

Endoscopic submucosal dissection

Initial experience in the Czech Republic

Ondřej Urban¹, Petr Vítek², Petr Fojtík¹, David Janík¹, Martin Kliment¹, Josef Chalupa², Vladimír Hořava Jr.³

¹ Centrum péče o zažívací trakt, Vítkovická nemocnice a.s., Ostrava, Česká republika / Gastroenterology centre, Vítkovice Hospital, Ostrava, Czech Republic

² Interní oddělení, Nemocnice ve Frýdku-Místku, p.o., Frýdek-Místek, Česká republika / Department of Internal Medicine, District Hospital, Frýdek-Místek, Czech Republic

³ Biocytolab s.r.o., Frýdek-Místek, Česká republika / Czech Republic

Urban O, Vítek P, Fojtík P, Janík D, Kliment M, Chalupa J, Hořava Jr V. Endoscopic submucosal dissection. Initial experience in the Czech Republic

Folia Gastroenterol Hepatol 2006; 4 (1): 4 – 10.

Abstract. Endoscopic submucosal dissection (ESD) enables en bloc resection of certain types of early gastrointestinal neoplasias with the help of different knives, of which the insulated-tip, or IT, knife is the most frequently used. The IT knife is a variant of the needle knife, tipped with a ceramic ball to prevent cutting through muscularis propria. ESD is applied throughout the gastrointestinal tract, mostly in the stomach and colon. Although widely used in Japan, reports on ESD from western countries are infrequent. A total of six cases of ESD from two Czech gastroenterology centers are presented here.

Key words: endoscopic submucosal dissection, endoscopic mucosal resection, insulated-tip needle knife

Urban O, Vítek P, Fojtík P, Janík D, Kliment M, Chalupa J, Hořava Jr V. Endoskopická submukózní disekce. První zkušenosti v České republice. Folia Gastroenterol Hepatol 2006; 4 (1): 4 – 10.

Souhrn. Metoda endoskopické submukózní disekce (ESD) umožňuje resekci některých časných gastrointestinálních neoplazií en bloc. Při této metodě se využívá speciálních nožů. Nejčastěji používaný je jehlový nůž s keramickou špičkou, která zabraňuje prořezání nože přes muscularis propria. Metoda ESD se v současnosti používá v celé trávicí trubici, především v žaludku, tračníku a rektu. Metoda je používána zejména v Japonsku, ojediněle byly publikovány soubory z evropských a amerických pracovišť. Autoři prezentují šest případů ESD ze dvou center v České republice.

Klíčová slova: endoskopická submukózní disekce, endoskopická mukózní resekce, jehlový nůž s keramickou špičkou

Gastrointestinal tract neoplasias are a major problem in Europe. Reports indicate that a total of 579,542 gastrointestinal tract cancers are expected to be diagnosed every year (7). Gastroenterologists are making all possible efforts to diagnose and treat precursor lesions and carcinomas at an early stage.

It is generally accepted that endoscopic treatment of certain types of gastrointestinal neoplasias is more effective than surgical intervention (10). The methods of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have proven effective in the treatment of superficial neo-

