



REVIEW

Recent approach for preventing complications in upper gastrointestinal endoscopic submucosal dissection

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Abstract

Although endoscopic submucosal dissection (ESD) is a minimally invasive treatment method for upper gastrointestinal (GI) tumors, patients undergoing upper GI ESD sometimes fall into a serious condition from complications. Thus, it is important to fully understand how to prevent complications when performing upper GI ESD. One of the major complications in esophageal and gastric ESD is intraoperative perforation. To prevent this complication, blind dissection should be avoided. Traction-assisted ESD is a useful technique for maintaining good endoscopic view. This method was proven to reduce the incidence of intraoperative perforation, which would become a standard technique in esophageal and gastric ESD. In gastric ESD, delayed bleeding is the most common complication. Recently, a novel prediction model (BEST-J score) consisting of 10 factors with four risk categories for delayed bleeding in gastric ESD was established, and a free mobile application is now available. For reducing delayed bleeding in gastric ESD, vonoprazan ≥ 20 mg/day is the sole reliable method in the current status. Duodenal ESD is still challenging with a much higher frequency of complications, such as perforation and delayed bleeding, than ESD in other organs. However, with the development of improved devices and techniques, the frequency of complications in duodenal ESD has been decreasing. To prevent intraoperative perforation, some ESD techniques, such as using the distal tips of the Clutch Cutter, were developed. An endoscopic mucosal defect closure technique would be mandatory for preventing delayed complications. However, several unresolved issues, including standardization of duodenal ESD, remain and further studies are demanded.

KEYWORDS

complications, duodenum, endoscopic submucosal dissection, esophagus, stomach

INTRODUCTION

Endoscopic submucosal dissection (ESD) is now widely accepted as a minimally invasive treatment method for early-stage esophageal and gastric cancers, particularly

in Eastern Asian countries.^{1–6} In addition, many reports have shown favorable long-term outcomes after ESD for such tumors, irrespective of the curative status,^{6–11} and risk of lymph node metastasis or recurrence in noncurative resection.^{12–16}

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TABLE 1 Major complications and management for preventing them in esophageal endoscopic submucosal dissection (ESD)

	Frequency	Preventative method
Intraoperative perforation	1.4%–4.6% ¹⁸	• Traction-assisted method to prevent “blind” dissection ^{20,21}
Delayed perforation	Rare (three cases; two of them required emergency surgery) ^{24,25}	• Prevention of excessive energizing during ESD ²³
Delayed bleeding	0.0%–6.7% ^{3,27–34}	• No established method
Aspiration pneumonia	1.6%–4.0% ^{3,38}	• Use of a tube or a mouthpiece for continuous saliva suction ^{39,40} • Use of a continuously liquid-sucking catheter attachment for the endoscope ³⁸
Stricture	0.7% (<1/2 circumferential lesion) 27.6% (1/2–3/4 circumferential lesion) 94.1% (>3/4 circumferential lesion) ⁴³	• Steroid injection ^{45–51} • Oral steroid intake ^{53–56,58} • Endoscopic balloon dilation ⁴⁴

Meanwhile, patients undergoing esophageal and gastric ESD sometimes fall into a serious condition from complications. Furthermore, duodenal ESD is still not standardized and appears to have a higher frequency of complications than ESD in other organs. For endoscopists performing upper gastrointestinal (GI) ESD, it is important to fully understand how to prevent complications. In this review, we focused on the complications in upper GI ESD and provide a summary of recent approach to prevent them.

ESOPHAGEAL ESD

Esophageal ESD has become the standard technique over endoscopic mucosal resection (EMR) in the treatment of esophageal cancer because it is associated with a lower recurrence rate and better survival.¹⁷ As major complications in esophageal ESD, intraoperative and delayed perforation, delayed bleeding, aspiration pneumonia, and stricture have been reported (Table 1).

