質問４．
患者さんの予後について、わかる範囲でお答え下さい。

１．生存　　→　付問５．へ

２．死亡　　→　付問６．へ

３．不明

付問５．　　最終生存確認日は？　　平成　　年　　月　　日

付問６．　　A. 死亡日は？（もし、おわかりになればご記入下さい）

平成　　年　　月　　日

B. その死因は？（もし、おわかりになればご記入下さい）

C. 死亡された病院はどちらですか？（もし、おわかりになればご記入下さい）

病院

住所

電話番号

担当医　　先生

質問５．
転居などのために他の施設へ紹介された場合、その施設についてわかる範囲でお答え下さい。

病院

住所

電話番号

担当医　　先生

以上

ご協力いただき、有り難うございました。

（資料4）：アンケート調査（患者用）

アンケート調査

患者符号化番号　　[　　]
（担当医が記入する匿名化のための番号です。）
内視鏡切除施行施設　　[　　]（担当医記入）
内視鏡切除施行日　　[　　]（担当医記入）

質問１．
このアンケート調査の記入日をお書き下さい。　　平成　　年　　月　　日

質問２．
内視鏡切除のあとに、上部内視鏡検査（胃カメラ検査）は受けられましたか？○をつけて下さい。

１．はい　　→　付問１．へ

２．いいえ　　→　質問３．へ

付問１．　A. 検査はいつ受けられましたか？　　平成　　年　　月　　日

B. 検査はどこで受けられましたか？　わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

C. 再発や新たな胃がんが発見されましたか？○をつけて下さい。

１．はい　　→　付問２．へ

２．いいえ　　→　質問４．へ

付問２．　その治療は受けられましたか（受けていますか）？○をつけて下さい。

１．はい　　→　付問３．へ

２．いいえ　　→　質問４．へ

付問３．　その治療はどこで受けられましたか（受けていますか）？
わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

質問３．
内視鏡切除後に上部内視鏡検査を受けられていない理由は何ですか？○をつけて下さい。

１．転居し、かかりつけの病院に行けなくなった。

２．大きな病気になった。

３．忙しかった。

４．その他　　[　　]