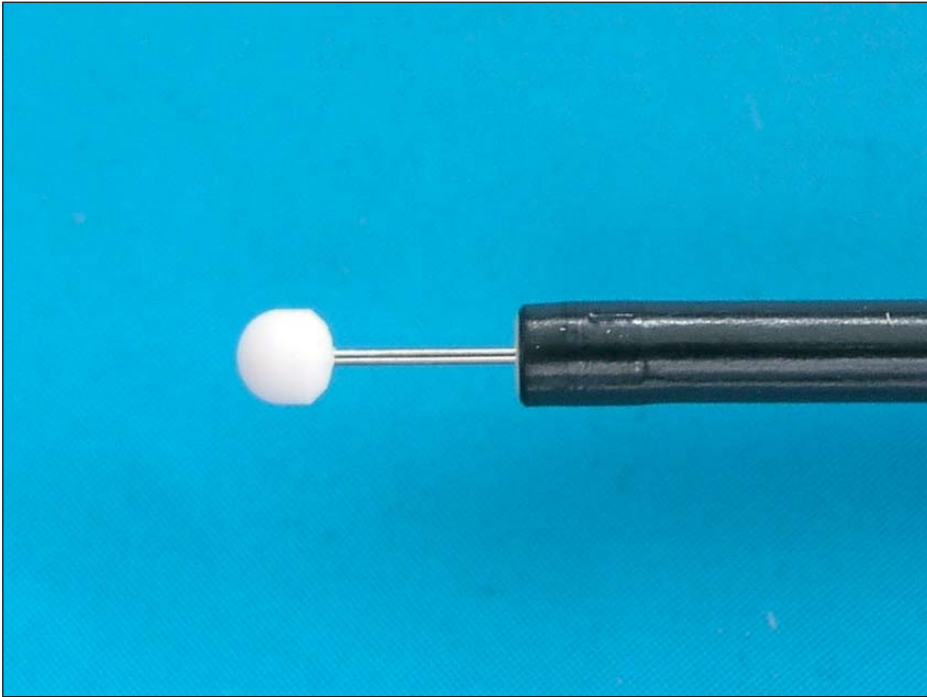


Figure 1 / Obr. 1
The insulated-tip needle knife (IT knife). Diameter of the tip 2.2mm, length 4 mm.
Jehlový nůž s keramickou špičkou. Průměr špičky 2,2 mm, délka 4mm.

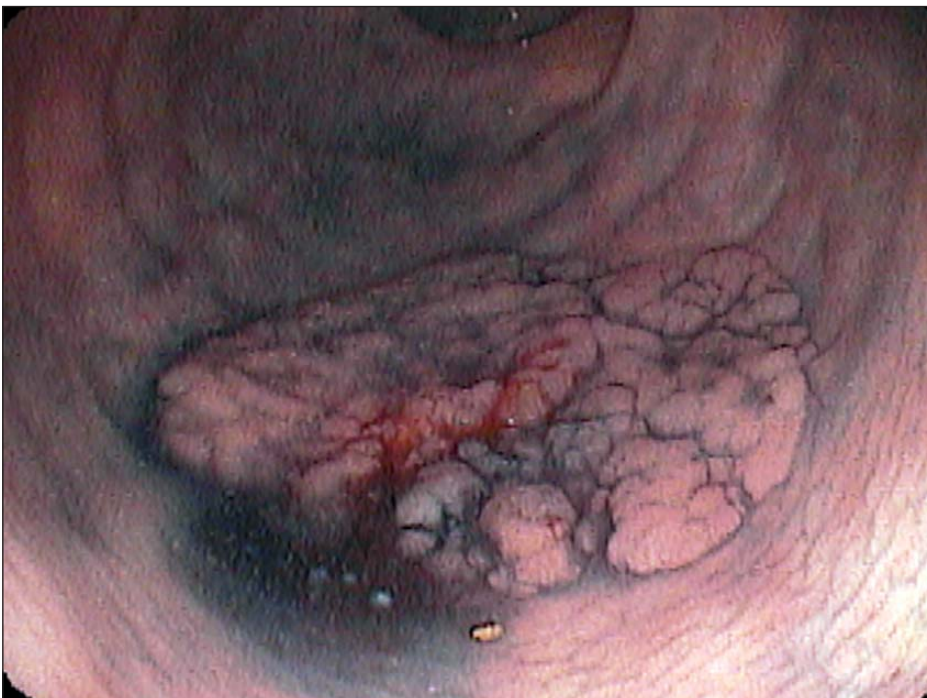


Figure 2 / Obr. 2
A flat neoplastic lesion LST-G 30 mm in diameter in the rectum. 0.1% indigo carmine solution staining. Patient No. 6 (see table).
Plochá neoplastická léze rekta typu LST-G o průměru 30mm. Chromodiagnostika 0,1% roztokem indigokarmínu. Pacient č. 6 (viz tabulka).

plastic lesions in the event that risk of lymph node metastasis is less than 3 % (5). That means that neoplastic invasion is limited to mucosa or the upper third portion of the submucosal layer, and lymphatic invasion is not observed. If, in such a case, the lesion can be completely removed, the endoscopist ought to consider a resection curative. Both EMR and ESD originated in Japan. While EMR is now widely used in the West and Czech Republic (13), reports on ESD are still scarce and the results not satisfactory (11). We present our initial experien-

ce with ESD using the IT knife (Fig. 1) on a group of 6 patients.

