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SPECIAL FEATURE: REVIEW ARTICLE

Cutting edge of EUS-FNA

Endoscopic ultrasound-guided fine-needle aspiration for gastrointestinal subepithelial lesions

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Abstract
Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is the first-choice procedure for obtaining pathological tissue samples from gastrointestinal (GI) subepithelial lesions (SELs). However, its diagnostic accuracy is lower than that for pancreatic masses owing to puncture difficulty and the need for immunostaining for definitive diagnosis. The advent of fine-needle biopsy needles, which have become well known in recent years, improves the diagnostic accuracy of EUS-FNA for GI SELs. The forward-viewing echoendoscope and rapid on-site evaluation (ROSE) have also helped to improve diagnostic accuracy. Furthermore, in facilities where ROSE is not available, endosonographers perform a macroscopic on-site evaluation. With these procedural innovations, EUS-FNA is now performed aggressively even for SELs smaller than 20 mm. The incidence of procedure-related adverse events such as bleeding and infection is low, and thus, EUS-FNA can be safely performed to diagnose SELs.

Keywords Endoscopic ultrasound-guided fine-needle aspiration · Endoscopic ultrasound-guided fine-needle biopsy · Gastrointestinal stromal tumor · Rapid on-site evaluation · Subepithelial lesions

Diagnosis of gastrointestinal subepithelial lesions

Gastrointestinal (GI) subepithelial lesion (SEL) is a general term referring to lesions that develop in the submucosal or muscular layer of the GI tract, with most lesions unexposed on the mucosal surface. However, even if lesions of mucosal origin can be considered an SEL, lesions originating from the lamina propria or muscularis mucosae with normal mucosal epithelium and SEL-like elevations can also be included. Thus, SEL includes gastrointestinal stromal tumors (GISTs), leiomyomas, schwannomas, SEL-like carcinomas, malignant lymphomas, neuroendocrine tumors, ectopic pancreas, lipomas, simple cysts, bronchogenic cysts, lymphangiomas, amyloidosis, and many other diseases [1–7].

Histological evaluation should be performed to diagnose these SELs. However, obtaining tissues from SELs is difficult with conventional endoscopic forceps biopsy, except for the so-called delle lesions with mucosal surface depressions, because these lesions are covered by normal epithelium. Conversely, endoscopic ultrasound (EUS) is useful for SEL imaging because it can infer a diagnosis based on the GI wall layers where the lesion and its internal echo patterns are located. A submucosal lesion with a uniform non-echoic pattern is diagnosed as a cyst or lymphangioma. A submucosal lesion with a uniform hyperechoic pattern is diagnosed as a lipoma. These SELs can be diagnosed using EUS imaging alone. However, SELs with a hypoechoic pattern in the muscular layer include different mesenchymal tumors, such as GISTs, leiomyomas, and schwannomas [1–3]. Moreover, these tumors cannot be differentiated with EUS imaging alone [8]. Since GISTs are malignant and leiomyomas/

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schwannomas are benign tumors, the differential diagnosis of "GIST or not" is important in determining the treatment strategy for SELs with hypoechoic patterns in the muscular layer. SEL-like carcinomas and malignant lymphomas invading from the submucosa to the muscular layer also present a hypoechoic pattern [6]. Therefore, hypoechoic SELs in the submucosal and muscular layers should be pathologically diagnosed using tissue samples (Fig. 1).

SEL tissue sampling methods

Previously, bite-to-bite biopsy (BBB) with forceps was performed to obtain tissue samples from SELs, a simple method of performing multiple biopsies obtained from the same site perpendicularly from the mucosal surface to the deeper layers of SELs. However, Ji et al. reported a low accuracy (38%) and a high bleeding rate (14%) [9]. Facciorusso et al. also performed propensity score matching between BBB and EUS-guided fine-needle aspiration (EUS-FNA) in upper GI and rectal SELs (120 patients in both groups) and found that the specimen collection rate (BBB vs. EUS-FNA, 77.5% vs. 94.1%) and accuracy (BBB vs. EUS-FNA, 67.1% vs. 89.3%) were significantly higher for EUS-FNA, whereas adverse events (BBB vs. EUS-FNA, 30% vs. 6.6%) were significantly lower for EUS-FNA [10].

On the other hand, mucosal incision-assisted biopsy (MIAB) based on endoscopic submucosal dissection (ESD) has been recently performed in East Asia, especially in Japan [11–15]. MIAB is performed by making a mucosal incision and submucosal dissection to expose the SEL, and the tissue is obtained under direct observation using forceps or other instruments. Its accuracy was reported to be 77.8%–100%, whereas some other studies reported it to be ≥ 90% [11, 12, 15, 16]. Especially in small SELs of < 20 mm in diameter, an accuracy of 75%–100% has been reported [16]. However, due to the complexity of the procedure, MIAB is limited to countries and institutions accustomed to ESD.

In 1992, Vilmann et al. used EUS-FNA as a method of performing needle biopsy under real-time EUS observation [17], which has become well known worldwide. EUS-FNA was first mainly indicated for pancreatic masses but later became the standard method of tissue sampling for SELs. Compared to MIAB, EUS-FNA has the advantage of simplicity, except for the need for a dedicated echoendoscope. Therefore, EUS-FNA is the first-choice technique for obtaining pathological findings from SELs.

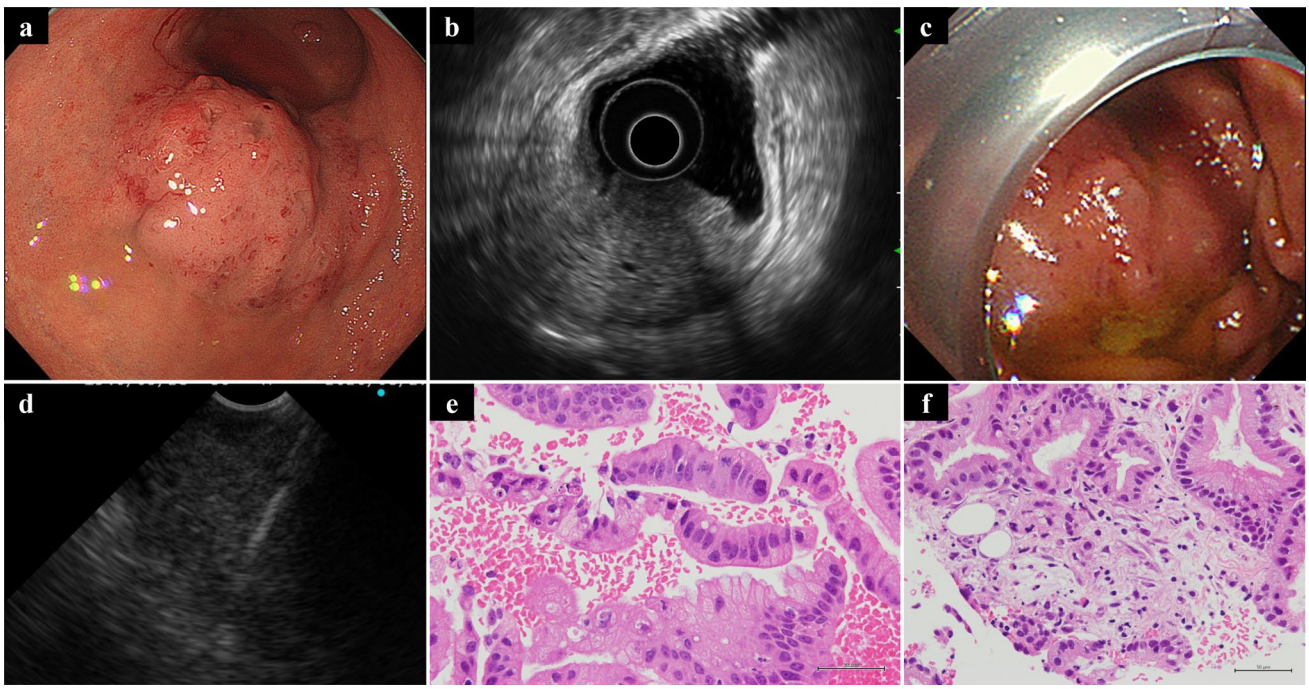

Fig. 1 EUS-FNA of SEL-like gastric cancer. A 3–4 cm mass lesion like an SEL was found in the greater curvature of the middle gastric body. **a** EUS using a radial-type echoendoscope revealed gastric carcinoma that invaded the muscular or serosal layers. **b** However, repeated forceps biopsies from the mucosal side did not yield tumor cells. Therefore, EUS-FNA was performed using a forward-viewing echoendoscope. **c** The puncture was performed using a 22-G fork-tip needle. **e/f** Hematoxylin/eosin staining showed mixed findings of poorly differentiated adenocarcinoma, well-differentiated tubular adenocarcinoma, and papillary adenocarcinoma. The patient was diagnosed with gastric cancer. *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *SEL* subepithelial lesion, *EUS* endoscopic ultrasound

Indications and diagnostic performance of EUS-FNA for SELs

EUS-FNA is indicated for SELs of submucosal or muscular origin that cannot be diagnosed with forceps biopsy [18–20]. However, cysts, lymphangiomas, and lipomas, which can be identified only on EUS images, are excluded. In practice, GISTs should be distinguished from other mesenchymal tumors, and since GISTs more frequently develop in the stomach, EUS-FNA for SELs has been commonly reported in gastric SELs [18]. EUS-FNA of esophageal and duodenal SELs has also been performed; however, the frequency of GISTs is lower than that of gastric SELs. In particular, leiomyoma, a benign tumor, is more commonly observed in esophageal SELs (Fig. 2) [21]. EUS-FNA of colorectal SELs has been performed for local recurrence after rectal cancer surgery, GIST, and ectopic endometriosis of the rectum, although only a few studies reported difficulty of deep insertion of the echoendoscope and the number of indicated lesions was small [22–24].