質問４．
ヘリコバクター・ピロリ菌について、○をつけて下さい。

１．感染歴あり　　→　付問４．へ

２．感染歴なし　　→　質問５．へ

３．不明（検査未施行）　→　質問５．へ

付問４．　除菌治療の有無について、○をつけて下さい。

１．除菌施行　→　付問５．へ

２．除菌未施行　→　質問５．へ

付問５．　A. 除菌治療開始日は？　平成　年　月　日頃

B. 除菌治療の成否について、○をつけて下さい。

１．除菌成功

２．除菌失敗

３．不明（判定未施行）

質問５．
内視鏡切除を行った後に、新たな大きな病気にかかりましたか？（風邪などの軽い病気は除きます。）○をつけて下さい。

４．はい　→　付問６．へ

５．いいえ　→　質問６．へ

付問６．
新たな大きな病気について、すべて記入して下さい。
（記入しきれない場合、裏面にご記入下さい。）

A. いつ頃からですか？　平成　年　月　頃

B. 病名は ＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

C. その病気でかかっている（かかっていた）病院はどちらですか？
わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

A. いつ頃からですか？　平成　年　月　頃

B. 病名は ＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

C. その病気でかかっている（かかっていた）病院はどちらですか？
わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

A. いつ頃からですか？　平成　年　月　頃

B. 病名は ＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

C. その病気でかかっている（かかっていた）病院はどちらですか？
わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

質問６．
アンケート記入は、ご本人が行いましたか？代理の方が行いましたか？○をつけて下さい。

１．ご本人

２．代理の方　→　付問７．へ

付問７．　残念ながら患者さんがお亡くなりになったために、代理の方が記入された場合、下記にお答えください。

A. いつ亡くなられましたか？　平成　年　月　日

B. その原因の病名は（もし、おわかりになればご記入下さい）

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

C. お亡くなりになった病院はどちらですか？
わかる範囲でお答え下さい。

＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院

住所＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

担当医＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿先生

以上

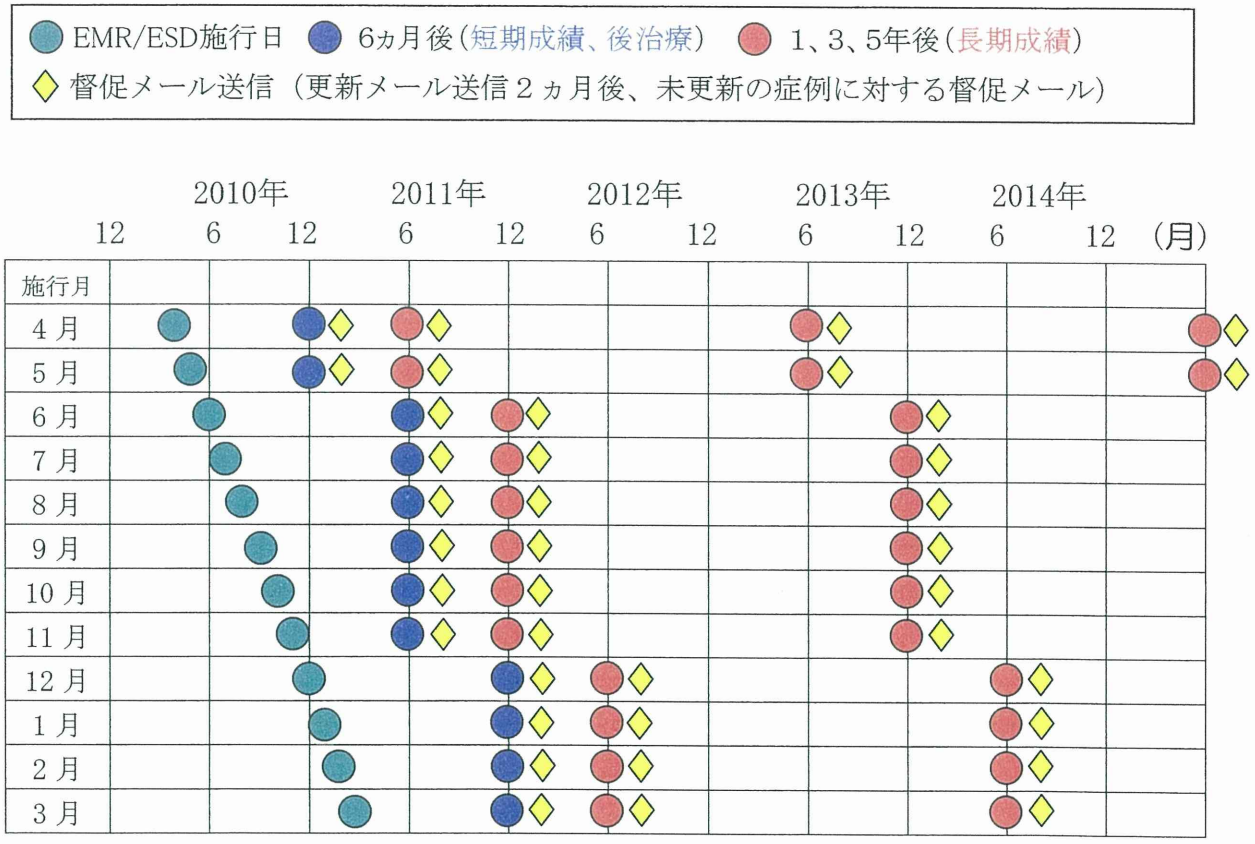
ご協力いただき、有り難うございました。

（資料5）：「自動Eメール送信機能」のシェーマ

内視鏡切除施行より 6 ヶ月後の C. 短期成績、D. 後治療の更新登録、1、3、5 年後の E. 長期成績の更新登録時期を１ヶ月以上経過して更新登録されていない症例について、年 2 回（6 月、12 月）各登録施設における登録代表者および当該登録担当医師に対し、更新登録を促すＥメールを送信する。

さらに、Ｅメール送信して２ヶ月経過しても未更新の症例に対し、再度督促Ｅメールを送信する。

これらの機能は、サーバ上で自動的・定期的に実行される。



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Gastric Cancer
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SHORT COMMUNICATION

Design of Japanese multicenter prospective cohort study of endoscopic resection for early gastric cancer using Web registry (J-WEB/EGC)

Ichiro Oda · Taichi Shimazu · Hiroyuki Ono · Satoshi Tanabe · Hiroyasu Iishi · Hitoshi Kondo · Motoki Ninomiya

Received: 26 March 2012 / Accepted: 4 April 2012

Abstract A Japanese multicenter prospective cohort study is currently being conducted on endoscopic resection (ER) for early gastric cancer (EGC) using a Web registry system developed to determine short-term and long-term outcomes based on the absolute and expanded indications. All consecutive patients with EGC or suspected EGC undergoing ER at the 41 participating institutions from July 2010 to June 2012 are being enrolled in the study cohort using the Web registry system, and each patient will be followed up for a minimum of 5 years. The study investigation includes baseline patient and lesion characteristics as well as short-term and long-term outcomes. A survey program to collect information on long-term outcomes is also being introduced for patients subsequently followed up in institutions other than their original participating institutions, as well as patients for whom the original participating institutions have been losing track of their follow-up. The primary endpoint is 5-year overall survival, with en bloc resection, curative resection, complication, local recurrence, distant metastasis, metachronous EGC, and recurrence-free survival being secondary endpoints in addition to the successful collection of long-term outcome data on enrolled patients utilizing the survey program.

Keywords Early gastric cancer · Endoscopic mucosal resection · Endoscopic submucosal dissection · Cancer registry

I. Oda (✉)
Endoscopy Division, National Cancer Center Hospital,
5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
e-mail: ioda@ncc.go.jp

T. Shimazu
Epidemiology and Prevention Division,
Research Center for Cancer Prevention and Screening,
National Cancer Center, Tokyo, Japan

H. Ono
Division of Endoscopy, Shizuoka Cancer Center,
Shizuoka, Japan

S. Tanabe
Department of Gastroenterology,
Kitasato University School of Medicine, Kanagawa, Japan

H. Iishi
Department of Gastrointestinal Oncology,
Osaka Medical Center for Cancer and Cardiovascular Diseases,
Osaka, Japan

H. Kondo
Center for Digestive Diseases, Tonan Hospital, Sapporo, Japan

M. Ninomiya
Department of Surgery, Hiroshima City Hospital,
Hiroshima, Japan

Introduction

Endoscopic resection (ER) is accepted as a less-invasive method for local resection of early gastric cancer (EGC), with a negligible risk of lymph node metastasis [1]. Remarkable progress has been made during the past decade in making technical improvements and expanding the indications for ER. Endoscopic treatment methods vary from conventional endoscopic mucosal resection (EMR) to endoscopic submucosal dissection (ESD) [2–9]. According to the Japanese gastric cancer treatment guidelines for 2010, the absolute indications for ER of EGC consist of a lesion clinically diagnosed as a differentiated histological type intramucosal cancer $\leq$2 cm in diameter with no ulcer findings [10]. Based on a retrospective analysis of the

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percentage of lymph node metastasis in a large number of surgical EGC cases, other groups of EGC patients with a negligible risk of lymph node metastasis have been identified to include patients with larger lesions and lesions with ulceration [11]. Such lesions were previously resected by surgery because of the difficulty in effectively using the EMR techniques then existing. Following the development of ESD, however, en bloc resections could be achieved even for larger and ulcerative lesions. As a result, the Japanese gastric cancer treatment guidelines for 2010 now include expanded indications for ER of EGC [10].