Patients and methods

A total of six patients were treated in two Czech gastroenterology centers during the period 8/2005 - 2/2006. Single working channel endoscopes were used (OLYMPUS CF 145, 160 and PENTAX EC 3880K). As soon as the lesion was diagnosed, either 0.1% indigo carmine or 0.1% methylene blue solutions were sprayed on the lesion using a spray catheter.

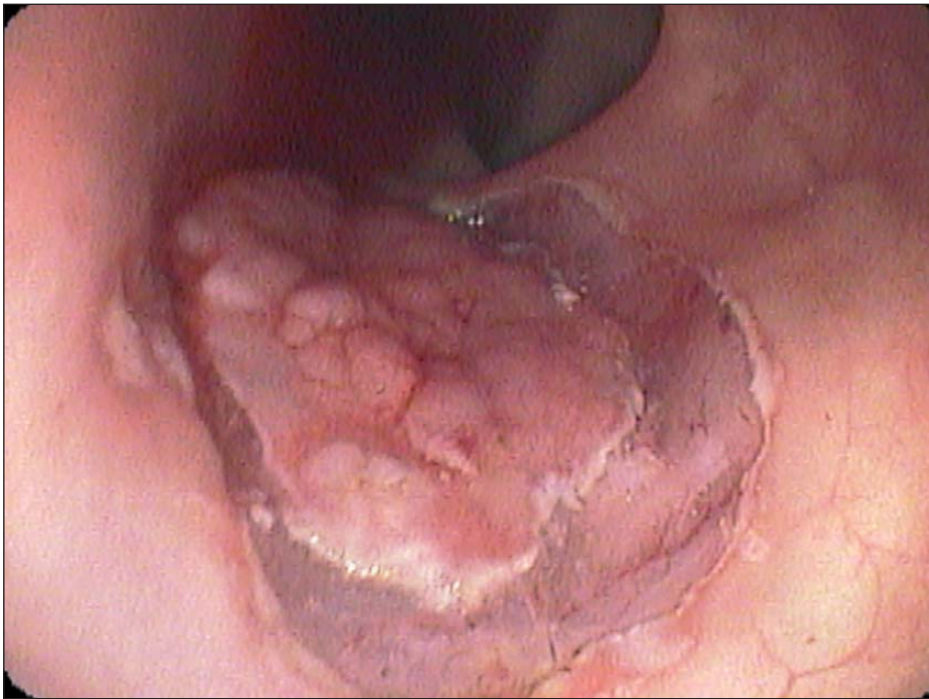


Figure 3 / Obr. 3
An endoscopic mucosal incision around the lesion. The same patient as in Fig. 2.
Incize mukózy kolem léze. Stejný pacient jako na obrázku 2.

