

<http://hdl.handle.net/1765/120419>



General summary and discussion



GENERAL SUMMARY AND DISCUSSION

This thesis explores how to improve the diagnostic outcome of Endoscopic ultrasound (EUS)-guided tissue sampling. First, it gains insight in the current international practice patterns of endosonographers. Then, it focusses on the performance of different EUS-sampling devices. We compared the diagnostic performance of a fine needle aspiration (FNA) and fine needle biopsy (FNB) device, their diagnostic reproducibility, and the value of their combined use, in a prospective randomized manner. In addition, a meta-analysis was performed, mutually comparing FNA and the novel-generation FNB devices, comprising the ProCore (Cook Medical), SharkCore (Medtronic) and Acquire (Boston Scientific) needles. In the third part of the thesis, we explore if EUS-FNA tissue preparation techniques can be optimized by training endoscopy personnel and by comparing specimen processing with liquid based cytology (LBC) to the conventional glass-smear technique.

Current practice in EUS-guided tissue sampling

EUS-guided tissue sampling is increasingly being used, due to its high diagnostic accuracy, minimal invasive character, and good tissue yield, which is of major importance in the current era of patient tailored medicine [1]. Because of its increased use, the technique is continuously evolving. This leaves the optimal sampling strategy a subject of debate, and clinicians with limited evidence for their daily practice [2-6].

In **chapter 2**, an online survey aimed to map the practice patterns for EUS-guided tissue sampling. We found considerable intercontinental differences and deviations from the guidelines. According to the questioned American endosonographers, their all-round use of propofol rather than conscious sedation may be explained by marketing strategies of anaesthesiologists [7-9]. If this practice pattern will spread to Europe, procedure costs are expected to rise [7, 10, 11]. Another difference was the use of periprocedural acetylsalicylic acid, which was generally continued in the United States (US), according to the guidelines, in contrast to Europe and Asia. In Asia, this may be explained by the believe that Asians are more susceptible to bleeding complications [12]. As for the use of rapid on-site pathological evaluation and preparation of the collected tissue (ROSE), our survey reported that it was used by virtually all respondents from the US, while in Europe and Asia, it was only available in half of the centers, due to cost issues and disbelief in its added value. Indeed, a recent meta-analysis could not proof its benefit and the European Society of Gastroenterology (ESGE) guidelines do not recommend its use [13].

Histology was uniformly stored in formalin. The preferred preservation fluid for cytological specimens, however, differed considerably. Asians generally use alcohol or saline, while European and US practitioners use Cytolyt. This reflects the lack of recommendations on preservation and specimen handling by the current guidelines. A practice pattern that did not differ between continents was the preferred needle size and number of passes. The survey identified the 22-gauge (G) needle as the preferred size for both FNA and FNB [14-17], and participants

reported to perform less passes with FNB than FNA. Although at the time of the survey, this was not yet recommended, the updated ESGE guidelines indeed advise to perform less passes with FNB [2-3] than FNA [3-4], in the absence of ROSE [13].

The optimal EUS-sampling device

As we discussed in the introduction of this thesis, EUS-needles are, and always have been a major target of innovation in EUS-guided tissue sampling. FNB devices were introduced to overcome the limitations of FNA, mainly by providing histological specimens rather than loose target cells. However, their diagnostic performance was not convincingly better than the FNA needles [18-22]. Some reported that FNB not so much harvested histological tissue fragments, but just improved the yield of loose target cells [18, 23-29]. Others claimed that histology can also be obtained with the conventional FNA needles [18, 30, 31]. Lastly, new tissue preparation techniques, such as cell block, allow for a 'histology like' analysis of cytological material.

The first FNB devices, TruCut[™] (Travenol Laboratories) and Quick-Core[®] (Cook Medical), were hampered by a rigid design and difficult deployment. In response, several novel FNB needles have been introduced in the last years, including the ProCore reversed and forward facing bevel, SharkCore, and Acquire needles. As the design of these needles significantly differs from the first FNB devices and from each other, there is a growing interest in their diagnostic performance.

The 20G ProCore forward facing bevel needle was introduced first, in 2015, and its diagnostic performance has been extensively assessed. The largest study available is the international multicenter trial that is presented in **chapter 3**. In this trial, the ASPRO study (ASpiration versus PROcore), we compared the ProCore forward facing FNB needle to a commonly used conventional FNA needle, the 25G EchoTip Ultra Needle (Cook Medical), which was chosen because of its optimal flexibility and yield [2, 13].