The accuracy of EUS-FNA for SELs varied from 43.3 to 100% depending on the study [16, 25–43], and the specimen collection rate and accuracy were considered lower than those for pancreatic masses. Most benign diseases such as leiomyoma and ectopic pancreas are diagnosed based on EUS-FNA and follow-up results without resection. In 2016, a meta-analysis reported by Zhang et al. demonstrated a pooled accuracy of 59.9% in 17 articles for EUS-FNA of upper GI SELs [44]. However, these articles were older, published from 2004 to 2014. Therefore, some overlap was found, and only two articles described the results of fine-needle biopsy (FNB) needles, which will be discussed later; five articles described Tru-Cut needle biopsy (TCB) needles [34, 45–48], which are no longer available; and 14 articles described FNA needles. The pooled accuracy for FNA needles was only 56%.

EUS-FNA for SELs has been used to diagnose gastric GISTs, the most common target among SELs, requiring a sufficient number of specimens for immunohistochemical staining. However, unlike pancreatic masses and swollen lymph nodes, obtaining specimens using EUS-FNA for SELs is difficult because the puncture target is within the GI tract wall, the lesion may escape with the wall during puncture, the lesion is hard to puncture, and even if the puncture is possible, moving the needle within the lesion is difficult [3, 20].

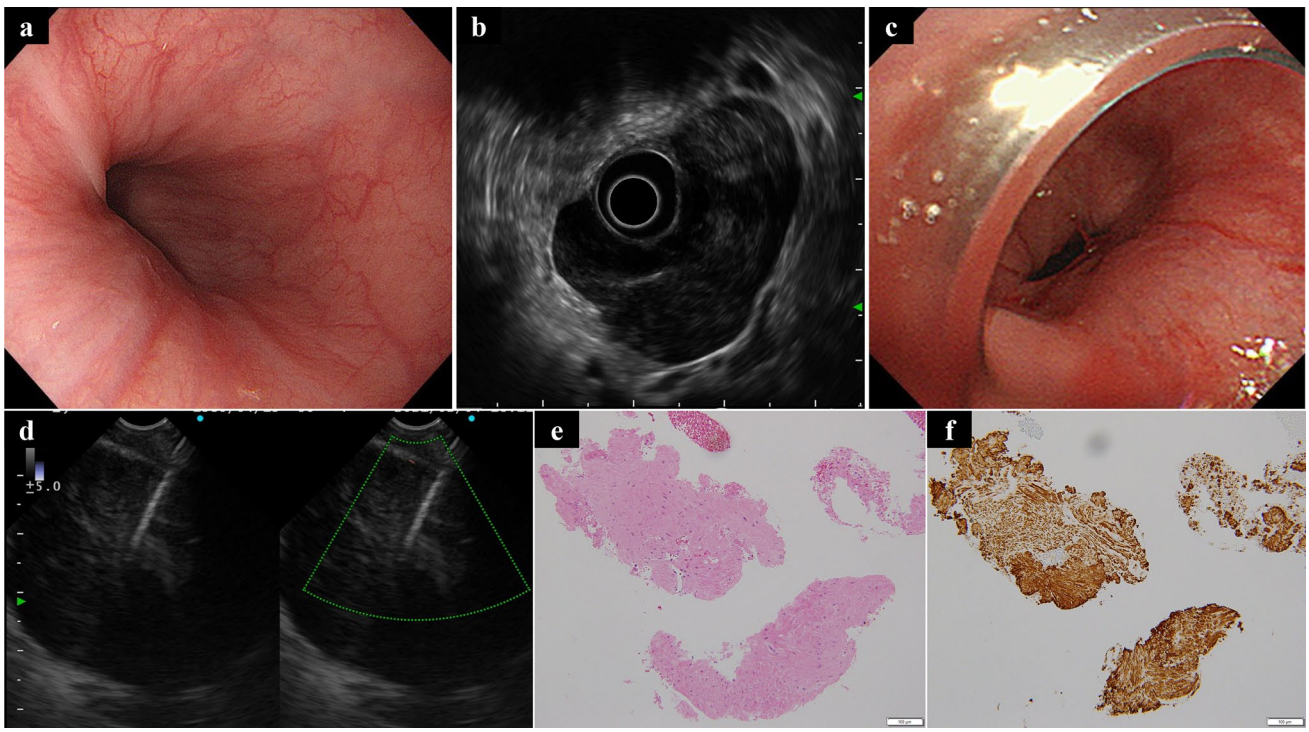

Fig. 2 EUS-FNA of esophageal leiomyoma. **a** The lumen of the lower thoracic esophagus was narrowed by an SEL. **b** EUS with a radial-type echoendoscope showed a hypoechoic mass surrounding the esophagus. **c** EUS-FNA was performed using a forward-viewing echoendoscope. **e** The puncture was performed using a 22-G fork-tip needle. **f** Hematoxylin/eosin staining showed clusters of spindle-shaped cells. **g** Tumor cells were positive for desmin staining; C-kit staining was negative, and a diagnosis of leiomyoma was made. **h** *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *SEL* subepithelial lesion

EUS-guided needle

As an alternative to the FNA needle, the TCB needle was expectedly useful as a puncture needle for obtaining core tissues [34, 45–48]. The TCB needle has the same structure as the needle used for liver biopsy. The inner needle was used to puncture the lesion, and the outer needle was inserted to cut out the lesion. However, use of the TCB needle was terminated in 2011, and it is no longer available due to its thick and rigid 19-G needle and the fact that it can only be used for lesions larger than 3 cm due to its structure.

To collect high-quality and high-quantity specimens, a puncture needle with a more improved shape compared to the conventional FNA needle known as an "FNB needle" is currently used [1, 49–73]. FNB needles include side-fenestrated reverse-bevel-type core trap, Franseen, and fork-tip needles. First, core trap needles with side-fenestrated reverse bevels were developed. Unlike core trap needles, the Franseen and fork-tip needles have an improved tip shape and are referred to as "new FNB needles."

Facciorusso et al. compared FNA and FNB needles for SELs in their meta-analysis [70] and extracted 10 articles [56–65], including six randomized controlled trials from 2014 to 2019. They found that FNB needles consisted of seven reverse-bevel needles, three Franseen needles, and two fork-tip needles. The analysis concluded that the specimen collection rate (FNA vs. FNB, 80.6 vs. 94.9%, odds ratio 2.54) and accuracy (FNA vs. FNB, 65% vs. 87.9%, odds ratio 4.10) of the FNB needle were higher than those of the FNA needle [70]. In addition, a meta-analysis of FNB needles by Tan et al. revealed sufficient results with a specimen collection rate of 98.8% and an accuracy of 85.7% based on 16 articles from 2015 to 2020 [71]. However, among FNB needles, differences in diagnostic performance were observed, and EUS-FNA for SELs using the new FNB needle (such as Franseen and fork-tip needles) has been reported to have a sufficient specimen collection rate of 74–100% and an accuracy of 88–92.3% [1, 66, 67, 72]. In particular, the fork-tip needle has high puncture performance and is expected to provide a smooth puncture of SELs with a sharp sensation similar to that of FNA needles. Takasumi et al. reported a specimen collection rate of 100% and an accuracy of 92.3% for EUS-FNA with a 22-G fork-tip needle in gastric SEL [1]. Yamashita et al. reported that the specimen collection rate with fork-tip needles was higher than that with Franseen needles in SELs of < 2 cm (Franseen vs. fork-tip, 74% vs. 96%) [72]. However, this study used fork-tip needles after using Franseen needles, which may have been related to an improved surgical technique. Moreover, when EUS-FNA is performed using an FNB needle, the 22-G needle is considered the most commonly used. However, Antonin et al. reported that when EUS-FNA of upper GI SELs with a 22-G FNB needle was technically difficult or the specimen was poor, switching to a 25-G FNB needle facilitated the diagnosis in 56.2% of patients [73].

In summary, the FNB needle has a higher specimen collection rate and accuracy than the FNA needle in EUS-FNA for SELs (Table 1). Although the FNA needle seems to have better puncture performance, the FNB needle should be selected for SELs where a puncture with the FNB needle seems feasible. The European Society of Gastrointestinal Endoscopy guidelines strongly recommend the use of the FNB needle for EUS-FNA with SELs of > 20 mm and weakly recommend the use of the FNB needle for SELs of < 20 mm [18].

Technological devices

The type of echoendoscope primarily used in EUS-FNA is a convex-type echoendoscope. However, the conventional type is an oblique-viewing (OV) echoendoscope, which is designed to facilitate puncture of pancreatic masses. Therefore, no problems were encountered in puncturing SELs located in the posterior wall or lesser curvature of the stomach; however, puncturing SELs located in the greater curvature or anterior wall of the stomach was difficult.