Perforation

According to a database analysis of 12,899 cases, the rates of perforation in very low to very high hospital volume were 4.6%–1.4%.¹⁸ Over three-fourths of circumferential resection of the esophagus¹⁹ and a lower hospital volume^{3,18} were reported as risk factors for perforation. Furthermore, blind dissection should be avoided to prevent intraoperative perforation.²⁰ In this regard, traction-assisted ESD is useful to maintain a good endoscopic view, which can overcome some of the technical difficulty associated with ESD. According to a multicenter randomized trial, no intraoperative perforation occurred in traction-assisted ESD using dental floss, whereas 4.3% of the cases had intraoperative perforation in conventional ESD.²¹ Nevertheless, esophageal ESD has the potential for a higher incidence of complications and, thus, it is preferable that an expert endoscopist performs this procedure.²²

Delayed perforation might be caused by tissue necrosis and degeneration by heat denaturation in the muscularis propria due to excessive energizing during ESD.²³ GI motility, digestive juice, and/or food may be the final trigger for delayed perforation.^{24,25} However, this complication is rare in esophageal ESD; indeed, there are only a few case reports about delayed perforation in esophageal ESD.^{23,26} Once delayed perforation occurs, surgical treatment is generally selected,²⁶ but a case was successfully treated by temporary stent replacement.²³

Delayed bleeding

Delayed bleeding in esophageal ESD is considered relatively rare, and the rate of this complication was reported as 0.0%–6.7%.^{3,27–34} No studies have reported the risk factors for delayed bleeding in esophageal ESD. Although the guidelines do not recommend proton pump inhibitor (PPI) after esophageal ESD,²² a recent large-scale database study revealed that vonoprazan, which is a novel oral potassium-competitive acid blocker with strong and sustained acid-inhibitory activity,³⁵ had a tendency to reduce delayed bleeding after esophageal ESD in the middle or lower part of the esophagus.³⁴ This report addressed the possible reasons as the lower clearance of refluxate by esophageal motility impairment after esophageal ESD³⁶ and the necessity of strict acid suppression to control bleeding (pH > 6 is required in upper GI bleeding³⁷). However, further studies are demanded for confirming the advantage of vonoprazan to prevent delayed bleeding in esophageal ESD and its cost-effectiveness should also be evaluated.³⁴

Aspiration pneumonia

Aspiration pneumonia occurs in 1.6%–4.0% of esophageal ESD.^{3,38} Although clinical symptoms are mild in most patients, symptoms can become serious

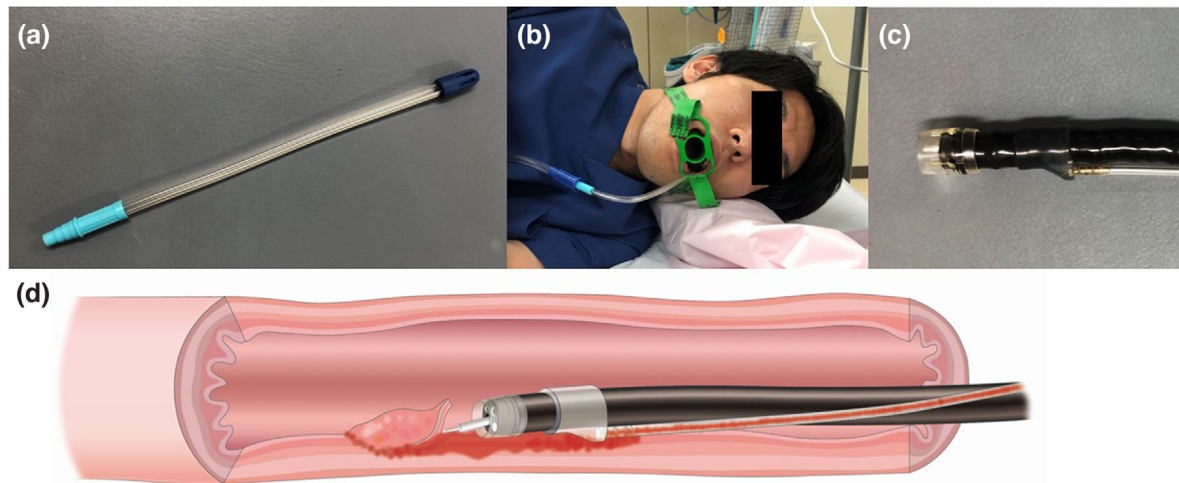


FIGURE 1 Preventative methods for aspiration pneumonia in esophageal endoscopic submucosal dissection (ESD). A tube for continuous saliva suction (a and b) and a continuously liquid-sucking catheter attachment for the endoscope (c and d)