We demonstrated that this 20G FNB needle achieves a higher diagnostic accuracy and tissue core yield within less passes than FNA. These findings equally applied for pancreatic and non-pancreatic lesions, and were irrespective of target lesion size, number of needle passes, and presence of an on-site pathologist. Moreover, despite of inter-center differences, the benefit of the new FNB needle was consistent amongst all 13 participating centers, supporting the general applicability of these findings.

The better performance of the new 20G FNB needle seems related to its design adaptations, which include a large diameter, a flexible needle sheath, a forward facing rather than a reversed bevel, and a Menghini rather than a lancet tip, which decreases resistance during tissue traversing. The fact that a large-bore FNB needle outperformed a thinner FNA needle is an important observation, because it counters the conception that the performance of larger-bore needles is hampered by their suboptimal performance in an angulated scope-position.

The better overall performance of the FNB needle was shown to be center independent, but we were well aware that all participating centers were high volume centers. To assess the

reproducibility in non-expert hands, we performed a second study. As described in **chapter 4**, we compared the diagnostic agreement between academic and non-academic pathologists. The first 125 pancreatic and lymph node cases, enrolled in the original ASPRO trial, were re-assessed by 5 academic and 5 non-academic pathologists from different countries. The diagnostic agreement on the final diagnosis was higher for FNB samples than for FNA, amongst expert academic as well as non-academic pathologists. Logistic regression analysis further showed that the pathologist's provenance (academic or non-academic) did not influence diagnostic accuracy. This endorses the use of the novel 20G FNB needle in academic as well as non-academic centers.

The most likely explanation for the better agreement on the FNB samples is their higher tissue core rate, which was positively associated with a better diagnostic agreement. Furthermore, the cytological yield of FNB was also higher than for FNA, but only the availability of tissue cores, and not cytology, contributed to a better diagnostic accuracy. Another quality parameter that seemed to contribute to the high diagnostic accuracy and agreement on samples obtained with FNB is the low sample artifact rate. Not only did the present study show a decrease in accuracy when artifacts were present, previous studies have also reported that artifacts may hamper ancillary testing [32]. Interestingly, agreement on the presence of artifacts was low for both needles (although slightly better for FNB than FNA). This is in line with the fact that agreement on all sample quality parameters was low in the current study, similar to reports from others [33, 34]. This likely results from the lack of uniform outcome definitions regarding the performance of EUS-guided tissue sampling.

To further explore the optimal sampling approach, in **chapter 5**, the role of combined FNA and FNB use is assessed. The benefits of an FNA needle; optimal flexibility to reach a target lesion and the possibility to perform on-site cytological evaluation, may complement the benefits of FNB; collection of histological tissue cores to optimize the diagnostic yield and harvest enough tissue for ancillary testing. To explore the incremental diagnostic yield of dual sampling, all ASPRO cases that were sampled with both needles during the same procedure were included. This resulted in 24 patients who were first sampled with the 25G FNA needle, and 49 cases who were first sampled with the 20G FNB device. Interestingly, dual sampling only improved diagnostic accuracy for malignancy if FNA was followed by sampling with FNB and not vice versa. The previously reported diagnostic benefit of the FNB over the FNA needle may very well explain why FNA followed by FNB resulted in a higher diagnostic accuracy than FNA alone, and also explains the limited value of the reversed approach. However, FNB may have caused blood contamination of subsequent specimens, or "tracking" within the target lesion, impeding the FNA needle from finding its own diagnostic route. Last, secondary FNA was mostly used to allow for ROSE. However, since the incremental yield of ROSE is questionable in academic high volume centers, the benefit of FNA to allow for ROSE is expected to be limited [35-37].

In **chapter 6** we zoom out from the diagnostic performance of the two specific needles and present an updated meta-analysis on the performance of all currently available EUS-FNA

and FNB needles. EMBASE, MEDLINE/PubMed, Web of Science, the Cochrane Library, and Google Scholar were systematically searched for studies comparing FNA to FNB. We included randomized controlled trials of at least 50 patients, and extracted data on diagnostic accuracy, adequacy, number of passes, presence of tissue cores, and adverse events. Study quality was assessed based on the QUADAS-2 tool.

