

Endoscopic submucosal dissection for duodenal tumors

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Abstract: Recently, endoscopic submucosal dissection (ESD) for the duodenal tumors has come to be treated in many institutions, but has also showed many problems of feasibility and safety compared with endoscopic mucosal resection (EMR). Although duodenal ESD is expected to be more effective for the prevention of postoperative local recurrence, high incidence rate of duodenal perforation and emergency surgical rescue are big problem. Prophylactic mucosal closure by clipping device, polyglycolic acid sheets shielding, and the laparoscopic and endoscopic cooperative surgery are reported to be effective measures to overwhelm the various problems associated with duodenal ESD. However, duodenal ESD still has quite a bit of room for improvement of the procedure, and currently the indication should be well discussed before treatment in consideration of the expected therapeutic effect and complications.

Keywords: Duodenal tumor; endoscopic submucosal dissection (ESD); endoscopic mucosal resection (EMR)

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Introduction

Endoscopic submucosal dissection (ESD) is widely adopted as an effective treatment strategy for esophageal, gastric, and colonic neoplasms. Recently, the therapeutic indication has been expanded to the duodenal neoplasms in many institutions, but it causes a lot of controversy because of unknown clinicopathological characteristics of the tumors and high incidence rate of complications associated with endoscopic procedures.

Clinicopathological characteristics of duodenal tumors

The prevalence of duodenal epithelial neoplasms is reported to be 0.03% to 0.4% of the patients undergoing the upper endoscopy (1,2), which is smaller than those of other digestive neoplasms. Majority of them are diagnosed as adenomas or mucosal adenocarcinomas located at descending part of the duodenum (3-6). The malignant

transformation rate of adenomas differs depending on the previous reports. Some suggested the duodenal adenomas progressed to adenocarcinomas in 30% to 80% of the cases (7,8), but Okada reported that only 4.7% of 47 duodenal adenomas progressed to the adenocarcinoma during follow-up and pointed out a high risk of progression to adenocarcinoma for high grade adenomas of 20 mm or more in size (9). The incidence rate of lymph node metastasis of duodenal adenocarcinomas is also unclear because of the lack of cases treated by surgical resection. Some previous case-series reports showed the mucosal cancers were free from lymph node metastasis, suggesting the endoscopic therapeutic indication for them (10,11).

Merits and faults of ESD and EMR

There are basically two ways of endoscopic resection of duodenal tumors, ESD and endoscopic mucosal resection (EMR). The advantage of ESD to EMR is higher en bloc resection rate and lower local recurrence rate regardless

Table 1 Previous reports regarding the outcomes of duodenal ESD

References	Year	Number of cases	Mean size (mm)	En bloc (%)	Perforation (%)	Bleeding (%)	Surgical rescue (%)
Hirasawa	1997	14	12.7	12 (86.0)	0	0	0
Ahmad	2002	27	2	23 (85.0)	0	9 (33.0)	0
Oka	2003	15	9.4	N.D	0	1 (6.0)	0
Apel	2005	20	med. 27.5	N.D	0	2 (10.0)	0
Lepilliez	2008	43	19	21 (48.8)	1 (2.3)	11 (25.6)	1 (2.3)
Alexander	2009	23	27.6	18 (78.0)	0	1 (4.0)	0
Honda	2009	6	7.5	5 (83.0)	0	1 (17.0)	1 (17.0)
Endo	2010	11	9.5	10 (90.1)	0	0	0
Sohn	2010	24	N.D	21 (87.5)	0	7 (29.0)	0
Kim	2010	17	15.1	14 (82.0)	0	1 (6.0)	0
Kedia	2010	33	N.D	23 (69.7)	0	5 (14.0)	0
Conio	2012	26	med. 15	N.D	0	3 (12.0)	0
Min	2013	23	12.9	20 (87.0)	1 (4.3)	2 (8.7)	0
Fanning	2013	50	N.D	25 (50.0)	2 (4.0)	20 (40.0)	2 (4)
Maruoka	2013	26	10	18 (69.2)	0	12 (46.2)	0
Matsumoto	2014	31	11.4	26 (83.9)	0	1 (3.2)	0
Yamamoto	2014	17	9.4	14 (82.0)	0	0	0
Basford	2014	34	25	17 (50.0)	0	3 (8.8)	0
Kakushima	2014	10	med. 15	10 (100.0)	0	0	0
Seo	2014	45	N.D	N.D	0	2 (6.0)	0
Park	2015	45	med. 8	35 (77.8)	2 (4.5)	1 (2.2)	0
Nonaka	2015	113	med. 12	71 (63.0)	0	14 (12.0)	0
Ono	2016	798	N.D	629 (79.0)	18 (2.3)	24 (3.0)	3 (0.4)
Kim	2016	38	18	37 (97.4)	0	3 (7.9)	0
Klein	2016	106	25	N.D	3 (2.8)	16 (15.0)	2 (1.9)

