

This is an Open Access article licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License (www.karger.com/OA-license), applicable to the online version of the article only. Distribution for non-commercial purposes only.

Is Endoscopic Submucosal Dissection the Option for Early Gastric Cancer Patients with Contraindication to Surgery?

Said Farhat^a Romain Coriat^{a, c} Virginie Audard^{a, b}
Sarah Leblanc^{a, c} Frederic Prat^{a, c} Stanislas Chaussade^{a, c}

^aService de gastroentérologie and ^bService d'anatomie et de cytologie pathologiques, Hôpital Cochin, GHU Ouest, Assistance Publique-Hôpitaux de Paris, and ^cUniversité Paris Descartes, Paris, France

Key Words

Gastric cancer · Surgery · Comorbidity · Elderly · Endoscopic treatment

Abstract

Surgical therapy is the traditional approach for early gastric cancer. Patients with comorbidities cannot benefit from this treatment because of high surgical morbidities and mortalities. Endoscopic submucosal dissection is a new technique for complete en bloc resection of early gastric cancer. We report the case of a patient with severe cardiomyopathy who developed early gastric cancer without metastases present on CT scan. The patient underwent endoscopic submucosal dissection because of the high risk associated to surgery due to severe comorbidity. The patient had complete submucosal dissection with complete en bloc resection. The lateral and deep margins were free of cancerous cells based on histopathology study. The patient was controlled every 6 months for 30 months by endoscopy. Systematic biopsies were done. No recurrences were diagnosed. This report supports the application of endoscopic treatment for patients with early gastric cancer and at high risk for surgery due to comorbidities.

Introduction

Early gastric cancer is defined as gastric cancer confined to the mucosa or submucosa, regardless of the presence or absence of lymph node metastasis. Surgery for early gastric cancer remains the mainstay of therapeutic approaches with 5- and 11-year survival rates of 90 and 57%, respectively, for T1 gastric cancer (mean survival 4.43 years for patients >70 years old) [1]. Recurrences occur within the first 2 years and are one of the major problems in gastric cancer with a local recurrence rate of 67% [2]. As a result, surgery is considered the standard in early gastric cancer treatment.

Improvement of endoscopic tools and techniques may change the style of treatment in certain cases. Despite advances in surgical techniques and skills, surgical morbidity for gastric cancer still ranges from 19 to 63% with a reported mortality from 1.7 to 11.4% [3, 4]. The prognosis of resectable gastric cancer is closely dependent on tumor depth, lymph node involvement, and whether a curative (R0) resection has been performed. The extension of surgical resection with curative intent may expose the patient to an increased risk of morbidity and mortality with a negative impact on long-term survival [5]. Age, preoperative performance status, tumor stage, surgeon skill, operating time and the type of surgery are the main risk factors related to surgical morbidity and mortality [4].

Comorbidities influence overall life expectancy and are an important consideration when evaluating risks over benefits. Of all comorbid conditions, cardiovascular disease is the most prevalent and a leading cause of severe perioperative complications and death. In cases with high surgical mortality, endoscopic treatment might be an attractive and less invasive option. Taking this into account, endoscopic mucosal resection has been successfully used to treat intramucosal gastric cancer worldwide, but unfortunately specimens resected with piecemeal are often misinterpreted and under- or overstaged. En bloc resection has been the cornerstone for the development of new endoscopic techniques. Endoscopic submucosal dissection (ESD) is the new technique for achieving en bloc resection of the tumor using Triangular Tip knife (TT KNIFE®, Olympus, Tokyo, Japan). ESD allows en bloc resection for intramucosal tumors and reduces local recurrences [6]. In patients who underwent ESD using the TT KNIFE® for early gastric cancer lesions, Oda et al. described a one-piece resection rate of 98%. A tumor-free margin was obtained in 93% of cases and all but one complication was managed by endoscopic treatment (immediate bleeding in 7%, delayed bleeding in 6% and perforation in 4%) [7].

As gastroenterologists become more familiar and experienced with ESD materials and techniques, high-risk patients not suitable for surgical therapy may benefit from these therapeutic techniques. We report a case with early gastric cancer treated by ESD because of severe underlying organ dysfunction.