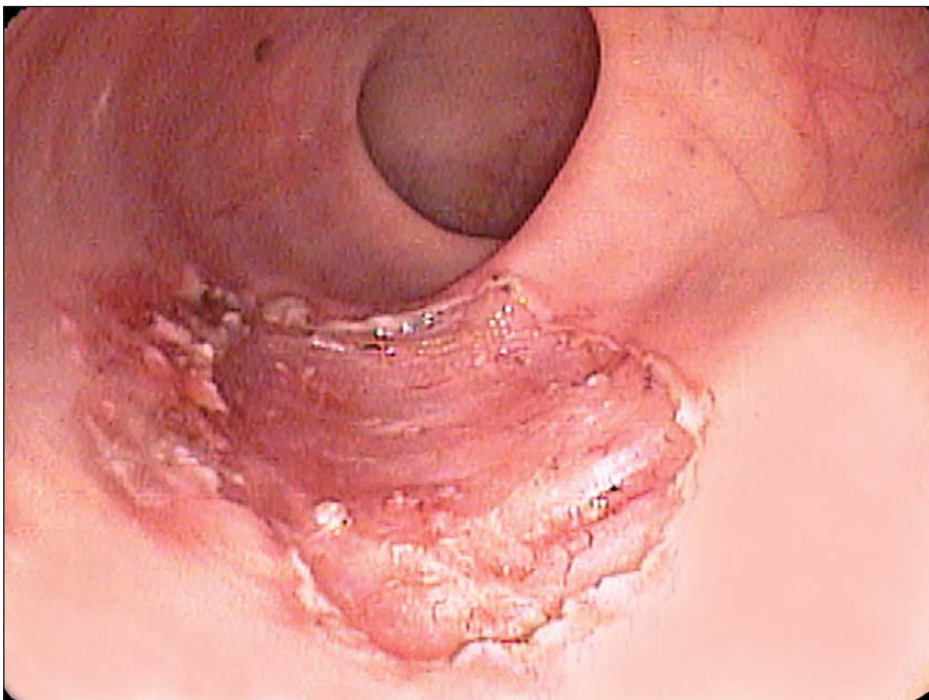


Figure 4 / Obr. 4
An artificial ulcer after endoscopic submucosal dissection.
A muscularis propria can be seen. The same patient as in Fig. 2.
Slizniční defekt po endoskopické submukózní disekci. Stejný pacient jako na obrázku 2.

ter (Spray catheter OLYMPUS PW-6C-1) to improve its delineation (2) (Fig. 2). Each lesion was then classified according to the Paris Endoscopic Classification of Superficial Neoplastic Lesions (6). The absence of a deep invasion into the submucosa was assumed by the absence of ulceration and the presence of a lifting sign after a submucosal injection (Injection needle OLYMPUS NM-200U-0525, length of needle 4 or 5 mm). We used a saline-epinephrine solution (dilution rate 20.000:1) and 10% glycerol solution for the submucosal injections. A total amount of 20 mL to 60 mL

of fluid was used. The needle was preferentially inserted through the surrounding, intact mucosa. Only lesions with complete lifting were considered for endoscopic treatment. In this case, small incisions into the submucosa were performed at a distance of 3-5 mm from the border of the lesion with the help of a needle knife. The ceramic ball of the IT knife (IT knife OLYMPUS KD10Q) was then introduced through the incision into submucosa (Figs 1 and 7). The cutting in the direction of the next incision followed. A blended (ENDOCUT) current was used.

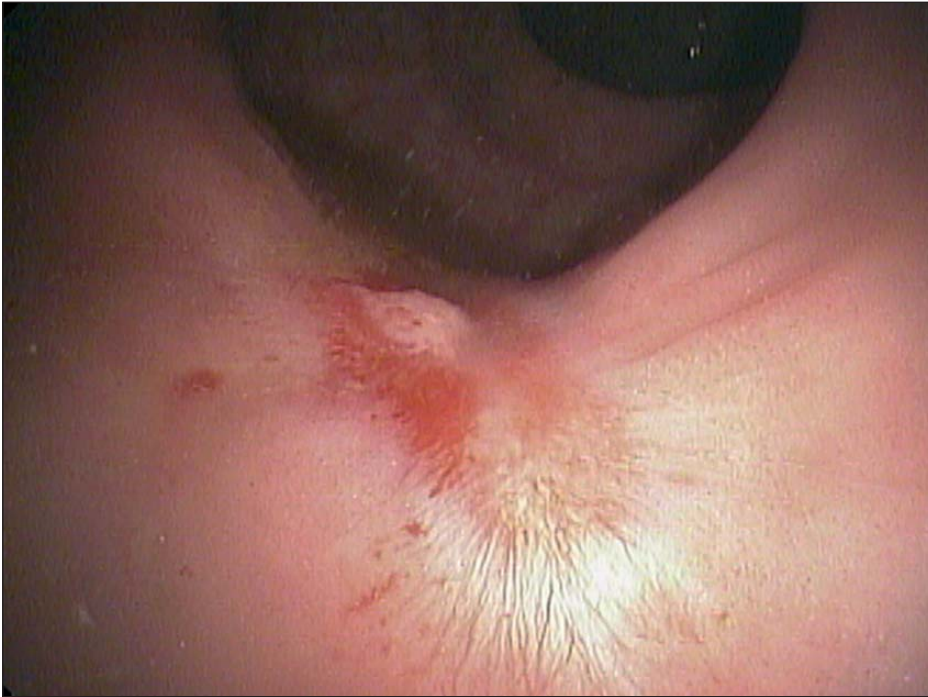


Figure 5
A scar 6 weeks after resection. There is a granulation tissue visible in the upper part of the scar. The same patient as in Fig. 2.
Jizva 6 týdnů po resekci. V horní části jizvy je patrná granulační tkáň. Stejný pacient jako na obrázku 2.

