (%)	
19G	15 (8.7)
22G	137 (79.2)
25G	21 (12.1)
The company providing EUS puncture needle, n (%)	
Cook Medical Corporation	147 (85)
Boston Scientific Corporation	15 (8.7)
Olympus Corporation	2 (1.2)
Medi-Globe Corporation	9 (5.2)
Location of puncture (Interaction location has been merged, n (%))	
Pancreatic head	95 (54.9)
Pancreatic neck	11 (6.4)

(continued)

**Table 1**

**Clinical characteristics of the study patients (n = 173), (continued)**

Characteristics	Values
Pancreatic body	37 (21.4)
Pancreatic tail	17 (9.8)
The probability of acquiring sufficient pancreatic tissue samples (>5 cells/HPF)	164 (94.8)
The level of IgG4-positive plasma cell per HPF by histology	
<10/HPF	86 (49.7)
>10/HPF	78 (45.1)

AIP: autoimmune pancreatitis; IgG: immunoglobulin G; SD: standard deviation; HPF: high-power field; EUS-FNA: ultrasound-guided fine-needle aspiration; EUS-FNB: EUS-guided fine-needle biopsy; 19G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.

patients (23.7%) were diagnosed with diabetes, and 27 (15.6%) had hypertension.

Upon initial evaluation, the study cohort included 104 cases (60.1%) suspected of AIP, 4 cases (2.3%) of chronic pancreatitis, 12 cases (6.9%) indicating pancreatic cancer, and 53 cases (30.6%) classified as unspecified. After undergoing EUS-TA procedures, 98 patients (56.6%) received a definitive pathological diagnosis of type 1 AIP. The remaining 75 patients (43.4%) were given a provisional diagnosis of AIP based on radiographic and clinical findings. Among these, 28 individuals (16.2%) were identified with type 2 AIP, although a definitive histopathological confirmation was not obtained.

Additionally, 103 patients (59.5%) exhibited elevated serum level 1 IgG4 levels, which were more than twice the upper limit of normal, whereas 32 patients (18.5%) had level 2 serum IgG4 levels, ranging from 1 to 2 times the upper limit of normal. Within the study group, 34 patients (19.7%) were diagnosed with sclerosing cholangitis, a condition characterized by narrowing of the proximal and distal bile ducts and thickening of the bile duct walls. Sialadenitis was observed in 2 patients (1.2%), and interstitial nephritis was found in 5 patients (2.9%). No cases of ulcerative colitis or Crohn disease were reported.

*Findings of EUS*

Table 1 displays the results of the EUS findings in the study. Typical changes in pancreatic tissue and ducts were observed, including widespread or localized areas of reduced echogenicity, overall or localized enlargement, swollen lymph nodes, and hypoechoic margins around the pancreas<sup>[12]</sup>. Eighty-three individuals (48.0%) showed diffuse enlargement of the pancreas, aligning with level 1 imaging evidence for type 1 AIP. Furthermore, 80 patients (46.2%) exhibited segmental or focal enlargement of the pancreas, indicative of level 2 imaging evidence. Segmental or focal narrowing was observed in 35 patients (20.2%), also suggesting level 2 imaging evidence. In a single case (0.6%), long strictures in the main pancreatic duct were noted, which aligned with level 1 imaging evidence for type 1 AIP.

Among the 173 patients diagnosed with AIP via EUS-TA, 104 patients (60.1%) underwent EUS-FNA, and 69 patients (39.9%) received EUS-FNB. The 22-gauge (22G) puncture needle was used most frequently, with a usage rate of 79.2%. The majority of EUS needles were supplied by the Cook Medical, constituting 85% of

total. Punctures were most commonly performed at the pancreatic head in 54.9% of cases, followed by the body (21.4%), tail (9.8%), and neck (6.4%). Adequate samples of pancreatic tissue (>5 cells/HPF) were obtained from 164 people (94.8%). Abundant IgG4-positive plasma cell infiltration (>10 cells/HPF) was observed in 45.4% of patients for the diagnosis of type 1 AIP.

