

# EUS-guided fine needle biopsy sampling in autoimmune pancreatitis: Is needle tip design more important than needle size?



## Authors

Per Hedenström<sup>1,2</sup>, Björn Lindkvist<sup>1,2</sup>

## Institutions

- 1 Division of Medical Gastroenterology, Department of Internal Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden
- 2 Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

## Bibliography

Endoscopy International Open 2020; 08: E1862–E1864  
 DOI 10.1055/a-1293-7890  
 ISSN 2364-3722

© 2020. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Corresponding author

Dr Per Hedenström, Medicinmottagningen, Sahlgrenska Universitetssjukhuset, Blå Stråket 3, 413 35 Göteborg, Sweden  
 Fax: +46 31827458.  
[per.hedenstrom@vgregion.se](mailto:per.hedenstrom@vgregion.se)

Endosonographers encounter a lot of puzzling situations and conditions. One such condition is autoimmune pancreatitis (AIP). The typical radiological presentation in autoimmune pancreatitis is a “sausage-shaped” pancreas with parenchymal enlargement, peripancreatic halo, and a general narrowing of the pancreatic duct [1]. However, AIP can also present with a focal pancreatic mass that may be impossible to distinguish from pancreatic ductal adenocarcinoma (PDAC) solely based on imaging [2, 3]. Clinical management of AIP and PDAC are completely different and misdiagnosis of AIP as PDAC may have deleterious consequences for the patient, including unnecessary and extensive pancreatic surgery, chemotherapy, and withholding of a potentially curative treatment (corticosteroids and/or other immunosuppressants) [2, 4, 5]. Moreover, the prognosis for AIP is far better than for PDAC, with long-term survival to be expected in the majority of patients.

These circumstances underscore the need for reliable pre-treatment diagnosis of AIP, which is based upon several modalities including imaging (computed tomography [CT]), serology (immunoglobulin [Ig] G4), histology, and the response to therapy [2, 6–9]. The International Consensus Diagnostic Criteria (ICDC) is one of the standards most widely used and applied in the work-up of suspected AIP [9].

Especially in cases with an unclear diagnosis after imaging and serology, endoscopic ultrasonography (EUS) is an informative diagnostic modality for suspected AIP. Typical endosonographic features often seen in AIP are an echo-poor parenchyma, sometimes with hyperechoic strands, a diffuse pancreatic

enlargement, an increased glandular volume, and in certain cases, a focal, hypoechoic mass in the pancreatic head that causes upstream dilatation of the MPD [10, 11]. Quite obviously and somewhat concerning there is a clear resemblance with many of the findings in PDAC. That is why an EUS image alone is not sufficient to confirm AIP [9, 12].

Consequently, EUS-guided sampling of the pancreas is required. EUS-guided fine-needle aspiration (EUS-FNA) with standard open tip needles aimed for cytology is the mainstay approach in various malignant conditions such as PDAC [13, 14]. However, the diagnostic capacity of EUS-FNA in AIP is suboptimal, with a sensitivity of around 60% at best, even when using a relatively large 22G needle [15–17]. EUS-guided fine-needle biopsy sampling (EUS-FNB) has significantly improved the diagnostic accuracy of, among others, subepithelial lesions [18, 19]. It goes without saying that there would be a huge diagnostic advantage if biopsy cores acquired with EUS-FNB also were sufficient for definitive histologic diagnosis of AIP.

In the current issue of Endoscopy International Open, Opong and colleagues assess the utility of EUS-FNB in the pre-treatment diagnosis of type 1 AIP. The authors conducted a retrospective, single-center study based on a prospectively maintained database of patients with AIP. Twenty-four patients with a final diagnosis of AIP who underwent EUS between 2011 and 2018 were included in the study. In total, 28 EUS procedures were performed. Notably, 38% of patients presented with a focal mass in the pancreatic head on CT and 79% had cholestasis. EUS was performed by using linear echo-endoscopes. At sam-

pling, a minimum of three passes were performed and standard suction was used. Given the retrospective study design, there was no restriction on the type of FNB needle used.

In a majority of procedures (n = 22), the fork-tip FNB-needle (Sharkcore, Medtronic, Minneapolis, United States) was used in a study of 18 individuals. The 25G needle was used in seven procedures and the 22G needle in 15 procedures. The reverse bevel FNB-needle (Procore, Cook Medical, Limerick, Ireland) was used in the remaining six cases. The diagnostic information gained from the acquired FNB-core tissue specimens was classified according to the ICDC pathology criteria [9] with a Level 1 or a Level 2 finding being accepted as a diagnostic sample. All slides were double reported by two pathologists. A minimum of 12 months of clinical follow-up was required and the HISORT criteria were used to establish the final diagnosis of the study patients.