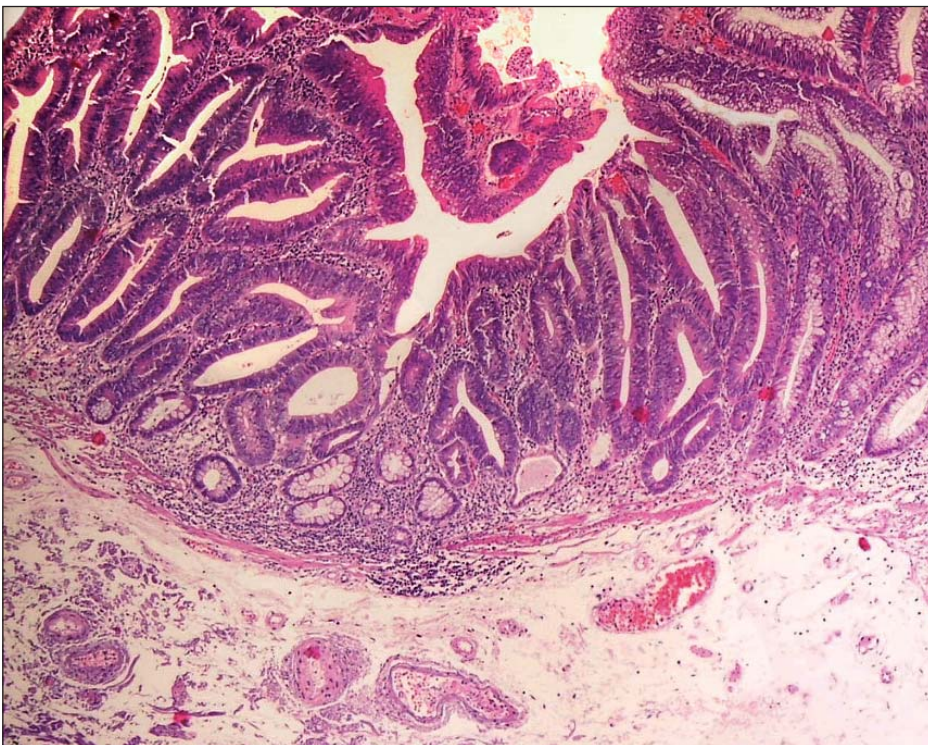


Figure 6 / Obr. 6
A resected specimen – HGD adenoma. Haematoxilin-eosin. The same lesion as in Fig. 2.
Resekát – adenom s těžkou dysplazií. Hematoxylin-eozin. Stejný pacient jako na obrázku 2.

A transparent cap attached to the distal tip of the endoscope was used in two cases (Figs 7 and 8). When cutting around the lesion was finished, retraction of the lesion could be observed (Fig. 3). The retracted lesion was resected with a mucosectomy snare in three cases. In the other three cases, the resection of the lesion was completed by lightly dissecting through the submucosal layer using the IT knife (Fig. 4). Whenever bleeding occurred, it was immediately stopped with hot biopsy forceps, argon plasma coa-

gulation, or endoclips. The resected specimens were removed, fixed on cork boards, and placed in 10% formaldehyde solution. Descriptions of the patients and their lesions are listed in the Table.

We have achieved curative treatment with ESD in 5 patients with rectal neoplasias. The resection margin of the specimens in these patients was free of any neoplastic tissue upon histopathological examination and no residual neoplastic tissue was diagnosed during follow-up endoscopy (Figs 5 and 6). The