In contrast, forward-viewing (FV) echoendoscopes are reportedly useful [74] and have the advantage of allowing puncture with the scope in front of SELs [74–78]. Yamabe et al. developed a method for performing EUS-FNA while aspirating the SEL by attaching a soft hood to the tip of the FV echoendoscope [77]. The lesion could not escape when aspirated into the hood, with a specimen collection rate of 87.5% in eight SELs of ≤ 15 mm (Fig. 3). Moreover, in a prospective, randomized, crossover study of 41 patients, Matsuzaki et al. reported no significant difference in the diagnostic yield (FV vs. OV, 80 vs. 73.3%) and accuracy (FV vs. OV, 77.2 vs. 72.7%) [78]. However, the FV echoendoscope had a larger median tissue sample area and a shorter median procedure time than the OV echoendoscope in patients with GIST. The use of FV echoendoscopes is expected to improve the success rate of SEL puncture from the greater curvature to the anterior wall in the gastric fornix and gastric body and contribute to the diagnostic performance of EUS-FNA. However, the usefulness of FV echoendoscopes for SELs should be validated in a prospective study.

Negative pressure is generally recommended for EUS-FNA specimen collection and is used in two methods: the standard syringe aspiration and the "slow-pull method," in which a stylet is slowly pulled out to apply low negative pressure [79, 80]. The advantage of the slow-pull method is the possibility to collect specimens with few

Table 1 Comparison of EUS-FNA with FNA and FNB needles in gastrointestinal SEL

First author	Year	Study design	Number of cases	Gastric SEL	FNA/FNB	FNB needle	Specimen collection rate (FNA vs FNB)	Accuracy (FNA vs FNB)	Needle pass (FNA vs FNB)
Kim [56]	2014	RCT	22	17	10/12	Reverse-bevel	20% vs 75%	N/A	4 vs 2
Han [57]	2016	Crossover RCT	22	22	22/22	Reverse-bevel	90.9% vs 95.5%	68.2% vs 81.8%	2 vs 1
Lee [58]	2017	RCT	14	9	6/8	Reverse-bevel	N/A	100% vs 100%	N/A
El Chafic [59]	2017	Retrospective	106	76	91/15	Fork-tip	64.8% vs 100%	52.7% vs 86.7%	3 vs 1
Nagula [60]	2018	RCT	18	12	6/12	Reverse-bevel	N/A	83.3% vs 75%	2 vs 2
Iwai [61]	2018	Crossover RCT	23	23	23/23	Reverse-bevel	78.3% vs 95.7%	73.9% vs 91.3%	2 vs 2
Fujita [62]	2018	Retrospective	61	55	44/17	Franseen	75% vs 94.1%	N/A	3 vs 3
Hedenstrom [63]	2018	Crossover RCT	70	52	70/70	Reverse-bevel	N/A	49% vs 83%	N/A
Inoue [64]	2019	Propensity score matching	114	71	57/57	Reverse-bevel, Franseen	63% vs 84%	60% vs 82%	2 vs 2
Bang [65]	2019	Retrospective	218	N/A	132/86	Franseen, fork-tip	74% vs 92%	N/A	2.5 vs 1.8
Trindade [66]	2019	Retrospective	147	115	46/101	Fork-tip	41.3% vs 89.1%	37% vs 89.1%	3.5 vs 3.5
de Moura [67]	2020	Retrospective	229	173	115/114	Franseen, fork-tip, Reverse-bevel	40% vs 69.3%	77.2% vs 88%	3.4 vs 2.9
Kuraoka [68]	2021	Retrospective	33	25	18/15	Franseen	N/A	100% vs 100%	2.5 vs 2
Nagai [69]	2021	Retrospective	150	125	64/86	Franseen	75% vs 85%	N/A	3 vs 2
Takasumi [1]	2021	Retrospective	79	79	66/13	Fork-tip	90.9% vs 100%	81.8% vs 92.3%	5 vs 5
Sekine [55]	2022	Retrospective	62	49	31/31	Franseen, Reverse-bevel	N/A	74.2% vs 87.1%	N/A

* "Accuracy" is referred to as "diagnostic rate" or "diagnostic yield" depending on the article, and may include cases that have not undergone resection and for which the final diagnosis is estimated based on follow-up

SEL subepithelial lesion, *FNA* fine-needle aspiration, *FNB* fine-needle biopsy, *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *RCT* randomized controlled trial, *N/A* not available

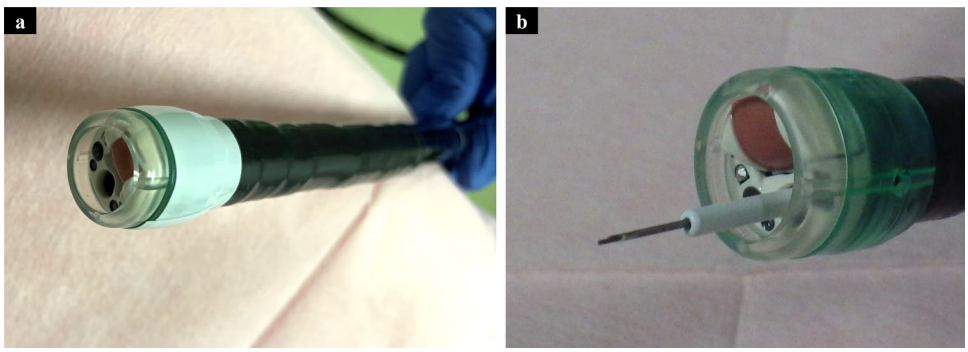

Fig. 3 A forward-viewing echoendoscope. **a** transparent hood made of polyvinyl chloride was attached to the tip of the scope for puncture while aspirating the mucosal surface of the lesion. **b** This figure shows the insertion of the FNA needle into the forceps channel of a forward-viewing echoendoscope. *FNA* fine-needle aspiration

blood components even in lesions with high blood flow. In particular, combining the FNB needle and the slow-pull method is expectedly useful. Lee et al. reported no difference in accuracy (standard vs. slow-pull, 81.5 vs. 83.3%) and volume of specimens collected between the standard suction and slow-pull methods in EUS-FNA of SELs using the FNB needle [81]. The results showed no difference in the number of specimens collected between the standard and slow-pull methods.

However, SELs may be hard and sometimes require slightly higher negative pressure. The "wet suction method," defined as the concept of maintaining negative pressure aspirated with a syringe to the lesion by filling the puncture needle with saline solution, is reportedly useful mainly in diagnosing pancreatic lesions using EUS-FNA [82–85]. This method is also expectedly useful for specimen collection in EUS-FNA of SELs. Pita et al. reported that EUS-FNA was performed in 87 SELs using the wet method, which could be performed up to immunostaining in 81% of the patients [86]. Takasumi et al. conducted a prospective, randomized, crossover study comparing the cellularity of specimens from upper GI SELs collected via conventional aspiration and wet suction, but they failed to demonstrate the superiority of the wet suction method [2]. The percentage of moderate-to-high cellularity tissues was higher with conventional aspiration than with the wet suction method (conventional vs. wet, 77 vs. 61.5%). However, FNA needles were used in this study.

EUS-FNA of colorectal SELs can be performed, but inserting an echoendoscope into the deep colon is difficult. However, EUS-FNA has been successfully used for deep colorectal lesions by inserting an OV echoendoscope with an overtube and a guidewire [22, 23] or a novel FV echoendoscope with a guidewire [87, 88].

EUS-FNA for SELs smaller than 20 mm

In the case of SELs, the stomach is the most important target organ for EUS-FNA due to the highest incidence of GISTs. Because most gastric SELs of < 20 mm are considered benign or low malignancy, and because collecting specimens via EUS-FNA is technically difficult, EUS-FNA has been recommended for gastric SELs of > 20 mm.

However, metastatic cases of gastric GISTs of < 20 mm have been reported [89–91], and the Japanese guidelines 4th edition for the treatment of GISTs in 2022 weakly recommend surgery for gastric GISTs of < 20 mm [92]. Therefore, considering that a hypoechoic SEL of gastric muscular origin without delle cannot be diagnosed, endoscopic tissue sampling is necessary for the diagnosis; even if the SEL is < 20 mm, surgical resection is performed if EUS-FNA results show a malignant tumor such as a GIST. Conversely, if the SEL is diagnosed as a benign tumor such as a leiomyoma or schwannoma, the patient can be followed up without unnecessary treatment. Surgical resection of GISTs does not require lymph node dissection, and diagnosis of GISTs at a small size allows for a reduction of the lesion size.

The accuracy of EUS-FNA for SELs of < 20 mm varied from 45 to 80%, including reports of FNB needles (Table 2) [25, 26, 33, 36, 37, 41, 42, 55, 61–64, 69, 86]. Among these articles, Akahoshi et al. [26] reported the largest number of cases in their study of 90 cases; however, the specimen collection rate was 62.2%, which was insufficient. This article was published in 2014, and only FNA needles were used. They noted that even in cases of inadequate specimen collection at the first EUS-FNA, the total specimen collection rate improved to 73.3% by repeating the EUS-FNA. In a retrospective study by Inoue et al., the accuracy after propensity score matching was significantly lower for SELs of ≤ 20 mm (≤ 20 vs. > 20 mm, 66.7% vs. 96.7%) [61]. In our study, the specimen collection rates for 140 gastric SELs that underwent EUS-FNA were 80% (28/35), 94.9% (94/99), and 100% (6/6) for specimens of < 20 mm, 20–49 mm, and ≥ 50 mm, respectively, i.e., it was lower for specimens of < 20 mm. Specimens were collected in 80% of patients with an SEL of < 20 mm and 85.7% (24/28) of patients with an SEL of 15–19 mm [93].