The authors report a low diagnostic sensitivity for AIP using the reverse-bevel FNB-needle (0/6; 0%) while the use of the fork-tip FNB-needle resulted in a relatively high diagnostic sensitivity of 77% in a per-procedure analysis. No serious adverse events were reported. Based on the presented results, the authors conclude that the 22/25 G fork-tip needle outperforms the 22G reverse bevel needle for diagnosis of AIP and, therefore, the former needle should be the needle of choice in this specific situation.

The study by Oppong and co-workers is of interest because there is a lack of studies comparing the fork-tip needle with the reverse bevel needle in the work-up of suspected AIP. The diagnostic support and impact of EUS-guided sampling is especially important in patients who present with a focal mass or with indeterminate findings at imaging or (low titer) IgG4-serology, hence a non-conclusive ICDC-based diagnosis. In the current study, a little less than half of the patients (44%) did not meet the criteria for the AIP diagnosis without histology. Hence, in this subgroup of patients, the pathology report for EUS-FNB was crucial to establish the diagnosis.

Besides the main results, there are some additional observations in the work by Oppong that merit attention. Somewhat surprisingly, the 25G fork-tip needle was sufficient for a level 1 definitive diagnosis of AIP in three cases and not obviously less sensitive than the 22G needle. This suggests that needle tip design may be more important than needle size for successful EUS-guided sampling in AIP. This interpretation is in line with the findings of a previous study investigating the largest available EUS-FNA needle (19G, Echotip, Cook Medical) in 44 patients. This approach only reached a histologic sensitivity for AIP of around 40% [20].

Although presenting valuable data, the study by Oppong and co-workers is not without weaknesses. The study is not a randomized trial and a bias related to preferential selection of needle based on patient characteristics cannot be ruled out. The number of patients examined using the reverse bevel needle was low, decreasing the statistical power of the head-to-head comparison of the two needle types. Furthermore, the needles used varied not only in tip type but also in size. Nevertheless, only 19G or 22G reverse bevel needles were used, ruling out small needle size as a plausible explanation for the poor

sensitivity of this needle type. A bias related to the learning curve of the endosonographer also needs to be taken into account as a consequence of the retrospective design of the study. When comparing the results of the current study with previous reports, the reader should pay close attention to how data are analyzed because per-procedure analysis and per-individual analysis (which excludes non-diagnostic samples in repeated procedures on the very same individual) will lead to markedly different results. Preferably, the former measurement should be used.

What else on this topic can be extracted from the literature? In the randomized, prospective COMPAS Trial performed by Kurita and co-workers on 110 patients with suspected AIP [21], the 22G Franseen tip needle (Acquire, Boston Scientific) showed a significantly higher sensitivity compared with the 20G forward-bevel needle (Procore, Cook Medical), 79% vs 42%. The FNB-core tissue volume, that is, the assessable number of high power fields at microscopy, was also significantly higher in the Franseen tip group. Hence, the conclusion in both the study by Oppong and the study by Kurita is similar, that is, the side bevel needles seem less appropriate for diagnosis of AIP. Moreover, the recorded high sensitivity of the 22G Franseen tip needle in AIP was confirmed in a very recent study on 56 patients conducted by Ishikawa et al [22].

To conclude, the study by Oppong adds valuable information to the body of knowledge regarding the utility of EUS-FNB in pancreatic diseases in general and in AIP in particular. With co-existing support from the large study by Kurita et al, the side bevel needles most probably should not be recommended as the first-line approach in EUS-guided sampling of suspected AIP. A future head-to-head study, with strict inclusion criteria and FNB needle-size restricted to one single, is needed to answer the question of whether the Franssen tip needle design or the fork-tip needle design is the preferable one. Indeed, such a comparison has been performed in 50 patients primarily with malignant diagnoses presenting as a solid pancreatic mass [23]. However, none of these patients had a final diagnosis of AIP.

It is hoped that implementation of modern type EUS-FNB sampling will facilitate histologic diagnosis in patients with AIP and thereby give support to clinicians in avoiding extensive surgery when imaging or serology cannot rule out a devastating false diagnosis of PDAC.

In a real-world EUS situation, the results of the current study should probably be interpreted by you as the endosonographer in such a way that the fork-tip needle is the needle of choice used when AIP is a probable diagnosis. Finally, we would like to take the opportunity to remind all endosonographers to consider AIP when examining patients with an unclear pancreatic condition, including those with a focal, solid mass. So, good luck with all your efforts!

## Competing interests

The authors declare that they have no conflict of interest.