*Comparison of histopathological findings of EUS-FNA and EUS-FNB*

As shown in Table 2, the baseline characteristics and histopathological findings of EUS-FNA and EUS-FNB are compared. No significant differences were observed between EUS-FNB and EUS-FNA in terms of gender ( $P > 0.05$ ), age ( $P = 0.19$ ), type of AIP ( $P > 0.05$ ), diameter size of puncture needles ( $P > 0.05$ ), puncture location ( $P > 0.05$ ), and initial diagnosis upon hospital admission ( $P > 0.05$ ). Sufficient pancreatic tissue samples (>5 cells/HPF) were obtained in 164 of 173 patients (94.8%), with success rates of 94.2% for EUS-FNA and 95.7% for EUS-FNB, showing no significant difference ( $P > 0.05$ ). In the final diagnosis, EUS-FNB was more likely to provide definitive type 1 AIP diagnosis supported by full histopathological evidence compared with EUS-FNA (71.0% vs. 26.9%,  $P < 0.001$ ). When complete tissue samples were available, EUS-FNB exhibited higher rates of reliable level 1 histopathological findings (40.9% vs. 16.3%,  $P < 0.001$ ) and reliable level 2 histopathological findings (33.3% vs. 12.2%,  $P < 0.001$ ) compared with EUS-FNA. Furthermore, a higher occurrence of IgG4-positive plasma cell infiltration (>10 cells/HPF) was observed in the EUS-FNB group compared with the EUS-FNA group (74.2% vs. 27.9%,  $P < 0.001$ ). For example, compared with the EUS-FNA group, the EUS-FNB group was more associated with a greater abundance of IgG4-positive plasma cells (>100 cells/HPF) (11.6% vs. 1.9%,  $P = 0.02$ ). Conversely, EUS-FNA was more associated with uncertain and suspicious histopathological evidence for type 1 AIP (suspected type 1 AIP) compared with EUS-FNB (32.7% vs. 4.5%,  $P < 0.001$ ). Similarly, a higher percentage of patients in the EUS-FNA group lacked full histopathological evidence compared with the EUS-FNB group (38.8% vs. 21.2%,  $P = 0.02$ ).

*Factors associated with level 1 histopathological finding of type 1 AIP*

Figures 2–4 show factors associated with the histopathological findings of type 1 AIP based on multivariate logistic regression analysis. The only variable that demonstrated an independent correlation with the quality of histopathological evidence was the type of puncture needle used. EUS-FNA was less effective than EUS-FNB in obtaining reliable evidence for diagnosing type 1 AIP, as evidenced by both level 2 ( $P = 0.002$ ; odds ratio [OR], 0.21; 95% confidence interval [CI], 0.08–0.56) and level 1 ( $P = 0.001$ ; OR, 0.19; 95% CI, 0.08–0.49) histopathological evidence. Conversely, EUS-FNA showed a stronger correlation with the likelihood of suspected type 1 AIP compared with EUS-FNB ( $P = 0.04$ ; OR, 4.06; 95% CI, 1.05–15.75). Other factors, including age, gender, diameter size of puncture needles, and parenchymal imaging via EUS, did not exhibit any significant correlations with the histopathological findings.

*Comparison of histopathological findings of 19G EUS-FNA and EUS-FNB*

To compare the diagnostic efficacy of EUS-FNA using a 19G puncture needle (19G EUS-FNA) and EUS-FNB, a detailed analysis was conducted, with results presented in Table 3. A total of 12 individuals underwent 19G EUS-FNA, whereas 69 individuals underwent EUS-FNB. Within the EUS-FNB group, the needle gauges were distributed as follows: 3 individuals used the 19G needle, 59 used the