A number of reports have been published on the short-term and long-term outcomes of EMR and ESD for EGC based on the absolute and expanded indications, but most of the reports were retrospective studies from single centers [12–17]. One published multicenter retrospective study reported a favorable 3-year survival rate, although about 20 % of the patients were excluded from the long-term outcome analysis because their follow-up information was unavailable [12].

As a result, a Japanese multicenter prospective cohort study of ER for EGC using a Web registry system (J-WEB/EGC) was developed and introduced in July 2010.

J-WEB/EGC design

Purpose

Our purpose is to determine in a multicenter prospective cohort study the short-term and long-term outcomes of EMR and ESD for EGC based on the absolute and expanded indications.

Endpoints

The primary endpoint is 5-year overall survival. Secondary endpoints are en bloc resection, curative resection, complication, local recurrence, distant metastasis, metachronous EGC, and recurrence-free survival in addition to the successful collection of long-term outcome data on enrolled patients at 5 years utilizing the survey program.

Study cohort

We set the 41 participating institutions to cover nearly all regions of Japan (Table 1). All consecutive patients with EGC or suspected EGC undergoing ER at the participating institutions from July 2010 to June 2012 are included in this study. A patient is excluded only if written informed consent is not obtained. All enrolled patients are prospectively registered to the Web registry system, and each patient will be followed up for a minimum of 5 years. This study is being conducted with the approval of every institutional review board; written informed consent is being required for enrollment from each patient; and the

Table 1 Participating institutions from north to south in Japan

1	Tonan Hospital, Hokkaido
2	Kin-Ikyou Chuo Hospital, Hokkaido
3	Akita University Hospital, Akita
4	Iwate Medical University Hospital, Iwate
5	Yamagata Prefectural Central Hospital, Yamagata
6	Sendai City Medical Center, Miyagi
7	Fukushima Medical University Hospital, Fukushima
8	Niigata University Medical & Dental Hospital, Niigata
9	Niigata Prefectural Central Hospital, Niigata
10	Jichi Medical University Hospital, Tochigi
11	Tochigi Cancer Center, Tochigi
12	National Cancer Center Hospital East, Chiba
13	National Cancer Center Hospital, Tokyo
14	Cancer Institute Hospital, Tokyo
15	Toranomon Hospital, Tokyo
16	The University of Tokyo Hospital, Tokyo
17	National Center for Global Health and Medicine, Tokyo
18	Chofu Touzan Hospital, Tokyo
19	Kitasato University East Hospital, Kanagawa
20	Yokohama City University Medical Center, Kanagawa
21	Saku Central Hospital, Nagano
22	Shizuoka Cancer Center Hospital, Shizuoka
23	Toyama Prefectural Central Hospital, Toyama
24	Ogaki Municipal Hospital, Gifu
25	Aichi Cancer Center Hospital, Aichi
26	Ishikawa Prefectural Central Hospital, Ishikawa
27	University Hospital, Kyoto Prefectural University of Medicine, Kyoto
28	Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka
29	Osaka Koseinenkin Hospital, Osaka
30	Kobe University Hospital, Hyogo
31	Hyogo Cancer Center, Hyogo
32	Tottori Red Cross Hospital, Tottori
33	Okayama University Hospital, Okayama
34	Tsuyama Central Hospital, Okayama
35	Tokushima University Hospital, Tokushima
36	Hiroshima University Hospital, Hiroshima
37	Hiroshima City Hospital, Hiroshima
38	Shikoku Cancer Center, Ehime
39	Fukuoka University Chikushi Hospital, Fukuoka
40	Saga University Hospital, Saga
41	Nagasaki University Hospital, Nagasaki

study has been registered in the UMIN Clinical Trial Registry (UMIN000005871).

Study methods

The study investigation is divided into baseline patient and lesion characteristics as well as short-term and long-term outcomes. Baseline patient and lesion characteristics are entered using the Web registry system by each of the 41 participating institutions before ER. Baseline patient characteristics include age, gender, performance status, body weight, body height, medical history, concomitant disease, regular use of anticoagulant and/or antiplatelet drugs, and information on *Helicobacter pylori* infection/eradication. Other personal identification information, such as name, date of birth, and institutional reference number for each patient, is not entered in the Web registry system database, but a conversion code is instead used, based on the applicable institutional reference number, to ensure patient confidentiality. Baseline lesion characteristics include endoscopic determinations on tumor location, size, and depth, macroscopic type, ulcer findings, and the histological diagnosis of any biopsy specimen.

Short-term outcomes are entered using the Web registry system by each of the participating institutions for 6 months following ER. Short-term outcomes include the day and method of ER, primary instrument used during ESD, type of anesthesia, procedure time, number of resected specimens, complications, histological findings from ER specimens, and any additional treatment. Histological findings include tumor histological type, size, depth, macroscopic type, ulcer finding, lymphatic involvement, vascular involvement, lateral margin, and vertical margin.

Long-term outcomes are entered using the Web registry system by each of the participating institutions at 1, 3, and 5 years following ER. Long-term outcomes include follow-up status, local recurrence, metastasis, metachronous EGC, information on *Helicobacter pylori* infection/eradication, and mortality. Follow-up status includes follow-up in the original participating institution, subsequent follow-up at another institution, and losing track of appropriate follow-up.