in elderly patients. The cause of this complication is considered to be liquid reflux from the esophagus to the mouth and saliva retention in the oral cavity.^{38,39} To prevent pneumonia, some methods have been developed. One is continuous saliva suction using a tube³⁹ (Figure 1a,b) or mouthpiece.⁴⁰ The other is a continuously liquid-sucking catheter attachment for the endoscope to reduce the volume of liquid reflux to the mouth (Figure 1c,d).³⁸ A randomized controlled trial revealed that the use of this device in esophageal ESD reduced the volume of liquid reflux to the mouth and contributed to the decreased incidence of aspiration pneumonia on computed tomography scan.³⁸ Since the age peak has risen in esophageal cancer in Japan,⁴¹ the issue of aspiration pneumonia in esophageal ESD will be more important in the near future. These devices might help reduce this complication.

Stricture

The circumferential range for resection is a well-known risk factor for a stricture after esophageal ESD.^{42,43} According to a previous study, the incidence of strictures after esophageal ESD was 0.7% in lesions with a circumferential range of $<1/2$, 27.6% for $>1/2$, and 94.1% for $>3/4$.⁴³ A stricture remarkably decreases the quality of life of the patients. Thus, a preventative method is recommended for lesions extending $>1/2$ of the esophageal circumference (expected mucosal defect is $\geq 2/3$ of the esophageal circumference) and mandatory in those $>3/4$ (expected mucosal defect is $\geq 5/6$ of the esophageal circumference).

Several methods have been proposed for preventing stricture after esophageal ESD. Prophylactic endoscopic balloon dilation (EBD) decreases the incidence of a stricture after ESD.⁴⁴ Local steroid injection is the

most frequent method for preventing a stricture, and several studies have demonstrated its efficacy for reducing strictures after ESD.^{45–47} In the guidelines,²² this method is recommended after ESD with mucosal defects affecting $\geq 3/4$ of the esophageal circumference. However, the details of local steroid injection have not been standardized. Triamcinolone was mostly used,^{45,46,48–50} but some studies used dexamethasone as well.^{47,51} The number and timing of steroid injection varied depending on the study, and the dose of steroid also varied (e.g., the dose of triamcinolone injection immediately after ESD varied from 40 to 100 mg among studies with single triamcinolone injection^{46,48,50}). Thus, standardization of the details of local steroid injection is needed. Furthermore, local steroid injection alone may not be sufficient for preventing stricture after 5/6 to entire circumferential resection.^{48,49,52}

Oral steroid intake is also proven to be effective for reducing strictures after esophageal ESD.^{53–56} Although the dose and duration varies across the studies, results from a recent network meta-analysis suggest that long-term (≥ 12 week) oral steroid intake appears to be an optimal method to prevent strictures after esophageal ESD among steroid application.⁵⁷ Iizuka et al.⁵⁸ also reported that 18-week oral steroid intake (30 mg prednisolone for 3 weeks and reduction in 5 mg decrements every 3 weeks) showed a significantly lower rate of strictures than 8-week oral steroid intake (30 mg prednisolone for 2 weeks and tapering) after entire circumferential ESD (36% vs. 82%), although local steroid injection was added as needed in both treatment groups. However, it has been noted that long-term or higher dose systemic steroid administration can cause several side effects including infection and diabetes mellitus.^{59,60} In fact, a case report indicated a risk of life-threatening infection when taking oral steroid after esophageal ESD.⁶¹