In a comparison of FNA and FNB needles for SELs of < 20 mm, Sekine et al. found no difference in accuracy at > 20 mm (FNA vs. FNB, 75% vs. 77.8%), but at < 20 mm, the accuracy of FNB needles was significantly higher (FNA vs. FNB, 72.7% vs. 100%) [55]. Nagai et al. also found that the specimen collection rate was significantly higher with the FNB needle when used as the historical control in SELs of ≤ 20 mm (FNA vs. FNB, 45.4% vs. 81.1%) [69]. The specimen collection rate was also higher with the FNB needle for SELs of ≤ 15 mm (FNA vs. FNB, 38.5% vs. 94.1%).

In summary, the specimen collection rate and accuracy of EUS-FNA for SELs of < 20 mm are insufficient; however, once a diagnosis is obtained, EUS-FNA is useful for determining the treatment strategy (Fig. 4). The specimen collection rate and accuracy of EUS-FNA for SELs of < 20 mm are expected to improve with use of new FNB needles, FV echoendoscopes, and other techniques.

Sample handling during on-site evaluation

Rapid on-site evaluation (ROSE) is a method to determine whether an evaluable specimen has been collected and to decide whether to terminate the puncture or perform an additional puncture during EUS-FNA (Fig. 5) [94, 95]. Several meta-analyses have shown that EUS-FNA with ROSE helps to improve the specimen collection rate and accuracy for pancreatic lesions [96–98], and the usefulness of EUS-FNA in SELs has also been reported [1, 99]. However, in real clinical practice, cytologists and cytology technologists in some facilities experience difficulties performing EUS-FNA, and endoscopists use these methods for performing ROSE [95, 100, 101]. Further, several methods of specimen confirmation performed by endoscopists, including macroscopic on-site evaluation (MOSE) [102–104], stereomicroscopic on-site evaluation (SOSE) [105–109], and visual on-site evaluation (VOSE) [110], have been reported. MOSE is a method to evaluate

Table 2 EUS-FNA for SELs < 20 mm or ≤ 20 mm

First author	Year	Study design	Number of cases	Location	Needle	Sample collection rate	Accuracy*
Sepe [33]	2009	Retrospective	37 (< 20mm vs 20-100mm vs > 100mm; 5 vs 28 vs 4))	Sto 32, Duo 3, Eso 1, Rec 1	FNA	N/A	< 20mm vs 20-100mm vs > 100mm; 80% vs 89.3% vs 0%
Suzuki [36]	2011	Retrospective	47 (< 20mm vs ≥ 20mm; 5 vs 42)	Sto 47	FNA	N/A	< 20mm vs ≥ 20mm; 80% vs 69%
Watson [41]	2011	Retrospective	66 (< 20mm vs ≥ 20mm; 22 vs 44)	Sto 55, Eso 7, Duo 4	FNA	N/A	< 20mm vs ≥ 20mm; 45% vs 80%
Akahoshi [26]	2014	Retrospective	90 (< 20mm)	Sto 90	FNA	62.20%	N/A
Sekine [25]	2015	Retrospective	67 (< 20mm vs ≥ 20mm; 19 vs 48)	N/A	FNA	< 20mm vs ≥ 20mm; 100% vs 100%	GIST < 20mm; sensitivity 82.9%, PPV 100%
Attila [37]	2018	Retrospective	22 (< 20mm vs > 20mm; 10 vs 12)	Sto 12, Eso 6, Duo 4	FNA	N/A	< 20mm vs > 20mm; 50% vs 91.6%
Lopes [42]	2018	Retrospective	89 (≤ 20mm vs > 20mm; 58 vs 34), 19G/22G (75/17)	Sto 89	FNA	19G (≤20mm vs > 20mm; 90.7% vs 93.7%), 22G N/A	N/A
Iwai [61]	2018	Crossover RCT	23 (≤ 20mm vs > 20mm; 6 vs 17)	Sto 23	FNA/FNB	N/A	FNA (≤ 20mm vs > 20mm; 83.3% vs 70.6%), FNB (≤ 20mm vs > 20mm; 83.3% vs 94.1%)
Fujita [62]	2018	Retrospective	61 (< 20mm vs ≥ 20mm; 20 vs 41)	Sto 55, Eso 5, Rec 1	FNA/FNB	FNA (< 20mm vs ≥20mm; 60% vs 82.8%), FNB (< 20mm vs ≥20mm; 100% vs 91.7%)	N/A
Hedenström [63]	2018	Crossover RCT	65 (≤ 20mm vs > 20mm; 14 vs 51)	Sto 52, Duo 7, Eso 6	FNA/FNB	N/A	Sensitivity; FNA (≤ 20mm vs > 20mm; 57% vs 45%), FNB (≤ 20mm vs > 20mm; 86% vs 82%)
Inoue [64]	2019	Retrospective	57 (≤ 20mm vs > 20mm; 27 vs 30)	Sto 38, Eso 11, Duo 4, Rec 4	FNA/FNB	N/A	≤ 20mm vs > 20mm; 66.7% vs 96.7%
Nagai [69]	2021	Retrospective	70 (≤ 20mm); 30 (≤ 15mm)	N/A	FNA/FNB	FNA (≤ 20mm; 45%, ≤ 15mm; 38%), FNB (≤ 20mm; 81%, ≤ 15mm; 94%)	N/A
Pita [86]	2021	Retrospective	87 (≤ 20mm vs > 20mm; 34 vs 53)	55	FNA	≤ 20mm vs > 20mm; 77% vs 91%	N/A
Sekine [55]	2022	Retrospective	62 (< 20mm vs ≥ 20mm; 24 vs38)	Sto 49, Duo 8, Eso 1, Rec 4	FNA/FNB	N/A	FNA (< 20mm vs ≥ 20mm; 72.7% vs 100%), FNB (< 20mm vs ≥ 20mm; 75% vs 77.7%)

* "Accuracy" is referred to as "diagnostic rate" or "diagnostic yield" depending on the article, and may include cases that have not undergone resection and for which the final diagnosis is estimated based on follow-up

Sto stomach, *Eso* esophagus, *Duo* duodenum, *Rec* rectum, *PPV* positive predictive rate, *N/A* not available

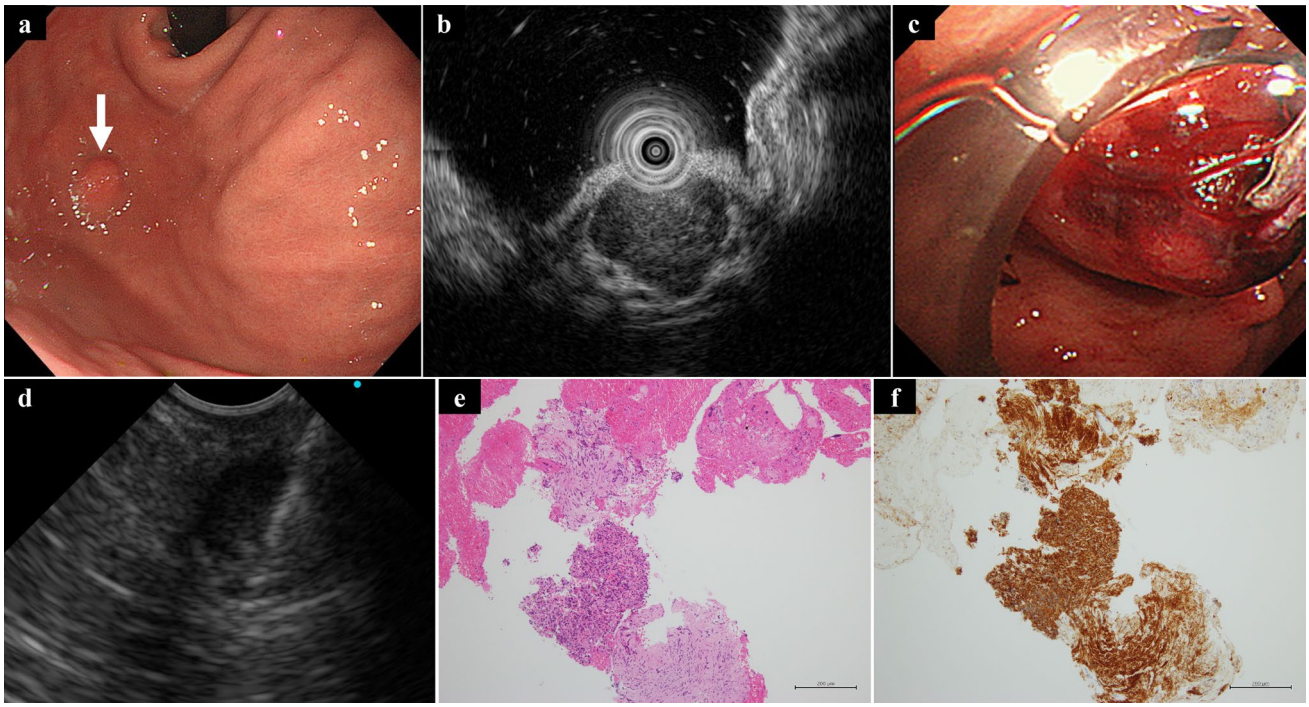

Fig. 4 EUS-FNA of a small gastric GIST. **a** small SEL was detected in the gastric fornix (white arrow). **b** EUS using an ultrasound probe revealed an 11-mm-sized hypoechoic lesion in the muscularis propria. **c** A forward-viewing echoendoscope with a transparent hood made of polyvinyl chloride was inserted at the tip of the scope. **d** The puncture was performed using a 22-G fork-tip needle. **e** Hematoxylin/eosin staining showed clusters of spindle-shaped cells. **f** C-kit staining was positive for tumor cells, and a diagnosis of GIST was made. *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *GIST* gastrointestinal stromal tumor