According to the Japanese gastric cancer treatment guidelines 2010, it is recommended each patient be followed up with an esophagogastroduodenoscopy at least annually for 5 years following ER. In the case of a histologically curative resection for EGC based on the expanded indications, an abdominal computed tomography or ultrasonography examination is also recommended at least annually.

Survey program for patients subsequently followed up at other institutions and patients whose follow-up has been lost

To collect information on the long-term outcomes for a patient subsequently followed up at an institution other than the original participating institution, a questionnaire survey is sent to such institution. For a patient for whom the original participating institution has lost track of their follow-up, and for whom there has been no response to the questionnaire survey from such other institution, a questionnaire survey is sent directly to the patient. If there is still no response, we refer to the patient's residential register for information on whether the patient has moved or is no longer living. For any patient who has moved, a questionnaire survey is sent to the new address provided by such patient's residential register. If it becomes necessary to identify a patient's cause of death, cause of death is confirmed by contacting the institution where the patient died, hospital-based cancer registries, the Ministry of Justice, or using mortality data from the Ministry of Health, Labour and Welfare.

The coordinating center for the J-WEB/EGC conducts these follow-up surveys as necessary after requesting the original participating institution for personal identification information on a particular patient, except for two participating institutions that conduct their own follow-up surveys without sending personal identification information on such a patient to the coordinating center as recommended by the institutional review boards of those two institutions. Long-term outcome data obtained from any follow-up survey for a particular patient are made available to the original participating institution through the Web registry system.

Discussion

J-WEB/EGC is a Japanese multicenter prospective cohort study of ER for EGC using a Web registry system that has several unique features. First, the follow-up survey program will be conducted for patients followed up at other institutions and patients whose follow-up has been lost. It can be quite difficult to follow up all consecutive patients in each participating institution for a lengthy period. Although a nationwide population-based cancer registry is currently being developed in Japan that will provide data on patient prognosis to hospital-based cancer registries, it may not be completed by the end of this study's initial 5-year follow-up period [18]. In this study, the patient is informed that the follow-up survey program will be conducted only when the patient is followed up in another institution or the original participating institution loses

track of the follow-up, and written informed consent is obtained from each patient before enrollment.

Second, the participating institutions cover nearly all regions of Japan for evaluating a large number of consecutive ER patients with EGC. Approximately 5,000 patients have already been enrolled during the first year from July 2010 (data not shown), so both short-term outcomes and long-term outcomes based on an expected high patient follow-up rate will become available from a very large number of cases as a result of this study.

Third, the Web registry system is being utilized in this study so each of the 41 participating institutions and the coordinating center can adequately handle an enormous amount of data from a very large number of EGC cases. The Web registry system is equipped with a number of security measures including a firewall, intrusion detection, antivirus program, secure socket layer, and access restriction. In addition, specific personal identification information such as name, date of birth, and institutional reference number for each patient is not entered in the Web registry system database; a conversion code based on a patient's institutional reference number being used instead to further protect patient confidentiality. The security of the Web registry system was also confirmed in a pilot study conducted before this study, and there have been no security-related problems since J-WEB/EGC was introduced in July 2010.

In summary, J-WEB/EGC became fully operational in July 2010. Short-term outcomes and long-term outcomes of ER for EGC based on a high patient follow-up rate will become available in a few years from a very large number of cases as a result of this comprehensive study.

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Clinical outcomes of endoscopic submucosal dissection for early gastric cancer in remnant stomach or gastric tube

Authors N. Nishide, H. Ono, N. Kakushima, K. Takizawa, M. Tanaka, H. Matsubayashi, Y. Yamaguchi

Institution Division of Endoscopy, Shizuoka Cancer Center, Shizuoka, Japan

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Corresponding author
N. Kakushima, MD, PhD
Division of Endoscopy
Shizuoka Cancer Center
1007 Shimonagakubo
Nagaizumi
Suntogun
Shizuoka, 411-8777
Japan
Phone: +81-55-9895222
Fax: +81-55-9895692
kakushin-tky@umin.ac.jp

Background and study aims: Little information exists regarding the optimal treatment of early gastric cancer (EGC) in a remnant stomach or gastric tube. The aim of this study was to assess the feasibility and clinical outcomes of endoscopic submucosal dissection (ESD) for EGC in a remnant stomach and gastric tube.

Patients and methods: Between September 2002 and December 2009, ESD was performed in 62 lesions in 59 patients with EGC in a remnant stomach (48 lesions) or gastric tube (14 lesions). Clinicopathological data were retrieved retrospectively to assess the en bloc resection rate, complications, and outcomes. Treatment results were assessed according to the indications for endoscopic resection, and were compared with those of ESD performed in a whole stomach during the same study period.

Results: The en bloc resection rates for lesions within the standard and expanded indication were 100% and 93%, respectively. Postoperative bleeding occurred in five patients (8%). The perforation rate was significantly higher (18%, 11/62) than that of ESD in a whole stomach (5%, 69/1479). Among the perforation cases, eight lesions involved the anastomotic site or stump line, and ulcerative changes were observed in five lesions. The 3-year overall survival rate was 85%, with eight deaths due to other causes and no deaths from gastric cancer.

Conclusion: A high en bloc resection rate was achieved by ESD for EGC in a remnant stomach or gastric tube; however, this procedure is still technically demanding due to the high complication rate of perforation.