**Table 2**  
**Comparison of baseline characteristics and histopathological findings of EUS-FNA and EUS-FNB**

	EUS-FNA	EUS-FNB	P
Time for hospital admission, n (%)			<0.001
2010–2016	45 (43.3%)	8 (11.6%)	
2017–2023	59 (56.7%)	61 (88.4%)	
Sex, n (%)			0.67
Male	88 (84.6)	60 (87.0)	
Female	16 (15.4)	9 (13.0)	
Age, mean ± SD (range), y	57.74 ± 11.81	60.10 ± 11.33	0.19
Type of AIP, n (%)			0.73
Type 1 AIP	88 (84.6)	57 (82.6)	
Type 2 AIP	16 (15.4)	12 (17.4)	
Diameter size of puncture needles, n (%)			0.18
19G	12 (11.5)	3 (4.3)	0.10
22G	78 (75%)	59 (85.5)	0.10
25G	14 (13.5)	7 (10.1)	0.51
Location of puncture (interaction location has been merged), n (%)			0.97
Pancreatic head	63 (60.6)	39 (56.5)	1.00
Pancreatic neck	6 (5.8)	5 (7.2)	0.70
Pancreatic body	28 (26.9)	13 (18.8)	0.90
Pancreatic tail	10 (9.6)	7 (10.1)	0.91
Initial diagnosis upon hospital admission, n (%)			0.09
Nonspecified diagnosis	32 (30.8)	21 (30.4)	0.96
Suspected as AIP	67 (64.4)	37 (53.6)	0.16
Chronic pancreatitis	1 (1.0)	3 (4.3)	0.30
Pancreatic cancer	4 (3.8)	8 (11.6)	0.07
The probability of acquiring sufficient pancreatic tissue samples (>5 cells/HPF)	98 (94.2)	66 (95.7)	1.00
The final diagnosis, n (%)			<0.001
Suspected as type 1 AIP without full histopathological evidence	76 (73.1)	20 (29.0)	<0.001
Definitive type 1 AIP supported by full histopathological evidence	28 (26.9)	49 (71.0)	<0.001
Histopathological evidence level, n (%)			<0.001
No full histopathological evidence for type 1 AIP	38 (38.8)	14 (21.2)	0.02
Uncertain and suspicious histopathological evidence for type 1 AIP (suspected type 1 AIP)	32 (32.7)	3 (4.5)	<0.001
Reliable level 2 histopathological evidence for type 1 AIP	12 (12.2)	22 (33.3)	<0.001
Reliable level 1 histopathological evidence for type 1 AIP	16 (16.3)	27 (40.9)	<0.001
The level of IgG4 per HPF by histology, n (%)			<0.001
<10/HPF	69 (66.3)	17 (25.8)	<0.001
>10/HPF	29 (27.9)	49 (74.2)	<0.001
The amount of IgG4-positive plasma cell per HPF by histology, n (%)			<0.001
0/HPF	37 (35.6)	14 (20.3)	0.03
(0–10)/HPF	33 (31.7)	3 (4.3)	<0.001
(10–20)/HPF	8 (7.7)	12 (17.4%)	0.05
(20–50)/HPF	11 (10.6)	16 (23.2)	0.03
(50–100)/HPF	7 (6.7)	13 (18.8)	0.02
>100/HPF	2 (1.9)	8 (11.6)	0.02

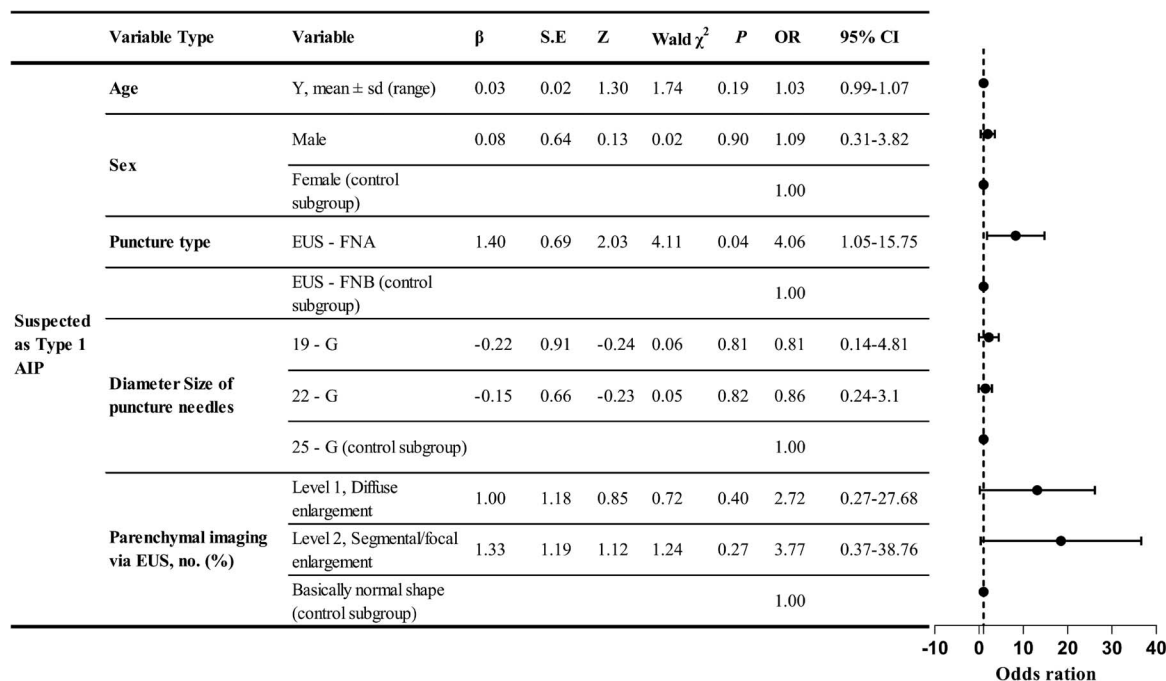
AIP: autoimmune pancreatitis; IgG: immunoglobulin G; SD: standard deviation; HPF: high-power field; EUS-FNA: ultrasound-guided fine-needle aspiration; EUS-FNB: EUS-guided fine-needle biopsy; 19G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.