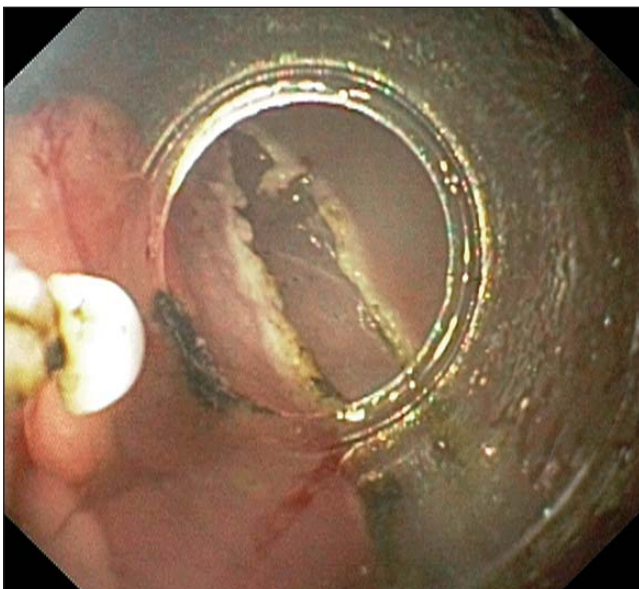


Figure 7 / Obr. 7

A mucosal incision with IT knife. A transparent cap is attached to the tip of the endoscope to improve visualization.
Incize mukózy s pomocí IT nože. Na konci endoskopu patrný průhledný nástavec pro zlepšení viditelnosti.

length of stay in hospital was 24 – 48 hours. One patient with a rectal carcinoid had minor rectal bleeding on the eighth day and was treated with argon plasma coagulation without the need for hospital admission. One patient with early gastric cancer had post-ESD bleeding that required urgent upper endoscopy to clip the bleeding vessel and a transfusion of two units of erythrocyte concentrate. He stayed in hospital for 7 days. This patient underwent gastric resection later on because of tumour infiltration in the lateral resection margin. The postoperative course was uneventful (stage pT1N0M0).

Discussion

EMR and ESD methods are used in the treatment of defined subgroups of superficial gastrointestinal neo-

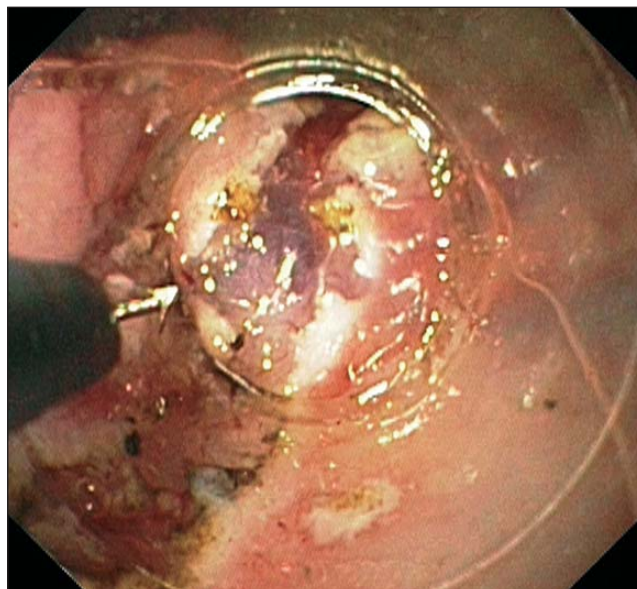


Figure 8 / obr. 8

Submucosal preparation with a triangle knife. The same lesion as in Fig. 7.
Preparace submukózy s pomocí trojúhelníkového nože. Stejná léze jako na obrázku 7.

plasias. A total of four principle methods of EMR and many modifications have been developed by Japanese endoscopists. These include lift and cut, cap-assisted EMR or suck and cut, band-assisted EMR, and EMR with a special overtube.

The EMR method is suitable for *en bloc* resection of superficial lesions with a diameter of up to 20-30 mm. Although larger lesions can be resected with a piecemeal EMR technique as well, a lower diagnostic accuracy of the final histopathological examination should be expected.

The ESD method with a diathermic knife (8,9) not only enables *en bloc* resection of large lesions (4) but also provides the advantage of direct visual control during the cutting process in the submucosal layer. After the initial success of applying ESD in the

Table / Tabulka

Endoscopic submucosal dissection with IT knife – characteristics of patients and lesions.
Endoskopická submukózní disekce s pomocí IT nože – charakteristika nemocných a jejich lézí.