Introduction

Little information exists regarding the optimal treatment of early gastric cancer (EGC) in a remnant stomach or a gastric tube. To obtain a radical cure, surgical resection has been considered the standard treatment; however, surgery is not usually preferred because of its high morbidity and mortality [1,2]. Endoscopic mucosal resection (EMR) including endoscopic submucosal dissection (ESD) has been widely accepted as a standard treatment for EGC in Japan [3–5]. Recently, the benefit of endoscopic treatment for metachronous EGC in a reconstructed stomach has been reported in several case series of small numbers of patients [6–13]. Although ESD is a minor invasive treatment compared with surgery, performing ESD is considered technically more difficult in a remnant stomach or a gastric tube than in a whole stomach because of the deformity and narrow space due to previous surgery. Therefore, ESD for EGC in a remnant stomach or gastric tube is not yet widespread. In this study, we characterize the feasibility and clinical outcome of ESD for EGC in a remnant stomach or a gastric tube.

Patients and methods

From a prospectively entered database, which contained findings of 1904 EGC lesions that were treated by ESD at Shizuoka Cancer Center, between September 2002 and December 2009, 62 lesions in 59 patients with a remnant stomach after distal gastrectomy (48 lesions) or a gastric tube (14 lesions) were selected as the main study group for analysis. Among 1824 lesions treated by ESD for EGC in a whole stomach, 775 lesions within the standard criteria and 704 lesions within the expanded criteria of indications for ESD, as described below, were selected as a control group. Patients who underwent ESD for EGC in a stomach after partial gastrectomy (11 lesions), for EGC in a stomach after proximal gastrectomy (4 lesions), and patients who under-

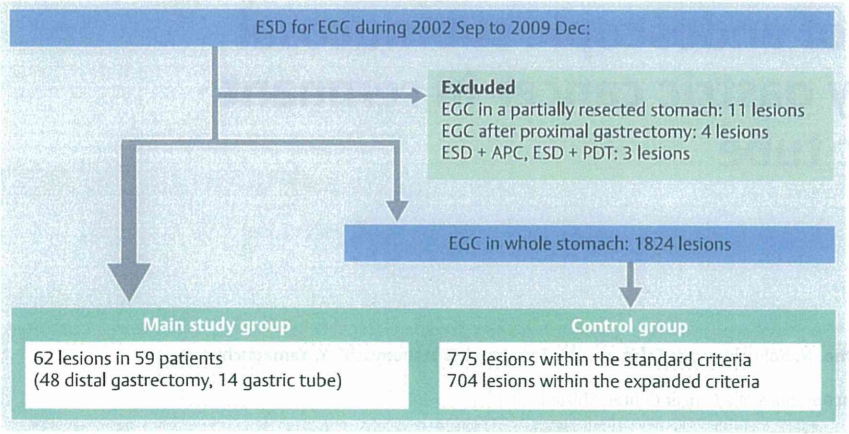


Fig. 1 Flow chart showing the patient inclusion in the study.

went combined therapy such as argon plasma coagulation and photodynamic therapy with ESD (3 lesions) were excluded (**Fig. 1**).

The general indications for ESD at the Shizuoka Cancer Center are lesions with the finding of EGC that meet the criteria for EMR proposed by the Japanese Gastric Cancer Society [14]. The criteria include: those with a preoperative diagnosis of differentiated-type intramucosal cancer without ulcer findings; differentiated-type intramucosal cancer that is no larger than 3 cm in diameter with ulcer findings; differentiated-type minute invasive submucosal cancer (invasion less than 500 µm below the muscularis mucosa) that is no larger than 3 cm in diameter; and undifferentiated-type intramucosal cancer that is no larger than 2 cm in diameter without ulcer findings.

Method of ESD

As described previously by Ono et al. [5, 15], an insulated-tip diathermic knife (IT Knife2; KD-611 L, Olympus, Tokyo, Japan) was used as the main electrosurgical endoscopic knife. An endoscope with a water-jet function (GIF-Q260 J or GIF-2T260 M, Olympus, Tokyo, Japan) and a high frequency generator (VIO300 D, ERBE, Elektromedizin, Tübingen, Germany) was used. After recognizing the lesion by observation during chromoendoscopy with indigo carmine (**Fig. 2a, b**), dots marking the area around the lesion were placed using an argon plasma coagulation (APC) probe (**Fig. 2c**). A commercially available solution of 0.4% sodium hyaluronate (MucoUp; Johnson and Johnson ASP Japan, Tokyo, Japan) was injected through a 25-gauge needle into the submucosal layer under the lesion. A 1–2-mm precut was made with a needle knife followed by a circumferential mucosal incision around the lesion with the IT Knife2 (**Fig. 2d, e**). The submucosal layer was then dissected by the IT Knife2 with an additional submucosal injection (**Fig. 2f**). When the tissue was too hard to cut with the IT Knife2 because of the existence of fibrosis or staples from the previous surgery, a needle knife was used as appropriate. After the resected specimen had been retrieved, the ulcer bed was carefully examined for residual blood vessels and coagulated with hot biopsy forceps (Boston Scientific, Tokyo, Japan), IT Knife2, or APC (**Fig. 2g, h**). Proton pump inhibitors were administered initially by injection and then orally after the procedure. A soft meal was started 2 days after ESD if there were no complications of postoperative bleeding or perforation.

Curability criteria from the histological assessment

The tumor size, depth of invasion, presence of ulcerative changes, existence of lymphovascular infiltration, and whether the specimen margins were free of cancer (R0) were assessed histopathologically. According to the criteria of the Japanese guidelines, the lesions were divided into one of three groups: standard indication, expanded criteria, and outside the criteria [14].

Lesions in the standard indication group consisted of differentiated-type mucosal cancer that was 2 cm or smaller in diameter, with no ulceration. The expanded criteria group consisted of differentiated-type mucosal cancer without ulceration; differentiated-type cancer that was 3 cm or smaller in diameter, with a depth of submucosal invasion less than 500 µm, with or without ulceration; or undifferentiated-type mucosal cancer that was 2 cm or smaller in diameter with no ulceration. Lesions that did not meet either the standard or the expanded criteria were defined as outside the criteria.