The recent wave of publications enabled us to include a significant number of new trials that compare FNA to FNB, and limit our evaluation to studies of high quality, as compared to previous meta-analyses [18-22]. Our analysis is the first to demonstrate a diagnostic benefit of FNB over FNA for pancreatic as well as non-pancreatic lesions, in terms of diagnostic accuracy, the number of needle passes performed, and tissue core yield. The adverse event rate was equally low for FNA and FNB. Other than diagnostic accuracy, sample adequacy did not differ between FNA and FNB. Sample adequacy or cellularity may be of less importance for a correct diagnosis than the presence histological tissue cores. Despite the use of new cytological preparation techniques like ThinPrep and cell block and the abundant use of ROSE, diagnostic accuracy was still better for FNB than FNA.

With regard to the general applicability of our results, it should be noted that there was a significant heterogeneity amongst the included studies. This is mainly due to the diversity in EUS-sampling protocols, and the inconsistent use of outcome definitions. Consequently, the outcomes of EUS-device studies remain difficult to interpret and should be extrapolated with caution.

Although the current analysis showed that FNB convincingly outperforms FNA, all included trials used the ProCore needle for FNB. As the use of the other new FNB needles, such as the Acquire and SharkCore needle, is increasing, we eagerly await head to head comparison studies between different FNB devices. Preferably, these should be (international) multicenter randomized controlled studies. According to ClinicalTrials.gov, a significant number of interesting studies investigating the performance of the novel generation of FNB devices is currently running.

Improving EUS-specimen preparation and handling

As mentioned in the previous section of this discussion, new FNA-tissue preparation techniques like ThinPrep and cell block increasingly enable pathologists to perform ancillary testing on cytological specimens. These techniques have been introduced to improve FNA-sample quality and accuracy, since the traditional, so called, smear-technique, is highly sensitive to preparation and contamination artifacts. Another way to solve this issue is to invest in a dedicated, on-site pathologist to handle the collected tissue. However, most centers omit this type of service. Therefore, EUS-FNA specimens are often prepared by the endoscopy staff, generally without a specialized training.

Chapter 7 explores if a one-day-hands-on tissue preparation training for endoscopy staff could improve sample quality and thus diagnostic accuracy of EUS-FNA in centers lacking ROSE. We performed a prospective pilot study, for which we invited 10 endosonographers and 12

endoscopy nurses from 7 regional EUS-centers in the Netherlands. Participants were educated on pancreas pathology, common diagnostic pitfalls, and the cause and prevention of smear-preparation-artifacts. Subsequently, they practiced smear preparation under the supervision of a team of academic (cyto)pathologists. After the training, 71 FNA-smears were prospectively collected from solid pancreatic lesions and compared to an equal number of pre-training 'control' slides.

Unfortunately, smear quality and diagnostic accuracy did improve after the training. The sample size did not allow us to assess individual results, to identify any trainees that did benefit from the training. There may be several reasons for the limited effect of our pilot-training. First, the training program may have been too short. As practical skills are better achieved after extensive training and tend to grow with exposure, it might have been more effective to intensify or repeat the training with one or more refresh sessions. In addition, the study period may have been too short to allow trainees to gain sufficient experience. Last, the lack of quality improvement may also be inherent to the nature of the smear technique itself, since it is a manual method that is sensitive to artifacts and prone to heterogeneous preparations. In contrast, cytological examination using LBC, i.e. ThinPrep and cell block, are associated with less contamination and drying artifacts [38].

Chapter 8 compares the diagnostic benefit of LBC to the conventional smear technique for the diagnosis of solid pancreatic lesions. The participating EUS personnel had been trained in the course of the previously described study. Two smears and a vial for ThinPrep and/or cell block were prepared from the first FNA-pass, without use of ROSE, and compared in terms of diagnostic accuracy for malignancy, sample quality, and diagnostic agreement between three (cyto)pathologists. The diagnostic accuracy was higher with the LBC technique as compared to the smear technique. However, this was only true when the yield of ThinPrep and cell block were collated. Artifacts were less present in both LBC techniques. The diagnostic agreement was comparable for LBC and smears, with the highest agreement on cell block samples. Given its higher accuracy and comparable agreement, LBC could be an alternative for centers lacking ROSE, especially cell block.