Patient	Gender	Age	Site	Type	Size (mm)	Histology	Complication
1	F	73	Rectum	LST	35x20	HGD adenoma	0
2	M	77	Stomach	0-IIc + Is	30x15	Well differentiated adenocarcinoma (sm1)	Bleeding
3	M	78	Rectum	LST	30x25	Intramucosal carcinoma	0
4	M	53	Rectum	LST	22x22	HGD adenoma	0
5	M	58	Rectum	Carcinoid	8x8	Carcinoid	Bleeding
6	M	73	Rectum	LST	30 x30	HGD adenoma	0

M – male; F – female; LST – laterally spreading tumour; HGD – high grade dysplasia

stomach, it is now also widely used in the oesophagus, colon, and rectum (15). ESD of early gastric carcinomas larger than 20 mm with a higher risk of lymphatic node metastasis can be accompanied by laparoscopic lymphatic node dissection to improve staging (1).

The ESD technique requires special endoscopic equipment. In addition to the IT knife, a TT (triangular-tip), HT (hook-tipped), flex knife and other knives were developed. There are few solutions used for submucosal injection. The most common is saline, by itself or with adrenalin 20.000:1, a glycerol solution, and hyaluronic acid. Special mixtures were developed to enable the safe resection of large lesions in the colon (3,16). It is quite useful to add a small amount of dye (indigo carmine or methylene blue) to the solution to improve the visualization of the whole thickness of the submucosal layer. Most of the authors report using a transparent distal cap to better control the procedure and maintain a stable distance between mucosa and the tip of the endoscope to allow safe cutting. Some of the authors use a small-caliber-tipped transparent hood to open incised mucosa for better visualizing submucosal tissue (14). The effectiveness of traction-assisted ESD in large flat adenomas (laterally spreading tumours) in the colon (12) has also been reported. This method is considered safe in experienced hands. The risk of perforation and severe bleeding was about 1% in a large series of cases from Japan (8).

As far as the authors are aware, this is the first report on ESD performed in the Czech Republic. In five of six patients curative resection could be achieved according to histopathological criteria. In case number 2 the procedure was not successful from the curative point of view because of positive lateral resection margin. Nevertheless histopathological examination of the resected specimen confirmed the diagnosis of cancer that was not certain from previous biopsy samples. We can only speculate here if in-

complete resection was due to factors on the lesion's or operator's side. The boundaries of this stomach cancer were quite ambiguous despite chromodiagnosis. We had to deal with the problem of a long horizontal cut that was not easy to perform and a spurting artery also had to be treated during the procedure.

The carcinoid tumour in case number 6 was sessile. These tumours are reported to develop in the deeper layer of mucosa, therefore they could invade like submucosal tumours. We preferred ESD to EMR in this situation, since careful dissection in the submucosal layer is much easier to control and cutting through the tumour base could thus be avoided.

From our point of view, ESD is a challenging procedure advantageous for a specific group of patients. Nevertheless, it must be emphasized that only very skilled and experienced endoscopists should offer it to well-informed patients. One must keep in mind that the risks are always the patient's to bear, and there are currently only a few centres worldwide available that teach this procedure. The procedure itself can also be very time consuming and costly. Our six cases required 40 to 100 minutes to achieve complete resection. Cost effectiveness is totally dependent on the local situation. At present, it is out of the question in the Czech Republic, where abdominal surgery is very inexpensive. In our opinion, ESD should be performed in well-equipped high-volume endoscopic centres. Of course, an experienced abdominal surgeon in the facility is a must.

Conclusion

ESD follows EMR as a procedure for the armamentarium of western therapeutic endoscopists. The careful adoption of this technique has a potential to minimize invasiveness in treating a selected group of patients. Having their benefit in mind, we can expect wider acceptance of ESD both in the Czech Republic and Europe. It is with great anticipation that we are prepared to accept this challenge.