ESD, endoscopic submucosal dissection; med., median; N.D, not described.

of the tumor size, location, and submucosal fibrosis, which has been much proven in the endoscopic treatment for esophageal, gastric, and colonic tumors (12). However, those advantages may be small for the endoscopic treatment for duodenal tumors compared with that for other digestive tumors (Tables 1,2). EMR seems inferior to ESD in en bloc resection and local recurrence without restriction of duodenal tumor size. However, several reports suggested a similarly good prognosis of the cases after piecemeal resection as those after en bloc resection (13-16), and the incidence of complication was apparently more frequent in

ESD than in EMR, especially for the duodenal perforation (Tables 1,2). Intraoperative perforation and delayed perforation after ESD were reported to be 6.3–50% and 0–14.3%, respectively (3-6). Recently, Ono *et al.* analyzed reported the clinical short-term outcomes of 1397 patients, who were endoscopically treated for duodenal neoplasms, by using questionnaire data taken from thirteen advanced institutions in Japan (4). In this large number of analysis, intraoperative perforation and delayed perforation each occurred in 12.1% (54/445) and 4.0% (18/445) of the cases of ESD and 1.6% (13/798) and 0.6% (5/798) of the cases of

Table 2 Previous reports regarding the outcomes of duodenal EMR

References	Year	Number of cases	Mean size (mm)	R0 resection (%)	Perforation (%)	Bleeding (%)	Surgical rescue (%)
Honda	2009	9	23.7	9 (100.0)	2 (22.2)	2 (22.2)	1 (11.0)
Takahashi	2009	4	20.5	4 (100.0)	2 (50.0)	0	0
Endo	2010	5	10	5 (100.0)	1 (20.0)	0	0
Jung	2013	14	17.1	12 (85.7)	5 (35.7)	1 (7.1)	2 (14.3)
Matsumoto	2014	15	12.9	13 (86.7)	3 (20.0)	3 (20.0)	2 (13.3)
Yamamoto	2014	30	13.7	27 (90.0)	3 (10.0)	0	1 (3.0)
Kakushima	2014	13	med. 13.5	13 (100.0)	4 (30.7)	0	1 (7.7)
Seo	2014	7	N.D	N.D	3 (42.9)	0	0
Park	2015	6	med. 8	5 (83.3)	2 (33.3)	0	N.D
Hoteya	2015	63	24.6	55 (87.3)	21 (31.3)	11 (17.5)	4 (6.2)
Ishii	2015	16	med. 13	13 (81.3)	1 (6.3)	0	1 (6.3)
Nonaka	2015	8	med. 18	4 (50.0)	2 (25.0)	0	1 (12.5)
Ono	2016	445	N.D	332 (75.0)	72 (16.2)	20 (4.5)	24 (5.4)
Kim	2016	8	8.5	3 (37.5)	3 (37.5)	1 (12.5)	0

N.D, not described; med., median.

EMR, showing a higher incidence of perforation in the cases of ESD. Additionally, emergency surgery was performed in 5.4% (24/445) of the cases of ESD and 0.4% (3/798) of the cases of EMR, and it was more frequently required in the cases of delayed perforation (52.2%: 12/23) than in the cases of intraoperative perforation (19.4%: 13/67). These results of advanced institutions in Japan show the difficulty to decrease the incidence of duodenal perforation associated with ESD only by the technical improvement.