Patient and Methods

A 78-year-old male patient with severe cardiomyopathy (arrhythmias, myocardial infarction and heart failure with on cardiac ultrasound akinesia of the inferior wall of the left ventricle with left ventricular ejection fraction of 45%) developed gastric cancer. The patient's cardiac function did not make him suitable for surgery. He had no metastases on CT scan. Endoscopic ultrasound before dissection showed a superficial lesion limited to the mucosa (usT1N0M0). The lesion was plane, slightly elevated and depressed, classified as IIa+IIc lesion following the Paris Classification (fig. 1a). The lesion measured 10 mm diameter and was located of the angulus. En bloc ESD was done using the TT KNIFE® with no operative complications.

ESD was done under sedation with propofol (2 mg/kg/h) and monitoring of cardiorespiratory function during the procedure. ESD was performed with a standard single accessory channel endoscope (Fujinon EG490ZW5 gastroscope; Fujinon Corp., Saitama City, Japan).

Sequences for ESD were as follows: marking, injection, incision, submucosal dissection and hemostasis. Marking was done with several marking dots 5–10 mm outside the margin of the target lesion, using the needle knife in forced coagulation mode (40 W). Injected solution was made with normal saline solution, epinephrine 1/40,000 and a small amount of indigo carmine 2%. The solution was injected using a 21-gauge needle into the submucosa to lift and detach the lesion with a volume of

50 cm³. The circumferential incision into the mucosa was made by using the back side of the TT KNIFE® in endocut mode (80 W) (fig. 1b, c). Direct dissection of the submucosal layer was carried out with the TT KNIFE® in endocut mode (80 W) and with the aid of a soft hood attached to the tip of the endoscope. Endoscopic hemostasis was performed during the procedure with the knife itself whenever active bleeding was noted. After the procedure, preventive endoscopic hemostasis was done for any oozing or exposed vessel with hemoclips (fig. 1d). Proton pump inhibitors were introduced 2 days before dissection. Postoperative evolution was restricted to abdominal pain successfully managed medically. There was no other postoperative complication. ESD was done on an inpatient basis, with a hospital stay of 3 days.

The resected specimen was fixed in formalin and sectioned into 2-mm slices, then embedded in paraffin. The pathology report confirmed the presence of a well-differentiated gastric adenocarcinoma infiltrating the submucosa over approximately 0.152 mm in length, without microemboli (fig. 2). The depth of the invasion was in contact with the limits of resection. One of the lateral margins of the resection was across an intramucosal adenocarcinoma. No local recurrences were observed after 23-month follow-up endoscopy and biopsies. The patient is disease-free at 30 months post therapy.

Discussion

Early gastric cancer is defined as gastric cancer confined to the mucosa or submucosa, regardless of the presence or absence of lymph node metastasis. ESD has been accepted as the endoscopic treatment of the localized intramucosal gastric neoplasm. However, tumor resection evaluation is difficult with piecemeal resection because complete reconstruction of the specimen is frequently impossible. En bloc resection has been proposed as a quality criterion for ESD because it allows for accurate histological assessment, while also reducing the risk of tumor recurrence [6]. ESD enables us to treat even large ulcerative lesions and lesions with a scar. A high en bloc resection rate, above 90%, has been reported in several Japanese studies [8]. Evaluation of the completeness of resection was easy in en bloc resected lesions. Complete resection was defined as microscopic findings of specimens showing intramucosal tumors without neoplastic components at both lateral and vertical margins, no lymphatic or venous invasion, and no undifferentiated-type nests.

ESD was done in the coagulation mode, which destroys approximately 1 mm around the dissected area at both sides. This justifies the marking spots of the tumor to control the lateral margins of the resection. Retrospectively, the patient is disease-free at 30 months and the control endoscopies with biopsies are still negative.

Over the past 20 years, since the introduction of these techniques, indications for ESDs for early gastric cancers have generally been accepted to include differentiated mucosal adenocarcinoma, elevated-type mucosal cancer less than 20 mm in largest diameter, and flat or depressed-type lesions (without ulceration) less than 10 mm in size [9]. Multivariate analysis suggests that if all three of these criteria are met and if no lymphatic involvement of the tumor is noted on histological evaluation, the incidence of lymph node involvement is less than 0.4% [10]. The incidence of lymph node metastasis was 15.9% in submucosal undifferentiated early gastric cancer [9]. As the presence of submucosal invasion, lymphatic or venous invasion or undifferentiated-type adenocarcinoma is considered to indicate higher risk of lymph node metastases, surgical treatment was strongly recommended [11].