22G needle, and 7 used the 25G needle. No significant differences were found between the groups in terms of gender ( $P > 0.05$ ), age ( $P > 0.05$ ), type of AIP ( $P > 0.05$ ), puncture location ( $P > 0.05$ ), and initial diagnosis upon hospital admission ( $P > 0.05$ ). Sufficient pancreatic tissue samples (>5 cells/HPF) were obtained in 77 of 81 patients (95.06%), with success rates of 91.7% for 19G EUS-FNA and 95.7% for EUS-FNB, indicating no significant difference in sample adequacy ( $P > 0.05$ ). In the final diagnosis, EUS-FNB was more likely to provide definitive type 1 AIP diagnosis supported by full histopathological evidence compared with 19G EUS-FNA (71.0% vs. 16.7%,  $P < 0.001$ ). When complete tissue samples were available, EUS-FNB exhibited higher rates of reliable level 1 histo-

pathological findings (40.9% vs. 9.1%,  $P = 0.049$ ). Furthermore, a higher occurrence of IgG4-positive plasma cell infiltration (>10 cells/HPF) was observed in the EUS-FNB group compared with the 19G EUS-FNA group (74.2% vs. 18.2%,  $P < 0.001$ ). Conversely, 19G EUS-FNA was more frequently associated with uncertain and suspicious histopathological evidence for type 1 AIP (suspected type 1 AIP) compared with EUS-FNB (27.3% vs. 4.5%,  $P = 0.04$ ).

## DISCUSSION

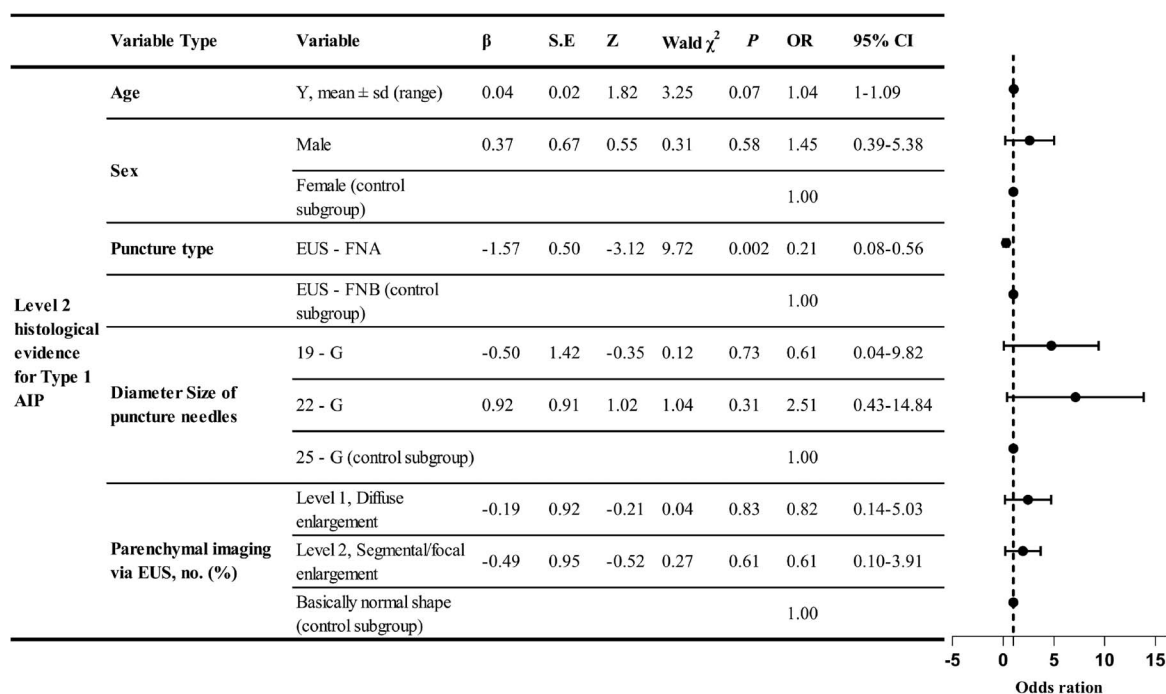
AIP presents a significant clinical challenge, often leading to unnecessary surgical interventions due to difficulties in differentiating it