REFERENCES

1. Abe N, Mori T, Takeuchi H, Yoshida T, Ohki A, Ueki H, Yanagida O, Masaki T, Sugiyama M, Atomi Y. Laparoscopic lymph node dissection after endoscopic submucosal dissection: A novel and minimally invasive approach to treating early-stage gastric cancer. *Am J Surg* 2005; 190: 496-503.
2. Bureš J, Rejchrt S, Repák R, Slezák L, Kopáčková M, Široký M. Chromo-endoskopie. *Čes Slov Gastroent* 2000; 54: 65-68.
3. Fujishiro M, Yahagi N, Nakamura M, Kakushima N, Kodashima S, Ono S, Kobayashi K, Hashimoto T, Yamamichi N, Tateishi A, Shimizu Y, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M. The successful outcome of a novel endoscopic treatment for GI tumors: endoscopic submucosal dissection with a mixture of high-molecular-weight hyaluronic acid, glycerin, and sugar. *Gastrointest Endosc* 2006; 63: 243-249.
4. Gotoda T. A large endoscopic resection by endoscopic submucosal dissection procedure for early gastric cancer. *Clin Gastroenterol Hepatol* 2005; 3 Suppl 1:71-73.
5. Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shi-

- moda T, Kato Y. Incidence of lymph node metastasis from early gastric cancer: Estimation with a large number of cases at two large centers. *Gastric Cancer* 2000; 3: 219-225.
6. Inoue H, Kashida H, Kudo S, Sasako M, Shimoda T, Watanabe H, Yoshida S, Guelrud M, Lightdale CJ, Wang K, Riddell RH, Diebold MD, Lambert R, Rey JF, Jung M, Neuhaus H, Axon AT, Genta RM, Gonvers JJ. The Paris endoscopic classification of superficial neoplastic lesions: Esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc* 2003; 58, Suppl 6: 3-43.
 7. Keighley MR. Gastrointestinal cancers in Europe. *Aliment Pharmacol Ther* 2003; 18, Suppl 3:7-30.
 8. Miyamoto S, Muto M, Hamamoto Y, Boku N, Ohtsu A, Baba S, Yoshida M, Ohkuwa M, Hosokawa K, Tajiri H, Yoshida S. A new technique for endoscopic mucosal resection with an insulated-tip electro-surgical knife improves the completeness of resection of intramucosal gastric neoplasms. *Gastrointest Endosc* 2002; 55: 576-581.
 9. Ohkuwa M, Hosokawa K, Boku N, Ohtu A, Tajiri H, Yoshida S. New endoscopic treatment for intramucosal gastric tumors using an insulated-tip diathermic knife. *Endoscopy* 2001; 33: 221-226.
 10. Rejchrt S. Gastrointestinal epithelial neoplasia. We can see only what we already know. *Folia Gastroenterol Hepatol* 2004; 2: 143-146.
 11. Rösch T, Sarbia M, Schumacher B, Deinert K, Frimberger E, Toermer T, Stolte M, Neuhaus H. Attempted endoscopic en bloc resection of mucosal and submucosal tumors using insulated-tip knives: a pilot series. *Endoscopy* 2004; 36: 788-801.
 12. Saito Y, Emura F, Matsuda T, Uraoka T, Nakajima T, Ikematsu H, Gotoda T, Saito D, Fujii T. A new sinker-assisted endoscopic submucosal dissection for colorectal cancer. *Gastrointest Endosc* 2005; 62:297-301.
 13. Urban O, Vítek P, Fojtík P, Chalupa J. Endoskopická diagnostika a léčba povrchových nepolypózních neoplazií trávicí trubice. *Folia Gastroenterol Hepatol* 2004; 2: 165-173.
 14. Yamamoto H. Endoscopic submucosal dissection of early cancers and large flat adenomas. *Clin Gastroenterol Hepatol* 2005; 3, Suppl 1:74-76.
 15. Yamamoto H, Yahagi N, Oyama T. Mucosectomy in the colon with endoscopic submucosal dissection. *Endoscopy* 2005; 37: 764-768.
 16. Yamasaki M, Kume K, Kanda K, Yoshikawa I, Otsuki M. A new method of endoscopic submucosal dissection using submucosal injection of jelly. *Endoscopy* 2005; 37: 1156-1157.

Correspondence to / adresa pro korespondenci:

MUDr. Ondřej Urban, Centrum péče o zažívací trakt,
Vítkovická nemocnice Ostrava, a.s., Zalužanského 15,
703 84 Ostrava-Vítkovice, Czech Republic.
E-mail: ondrej.urban@nemvitkovice.cz