Future perspectives and recommendations

The historical line between FNA and FNB is fading with the current pool of EUS-devices containing FNA and FNB needles of comparable sizes and flexibility. To complicate things even further, needle designs differ significantly within the FNA and FNB groups. Therefore, we propose to discard the distinctive nomenclature of FNA and FNB, and instead, focus on the performance of individual EUS-sampling devices.

The current thesis provides significant new information that may be used to improve EUS-guided tissue sampling. However, there is room for further development, as the updated meta-analysis in this thesis found that the diagnostic accuracy for traditional FNA ranged between 67% and 100% and for FNB between 69% and 100%. This thesis states that an FNB needle

outperforms FNA, and should be the first-choice device for EUS-guided tissue acquisition, independent of the type of solid target lesion. However, before any specific needle FNB type or design can be recommended, newer generation FNB needles need to be assessed.

Ideally, one would want to compare each available EUS-sampling device head to head, but this is challenging. First of all, due to the many available FNA and FNB sizes and designs this will be time consuming but not impossible. Other complicating issues that make it difficult to compare the result are the heterogeneity in EUS-sampling protocols and lack of uniform outcome definitions. As long as there is no evidence which sampling strategy is optimal, it will be difficult to standardize practice patterns. To overcome some of the issues, uniform outcome definitions need to be created. For this there may be a role for the European and American Societies for Gastroenterology, as was the case for the diagnostic classification of pathology samples by the Papanicolaou Society.

In addition to the optimal EUS-needle design, this thesis also focused on the optimal tissue preparation of FNA specimens. One may question if future research should continue to focus on this, since our study proved FNB to be superior to FNA. However, we did not directly compare FNA specimens in liquid-based cytology to FNB cores in formalin. It would be interesting to compare this in an international multicenter setting. Furthermore, it should be noted that tissue collection for liquid preparation techniques is easy for the endosonographer, but requires a well-equipped pathology laboratory and trained personnel. Therefore, introducing and implementing novel techniques and innovations for EUS-guided tissue sampling should always be done in close cooperation with the pathology department.

Lastly, in light of ever-increasing burden of health-care costs, it is crucial that, before making any recommendation regarding the most optimal EUS-guided sampling technique and tool, cost-effective analyses should be performed.

REFERENCES

1. Wani S, Muthusamy VR, McGrath CM, Sepulveda AR, Das A, Messersmith W, et al. AGA White Paper: Optimizing Endoscopic Ultrasound-Guided Tissue Acquisition and Future Directions. *Clin Gastroenterol Hepatol*. 2018;16(3):318-27.
2. Polkowski M, Larghi A, Weynand B, Boustiere C, Giovannini M, Pujol B, et al. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy*. 2012;44(2):190-206.
3. Committee ASoP, Anderson MA, Ben-Menachem T, Gan SI, Appalaneni V, Banerjee S, et al. Management of antithrombotic agents for endoscopic procedures. *Gastrointest Endosc*. 2009;70(6):1060-70.
4. Committee ASoP, Early DS, Acosta RD, Chandrasekhara V, Chathadi KV, Decker GA, et al. Adverse events associated with EUS and EUS with FNA. *Gastrointest Endosc*. 2013;77(6):839-43.
5. Committee ASoP, Jue TL, Sharaf RN, Appalaneni V, Anderson MA, Ben-Menachem T, et al. Role of EUS for the evaluation of mediastinal adenopathy. *Gastrointest Endosc*. 2011;74(2):239-45.
6. Committee ASoP, Khashab MA, Chithadi KV, Acosta RD, Bruining DH, Chandrasekhara V, et al. Antibiotic prophylaxis for GI endoscopy. *Gastrointest Endosc*. 2015;81(1):81-9.
7. Standards of Practice Committee of the American Society for Gastrointestinal E, Lichtenstein DR, Jagannath S, Baron TH, Anderson MA, Banerjee S, et al. Sedation and anesthesia in GI endoscopy. *Gastrointest Endosc*. 2008;68(5):815-26.
8. Ootaki C, Stevens T, Vargo J, You J, Shiba A, Foss J, et al. Does general anesthesia increase the diagnostic yield of endoscopic ultrasound-guided fine needle aspiration of pancreatic masses? *Anesthesiology*. 2012;117(5):1044-50.
9. Aisenberg J, Brill JV, Ladabaum U, Cohen LB. Sedation for gastrointestinal endoscopy: new practices, new economics. *Am J Gastroenterol*. 2005;100(5):996-1000.
10. McQuaid KR, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. *Gastrointest Endosc*. 2008;67(6):910-23.
11. Dewitt J, McGreevy K, Sherman S, Imperiale TF. Nurse-administered propofol sedation compared with midazolam and meperidine for EUS: a prospective, randomized trial. *Gastrointest Endosc*. 2008;68(3):499-509.
12. Lee SY, Tang SJ, Rockey DC, Weinstein D, Lara L, Sreenarasimhaiah J, et al. Managing anticoagulation and antiplatelet medications in GI endoscopy: a survey comparing the East and the West. *Gastrointest Endosc*. 2008;67(7):1076-81.
13. Polkowski M, Jenssen C, Kaye P, Carrara S, Deprez P, Gines A, et al. Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline - March 2017. *Endoscopy*. 2017.
14. Affolter KE, Schmidt RL, Matynia AP, Adler DG, Factor RE. Needle size has only a limited effect on outcomes in EUS-guided fine needle aspiration: a systematic review and meta-analysis. *Dig Dis Sci*. 2013;58(4):1026-34.
15. Madhoun MF, Wani SB, Rastogi A, Early D, Gaddam S, Tierney WM, et al. The diagnostic accuracy of 22-gauge and 25-gauge needles in endoscopic ultrasound-guided fine needle aspiration of solid pancreatic lesions: a meta-analysis. *Endoscopy*. 2013;45(2):86-92.