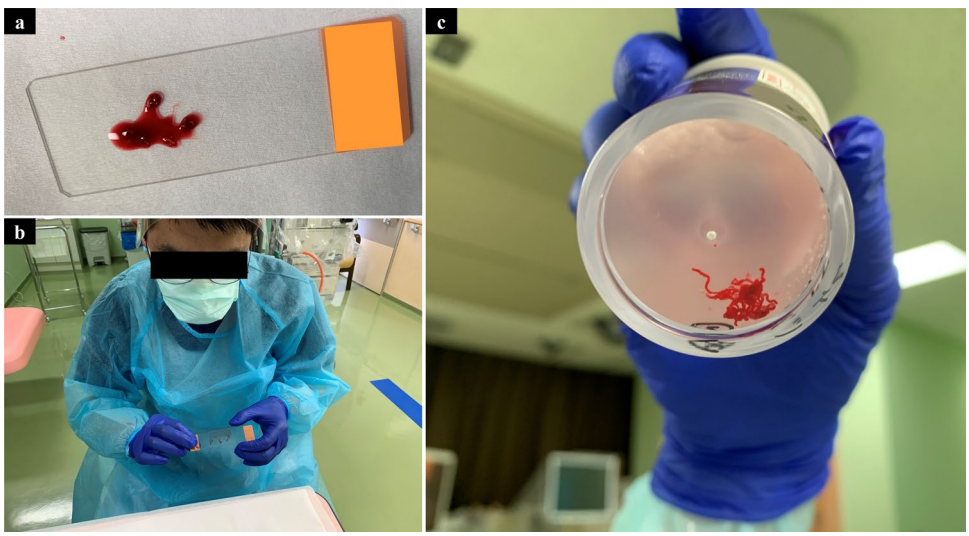

Fig. 5 Specimen handling in EUS-FNA of SELs. **a** The specimen collected using an FNA or FNB needle was extruded onto a glass slide using a stylet. **b** The specimens were divided into two groups: one for cytology and the other for histology. One specimen for cytology was fixed dry and ROSE stained with Cyto-quick stain, and the other specimen was fixed wet and Papanicolaou stained. **c** The specimen for histological examination was placed in a formalin bottle. *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *SEL* subepithelial lesion, *FNA* fine-needle aspiration, *FNB* fine-needle biopsy; ROSE, rapid on-site evaluation

the macroscopically visible core (MVC), a white, elongated portion of a specimen extruded on a glass slide. VOSE is a method used to confirm MVC by directly placing the specimen in a formalin solution, whereas SOSE is a method used to perform MOSE under a stereomicroscope.

Conversely, the significance of ROSE may differ in EUS-FNA with the FNB needle because obtaining a proper specimen is easier than with the FNA needle. The diagnostic performance of the FNB needle is reportedly higher than that of the FNA needle used with ROSE, even without ROSE [111]. In a meta-analysis of SEL by Facciorusso et al., no difference in the specimen collection rate was observed between FNA and FNB needles in EUS-FNA with ROSE (odds ratio, 1.60); however, the FNB needle was superior to the FNA needle in terms of the specimen collection rate without ROSE (odds ratio, 9.85) [70]. Therefore, the FNB needle provides sufficient diagnostic performance for SEL without ROSE. Regarding the number of punctures for SELs, Suzuki et al. [112] reported that 2–3 punctures are recommended for EUS-FNA using the FNB needle without ROSE, depending on the lesion location and needle type.

In the case of EUS-FNA with the FNA needle, ROSE contributes to the improvement of diagnostic performance; whereas with the FNB needle, ROSE has a slight additional effect on diagnostic performance because of excellent original specimen collection. However, Han et al. reported that the FNB needle for SELs with ROSE provided adequate specimens in a single puncture [57]. Therefore, the significance of ROSE in EUS-FNA of SEL cannot be denied, and the combined use of the FNB needle and ROSE can effectively reduce the number of punctures and yield a sufficient specimen. In particular, ROSE for SELs can be used to successfully confirm the presence or absence of spindle-shaped cells, suggesting that mesenchymal tumors should be immunostained.

The evidence for MOSE, SOSE, and VOSE as on-site evaluations other than ROSE is insufficient. However, a meta-analysis by Mohan et al. in 2022 (including pancreatic masses and lymph nodes in addition to SELs) revealed that EUS-FNA with MOSE combined with a new FNB, Franseen, and fork-tip needle showed a sufficient specimen collection rate [104]. The specimen collection rate and accuracy were 94.7% and 90.6%, respectively.

Other specimen handling techniques include the cell block method reported for EUS-FNA in SELs [86, 113].

Adverse events

Although performing EUS-FNA for SELs is considered safe, potential adverse events associated with the procedure include bleeding, perforation, and infection. In a meta-analysis of upper GI SELs, three serious adverse events (0.3%) occurred after performing 978 EUS-FNAs, including FNB and TCB needles [44]. All these adverse events occurred in patients in whom 19-G needles were used: two patients had sepsis [48] and one died due to multiple organ failure after complications caused by FNA of a large centrally necrotic GIST [43]. Regarding GIST, Takasumi et al. reported a case of intratumoral infection in a patient with a GIST who underwent EUS-FNA with a 22-G fork-tip needle for gastric SELs, which conservatively improved with oral antimicrobial administration (Fig. 6) [1]. As for infections, EUS-FNA of cysts is problematic because of post-puncture infection within the cyst, and care should be taken when performing EUS-FNA of bronchogenic cysts, which may be difficult to diagnose on EUS imaging [4]. Therefore, EUS-FNA of

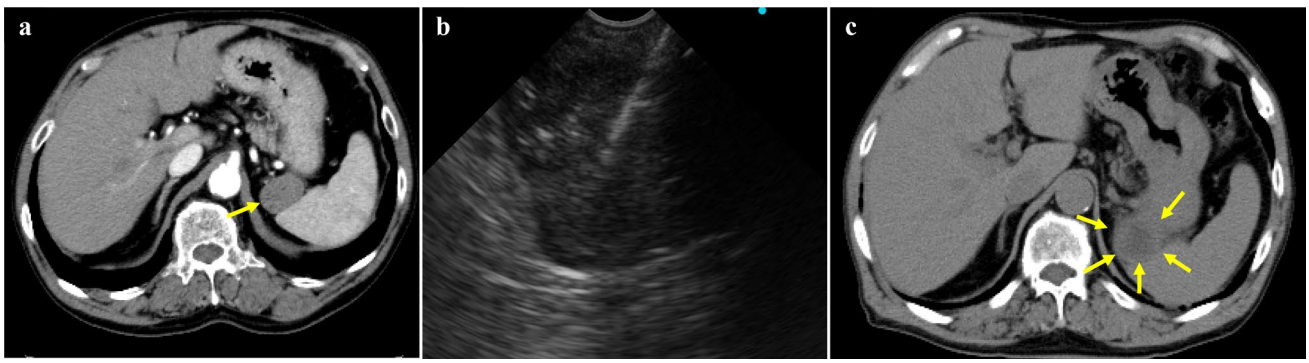

Fig. 6 Intratumoral infection after EUS-FNA. **a** Contrast-enhanced CT before EUS-FNA shows an SEL of the extragastric wall development type (yellow arrow). **b** EUS-FNA was performed using a 22-G fork-tip needle using a forward-viewing echoendoscope, and a diagnosis of GIST was made. **c** The patient had abdominal pain and fever after EUS-FNA, and CT showed hypoabsorption inside the tumor and increased fatty tissue density surrounding the tumor (yellow arrow). A diagnosis of intratumor infection or abscess formation was made. *EUS-FNA* endoscopic ultrasound-guided fine-needle aspiration, *CT* computed tomography, *SEL* subepithelial lesion, *GIST* gastrointestinal stromal tumor

cysts in the GI wall should not be performed without drainage of cyst contents. In addition, EUS-FNA of colonic SELs should be performed after colonic lavage even if the cyst is not a cyst. Levy et al. reported that adverse events occurred in 20.5% of 502 patients who underwent EUS-FNA through the colon wall, including lesions other than SELs, with pain, bleeding, and infection as the most common events [114].

Regarding bleeding after EUS-FNA, among 1,135 EUS-FNA cases of SELs based on the Japanese Diagnosis Procedure Combination database, five (0.4%) of them had severe bleeding requiring blood transfusion or endoscopic treatment [115]. Among the 908 EUS-FNA cases, including 56 SEL cases, 114 were on antithrombotic drugs, and Polmanee et al. reported four cases (3.5%) of post-EUS-FNA bleeding in patients on antithrombotic drugs [116]. Of the four cases, two continued to take antithrombotic agents, one had heparin replacement, and one was off antithrombotic agents when EUS-FNA was performed. However, none of the patients had serious bleeding. Inoue et al. reported that in 742 patients who underwent EUS-FNA, including 129 SELs, 131 (17.7%) were on antithrombotic drugs; however, only one patient with SEL-like gastric cancer had intraoperative bleeding and no postoperative bleeding [117].