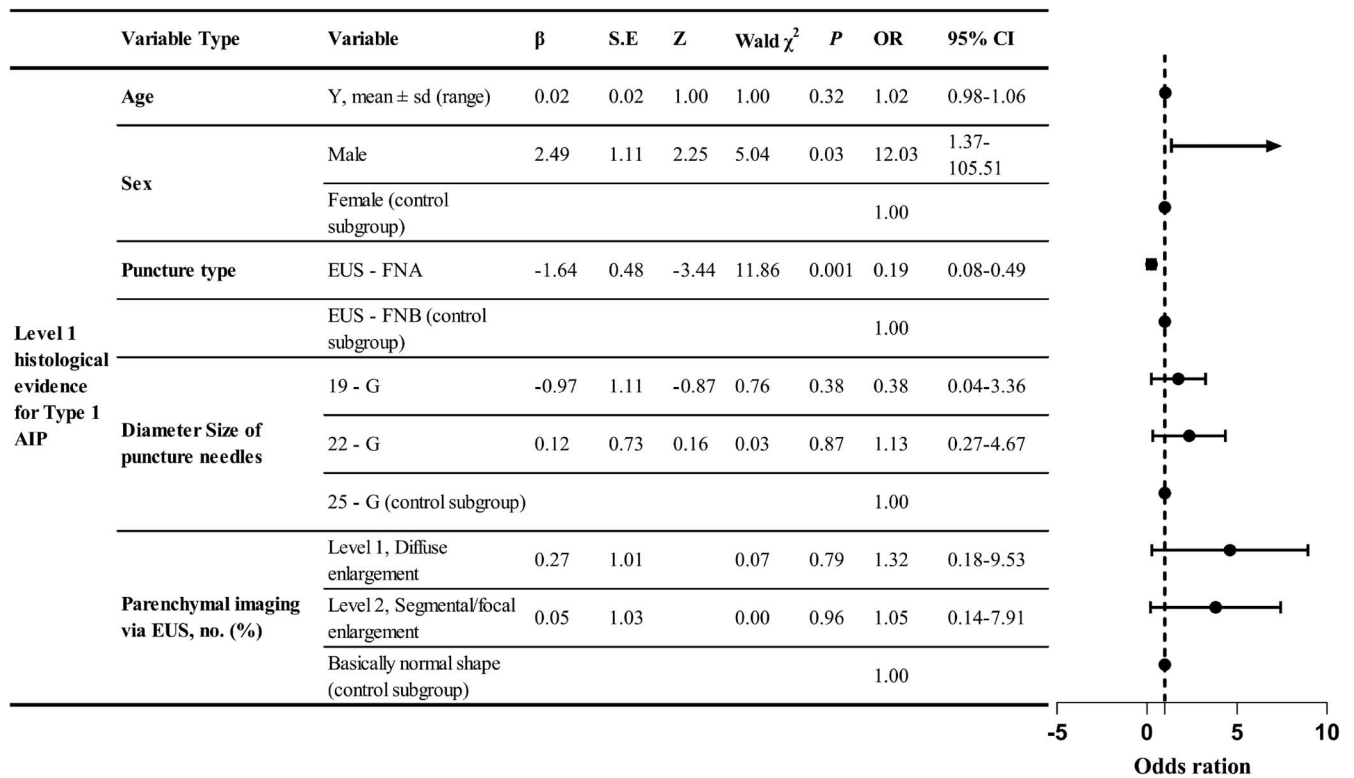
**Figure 2.** Multivariable logistic regression analysis of factors associated with suspected type 1 AIP. Control group: insufficient histological evidence. AIP: autoimmune pancreatitis; SD: standard deviation; EUS-FNA: ultrasound-guided fine-needle aspiration; EUS-FNB: EUS fine-needle biopsy; 19-G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.