TABLE 2 Major complications and management for preventing them in gastric endoscopic submucosal dissection (ESD)

	Frequency	Preventative method
Intraoperative perforation	2.3% (3.2% of such cases required emergency surgery) ⁶⁴	• Traction-assisted method ⁷³
Delayed perforation	0.4% (35.0% of such cases required emergency surgery) ⁶⁴	• Prevention of excessive thermal damage on muscularis propria ⁷⁵
Delayed bleeding	4.1%–8.5% ^{66,76–80}	• The use of vonoprazan ≥ 20 mg/day ³⁴
Thromboembolism	0.03% ⁹¹	• Continuation of antiplatelet agents? ^{80,91–94}
Stricture	21.3% in cardiac resection 3.2% in antral resection ¹⁰⁰	• No established method

GASTRIC ESD

Gastric ESD has replaced EMR as a standard method for endoscopic resection for early-stage gastric tumors in Eastern Asian countries. Indeed, over 90% of endoscopic resections for early gastric cancers are ESD in Japan.⁶² In gastric ESD, the major complications include intraoperative and postoperative perforation, delayed bleeding, thromboembolism, and stricture (Table 2).

Perforation

A meta-analysis that included 24,855 patients reported a rate of intraoperative perforation in gastric ESD as 2.7% (95% CI, 2.1%–3.3%).⁶³ According to a large-scale multicenter prospective study in Japan,⁶⁴ intraoperative perforation occurred in 2.3% (218/10,821), but only 3.2% of such cases (7/218) required emergency surgery. Thus, conservative management without surgical intervention is sufficient in most cases with intraoperative perforation. Many risk factors for intraoperative perforation, including invasion depth and submucosal fibrosis, have been reported. Among them, the upper-third of the stomach and longer procedure time might be especially important since many reports have identified them as risk factors.^{65–72} Obviously, endoscopist-related factors as well as tumor-related factors would affect the incidence of perforation. Also, in gastric ESD, traction-assisted ESD is useful for preventing intraoperative perforation. A multicenter randomized controlled trial demonstrated a lower incidence of intraoperative perforation in traction-assisted ESD using dental floss than that in conventional ESD (2.2% vs. 0.3%).⁷³

Delayed perforation is generally considered as a more serious complication than intraoperative perforation. In fact, although delayed perforation occurred in 0.4% of cases with gastric ESD, 35.0% of such cases required emergency surgery.⁶⁴ The discrepancy in the rate of emergency surgery between intraoperative and delayed perforation may be due to the larger sized perforation and the condition after starting a meal in delayed perforation. To date, the small number of such complica-

tions has made it difficult to investigate risk factors; however, a previous report identified that gastric tube cases were significantly associated with delayed perforation.⁷⁴ Furthermore, a possible cause of delayed perforation is necrosis of the muscularis layer due to excessive thermal damage of this layer.⁷⁵ Therefore, to prevent delayed perforation, excessive coagulation should be avoided. If the muscularis layer is excessively coagulated, closure of the ESD ulcer might be useful for preventing delayed perforation.

Delayed bleeding

Delayed bleeding is the most common complication in gastric ESD and this adverse event is reported to occur in 4.1%–8.5% of cases.^{66,76–80} However, the risk of delayed bleeding differs depending on various factors, such as anticoagulants.⁸¹ Recently, a novel prediction model (BEST-J score) for delayed bleeding in ESD for early gastric cancers was established.⁸² In this model, points were assigned to factors: 4 points each for warfarin and direct oral anticoagulants (DOACs), 3 points for chronic kidney disease with hemodialysis, 2 points each for P2Y12 receptor antagonist and aspirin, 1 point each for cilostazol, a tumor size >30 mm, lower-third in tumor location, and the presence of multiple tumors, and -1 point for the interruption of each kind of antithrombotic (AT) agents (Figure 2). The rates of bleeding for low- (0–1 points), intermediate- (2 points), high- (3–4 points), and very high-risk (≥ 5 points) categories were 2.8%, 6.1%, 11.4%, and 29.7%, respectively (Figure 2). A mobile application of this model was also developed (<https://apps.apple.com/app/id1492914336> for iOS, https://play.google.com/store/apps/details?id=hatta.best_j for Android). Based on the results in this study, anticoagulants have the highest risk for delayed bleeding with a similar risk between warfarin and DOACs, followed by hemodialysis and antiplatelet agents, in gastric ESD.