Furthermore, there are no reports of tumor seeding after EUS-FNA for SELs. Therefore, EUS-FNA for SELs can be performed safely; however, large blood vessels in the puncture route and puncturing through the GI tract wall should be avoided.

Conclusion

EUS-FNA has become the first choice for obtaining pathological tissue samples from GI SELs. With the advent of FNB needles, its diagnostic accuracy for GI SELs is improving. Furthermore, an FV echoendoscope and ROSE have also helped improve diagnostic accuracy. Therefore, EUS-FNA is currently performed aggressively even for SELs of < 20 mm. However, the difference between using EUS-FNA and MIAB should be discussed in the future.

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Author contributions Conceptualization: TH. Methodology: TH Formal Analysis: TH, MH, JN. Investigation: TY and TK. Data Curation: TH. Writing—original draft preparation: TH. Writing—review and editing: MH, TY, TK, JN project administration: TH.

Data availability Data are available upon request due to restrictions, for example, privacy or ethical considerations.

Declarations

Conflict of interest Takuto Hikichi, Minami Hashimoto, Takumi Yanagita, Tsunetaka Kato, and Jun Nakamura declare that there are no conflicts of interest.

Ethical approval This is a review article based on the previously reported literature. However, regarding EUS-FNA performed at our institution, all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all EUS-FNA patients.

References

1. Takasumi M, Hikichi T, Hashimoto M, et al. Usefulness of a forktip needle in endoscopic ultrasound-guided fine-needle biopsy for gastric subepithelial lesions. Diagnostics. 2021;11:1883.
2. Takasumi M, Hikichi T, Hashimoto M, et al. A pilot randomized crossover trial of wet suction and conventional techniques of endoscopic ultrasound-guided fine-needle aspiration for upper gastrointestinal subepithelial lesions. Gastroenterol Res Pract. 2021;2021:4913107.
3. Takasumi M, Hikichi T, Takagi T, et al. Efficacy of endoscopic ultrasound-guided fine-needle aspiration for schwannoma: six cases of a retrospective study. Fukushima J Med Sci. 2017;63:75–80.
4. Sato M, Irisawa A, Bhutani MS, et al. Gastric bronchogenic cyst diagnosed by endosonographically guided fine needle aspiration biopsy. J Clin Ultrasound. 2008;36:237–9.
5. Hashimoto C, Hikichi T, Hashimoto M, et al. Localized gastric amyloidosis diagnosed by endoscopic ultrasound-guided fine-needle aspiration. Clin J Gastroenterol. 2021;14:1036–41.
6. Yanagita T, Hikichi T, Nakamura J, et al. Gastric carcinoma with lymphoid stroma diagnosed by endoscopic ultrasound–guided fine-needle aspiration. Clin J Gastroenterol. 2021;14:471–7.
7. Watanabe K, Irisawa A, Hikichi T, et al. Acute inflammation occurring in gastric aberrant pancreas followed up by endoscopic ultrasonography. World J Gastrointest Endosc. 2012;4:331–4.
8. Lim TW, Choi CW, Kang DH, et al. Endoscopic ultrasound without tissue acquisition has poor accuracy for diagnosing gastric subepithelial tumors. Medicine. 2016;95: e5246.
9. Ji JS, Lee BI, Choi KY, et al. Diagnostic yield of tissue sampling using a bite-on-bite technique for incidental subepithelial lesions. Korean J Intern Med. 2009;24:101–5.
10. Faccirusso A, Crino SF, Rabai D, et al. Comparison between endoscopic ultrasound-guided fine-needle biopsy and bite-on-bite jumbo biopsy for sampling of subepithelial lesions. Dig Liver Dis. 2022;654:676–83.
11. Minoda Y, Chinen T, Osoegawa T, et al. Superiority of mucosal incision-assisted biopsy over ultrasound-guided fine needle aspiration biopsy in diagnosing small gastric subepithelial lesions: a propensity score matching analysis. BMC Gastroenterol. 2020;20:19.
12. Osoegawa T, Minoda Y, Ihara E, et al. Mucosal incision-assisted biopsy versus endoscopic ultrasound-guided fine-needle aspiration with a rapid on-site evaluation for gastric subepithelial lesions: a randomized cross-over study. Dig Endosc. 2019;13:413–21.
13. Kobara H, Mori H, Fujiwara S, et al. Bloc biopsy by tunneling method using endoscopic submucosal dissection for an upper gastrointestinal submucosal tumor. Endoscopy. 2012;44:E197–8.

14. Kobara H, Mori H, Fujiwara S, et al. Bloc biopsy by using submucosal endoscopy with a mucosal flap method for gastric subepithelial tumor tissue sampling (with video). Gastrointest Endosc. 2013;77:141–5.
15. Kobara H, Mori H, Nishiyama N, et al. Comparison of submucosal tunneling biopsy versus EUS-guided FNA for gastric subepithelial lesions: a prospective study with gastric crossover design. Endosc Int Open. 2017;5:E695-705.
16. Furukawa K, Nakamura M, Kawashima H. Tissue sampling methods for gastric subepithelial tumors. Gastroenterol Endosc. 2023;65:214–28.
17. Vilmann P, Jacobsen GK, Henriksen FW, et al. Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. Gastrointest Endosc. 1992;38:172–3.
18. Deprez PH, Moons LMG, O'Toole D, et al. Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2022;54:412–29.
19. Dumonceau JM, Polkowski M, Larghj A, et al. Indication, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy. 2011;43:897–909.
20. Goto O, Kaise M, Iwakiri K. Advancements in the diagnosis of gastric subepithelial tumors. Gut Liver. 2022;16:321–30.
21. Kang S, Kim DH, Kim Y, et al. Natural history of asymptomatic esophageal subepithelial tumors of 30 mm or less in size. J Korean Med Sci. 2022;37:e184.
22. Sasaki Y, Niwa Y, Hirooka Y, et al. The use of endoscopic ultrasound-guided fine-needle aspiration for investigation of submucosal and extrinsic masses of the colon and rectum. Endoscopu. 2005;37:154–60.
23. Cheng S, Tatuguma SE, de Oliveira GHP, et al. Colonoscopic ultrasound-guided fine-needle aspiration using a curvilinear array transducer: a single-center retrospective cohort study. Dis Colon Rectum. 2022;65:e80–4.
24. Fenandez-Esparrach G, Alberghina N, Subtil JC, et al. Endoscopic ultrasound-guided fine needle aspiration is highly accurate for the diagnosis of perirectal recurrence of colorectal cancer. Dis Colon Rectum. 2015;58:469–73.
25. Sekine M, Imaoka H, Mizuno N, et al. Clinical course of gastrointestinal stromal tumor diagnosed by endoscopic ultrasound-guided fine-needle aspiration. Dig Endosc. 2015;27:44–52.
26. Akahoshi K, Oya M, Koga T, et al. Clinical usefulness of endoscopic ultrasound-guided fine needle aspiration for gastric subepithelial lesions smaller than 2 cm. J Gastrointestin Liver Dis. 2014;23:405–12.
27. Kida M, Araki M, Miyazawa S, et al. Comparison of diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration with 22- and 25-gauge needles in the same patients. J Interv Gastroenterol. 2011;1:102–7.
28. Mekky M, Yamao K, Sawaki A, et al. Diagnostic utility of EUS-guided FNA in patients with gastric submucosal tumors. Gastrointest Endosc. 2010;71:913–9.
29. Kim DH, Park CH, Park SY, et al. Diagnostic yields of endoscopic ultrasound-guided fine-needle tissue acquisition according to the gastric location. Medicine. 2021;100:e26477.
30. Kawahara W, Ewaz A, Chang KHF, et al. Efficacy of endoscopic ultrasound-guided fine-needle aspiration and core needle biopsy in the diagnosis of upper gastrointestinal submucosal lesions. J Am Soc Cytopathol. 2017;6:254–64.
31. Turhan N, Aydog G, Ozin Y, et al. Endoscopic ultrasonography-guided fine-needle aspiration for diagnosing upper gastrointestinal submucosal lesions: a prospective study of 50 cases. Diagn Cytopathol. 2011;39:808–17.
32. Chatzipantelis P, Salla C, Karoumpalis I, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy in the diagnosis of gastrointestinal stromal tumors of the stomach. A study of 17 cases. J Gastrointestin Liver Dis. 2008;17:15–20.
33. Sepe PS, Moparty B, Pitman MB, et al. EUS-guided FNA for the diagnosis of GI stromal cell tumors: sensitivity and cytologic yield. Gastrointest Endosc. 2009;70:254–61.
34. Hoda KM, Rodriguez SA, Faigel DO. EUS-guided sampling of suspected GI stromal tumors. Gastrointest Endosc. 2009;69:1218–23.
35. Rong L, Kida M, Yamauchi H, et al. Factors affecting the diagnostic accuracy of endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) for upper gastrointestinal submucosal or extraluminal solid mass lesions. Dig Endosc. 2012;24:358–63.
36. Suzuki T, Arai M, Matsumura T, et al. Factors associated with inadequate tissue yield in EUS-FNA for gastric SMT. ISRN Gastroenterol. 2011;2011:619128.
37. Attila T, Aydın Ö. Lesion size determines diagnostic yield of EUS-FNA with onsite cytopathologic evaluation for upper gastrointestinal subepithelial lesions. Turk J Gastroenterol. 2018;29:436–41.
38. Akahoshi K, Sumida Y, Matsui N, et al. Preoperative diagnosis of gastrointestinal stromal tumor by endoscopic ultrasound-guided fine needle aspiration. World J Gastroenterol. 2007;13:2077–82.
39. Okasha HH, Naguib M, El Nady M, et al. Role of endoscopic ultrasound and endoscopic-ultrasound-guided fine-needle aspiration in endoscopic biopsy negative gastrointestinal lesions. Endosc Ultrasound. 2017;6:156–61.
40. Ando N, Goto H, Niwa Y, et al. The diagnosis of GI stromal tumors with EUS-guided fine needle aspiration with immunohistochemical analysis. Gastrointest Endosc. 2002;55:37–43.
41. Watson RR, Binmoeller KF, Hamerski CM, et al. Yield and performance characteristics of endoscopic ultrasound-guided fine needle aspiration for diagnosing upper GI tract stromal tumors. Dig Dis Sci. 2011;56:1757–62.
42. Lopes CV, Hartmann AA, de Almeida Artifan EL. EUS-FNA with 19 or 22 gauges needles for gastric subepithelial lesions of the muscle layer. Arq Bras Cir Dig. 2018;31:e1350.
43. Eckardt AJ, Adler A, Gomes EM, et al. Endosonographic large-bore biopsy of gastric subepithelial tumors: a prospective multicenter study. Eur J Gastrotenterol Hepatol. 2012;24:1135–44.
44. Zhang XC, Li QL, Yu YF, et al. Diagnostic efficacy of endoscopic ultrasound-guided needle sampling for upper gastrointestinal subepithelial lesions: a meta-analysis. Surg Endosc. 2016;30:2431–41.
45. Fernandez-Esparrach G, Sendino O, Sole M, et al. Endoscopic ultrasound-guided fine-needle aspiration and trucut biopsy in the diagnosis of gastric stromal tumors: a randomized crossover study. Endoscopy. 2010;42:292–9.
46. Lee JH, Choi KD, Kim MY, et al. Clinical impact of EUS-guided Trucut biopsy results on decision making for patients with gastric subepithelial tumors ≥ 2 cm in diameter. Gastrointest Endosc. 2011;74:1010–8.
47. DeWitt J, Emerson RE, Sherman S, et al. Endoscopic ultrasound-guided Trucut biopsy of gastrointestinal mesenchymal tumor. Surg Endosc. 2011;25:2192–202.
48. Polkowski M, Gerke W, Jarosz D, et al. Diagnostic yield and safety of endoscopic ultrasound-guided trucut [corrected] biopsy in patients with gastric submucosal tumors: a prospective study. Endoscopy. 2009;41:329–34.
49. Joo DC, Kim GH, Lee MW, et al. Diagnostic performance of endoscopic ultrasonography-guided fine-needle biopsy in upper gastrointestinal subepithelial tumors measuring 2–5 cm in size. Surg Endosc. 2022;36:8060–6.