The clinical characteristics of the perforation are different between ESD and EMR. ESD-associated perforation usually occurs as a small linear hole at early stage and tears easily to be gradually enlarged along with the endoscopic procedures. Additionally, the endoscopic resection becomes technically more difficult to continue (*Figure 1*). On the other hand, EMR-associated perforation occurs as a small roundish hole by an incidental whole layer resection on snaring. However, the lesion has already been resected, and it is usually relatively easy to close the small perforation by using clipping devices.

Some specific anatomical features of the duodenum can be given as the reason why the duodenal ESD frequently complicates a perforation. First, the narrow, crooked, and deeply located lumen makes it difficult to keep an adequate visual field for ESD. Second, the submucosal injection is

difficult due to abundant Brunner's glands and fibrosis in the submucosal layer, leading to the intraoperative severe conditions for submucosal dissection. Lastly, the duodenal muscle layer is very thin compared with other digestive tract (*Figure 2*), which is probably the biggest cause of perforation by minor physical or chemical damage including burning effect, compression of endoscopic devices, and tissue damage by bile and pancreatic juice.

Countermeasure for the duodenal perforations by ESD and EMR

Some countermeasures for the duodenal perforation have been suggested; carbon dioxide (CO₂) supply, prophylactic clipping, polyglycolic acid (PGA) sheets shielding, and the laparoscopic and endoscopic cooperative surgery (LECS). Using CO₂ for the air supply during ESD is necessary for the possible intraoperative perforation, regardless of the kind of digestive tract (12). The following two measures aim not for the prevention of an intraoperative perforation but for that of a delayed perforation. Prophylactic mucosal closure by clipping device after ESD is effective for the protection of the exposed muscle layer (*Figure 3*). However, the achievement depends on the size and location of the resected bed and scope instability (16,17). PGA sheet,