Curative resection was considered to be lesions that fitted the standard or expanded criteria with no lymphovascular infiltration, and that were resected en bloc with R0 resection.

For patients who were considered to have undergone curative resection for a lesion within the standard indication, follow-up by annual endoscopy with chromoendoscopy was performed. For patients who were considered to have undergone curative resection for a lesion within the expanded criteria, follow-up was performed by annual endoscopy with chromoendoscopy, and by abdominal computed tomography or abdominal ultrasonography. For patients who had undergone a non-curative resection, additional surgery was recommended.

Measurements

Operative time (from marking to complete lesion removal), en bloc resection rate, en bloc with R0 resection rate, complications (perforation and postoperative bleeding), and recurrence during the follow-up were retrieved for data analysis. Treatment results of ESD in a remnant stomach or gastric tube according to the indications for endoscopic resection were assessed, and compared with the results of ESD performed in a whole stomach. In this study, postoperative bleeding was defined as cases with hematemesis or melena requiring endoscopic intervention. Overall survival was measured from the date of ESD to death or to the confirmed date of the last follow-up visit. Survival time was calculated by the Kaplan–Meier method.

Statistical analysis was done using the Mann–Whitney's U test and chi-squared test, to describe certain differences in an ex-

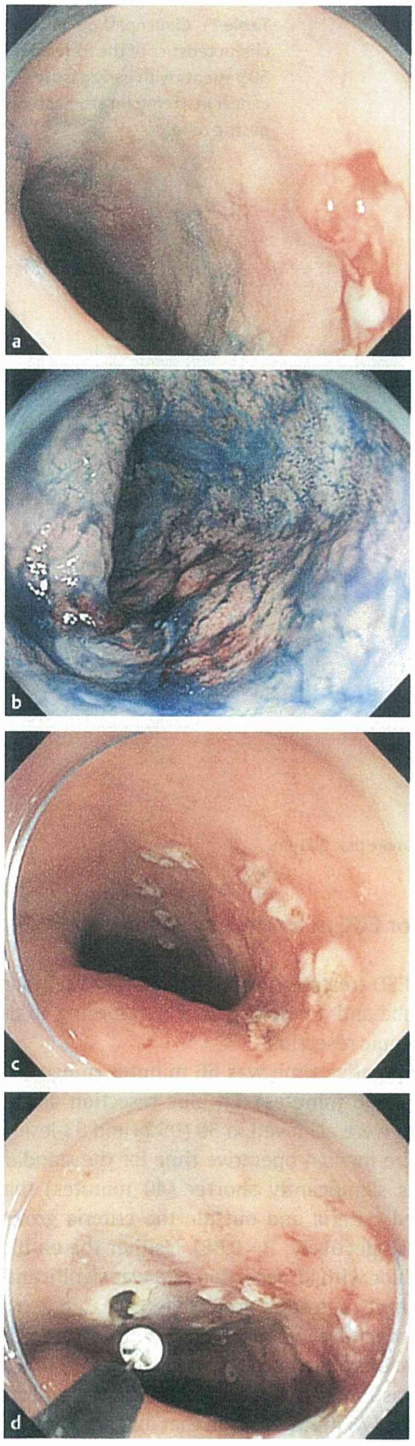
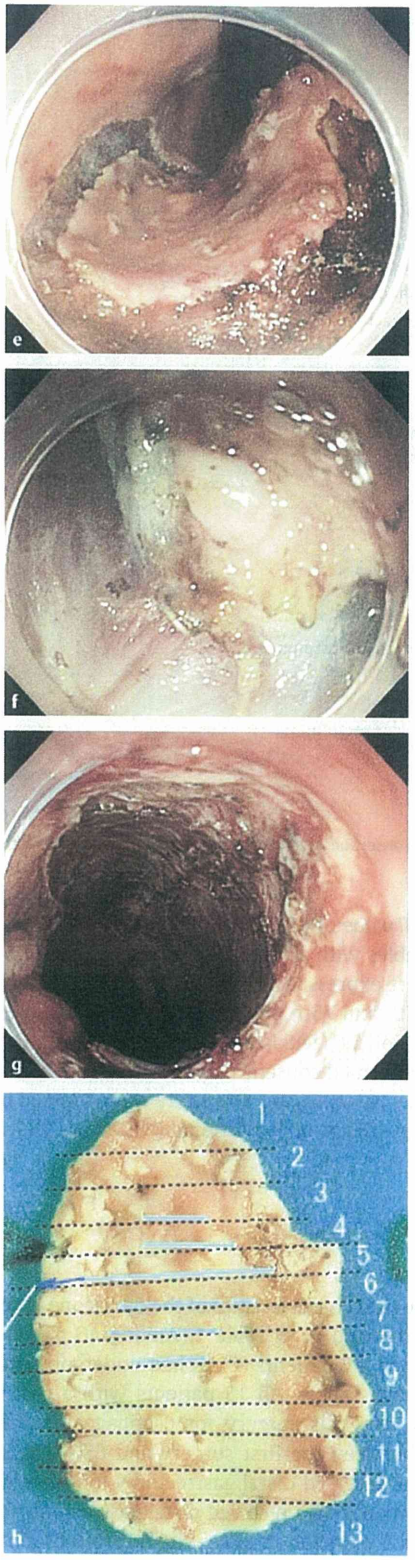


Fig. 2 The endoscopic submucosal dissection procedure. **a** A reddish, slightly depressed lesion with a small nodule is observed in a narrow area of a gastric tube. **b** Chromoendoscopy with indigo carmine is performed to determine the border of the lesion. **c** Marking dots were placed around the lesion using an argon plasma coagulation probe. **d, e** Circumferential cutting was performed with an insulated-tip diathermic knife (IT Knife2). **f** The presence of staples was revealed during submucosal dissection. **g** The artificial ulcer after removing the lesion is carefully observed for residual vessels. **h** The lesion proved to be a mucosal cancer (blue lines, number 3 – 8), and was removed en bloc with negative margins.