50. Kim GH, Ahn JY, Gong CS, et al. Efficacy of endoscopic ultrasound-guided fine-needle biopsy in gastric subepithelial tumors located in the Cardia. Dig Dis Sci. 2020;65:583–90.
51. Antonini F, Delconte G, Fuccio L, et al. EUS-guided tissue sampling with a 20-gauge core biopsy needle for the characterization of gastrointestinal subepithelial lesions: a multicenter study. Endosc Ultrasound. 2019;8:105–10.
52. Lee M, Min BH, Lee H, et al. Feasibility and diagnostic yield of endoscopic ultrasonography-guided fine needle biopsy with a new core biopsy needle device in patients with gastric subepithelial tumors. Medicine. 2015;94:e1622.
53. Kim DH, Kim GH, Cho CM, et al. Feasibility of a 20-gauge ProCore needle in EUS-guided subepithelial tumor sampling: a prospective multicenter study. BMC Gastrotenterol. 2018;18:151.
54. Kamata K, Kurita A, Yasukawa S, et al. Utility of a 20G needle with a core trap in EUS-guided fine-needle biopsy for gastric submucosal tumors: a multicentric prospective trial. Endosc Ultrasound. 2021;10:134–40.
55. Sekine M, Miura T, Fujiwara J, et al. Utility of endoscopic ultrasonography-guided fine-needle biopsy (EUS-FNB) for diagnosing small subepithelial lesions (< 20 mm). J Ultrasound. 2022;25:35–40.
56. Kim GH, Cho YK, Kim EY, et al. Comparison of 22-gauge aspiration needle with 22-gauge biopsy needle in endoscopic ultrasonography-guided subepithelial tumor sampling. Scand J Gastroenterol. 2014;49:347–54.
57. Han JP, Lee TH, Hong SJ, et al. EUS-guided FNA and FNB after on-site cytological evaluation in gastric subepithelial tumors. J Dig Dis. 2016;17:582–7.
58. Lee BS, Cho CM, Jung MK, et al. 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;11:559–66.
59. El Chafic AH, Loren D, Siddiqui A, et al. Comparison of FNA and fine-needle biopsy for EUS-guided sampling of suspected GI stromal tumors. Gastrointest Endosc. 2017;86:510–5.
60. Nagula S, Pourmand K, Aslanian H, et al. Comparison of endoscopic ultrasound-fine-needle aspiration and endoscopic ultrasound-fine-needle biopsy for solid lesions in a multicenter, randomized trial. Clin Gastroenterol Hepatol. 2018;16:1307–13.
61. Iwai T, Kida M, Imaizumi H, et al. Randomized crossover trial comparing EUS-guided fine-needle aspiration with EUS-guided fine-needle biopsy for gastric subepithelial tumors. Diagn Cytopathol. 2018;46:228–33.
62. Fujita A, Ryozawa S, Kobayashi M, et al. Diagnostic ability of a 22G Franseen needle in endoscopic ultrasound- guided fine needle aspiration of subepithelial lesions. Mol Clin Oncol. 2018;9:527–31.
63. Hedenström 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;32:1304–13.
64. Inoue T, Okumura F, Sano H, et al. Impact of endoscopic ultrasound-guided fine-needle biopsy on the diagnosis of subepithelial tumors: a propensity score-matching analysis. Dig Endosc. 2019;31:156–63.
65. Bang JY, Kirtane S, Krall K, et al. In memoriam: fine-needle aspiration, birth: fine-needle biopsy: the changing trend in endoscopic ultrasound-guided tissue acquisition. Dig Endosc. 2019;31:197–202.
66. Trindade AJ, Benias PC, Alshelleh M, et al. Fine-needle biopsy is superior to fine-needle aspiration of suspected gastrointestinal stromal tumors: a large multicenter study. Endosc Int Open. 2019;7:E931–6.
67. 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;92:108-19.e3.
68. Kuraoka N, Hashimoto S, Matsui S, et al. Effectiveness of EUS-guided fine-needle biopsy versus EUS-guided fine-needle aspiration: a retrospective analysis. Diagnostics. 2021;11:965.
69. Nagai K, Sofuni A, Tsuchiya T, et al. Efficacy of the Franseen needle for diagnosing gastrointestinal submucosal lesions including small tumors. Endosc Ultrasound. 2021;10:424–30.
70. Facciorusso A, Sunny SP, Del Prete V, et al. Comparison between fine-needle biopsy and fine-needle aspiration for EUS-guided sampling of subepithelial lesions: a meta-analysis. Gastrointest Endosc. 2020;91:14-22.e2.
71. Tan Y, Tang X, Huang J, et al. Efficacy, feasibility, and safety of endoscopic ultrasound-guided fine-needle biopsy for the diagnosis of gastrointestinal subepithelial lesions: a systematic review and meta-analysis. J Clin Gastroenterol. 2022;56:e283–92.
72. Yamashita Y, Ashida R, Yamazaki H, et al. Comparison of 22G fork-tip and franseen needles and usefulness of contrast-enhanced endoscopic ultrasound for diagnosis of upper gastrointestinal subepithelial lesions. Diagnositcs. 2022;12:3122.
73. Antonini F, Giorgini S, Fuccio L, et al. EUS-guided sampling with 25G biopsy needle as a rescue strategy for diagnosis of small subepithelial lesions of the upper gastrointestinal tract. Endosc Int Open. 2018;6:E892–7.
74. Irisawa A, Hikichi T, Takagi T, et al. Feasibility of interventional endoscopic ultrasound using forward-viewing and curved linear-array echoendoscope: a literature review. Dig Endosc. 2010;22:S128–31.
75. Larghi A, Fuccio L, Chiarello G, et al. Fine-needle tissue acquisition from subepithelial lesions using a forward-viewing linear echoendoscope. Endoscopy. 2014;46:39–45.
76. Lee S, Seo DW, Choi JH, et al. Evaluation of the feasibility and efficacy of forward-viewing endoscopic ultrasound. Gut Liver. 2015;9:679–84.
77. Yamabe A, Irisawa A, Bhytani MS, et al. Usefulness of endoscopic ultrasound-guided fine-needle aspiration with a forward-viewing and curved linear-array echoendoscope for small gastrointestinal subepithelial lesions. Endosc Int Open. 2015;3:E161–4.
78. Matsuzaki I, Miyahara R, Hirooka Y, et al. Forward-viewing versus oblique-viewing echoendoscopes in the diagnosis of upper GI subepithelial lesions with EUS-guided FNA: a prospective, randomized, crossover study. Gastrointest Endosc. 2015;82:287–95.
79. Nakai Y, Isayama H, Chang KJ, et al. Slow pull versus suction in endoscopic ultrasound-guided fine-needle aspiration of pancreatic solid masses. Dig Dis Sci. 2014;59:1578–85.
80. Nakai Y, Hamada T, Hakuta R, et al. A meta-analysis of slow pull versus suction for endoscopic ultrasound-guided tissue acquisition. Gut Liver. 2021;15:625–33.
81. Lee JS, Cho CM, Kwon YH, et al. Comparison of diagnostic performances of slow-pull suction and standard suction in endoscopic ultrasound-guided fine needle biopsy for gastrointestinal subepithelial tumors. Clin Endosc. 2022;55:637–44.
82. Attam R, Arain MA, Bloechl SJ, et al. Wet suction technique (WEST)": a novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions. Gastrointest Endosc. 2015;81:1401–7.
83. Sugimoto M, Takagi T, Suzuki R, et al. Can the wet suction technique change the efficacy of endoscopic ultrasound-guided fine-needle aspiration for diagnosing autoimmune pancreatitis type 1? A prospective single-arm study. World J Clin Cases. 2020;8:88–96.
84. Wang Y, Chen Q, Wang J, et al. Comparison of modified wet suction technique and dry suction technique in endoscopic