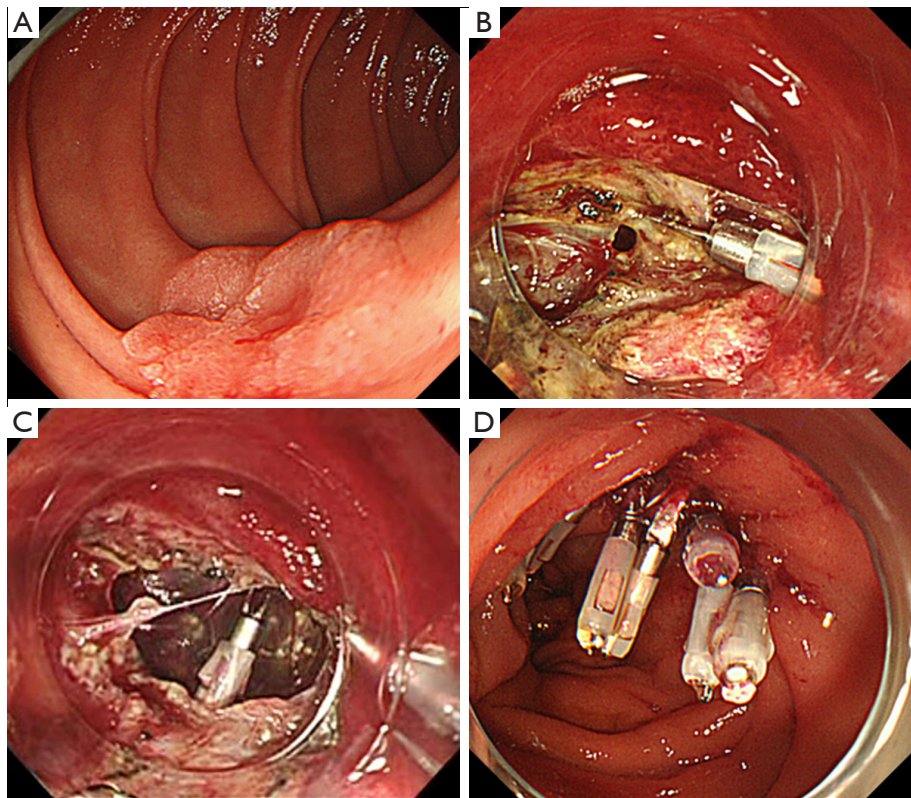


Figure 1 A case of early duodenal cancer located at the descending part of the duodenum (A). Perforation was complicated on submucosal dissection as a small hole of the proper muscle layer, and the endoscopic suture was attempted by using clipping device (B). However, the perforated site was gradually torn to become a large hole during the endoscopic procedure and a failed clip was dropped into the retroperitoneum (C). After removing a failed clip, the perforation was completely closed, but ESD had become difficult to continue, resulting in the piecemeal resection by snaring (D). Administration of the carbapenem antibiotic was started during the procedure, and the patient was treated conservatively to be discharged a week after ESD.

an absorbable mesh used to seal tissue defects with fibrin glue, was reported to be effective for the prevention of delayed bleeding after gastric ESD (18) and postoperative stenosis after esophageal extensive ESD (19). Recently, this shielding method has been reported to be also effective for the prevention of delayed perforation after duodenal ESD (20). LECS has been developed as a minimally invasive surgery for the gastrointestinal stromal tumor (21), and also proposed as an alternative method of ESD for the case of early stage digestive cancers which is difficult to treat by ESD. Some case series reports have suggested the efficacy of LECS for the treatment of duodenal tumors; the partial duodenal resection or seromuscular suturing of resection bed after ESD by using LECS technique (22,23). However, the extensive resection by LECS is considered to cause the

postoperative stenosis, and is inadaptible to the lesions near the duodenal papilla.

Current status and future prospects of duodenal ESD

Thus, duodenal ESD has not yet reached the recommendable measure for the endoscopic treatment of duodenal tumors. To overwhelm the various problems concerning the duodenal ESD, the endoscopic skill-up is necessary but insufficient, because a high incidence of complications has been experienced in the advanced Japanese institutions. Nevertheless, to reduce the incidence of complications as much as possible, the cases of possible indication of duodenal ESD should be collected to such specific institutions with advanced techniques and

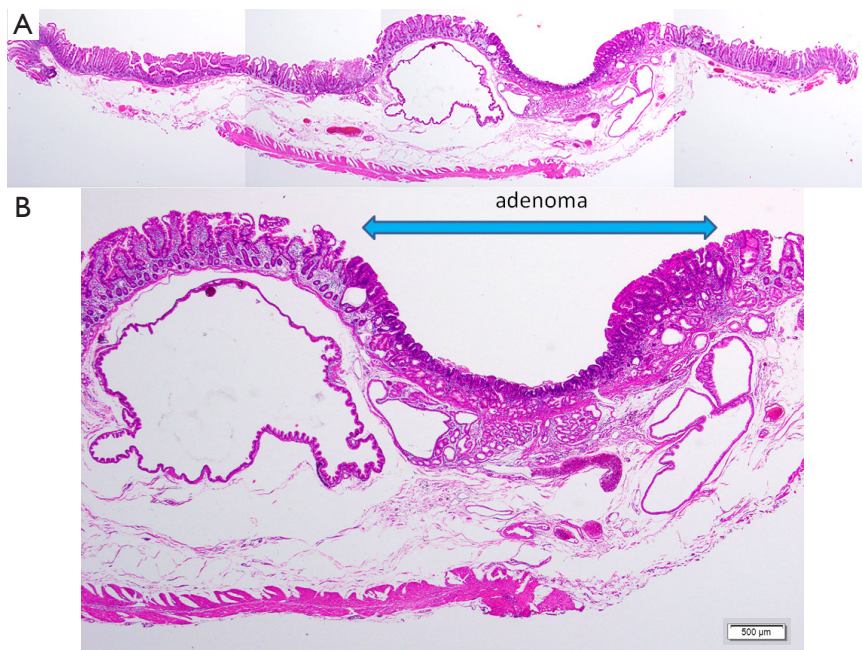


Figure 2 The whole layer-resected specimen by duodenal EMR complicating a perforation (A). This histopathologic picture shows abundant Brunner's gland at submucosal layer and a very thin proper muscle layer as 300–500 µm (B). This histopathologic picture makes it easy to understand the reason for high incidence rate of perforation associated with duodenal ESD.