## References

- [1] Löhr JM, Beuers U, Vujasinovic M et al. European Guideline on IgG4-related digestive disease – UEG and SGF evidence-based recommendations. *United Europ Gastroenterol J* 2020; 8: 637–666
- [2] Fritz S, Bergmann F, Grenacher L et al. Diagnosis and treatment of autoimmune pancreatitis types 1 and 2. *Br J Surg* 2014; 101: 1257–1265
- [3] Agrawal S, Daruwala C, Khurana J. Distinguishing autoimmune pancreatitis from pancreaticobiliary cancers: current strategy. *Ann Surg* 2012; 255: 248–258
- [4] Gardner TB, Levy MJ, Takahashi N et al. Misdiagnosis of autoimmune pancreatitis: a caution to clinicians. *Am J Gastroenterol* 2009; 104: 1620–1623
- [5] Ivan Heerde MJ, Biermann K, Zondervan PE et al. Prevalence of autoimmune pancreatitis and other benign disorders in pancreatoduodenectomy for presumed malignancy of the pancreatic head. *Dig Dis Sci* 2012; 57: 2458–2465
- [6] Chari ST. Diagnosis of autoimmune pancreatitis using its five cardinal features: introducing the Mayo Clinic's HISORT criteria. *J Gastroenterol* 2007; 42: 39–41
- [7] Chang MC, Liang PC, Jan S et al. Increase diagnostic accuracy in differentiating focal type autoimmune pancreatitis from pancreatic cancer with combined serum IgG4 and CA19-9 levels. *Pancreatology* 2014; 14: 366–372
- [8] Shimosegawa T, Chari ST, Frulloni L et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology. *Pancreas* 2011; 40: 352–358
- [9] Song TJ, Kim MH, Kim MJ et al. Clinical validation of the international consensus diagnostic criteria and algorithms for autoimmune pancreatitis: combined IAP and KPBA meeting 2013 report. *Pancreatology* 2014; 14: 233–237
- [10] Buscarini E, De Lisi S, Arcidiacono PG et al. Endoscopic ultrasonography findings in autoimmune pancreatitis. *World J Gastroenterol* 2011; 17: 2080–2085
- [11] Kamisawa T, Ohara H, Kim MH et al. Role of endoscopy in the diagnosis of autoimmune pancreatitis and immunoglobulin G4-related sclerosing cholangitis. *Digest Endosc* 2014; 26: 627–635
- [12] Chari ST, Takahashi N, Levy MJ et al. A diagnostic strategy to distinguish autoimmune pancreatitis from pancreatic cancer. *Clin Gastroenterol Hepatol* 2009; 7: 1097–1103
- [13] Hebert-Magee S, Bae S, Varadarajulu S et al. The presence of a cytopathologist increases the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology for pancreatic adenocarcinoma: a meta-analysis. *Cytopathology* 2013; 24: 159–171
- [14] Hewitt MJ, McPhail MJ, Possamai L et al. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. *Gastrointest Endosc* 2012; 75: 319–331
- [15] Cao L, Wang Y, Wang J et al. The role of EUS-guided fine needle aspiration in autoimmune pancreatitis: a single center prospective study. *Scand J Gastroenterol* 2018; 53: 1604–1610
- [16] Kanno A, Masamune A, Fujishima F et al. Diagnosis of autoimmune pancreatitis by EUS-guided FNA using a 22-gauge needle: a prospective multicenter study. *Gastrointest Endosc* 2016; 84: 797–804.e791
- [17] Morishima T, Kawashima H, Ohno E et al. Prospective multicenter study on the usefulness of EUS-guided FNA biopsy for the diagnosis of autoimmune pancreatitis. *Gastrointest Endosc* 2016; 84: 241–248
- [18] de Moura DTH, McCarty TR, Jirapinyo P et al. EUS-guided fine-needle biopsy sampling versus FNA in the diagnosis of subepithelial lesions: a large multicenter study. *Gastrointest Endosc* 2020; 92: 108–119.e103
- [19] Hedenstrom P, Marschall HU, Nilsson B et al. High clinical impact and diagnostic accuracy of EUS-guided biopsy sampling of subepithelial lesions: a prospective, comparative study. *Surg Endosc* 2018; 32: 1304–1313
- [20] Iwashita T, Yasuda I, Doi S et al. Use of samples from endoscopic ultrasound-guided 19-gauge fine-needle aspiration in diagnosis of autoimmune pancreatitis. *Clin Gastroenterol Hepatol* 2012; 10: 316–322
- [21] Kurita A, Yasukawa S, Zen Y et al. Comparison of a 22-gauge Franseen-tip needle with a 20-gauge forward-bevel needle for the diagnosis of type 1 autoimmune pancreatitis: a prospective, randomized, controlled, multicenter study (COMPAS study). *Gastrointest Endosc* 2020; 91: 373–381.e372
- [22] Ishikawa T, Kawashima H, Ohno E et al. Usefulness of endoscopic ultrasound-guided fine-needle biopsy for the diagnosis of autoimmune pancreatitis using a 22-gauge Franseen needle: a prospective multicenter study. *Endoscopy* 2020; doi:10.1055/a-1183-3583
- [23] Bang JY, Hebert-Magee S, Navaneethan U et al. Randomized trial comparing the Franseen and fork-tip needles for EUS-guided fine-needle biopsy sampling of solid pancreatic mass lesions. *Gastrointest Endosc* 2018; 87: 1432–1438