from PDAC. According to the ICDC,<sup>[13-16]</sup> histopathological examination emerges as crucial for accurately distinguishing between these diseases. EUS, initially developed in Japan in the

1980s,<sup>[17]</sup> not only improves the imaging of pancreatic lesions using higher ultrasonic frequencies but also serves as an excellent technique for obtaining histological evidence. At present, EUS



**Figure 3.** Multivariable logistic regression analysis of factors associated with level 2 histopathological evidence for type 1 AIP. Control group: insufficient histological evidence. AIP: autoimmune pancreatitis; SD: standard deviation; EUS-FNA: ultrasound-guided fine-needle aspiration; EUS-FNB: EUS-guided fine-needle biopsy; 19G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.



**Figure 4.** Multivariable logistic regression analysis of factors associated with level 1 histopathological evidence for type 1 AIP. Control group: insufficient histological evidence. AIP: autoimmune pancreatitis; SD: standard deviation; EUS-FNA: ultrasound-guided fine-needle aspiration; EUS-FNB: EUS-guided fine-needle biopsy; 19G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.

has developed considerably in China.<sup>[18]</sup> The EUS-FNA technique was first used in pancreatic head lesions in 1992, utilizing a curved linear array endoscope.<sup>[19]</sup> Since then, numerous uses for EUS-FNA have been documented, particularly in the field of gastrointestinal disorders.<sup>[20]</sup> Due to the growing need for precise tumor treatment and personalized medicine, the EUS-FNB was developed in 2002.<sup>[21]</sup> In recent years, the EUS-TA procedure, which includes EUS-FNA and EUS-FNB, has been implemented globally.<sup>[22-25]</sup> In our current study, we compared the ability to acquire high-quality tissue samples between EUS-FNA and EUS-FNB in a large cohort of 173 patients with AIP. The results showed higher rates of level 1 and level 2 histopathological findings and more abundant IgG4-positive plasma cell infiltration in the EUS-FNB group compared with the EUS-FNA group. A multivariate logistic analysis further demonstrated that only the type of puncture independently correlated with the quality level of histopathological evidence. Additionally, we conducted a comparative analysis of 19G EUS-FNA and EUS-FNB, revealing that EUS-FNB had higher rates of level 1 histopathological findings and a greater incidence of IgG4-positive plasma cell infiltration (>10 cells/HPF). EUS-FNB provided more high-quality histopathological evidence for diagnosing type 1 AIP than 19G EUS-FNA. Similarly, previous studies have verified that EUS-FNB needles achieve a higher yield of histologic core tissue compared with 19G FNA needles in patients with solid mass lesions.<sup>[26]</sup> However, it is important to note that the sample size could affect the statistical reliability of these results, and further data are required for validation.

Our study findings are consistent with multiple recent studies that advocate for the use of EUS-FNB for diagnosing AIP.<sup>[25]</sup> Thomsen et al.

verified a sensitivity of 83.3% and an accuracy of 99.2% for EUS-FNB in diagnosing AIP, with sufficient tissue samples (>5 cells/HPF) obtained in 93.4% of cases.<sup>[27]</sup> In our study, we detected sufficient pancreatic tissue in 95.7% of the patients using EUS-FNB. Additionally, a systematic review from Korea also indicated higher diagnostic yields for EUS-FNB compared with EUS-FNA in the context of AIP.<sup>[28]</sup> Zhao et al. also suggested that EUS-FNB should be considered a first-line modality in the diagnosis of IHC-required lesions, especially AIP and mesenchymal tumors.<sup>[29]</sup> Similar results could be observed in other diseases. For example, Bueno et al. demonstrated diagnostic accuracies of 85.8% for EUS-FNA and 89.2% for EUS-FNB in the PDCA field.<sup>[30]</sup> Similarly, Verloop et al. reported diagnostic accuracy rates of 74.6% for EUS-FNA and 84.2% for EUS-FNB in the realm of upper gastrointestinal diseases.<sup>[31]</sup>