Then, how can clinicians prevent delayed bleeding especially in patients at high risk? Several methods, such as the use of polyglycolic acid (PGA) sheet,⁸³ closure with clips,⁸⁴ and second-look endoscopy (SLE),⁸⁵

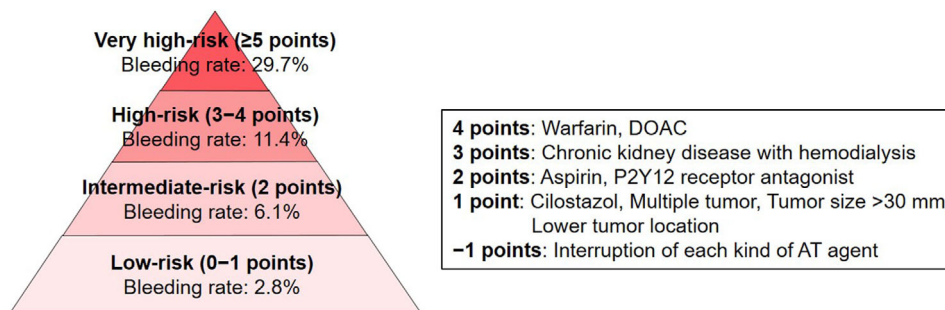


FIGURE 2 BEST-J score for predicting delayed bleeding risk after endoscopic submucosal dissection (ESD) for early gastric cancer. AT, antithrombotic; DOAC, direct oral anticoagulant

have been proposed. However, most methods had no significant effect in reducing delayed bleeding in gastric ESD (Table 3).^{82,86,87} Regarding SLE, noninferiority of patients with non-SLE compared to those with SLE was also confirmed in a randomized trial.⁸⁸ A recent database analysis using propensity-score methods demonstrated that vonoprazan had a significant reducing effect of approximately 30% on delayed bleeding compared with PPI (Table 3).³⁴ Furthermore, vonoprazan ≥ 20 mg/day, but not < 20 mg/day, showed a reduced risk of bleeding in comparison with standard/high-dose PPI in gastroduodenal ESD. Similar results were achieved when gastroduodenal ESD was limited to ESD for gastric tumors. Therefore, vonoprazan ≥ 20 mg/day would be useful for reducing delayed bleeding in gastric ESD. However, it should be noted that this study has some limitations due to the nature of a retrospective database analysis, such as unmeasured confounder and potential inaccuracy of coding.

In patients with delayed bleeding, clinicians should be careful for further bleeding. According to the largest study to date,^{89,90} the rate of delayed bleeding rate was 4.7% (489/10,320), and rebleeding occurred in 11.2% (55/489) of patients with delayed bleeding (Figure 3). Furthermore, 18.2% (10/55) of patients with rebleeding underwent further bleeding (Figure 3). Thus, the risk of repeated bleeding might gradually increase as the number of bleeding events increases.