Age, median (range), years	74 (53–84)
Sex, male/female, n	56/3
Remnant stomach, n	48
Gastric tube, n	14
Reason for previous surgery, benign disease/cancer, n	
Remnant stomach	17/29
Gastric tube	0/13
Period between previous surgery and ESD, median (range), years	
Remnant stomach for benign disease	30 (6–50)
Remnant stomach for gastric cancer	6 (1–30)
Gastric tube for esophageal cancer	4.5 (1–14)
Location of lesion in stomach, n	
Upper	24
Middle	34
Lower	4
Tumor diameter, median (range), mm	22 (5–59)
Pathological tumor depth	
M	43
SM1	10
SM2	9
Pathological ulceration	
Present	19
Absent	43
Involving the anastomotic site or stump line	
Yes	29
No	33
Indication for endoscopic resection	
Standard	16
Expanded	29
Outside of criteria	17

Table 1 Clinicopathological characteristics of the 62 lesions in 59 patients with early gastric cancer in a remnant stomach or a gastric tube.

ESD, endoscopic submucosal dissection; M, mucosal; SM1, submucosal invasion up to 500µm; SM2, submucosal invasion more than 500 µm.

ploratory way, and a *P* value of <0.05 was considered significant. For quantitative variables with apparently skewed distributions, the summary data were expressed as median (interquartile range [IQR] between the 25th and 75th percentiles). All analyses were done by StatView version 5.0 (SAS Institute Inc., Cary, North Carolina, USA). Written informed consent was obtained from all patients undergoing ESD. This retrospective study was endorsed by the institutional review board of our hospital (No.23-J2–23–1-3).

Results

Overall clinicopathological characteristics of the 62 lesions in the 59 patients are summarized in **Table 1**. Among 46 patients with a residual stomach, 29 patients (63%) had undergone previous surgery for gastric cancer. All 13 patients with a gastric tube had undergone previous surgery for esophageal cancer. The median period between the first surgery and ESD was 30 years for patients who received distal gastrectomy for a benign disease, 6 years for patients who received distal gastrectomy for a gastric cancer, and 4.5 years for patients who received esophagectomy for an esophageal cancer. Most of the patients were male (56/59, 95%) and the lesions were mostly located in the upper (39%) or middle (55%) portion of the stomach. The median diameter of the tumors was 22 mm. Ulceration was present in 19 lesions (31%). In 29 lesions (47%) the anastomotic site or the stump line from the previous surgery were involved.

Feasibility of ESD for EGC in a remnant stomach or gastric tube

Table 2 shows the ESD treatment results for EGC in a remnant stomach or gastric tube and a whole stomach, according to the indications for endoscopic resection.

The overall median operative time was 66 minutes (range 13–270 minutes, IQR 37.7–96 minutes). En bloc resection and en bloc with R0 resection were achieved in 59 (95%) and 53 lesions (85%), respectively. The median operative time for the standard indication group was significantly shorter (40 minutes) than that for the expanded criteria and outside the criteria groups (72 and 90 minutes, respectively; P <0.05). Neither the en bloc resection rate nor en bloc with R0 resection rate was significantly different among the three indication groups.

Treatment results between lesions with or without involvement of the anastomotic site or stump line were compared (**Table 3**). The operative time was longer for lesions involving the anastomotic site or stump line (78 minutes) than that for those without involvement (60 minutes), but the difference was not significant. En bloc with R0 resection rate was apparently lower for lesions with involvement of the anastomotic site or stump line.

Comparison of treatment results between ESD in a remnant stomach or gastric tube and ESD in a whole stomach (Table 2)

The operative time for standard (40 minutes) and expanded (72 minutes) criteria groups in a remnant stomach or gastric tube were longer than that for standard (33 minutes) and expanded (51 minutes) criteria groups in a whole stomach, however the differences were not significant.

Table 2 Endoscopic submucosal dissection treatment results for early gastric cancer in a remnant stomach or gastric tube and a whole stomach, according to the indications for endoscopic resection.

	ESD for remnant stomach or gastric tube				ESD for whole stomach	
	Total (n=62)	Standard (n=16)	Expanded (n=29)	Outside of criteria (n=17)	Standard (n=775)	Expanded (n=704)
Lesion size, median (IQR), mm	22 (14–33)	16* (9–18)	22* (13–30)	39* (25–46)	11 (8–15)	28* (22–37)
Presence of ulceration, n (%)	19 (31)	0	9 (31)	10 (26)	0	272 (39)
Involving anastomosis or stump line, n (%)	29 (47)	7 (44)	12 (41)	10 (59)	–	–
Operative time, median (IQR), minutes	66 (37–96)	40* (22–55)	72* (57–93)	90* (78–133)	33 (19–45)	51 33–80)
En bloc resection, n (%)	59 (95)	16 (100)	27 (93)#	16 (94)	774 (99.8)	700 (99)#
En bloc with R0 resection, n (%)	53 (85)	15 (94)#	26 (90)	12 (71)	774 (98)#	665 (94)
Perforation, n (%)	11 (18)	1 (6)	7 (24)#	3 (18)	17 (2)	52 (7)#
Bleeding, n (%)	5 (8)	1 (6)	2 (7)	2 (12)	65 (8)	93 (13)

ESD, endoscopic submucosal dissection; IQR, interquartile range.
* Mann–Whitney's U test: $P<0.05$. All other comparisons non-significant.
# Chi-squared test: $P<0.05$. All other comparisons non-significant.