ultrasound-guided fine-needle aspiration (EUS-FNA) for solid lesions: study protocol for a randomized controlled trial. Trials. 2018;19:45.
85. Villa NA, Berzosa M, Wallace MB, et al. Endoscopic ultrasound-guided fine needle aspiration: the wet suction technique. Endosc Ultrasound. 2016;5:17–20.
86. Pita I, Pimentel-Nunes P, Dinis-Ribeiro M, et al. Endoscopic ultrasound-guided sampling of gastrointestinal subepithelial lesions: just wet it. Eur J Gastroenterol Hepatol. 2021;33:1533–8.
87. Kawakami H, Ban T, Kubota Y, et al. Endoscopic ultrasonography-guided fine-needle biopsy from ascending colon using a novel curved linear echoendoscope. Endoscopy. 2020;52:E24–6.
88. Nguyen-Tang T, Shah JN, Sanchez-Yague A, et al. Use of the front-view forward-array echoendoscope to evaluate right colonic subepithelial lesions. Gastrointest Endosc. 2010;72:606–10.
89. Rossi S, Gasparotto D, Toffolatti L, et al. Molecular and clinicopathologic characterization of gastrointestinal stromal tumors (GISTs)of small size. Am J Surg Pathol. 2010;34:1480–91.
90. Yegin EG, Kani T, Banzragch M, et al. Survival in patients with hypoechoic muscularis propria lesions suggestive of gastrointestinal stromal tumors in gastric wall. Acta Gastroenterol Belg. 2015;78:12–7.
91. Asao A, Ihara E, Kubo H, et al. Gastric gastrointestinal stromal tumor smaller than 20 mm with liver metastasis. Clin J Gastroenterol. 2013;6:29–32.
92. Japan Society of Clinical Oncology (2022) Japanese clinical practice guidelines for gastrointestinal stromal tumors (GIST), Fourth edition. Tokyo (Japan): Kanehara (Japanese)
93. Hikichi T, Kikuchi H, Nakamura J, et al. Tissue biopsy method for gastric subepithelial lesion. Stomach Intest. 2017;52:1301–15.
94. Tournoy KG, Praet MM, Van Maele G, et al. Esophageal endoscopic ultrasound with fine-needle aspiration with an on-site cytopathologist: high accuracy for the diagnosis of mediastinal lymphadenopathy. Chest. 2005;128:3004–9.
95. Hikichi T, Irisawa A, Bhutani MS, et al. Endoscopic ultrasound-guided fine-needle aspiration of solid pancreatic masses with rapid on-site cytological evaluation by endosonographers without attendance of cytopathologists. J Gastroenterol. 2009;44:322–8.
96. Schmidt RL, Witt BL, Matynia AP, et al. Rapid on-site evaluation increases endoscopic ultrasound-guided fine-needle aspiration adequacy for pancreatic lesions. Dig Dis Sci. 2013;58:872–82.
97. Chen J, Yang R, Lu Y, et al. Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration for solid pancreatic lesion: a systematic review. J Cancer Res Clin Oncol. 2012;138:1433–41.
98. Matynia AP, Schmidt RL, Barraza G, et al. Impact of rapid on-site evaluation on the adequacy of endoscopic-ultrasound guided fine-needle aspiration of solid pancreatic lesions: a systematic review and meta-analysis. J Gastroenterol Hepatol. 2014;29:697–705.
99. Khoury T, Kadah A, Farraj M, et al. The role of rapid on-site evaluation on diagnostic accuracy of endoscopic ultrasound fine needle aspiration for pancreatic, submucosal upper gastrointestinal tract and adjacent lesions. Cytopathol. 2019;30:499–503.
100. Hayashi T, Ishiwatari H, Yoshida M, et al. Rapid on-site evaluation by endosonographer during endoscopic ultrasound-guided fine needle aspiration for pancreatic solid masses. J Gastroenterol Hepatol. 2013;28:656–63.
101. Nebel JA, Soldan M, Dumonceau JM, et al. Rapid on-site evaluation by endosonographer of endoscopic ultrasound fine-needle aspiration of solid pancreatic lesions: A randomized controlled trial. Pancreas. 2021;50:815–21.
102. Iwashita T, Yasuda I, Mukai T, et al. Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: a single-center prospective pilot study (MOSE study). Gastrointest Endosc. 2015;81:177–85.
103. Chong CCN, Lakhtakia S, Nguyen N, et al. Endoscopic ultrasound-guided tissue acquisition with or without macroscopic on-site evaluation: randomized controlled trial. Endoscopy. 2020;52:856–63.
104. Mohan BP, Madhu D, Reddy N, et al. Diagnostic accuracy of endoscopic ultrasound EUS-guided fine needle biopsy (FNB) by macroscopic on-site evaluation (MOSE): a systematic review and meta-analysis. Gastrointest Endosc. 2022;96:909-17.e11.
105. Masutani H, Okuwaki K, Kida M, et al. On-site stereomicroscope quality evaluations to estimate white core cutoff lengths using EUS-FNA biopsy sampling with 22-gauge needles. Gastrointest Endosc. 2019;90:947–56.
106. Ishikawa T, Ohno E, Mizutani Y, et al. Usefulness of macroscopic on-site evaluation using a stereomicroscope during EUS-FNB for diagnosing solid pancreatic lesions. Can J Gastroenterol Hepatol. 2022;2022:2737578.
107. Watanabe M, Okuwaki K, Kida M, et al. Multicenter prospective study of the efficacy of stereomicroscopic on-site evaluation in endoscopic ultrasound-guided tissue acquisition in patients with pancreatic cancer. Pancreatology. 2022;22:311–6.
108. Okuwaki K, Masutani H, Kida M, et al. Diagnostic efficacy of white core cutoff lengths obtained by EUS-guided fine-needle biopsy using a novel 22G franseen biopsy needle and sample isolation processing by stereomicroscopy for subepithelial lesions. Endosc Ultrasound. 2020;9:187–92.
109. Watanabe M, Okuwaki K, Kida M, et al. Histopathological comparison of aspiration and biopsy needles in endoscopic ultrasound-guided tissue acquisition in patients with subepithelial lesions. Diagn Cytopathol. 2021;49:856–63.
110. Stigliano S, Balassone V, Biasutto D, et al. Accuracy of visual on-site evaluation (Vose) In predicting the adequacy of Eus-guided fine needle biopsy: A single center prospective study. Pancreatology. 2021;21:312–7.
111. Crinó SF, Mitri RD, Nguyen NQ, et al. Endoscopic ultrasound-guided fine-needle biopsy with or without rapid on-site evaluation for diagnosis of solid pancreatic lesions: a randomized controlled non-inferiority trial. Gastroenterology. 2021;161:899-909.e5.
112. Suzuki M, Sekino Y, Hosono K, et al. Optimal number of needle punctures in endoscopic ultrasound-guided fine-needle biopsy for gastric subepithelial lesions without rapid on-site evaluation. J Med Ultra. 2021;48:623–9.
113. Shimizu T, Koshita S, Ohira T, et al. Endoscopic ultrasonography-guided fine-needle aspiration cytology combined with a cell-block method for gastrointestinal subepithelial lesions. Int Med. 2022;61:935–42.
114. Levy MJ, Abu Dayyeh BK, Fujii LL, et al. Prospective evaluation of adverse events following lower gastrointestinal tract EUS FNA. Am J Gastroenterol. 2014;109:676–85.
115. Hamada T, Yasunaga H, Nakai Y, et al. Rarity of severe bleeding and perforation in endoscopic ultrasound-guided fine needle aspiration for submucosal tumors. Dig Dis Sci. 2013;58:2634–8.
116. Polmanee P, Hara K, Mizuno N, et al. Outcomes of EUS-FNA in patients receiving antithrombotic therapy. Endosc Int Open. 2019;7:E15-25.
117. Inoue T, Okumura F, Sano H, et al. Bleeding risk of endoscopic ultrasound-guided fine-needle aspiration in patients undergoing antithrombotic therapy. Dig Endosc. 2017;29:91–6.