Thromboembolism

Regarding thromboembolism in the perioperative period of gastric ESD, only several cases have been reported (Table 4).^{80,90–94} According to a recent large-scale study by Shiroma et al.,⁹⁰ the rate of thromboembolism in gastric ESD was 0.03% (3/10,320). In reports published until 2017,^{80,91–94} most patients who underwent thromboembolism took antiplatelet agents with their discontinuation at the time of the thromboembolic events. These studies included a lot of patients who were treated under

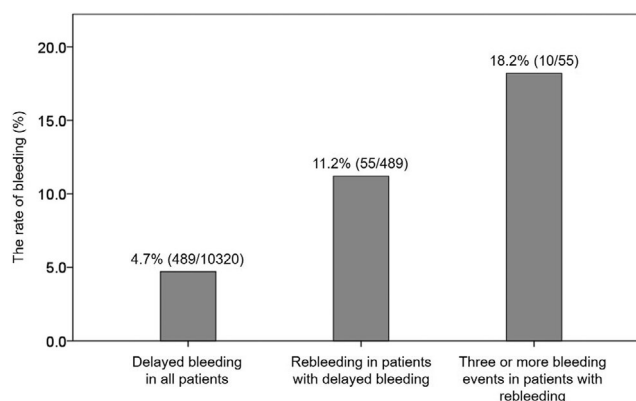


FIGURE 3 Increased bleeding risk in the cases with repeated bleeding after endoscopic submucosal dissection (ESD) for early gastric cancer. The rate of repeated bleeding gradually increases as the number of bleeding events experienced increases

the discontinuation of antiplatelet agents because the Japanese guidelines recommended discontinuation of them until 2012. By contrast in a study by Shiroma et al. (study period, 2013–2016),⁹⁰ the rate of patients who discontinued antiplatelet agents in the perioperative period of gastric ESD was rather low (6.3%) owing to the change of recommendation for their management in the guidelines,⁹⁵ and no thromboembolic events occurred in those with antiplatelet agents (0/1428). Thus, the change of the management of patients with antiplatelet agents (i.e., no discontinuation of these agents) might have reduced the frequency of this complication in gastric ESD. Meanwhile, anticoagulants were prescribed in all three patients with thromboembolism in the recent study.⁹⁰ In 2017, the management of patients with anticoagulants in the guidelines was further changed⁹⁶ because of the continuing risk of major bleeding in heparin replacement of anticoagulants without any significant effect for preventing thromboembolism.⁹⁷ However, the knowledge of delayed bleeding and thromboembolism in patients with anticoagulants after the latest guidelines is still not sufficient; thus, further studies in this field are required.

TABLE 3 Reports about preventative method for delayed bleeding in gastric endoscopic submucosal dissection (ESD)

Author, year	Study population	Preventative method	Control	Study design	No. of cases	Results for delayed bleeding (bleeding rate, preventative method vs. control)
Kataoka et al., 2019 ⁸⁶	Patients on AT agents or those with large mucosal resection	PGA sheet	Non-PGA sheet	RCT	137	No significant difference (4.5% vs. 5.7%)
Ego et al., 2020 ⁸⁷	Patients on AT agents	Mucosal closure	Nonclosure	Retrospective cohort study	400	No significant difference (11.5% vs. 11.9%)
Hatta et al., 2021 ⁸²	All patients	SLE	Non-SLE	Retrospective case-control study	10,319	No significant difference <ul style="list-style-type: none"> • 2.7% vs. 3.1% in low risk • 5.7% vs. 5.9% in intermediate risk • 12.9% vs. 9.6% in high risk • 29.0% vs. 33.3% in very high risk
Abe et al., 2021 ³⁴	Patients on vonoprazan or PPI	Vonoprazan	PPI	Retrospective cohort study using database (PS matching)	39,740	Reducing effect in the use of vonoprazan (5.4% vs. 7.5%)

Abbreviations: AT, antithrombotic; PGA, polyglycolic acid; PPI, proton pump inhibitor; PS, propensity score; RCT, randomized controlled trial; SLE, second-look endoscopy.