Different studies have presented conflicting views on the diagnostic accuracy of EUS-FNA for AIP. Some studies have shown that obtaining adequate tissue samples through EUS-FNA is challenging.<sup>[11,32]</sup> For example, Morishima et al. argued that EUS-FNA was ineffective for AIP diagnosis.<sup>[33]</sup> One possible explanation is that EUS-FNA is associated with obtaining small tissue strips and has a limited ability to examine histopathological structures. Additionally, EUS-FNA requires more punctures to acquire a core tissue mass, increasing the potential for injury and bleeding. Conversely, other studies have suggested that the EUS-FNA is effective in diagnosing pancreatic lesions.<sup>[34]</sup> Ishikawa also confirmed the usefulness of EUS-FNA in differentiating between AIP and cancer.<sup>[35]</sup> One possible explanation is that EUS-FNA offers advantages in terms of scope placement, tip flexibility, and the ability to use an elevator

**Table 3**  
**Comparison of baseline characteristics and histopathological findings of 19G EUS-FNA and EUS-FNB.**

	19G EUS-FNA	FNB	P
Time for hospital admission, n (%)			0.01
2010–2016	6 (50.0)	8 (11.6)	
2017–2023	6 (50.0)	61 (88.4)	
Sex, n (%)			1.00
Male	11 (91.7)	60 (87.0)	
Female	1 (8.3)	9 (13.0)	
Age, mean ± SD (range), y	58.75 ± 13.54	60.10 ± 11.33	0.71
Type of AIP, n (%)			1.00
Type 1 AIP	10 (83.3)	57 (82.6)	
Type 2 AIP	2 (16.7)	12 (17.4)	
Location of puncture (Interaction location has been merged), n (%)			0.65
Pancreatic head	8 (66.7)	39 (56.5)	0.76
Pancreatic neck	0 (0.0)	5 (7.2)	1.00
Pancreatic body	2 (16.7)	13 (18.8)	0.72
Pancreatic tail	0 (0.0)	7 (10.1)	0.59
Initial diagnosis upon hospital admission, n (%)			0.71
Nonspecified diagnosis	2 (16.7)	21 (30.4)	0.49
Suspected type 1 AIP	9 (75.0)	37 (53.6)	0.17
Chronic pancreatitis	0 (0.0)	3 (4.3)	1.00
Pancreatic cancer	1 (8.3)	8 (11.6)	1.00
The probability of acquiring sufficient pancreatic tissue samples (>5 cells/HPF)	11 (91.7)	66 (95.7)	0.48
The final diagnosis, n (%)			<0.001
Suspected as type 1 AIP without full histopathological evidence	10 (83.3)	20 (29.0)	<0.001
Definitive type 1 AIP supported by full histopathological evidence	2 (16.7)	49 (71.0)	<0.001
Histopathological evidence level, n (%)			0.002
No full histopathological evidence for type 1 AIP	6 (54.5)	14 (21.2)	0.06
Uncertain and suspicious histopathological evidence for type 1 AIP (suspected type 1 AIP)	3 (27.3)	3 (4.5)	0.04
Reliable level 2 histopathological evidence for type 1 AIP	1 (9.1)	22 (33.3)	0.16
Reliable level 1 histopathological evidence for type 1 AIP	1 (9.1)	27 (40.9)	0.049
The level of IgG4-positive plasma cell per HPF by histology, n (%)			<0.001
<10/HPF	9 (81.8)	17 (25.8)	0.001
>10/HPF	2 (18.2)	49 (74.2)	<0.001

AIP: Autoimmune pancreatitis; IgG: Immunoglobulin G; SD: Standard deviation; HPF: high-power field; 19G EUS-FNA: EUS-guided fine-needle aspiration using a 19-gauge puncture needle; EUS-FNB: EUS-guided fine-needle biopsy; 19G: 19-gauge; 22G: 22-gauge; 25G: 25-gauge.

function,<sup>[36]</sup> even though it carries a higher risk of complications such as bleeding.<sup>[37]</sup> Collectively, the combined use of EUS-FNA and EUS-FNB maximizes their strengths in identifying AIP, significantly enhancing the diagnostic capabilities of EUS in pancreatic conditions such as AIP.