Surgical resection of early gastric cancers offers an excellent (90–100%) chance of curing the disease based on several Japanese series [12]. Any major surgical intervention, however, carries risks of complications including wound infection, prolonged hospital stay, anesthetic complication and death. This is especially problematic in elderly patients or those patients with concomitant severe organ dysfunction including heart failure, kidney failure, and lung disease. For this reason, endoscopic therapy may provide an attractive and less invasive treatment option that may ultimately prove to be safer in this selected subgroup of patients. Although no head to head prospective trials have been performed looking at long-term survival for ESD versus surgery, 2- and 5-year survival rates for ESD are 100 and 95%, respectively, whereas they are 100 and 100% for patients who underwent surgery [12]. On the other hand, Isomoto et al. showed that non-curative ESD required close follow-up surveillance for recurrence for up to 2 years at least, as the recurrent tumors developed 13–24 months after ESD [13]. Tada et al. have shown no differences in survival rates after 5- and 10-year periods for ESD compared with surgery [14].

The incidence of gastric cancer is high in elderly patients. Surgery is the only curative treatment for gastric cancer. Comorbidities are common in elderly patients. ESD might be the best option in elderly patients with a high surgical morbidity.

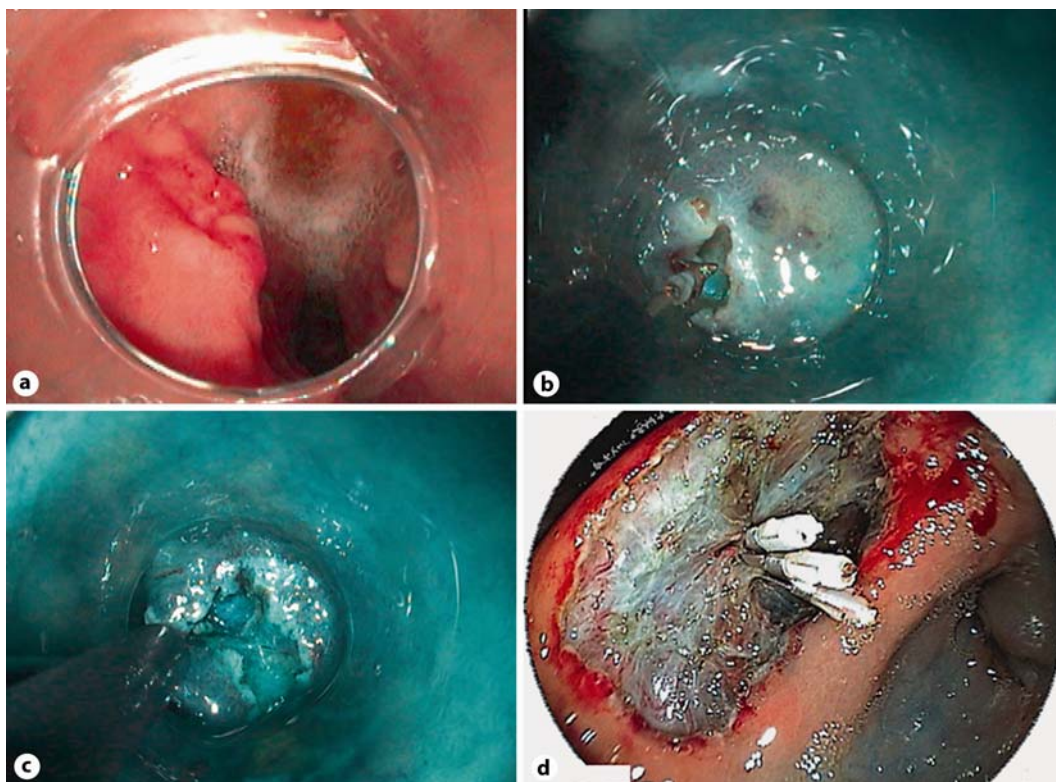


Fig. 1. ESD of early gastric lesion. **a** Slightly elevated and depressed lesion (IIa+IIc). **b** Direct incision using the back side of the TT KNIFE®. **c** Circumferential incision into the mucosa. **d** Preventive endoscopic hemostasis performed at the end of the procedure.