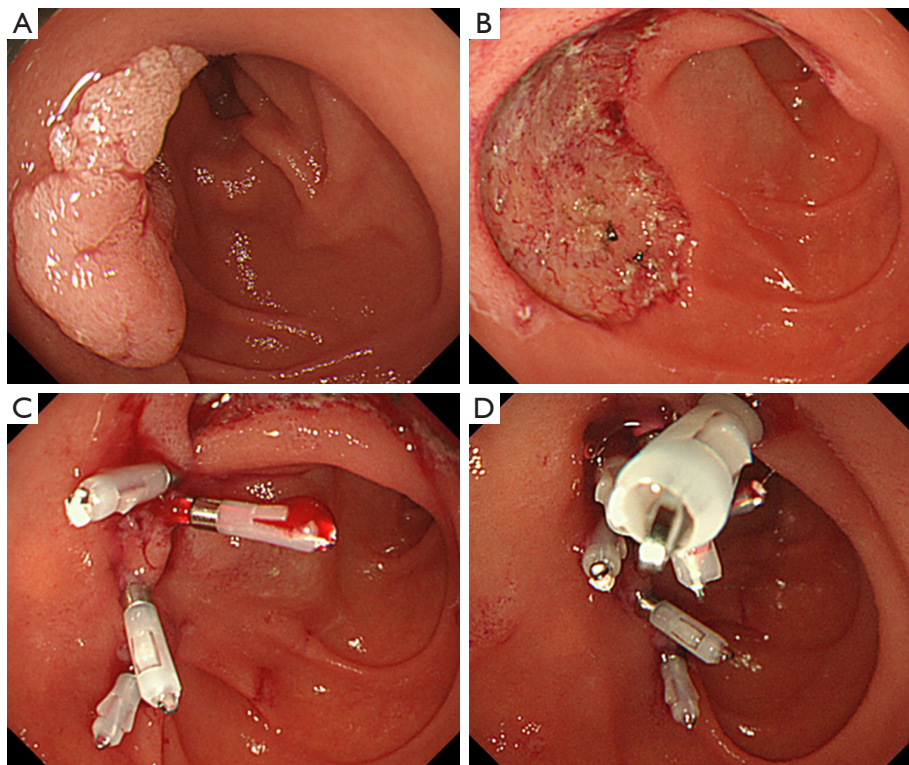


Figure 3 A case of early duodenal cancer located at the superior duodenal angle (A). The lesion was resected by ESD, and the postoperative mucosal defect reached half of the circumference (B). To prevent a delayed perforation, the resected bed was sutured from the end of it by using a clipping device (C). The resected bed has been completely sutured (D).

experiences. Additionally, the lesions likely to be resectable by EMR should not be treated by ESD, and we should have the prudence in aggressively performing duodenal ESD.

The complication of duodenal ESD we should overcome the most is an intraoperative perforation, which is most frequently experienced but has a lack of effective preventive measures. It seems difficult to prevent the intraoperative perforation singly by the progress of ESD techniques or related devices, implying the necessity of a fundamental change of the therapeutic method. From the perspective of a combined treatment, the further radical progress of LECS may possibly change the treatment for the duodenal tumors to more safe and feasible one.

Conclusions

The duodenal ESD still have many unsolved problems regarding feasibility and safety even by introducing various ideas, and the indication should be well discussed in consideration of the expected therapeutic effect and complications.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