TABLE 4 Reports about thromboembolism in gastric endoscopic submucosal dissection (ESD)

Author, year	Study population	No. of cases	No. of events (rate)	Type of thromboembolic event	Status of AT agents in cases with event
Lim et al., 2012 ⁸⁰	All patients	1503	1 (0.07%)	Cerebral infarction	Discontinuation of antiplatelet agents
Takeuchi et al., 2013 ⁹⁴	All patients	833	1 (0.12%)	Cerebral infarction	Discontinuation of AT agent (detail unclear)
Yoshio et al., 2013 ⁹³	All patients	1250	1 (0.08%)	Cerebral infarction	Discontinuation of aspirin, P2Y ₁₂ receptor antagonist, and cilostazol with heparin bridging
Sanomura et al., 2014 ⁹²	Patients on aspirin	78	4 (5.1%)	2, cerebral infarction; 2, myocardial infarction	All, discontinuation of aspirin
Igarashi et al., 2017 ⁹¹	Patients on AT agents	367	4 (1.1%)	2, cerebral infarction; 1, TIA; 1, angina pectoris	All, discontinuation of antiplatelet agents
Shiroma et al., 2021 ⁹⁰	All patients	10,320	3 (0.03%)	2, cerebral infarction; 1, TIA	1, discontinuation of warfarin; 1, discontinuation of warfarin with heparin bridging; 1, continuation of DOAC with heparin bridging

Abbreviations: AT, antithrombotic; DOAC, direct oral anticoagulant; TIA, transient ischemic attack.

TABLE 5 Major complications and management for preventing them in duodenal endoscopic submucosal dissection (ESD)

	Frequency	Preventative method
Intraoperative perforation	6.0%–31.6% (emergency surgery was required in 3.1%–23.1% of such cases) ^{105–109}	<ul style="list-style-type: none"> • The use of the Clutch Cutter¹⁰⁵ • Pocket-creation method¹⁰⁶ • Water pressure method¹¹¹
Delayed perforation	1.5%–4.8% ^{105–109} (emergency surgery was required in 25.0%–100.0% of such cases ^{106–109})	<ul style="list-style-type: none"> • Mucosal defect closure (clips, clips with string, an endoloop, over-the-scope clips)^{105,112–114} • Coverage of mucosal defect with a PGA sheet^{115,116}
Delayed bleeding	0.0%–18.4% ^{105,106,108,109,118}	<ul style="list-style-type: none"> • Mucosal defect closure (clips, clips with string, an endoloop, over-the-scope clips)¹¹⁷ • Coverage of mucosal defect with PGA sheet¹¹⁷ • The use of vonoprazan ≥ 20 mg/day³⁴

Abbreviation: PGA, polyglycolic acid.

Stricture

The most frequent location of stricture after gastric ESD is the cardia, followed by the antrum.^{98,99} Over three-fourths of the circumferential extent^{99,100} and extension of the mucosal defect to pyloric ring^{100,101} were independent risk factors for gastric stricture.

Although EBD and steroid application are well-established preventative methods for stricture in esophageal ESD, their effect in gastric ESD remains unclear. Kishida et al.¹⁰⁰ reported that early steroid treatment did not have a significant effect on stricture prevention after wide gastric ESD. Sumiyoshi et al.⁹⁹ compared the clinical characteristics between cases with and without prophylactic EBD. However, all were single-institution studies with small numbers of cases; thus, it is difficult to reach a definite conclusion. A multicenter study with a larger cohort is required for confirming the effect of preventative methods. Furthermore, surgical resection might be more appropriate as a therapeutic approach when suspecting high risk for refractory strictures after ESD, such as an entire circumferential lesion of the pyloric ring.

DUODENAL ESD

Duodenal ESD is technically more difficult and has greater risk of complications than ESD in other organs. Several reasons for the difficulty in this procedure have been raised.^{102,103} First, since the duodenal wall is thinner, the muscular layer is more vulnerable to electric damage. Second, the presence of Brunner's glands leads to poor submucosal elevation after submucosal injection. Third, the curved shape of the duodenum and its narrow lumen reduce the maneuverability of the endoscope. In addition, exposure to pancreatic and bile juice is also problematic. Thus, this procedure should be confined to endoscopists with extensive experience in performing ESD in other organs.¹⁰⁴ The major complications in duodenal ESD are intraoperative and delayed

perforation and delayed bleeding (Table 5). With the development of devices and techniques, the frequency of complications in duodenal ESD has been decreasing.