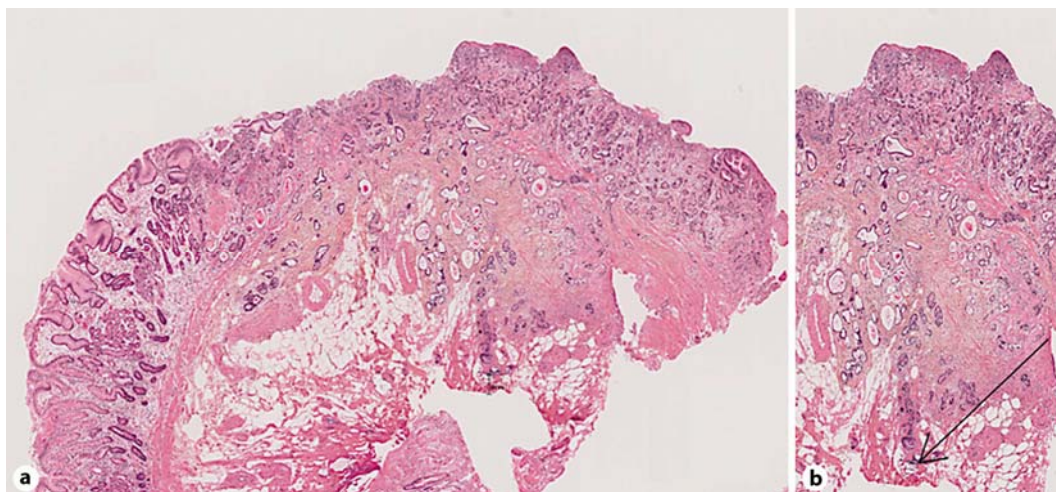


Fig. 2. Histopathology. **a** Well-differentiated gastric adenocarcinoma infiltrating the submucosa. **b** The depth of the invasion was close to the limits of resection.

References

- 1 Hartgrink HH, van de Velde CJ, Putter H, et al: Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. *J Clin Oncol* 2004;22:2069–2077.
- 2 Gunderson LL, Sosin H: Adenocarcinoma of the stomach: areas of failure in a re-operation series (second or symptomatic look) clinicopathologic correlation and implications for adjuvant therapy. *Int J Radiat Oncol Biol Phys* 1982;8:1–11.
- 3 Siewert JR, Bottcher K, Roder JD, et al: Prognostic relevance of systematic lymph node dissection in gastric carcinoma. German Gastric Carcinoma Study Group. *Br J Surg* 1993;80:1015–1018.
- 4 Park DJ, Lee HJ, Kim HH, et al: Predictors of operative morbidity and mortality in gastric cancer surgery. *Br J Surg* 2005;92:1099–1102.
- 5 Nanthakumaran S, Fernandes E, Thompson AM, et al: Morbidity and mortality rates following gastric cancer surgery and contiguous organ removal, a population based study. *Eur J Surg Oncol* 2005;31:1141–1144.
- 6 Ono H, Kondo H, Gotoda T, et al: Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001;48:225–229.
- 7 Oda I, Gotoda T, Hamanaka H, et al: Endoscopic submucosal dissection for early gastric cancer: Technical feasibility, operation time and complications from a large consecutive series. *Dig Endosc* 2005;17:54–58.
- 8 Onozato Y, Ishihara H, Iizuka H, et al: Endoscopic submucosal dissection for early gastric cancers and large flat adenomas. *Endoscopy* 2006;38:980–986.
- 9 Li C, Kim S, Lai JF, et al: Risk factors for lymph node metastasis in undifferentiated early gastric cancer. *Ann Surg Oncol* 2008;15:764–769.
- 10 Yamao T, Shirao K, Ono H, et al: Risk factors for lymph node metastasis from intramucosal gastric carcinoma. *Cancer* 1996;77:602–606.
- 11 Gotoda T, Yanagisawa A, Sasako M, et al: 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.
- 12 Kim HS, Lee DK, Baik SK, et al: Endoscopic mucosal resection with a ligation device for early gastric cancer and precancerous lesions: comparison of its therapeutic efficacy with surgical resection. *Yonsei Med J* 2000;41:577–583.
- 13 Isomoto H, Shikuwa S, Yamaguchi N, et al: Endoscopic submucosal dissection for early gastric cancer: a large-scale feasibility study. *Gut* 2009;58:331–336.
- 14 Tada M, Tanaka Y, Matsuo N, Shimamura T, Yamaguchi K: Mucosectomy for gastric cancer: current status in Japan. *J Gastroenterol Hepatol* 2000;15(suppl):D98–D102.

S. Farhat and R. Coriat contributed equally to the work.