16. Guedes HG, De Moura DT, Duarte RB, Coronel MA, Dos Santos ME, Cheng S, et al. A comparison of the efficiency of 22g versus 25g needles in EUS-FNA for solid pancreatic mass assessment: A systematic review and metaanalysis. *Gastrointest Endosc.* 2018;87(6):AB427.
17. Oh HC, Kang H, Do JH. Diagnostic accuracy of 22/25-gauze core needle in endoscopic ultrasound-guided sampling of solid pancreatic lesions: Systematic review and metaanalysis. *United Eur Gastroenterol J.* 2015;3(5):A210.
18. Bang JY, Hawes R, Varadarajulu S. A meta-analysis comparing ProCore and standard fine-needle aspiration needles for endoscopic ultrasound-guided tissue acquisition. *Endoscopy.* 2016;48(4):339-49.
19. Khan MA, Grimm IS, Ali B, Nollan R, Tombazzi C, Ismail MK, et al. A meta-analysis of endoscopic ultrasound-fine-needle aspiration compared to endoscopic ultrasound-fine-needle biopsy: diagnostic yield and the value of onsite cytopathological assessment Review. *Endosc Int Open.* 2017;5(5):E363-E75.
20. Li H, Li W, Zhou QY, Fan B. Fine needle biopsy is superior to fine needle aspiration in endoscopic ultrasound guided sampling of pancreatic masses. *Medicine.* 2018;97(13).
21. Oh HC, Kang H, Lee JY, Choi GJ, Choi JS. Diagnostic accuracy of 22/25-gauge core needle in endoscopic ultrasound-guided sampling: Systematic review and meta-analysis. *Korean J Intern Med.* 2016;31(6):1073-83.
22. Wang J, Zhao S, Chen Y, Jia R, Zhang X. Endoscopic ultrasound guided fine needle aspiration versus endoscopic ultrasound guided fine needle biopsy in sampling pancreatic masses. *Medicine.* 2017;96(28).
23. Iglesias-Garcia J, Dominguez-Munoz JE, Abdulkader I, Larino-Noia J, Eugenyeva E, Lozano-Leon A, et al. Influence of on-site cytopathology evaluation on the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of solid pancreatic masses. *Am J Gastroenterol.* 2011;106(9):1705-10.
24. Kim GH, Cho YK, Kim EY, Kim HK, Cho JW, Lee TH, et al. Comparison of 22-gauge aspiration needle with 22-gauge biopsy needle in endoscopic ultrasonography-guided subepithelial tumor sampling. *Scand J Gastroenterol.* 2014;49(3):347-54.
25. Iwashita T, Nakai Y, Samarasena JB, Park do H, Zhang Z, Gu M, et al. High single-pass diagnostic yield of a new 25-gauge core biopsy needle for EUS-guided FNA biopsy in solid pancreatic lesions. *Gastrointest Endosc.* 2013;77(6):909-15.
26. Larghi A, Iglesias-Garcia J, Poley JW, Monges G, Petrone MC, Rindi G, et al. Feasibility and yield of a novel 22-gauge histology EUS needle in patients with pancreatic masses: a multicenter prospective cohort study. *Surg Endosc.* 2013;27(10):3733-8.
27. Bang JY, Hebert-Magee S, Trevino J, Ramesh J, Varadarajulu S. Randomized trial comparing the 22-gauge aspiration and 22-gauge biopsy needles for EUS-guided sampling of solid pancreatic mass lesions. *Gastrointest Endosc.* 2012;76(2):321-7.
28. Inoue T, Okumura F, Mizushima T, Nishie H, Iwasaki H, Anbe K, et al. Assessment of Factors Affecting the Usefulness and Diagnostic Yield of Core Biopsy Needles with a Side Hole in Endoscopic Ultrasound-Guided Fine-Needle Aspiration. *Gut Liver.* 2016;10(1):51-7.
29. Hucl T, Wee E, Anuradha S, Gupta R, Ramchandani M, Rakesh K, et al. Feasibility and efficiency of a new 22G core needle: A prospective comparison study. *Endoscopy.* 2013;45(10):792-8.