- Jepsen JM, Persson M, Jakobsen NO, et al. Prospective study of prevalence and endoscopic and histopathologic characteristics of duodenal polyps in patients submitted to upper endoscopy. *Scand J Gastroenterol* 1994;29:483-7.
- Jung SH, Chung WC, Kim EJ, et al. Evaluation of non-ampullary duodenal polyps: comparison of non-neoplastic and neoplastic lesions. *World J Gastroenterol* 2010;16:5474-80.
- Fujihara S, Mori H, Kobara H, et al. Management of a large mucosal defect after duodenal endoscopic resection. *World J Gastroenterol* 2016;22:6595-609.
- Ono H, Kaise M, Nonaka S, et al. Clinical Issues of Duodenal Endoscopic Treatment. *Stomach and Intestine* 2016; 51: 1585-92. Available online: <http://medicalfinder.jp/doi/10.11477/mf.1403200770>
- Kim TW, Kim GH, Park DY, et al. Endoscopic resection for duodenal subepithelial tumors: a single-center experience. *Surg Endosc* 2017;31:1936-46.
- Klein A, Nayyar D, Bahin FF, et al. Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes. *Gastrointest Endosc* 2016;84:688-96.
- Sakorafas GH, Friess H, Derveniz CG. Villous tumors of the duodenum: biologic characters and clinical implications. *Scand J Gastroenterol* 2000;35:337-44.
- Galandiuk S, Hermann RE, Jagelman DG, et al. Villous tumors of the duodenum. *Ann Surg* 1988;207:234-9.
- Okada K, Fujisaki J, Kasuga A, et al. Sporadic nonampullary duodenal adenoma in the natural history of duodenal cancer: a study of follow-up surveillance. *Am J Gastroenterol* 2011;106:357-64.
- Abbass R, Rigaux J, Al-Kawas FH. Nonampullary duodenal polyps: characteristics and endoscopic management. *Gastrointest Endosc* 2010;71:754-9.
- Poultides GA, Huang LC, Cameron JL, et al. Duodenal adenocarcinoma: clinicopathologic analysis and implications for treatment. *Ann Surg Oncol* 2012;19:1928-35.
- Technology status report evaluation. Endoscopic mucosal resection. *Gastrointest Endosc* 2000;52:860-3.
- Alexander S, Bourke MJ, Williams SJ, et al. EMR of large, sessile, sporadic nonampullary duodenal adenomas: technical aspects and long-term outcome (with videos). *Gastrointest Endosc* 2009;69:66-73.
- Fanning SB, Bourke MJ, Williams SJ, et al. Giant laterally spreading tumors of the duodenum: endoscopic resection outcomes, limitations, and caveats. *Gastrointest Endosc* 2012;75:805-12.
- Maruoka D, Arai M, Kishimoto T, et al. Clinical outcomes of endoscopic resection for nonampullary duodenal high-grade dysplasia and intramucosal carcinoma. *Endoscopy* 2013;45:138-41.
- Nonaka S, Oda I, Tada K, et al. Clinical outcome of endoscopic resection for nonampullary duodenal tumors. *Endoscopy* 2015;47:129-35.
- Hoteya S, Kaise M, Iizuka T, et al. Delayed bleeding after endoscopic submucosal dissection for non-ampullary superficial duodenal neoplasias might be prevented by prophylactic endoscopic closure: analysis of risk factors. *Dig Endosc* 2015;27:323-30.
- Tsuji Y, Fujishiro M, Kodashima S, et al. Polyglycolic acid sheets and fibrin glue decrease the risk of bleeding after endoscopic submucosal dissection of gastric neoplasms

- (with video). *Gastrointest Endosc* 2015;81:906-12.
19. Iizuka T, Kikuchi D, Yamada A, et al. Polyglycolic acid sheet application to prevent esophageal stricture after endoscopic submucosal dissection for esophageal squamous cell carcinoma. *Endoscopy* 2015;47:341-4.
 20. Takimoto K, Imai Y, Matsuyama K. Endoscopic tissue shielding method with polyglycolic acid sheets and fibrin glue to prevent delayed perforation after duodenal endoscopic submucosal dissection. *Dig Endosc* 2014;26 Suppl 2:46-9.
 21. Hiki N, Yamamoto Y, Fukunaga T, et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. *Surg Endosc* 2008;22:1729-35.
 22. Tamaki I, Obama K, Matsuo K, et al. A case of primary adenocarcinoma of the third portion of the duodenum resected by laparoscopic and endoscopic cooperating surgery. *Int J Surg Case Rep* 2015;9:34-8.
 23. Irino T, Nunobe S, Hiki N, et al. Laparoscopic-endoscopic cooperative surgery for duodenal tumors: a unique procedure that helps ensure the safety of endoscopic submucosal dissection. *Endoscopy* 2015;47:349-51.

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