Currently, research is ongoing to introduce new EUS-FNB needles annually.<sup>[38]</sup> In our study, we included only the Franseen-type needle (Acquire; Boston Scientific) and the antegrade core trap (ProCore; Cook Medical) in the EUS-FNB group. However, recent new needles such as the fork-tip needles (SharkCore; Medtronic) have been introduced to the market as well. A comparison of their

effectiveness has been conducted. For example, Akira et al. suggested that the 22G Franseen needle should be superior for histopathological diagnosis of type 1 AIP compared with the 20G forward-bevel needle.<sup>[39]</sup> Karsenti et al. found that the 22G Acquire needle provided more tissue samples for histopathological evaluation and offered better diagnostic accuracy than the 20G Procore needle.<sup>[40]</sup> Kovacevic et al. verified that the Franseen-type FNB needle seemed to be significantly superior to a conventional FNA needle.<sup>[41]</sup> Thomsen et al. also found a high accuracy of SharkCore EUS-FNB across all pancreatic disease categories.<sup>[27]</sup>

Furthermore, the various needle sizes—19G for aspiration and core biopsy, 20G for core biopsy, 22G for standard aspiration and core biopsy, and ultrathin 25G needles—provide doctors with additional options.<sup>[20]</sup> In our study, only 19G, 22G, and 25G needles were included. The impact of using varying needle sizes has been reported by several investigations. There is an ongoing debate regarding the impact of 19G needles. Some studies have suggested that 19G and 22G needles perform identically.<sup>[42]</sup> Other studies have found that the 19G EUS-FNB needle outperforms the 22G FNA/FNB needles in acquiring genomic profiling of incurable pancreatic cancer. Despite the excellent sensitivity, specificity, and accuracy of 19G TopGain FNB needles, Kotaro et al. revealed that the use of 19G needles might increase the risk of adverse events, including 2.0% of severe adverse events.<sup>[43]</sup> As for the 25G needles, they have also been a subject of controversy. Young et al. revealed that 25G needles had fewer advantages compared with 22G needles, as the former required more than 3 times the number of needle passes.<sup>[44]</sup> However, other studies have demonstrated that the 25G needles yield a higher quantity of diagnostic cellular material than 22G FNA needles.<sup>[45]</sup> Similarly, Carrara et al. verified a higher rate of obtaining adequate samples with 25G FNA needles.<sup>[46]</sup>

Our study presents several notable advantages. First, it includes a large cohort of more than 100 patients, providing a comprehensive overview of 12 years of EUS-TA therapy for AIP in China. Additionally, our research addresses gaps in the literature by comparing EUS-FNA and EUS-FNB in the diagnosis of AIP among Chinese patients. Lastly, this study emphasizes a detailed analysis of individual components within the ICDC diagnostic criteria.

However, our study has several limitations that should be acknowledged. First, comprehensive data on puncture times, adverse events, and the effects of steroid use have not been fully collected. Second, we did not include other diseases to evaluate the accuracy and sensitivity of EUS-TA.

**CONCLUSION**

EUS-FNB demonstrates higher rates of level 1 and level 2 histopathological findings and a greater degree of IgG4-positive plasma cell infiltration, compared with EUS-FNA. The increasing popularity of EUS-FNB in recent years is attributed to its ability to obtain high-quality tissue samples for diagnosing AIP. The combined use of EUS-FNA and EUS-FNB optimizes their respective advantages in detecting AIP.

**Conflict of Interest**

Zhendong Jin is an Associate Editor of the journal. The article was subjected to the standard procedures of the journal, with a review



process independent of the editor and his research group. The authors declare that they have no financial conflict of interest with regard to the content of this report.

### Data Availability Statement

The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

### Source of Funding

This work was supported by the National Natural Science Foundation of China (grants 82370658 and 82170657).

### Author contributions

Yuyan Zhou, Liqi Sun, and Xinyue Wang contributed equally to this work and should be considered co-first authors. Zhendong Jin and Haojie Huang contributed equally to this work and should be considered as co-corresponding authors.

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