Perforation

The rate of intraoperative perforation in duodenal ESD was reported to be 6.0%–31.6%,^{105–109} which is about 3–14 times higher than that in gastric ESD.⁶⁴ Emergency surgery was required in 23.1% (6/26) of such cases when combining the results of four studies.^{104,105,107,108} On the other hand, the largest study to date revealed that additional intervention is required in 3.1% of cases with perforation.¹⁰⁷ This is surprising because the rate of requiring additional intervention in duodenal ESD was similar to those in esophageal and gastric ESD,^{64,110} although it should be noted that differences in the study period may have affected the frequency of perforation and additional intervention in duodenal ESD. Furthermore, when complete mucosal closure was achieved, no cases required additional intervention and the clinical course did not significantly differ between these cases and those without perforation.¹⁰⁷ Meanwhile, in patients in whom the lesions are located distal to the superior duodenal angle and complete mucosal closure cannot be achieved after perforation, an endoscopic nasobiliary and pancreatic duct drainage tube, and preventing the exposure of pancreatic and bile juice to the mucosal defect may be effective in preventing a worse clinical course.¹⁰⁷ To reduce intraoperative perforation, several methods have been proposed. Dohi et al.¹⁰⁵ reported that no perforation occurred in 47 cases with duodenal ESD using the Clutch Cutter, which is one of the scissors-type knives. Using this knife in ESD is relatively simple and safe for dissecting a narrow space and, even if the lesion has severe fibrosis, ESD can be safely performed using the distal tips of the Clutch Cutter.¹⁰⁵ A pocket-creation method¹⁰⁶ and water pressure method¹¹¹ were also developed for safe ESD.

Delayed perforation was reported to occur in 1.5%–4.8% of cases with duodenal ESD,^{105–109} which is about 5–16 times higher than that in gastric ESD.⁶⁴ Emergency surgery was required in all of such cases (3/3) in the results of three studies (no data were available in one study),^{106,108,109} whereas the largest study reported a rate of 25.0% (1/4).¹⁰⁷ To prevent this complication, various endoscopic mucosal defect closure techniques, including closure with clips, clips with string,¹¹² an endoloop,¹¹³ over-the-scope clips,^{105,114} and coverage with a PGA sheet,^{115,116} have been performed. A meta-analysis revealed that the rates of delayed perforation in patients with and without mucosal defect closure after duodenal endoscopic resection were 1.6% and 3.8%, respectively.¹¹⁷ The reduction by mucosal defect closure techniques for perforation did not reach statistical significance ($p = 0.13$) in this meta-analysis possibly due to the small number of cases, but the risk ratio was low (0.39). Mucosal defect closure techniques have a potential to prevent delayed perforation, and a future large-scale study or meta-analysis may demonstrate their significant effect.

Delayed bleeding

The rate of delayed bleeding is reported to be 0.0%–18.4%.^{105,106,108,109,118} A meta-analysis revealed that endoscopic mucosal defect closure techniques significantly reduced delayed bleeding in duodenal endoscopic resection (risk ratio, 0.14; delayed bleeding rate, 2.0% vs. 17.3%).¹¹⁸ Furthermore, a recent database analysis found that the use of vonoprazan showed a significant reduction of delayed bleeding compared to PPI in ESD for duodenal tumors,³⁴ although this study did not consider the effect of endoscopic preventive procedures after ESD. Thus, endoscopic mucosal defect closure techniques should now be mandatory for preventing delayed bleeding, and vonoprazan intake has the possibility to reduce this complication as compared to PPI.

CONCLUSIONS

We showed the current status of major complications in upper GI ESD and discussed recent approach for preventing them. Although many methods have been developed to prevent complications in esophageal and gastric ESD, several issues, including the prevention of delayed bleeding after gastric ESD, have remained unresolved. For duodenal ESD, which is still challenging in the current status, a future large-scale study is demanded to accumulate more evidence.

CONFLICT OF INTEREST

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