30. Lee BS, Cho CM, Jung MK, Jang JS, Bae HI. Comparison of Histologic Core Portions Acquired from a Core Biopsy Needle and a Conventional Needle in Solid Mass Lesions: A Prospective Randomized Trial. *Gut Liver*. 2017.
31. Cheng B, Zhang Y, Chen Q, Sun B, Deng Z, Shan H, et al. Analysis of Fine-Needle Biopsy Versus Fine-Needle Aspiration in Diagnosis of Pancreatic and Abdominal Masses: A Prospective, Multicenter, Randomized Controlled Trial. *Clin Gastroenterol Hepatol*. 2017.
32. Ooi M, Phan A, Nguyen NQ. Future role of endoscopic ultrasound in personalized management of pancreatic cancer. *Endosc Ultrasound*. 2017;6(5):300-7.
33. Mounzer R, Yen R, Marshall C, Sams S, Mehrotra S, Said MS, et al. Interobserver agreement among cytopathologists in the evaluation of pancreatic endoscopic ultrasound-guided fine needle aspiration cytology specimens. *Endosc Int Open*. 2016;4(7):E812-9.
34. Marshall C, Mounzer R, Hall M, Simon V, Centeno B, Dennis K, et al. Suboptimal Agreement Among Cytopathologists in Diagnosis of Malignancy Based on Endoscopic Ultrasound Needle Aspirates of Solid Pancreatic Lesions: A Validation Study. *Clin Gastroenterol Hepatol*. 2018;16(7):1114-22 e2.
35. Kappelle WFW, Van Leerdam ME, Schwartz MP, Bulbul M, Buikhuisen WA, Brink MA, et al. Rapid on-site evaluation during endoscopic ultrasound-guided fine-needle aspiration of lymph nodes does not increase diagnostic yield: A randomized, multicenter trial. *Am J Gastroenterol*. 2018.
36. van Riet PA, Larghi A, Attili F, Rindi G, Nguyen NQ, Ruzskiewicz A, et al. A multicenter randomized trial comparing a 25-gauge EUS fine-needle aspiration device with a 20-gauge EUS fine-needle biopsy device. *Gastrointest Endosc*. 2018.
37. Keswani RN, Krishnan K, Wani S, Keefer L, Komanduri S. Addition of Endoscopic Ultrasound (EUS)-Guided Fine Needle Aspiration and On-Site Cytology to EUS-Guided Fine Needle Biopsy Increases Procedure Time but Not Diagnostic Accuracy. *Clin Endosc*. 2014;47(3):242-7.
38. Hashimoto S, Taguchi H, Higashi M, Hatanaka K, Fujita T, Iwaya H, et al. Diagnostic efficacy of liquid-based cytology for solid pancreatic lesion samples obtained with endoscopic ultrasound-guided fine needle aspiration: A propensity score-matched analysis. *Dig Endosc*. 2017.