Table 3 Comparison of treatment results of endoscopic submucosal dissection in a remnant stomach or gastric tube between lesions with or without involvement of anastomotic site or stump line.

	Involvement of anastomotic site or stump line		*P* value*
	Yes N=29	No n=33	
Operative time, median (IQR), minutes	78 (50–97)	60 (35–93)	n.s.
En bloc resection, n (%)	28 (97)	31 (94)	n.s.
En bloc with R0 resection, n (%)	23 (79)	30 (91)	n.s.
Perforation, n (%)	8 (28)	3 (9)	0.057
Bleeding, n (%)	4 (14)	1 (3)	n.s
Local recurrence, n (%)	1 (4)	1 (3)	n.s

IQR, interquartile range; n.s., not significant.
* Chi-squared test.

The en bloc resection rate for lesions within the expanded criteria (93%) and the en bloc with R0 resection rate for lesions within the standard criteria (94%) for ESD in a remnant stomach or gastric tube were significantly lower ($P<0.05$) than those of ESD in a whole stomach (99% and 98%, respectively).

Complications of ESD for EGC in a remnant stomach or gastric tube

As shown in **Table 2**, the overall perforation rate was 18% (11/62) for ESD in a remnant stomach or gastric tube. Among the 11 cases, perforation occurred in lesions in the expanded criteria (seven cases) or outside the criteria group (three cases). The lesion involved the anastomotic site or stump line in eight cases, and ulcerative changes were observed in five lesions. The perforation rate for lesions within the expanded criteria was significantly higher (24%) than that of lesions within the expanded criteria in a whole stomach (7%) ($P<0.05$). All of the perforations occurring during the ESD procedure were sealed immediately with endoclips. All patients were treated by fasting and with nasogastric suction and administration of antibiotics. No emergency surgery was required. The median hospitalized period for the perforation cases and non-perforation cases was 7 and 5 days, respectively ($P=0.04$).

Postoperative bleeding occurred in five lesions (8%). All hemorrhagic episodes were successfully treated by endoscopic clipping or coagulation, with no patient requiring a blood transfusion. Among the three lesion groups, the complication rates of perforation and bleeding were high in the expanded criteria and outside the criteria groups compared with the standard indication group but these differences were not significant.

The complication rate of perforation was as high as 28% for lesions with involvement of the anastomotic site or stump line, which was higher than that of lesions without involvement ($P=0.057$) (**Table 3**).

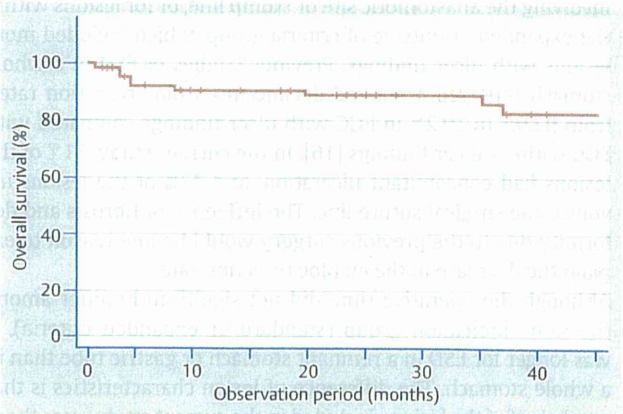


Fig. 3 Kaplan–Meier estimation of survival for patients who underwent endoscopic submucosal dissection in a remnant stomach or a gastric tube. The 3-year overall survival was 85%. There were eight deaths from other causes during the observation period.

Recurrence and overall survival of ESD for EGC in a remnant stomach or a gastric tube

According to the pathology results, the ESD treatment was considered non-curative in 25 lesions (21 in the outside the criteria group, one with lymphovascular infiltration, and three lesions with positive surgical margins). Among these non-curative cases, six patients with a remnant stomach underwent additional surgery. The other patients refused surgery because of old age or coexisting diseases and were followed in an outpatient setting. Local recurrence occurred in two of these patients, at 14 and 15 months, respectively, during a median follow-up of 27 months after ESD. Both patients were considered to have undergone non-curative resections, but refused additional surgery. A second ESD was performed in one patient, and the other patient was treated by coagulation with a hot biopsy forceps and additional photodynamic therapy. The cumulative overall 3-year survival rate was 85% (**Fig. 3**). No patient died from gastric cancer. Eight patients died from other malignancies, pulmonary infarction, and peritonitis. A metachronous EGC was found in two patients during the observation period, and these were treated by another ESD procedure.

Discussion

Compared with surgery, endoscopic treatment including EMR is a minor invasive treatment and has been performed for the treatment of EGC in a remnant stomach or gastric tube. The reported en bloc resection rate of EMR performed for EGC in a remnant stomach or gastric tube is 14.3%–40.9% [8, 10,11]. ESD has the potential to achieve a higher en bloc resection rate than EMR, and several investigators have reported the application of ESD for EGC in a remnant stomach [9–12] or gastric tube [8,13]. Among the case series of 13 to 40 patients, the en bloc resection rate of ESD in a remnant stomach has been reported as 95%–100% [9–12]. Among the case series of 8–10 patients of ESD in a gastric tube, the en bloc resection rate was reported as 88%–90% [8, 13]. The current study therefore represents the largest experience in this patient population, and showed a high en bloc resection rate of 95%.

The en bloc resection rate of ESD for a remnant stomach or gastric tube was slightly lower than that of ESD in a whole stomach in our study. The en bloc resection rate was rather low for lesions involving the anastomotic site or stump line, or for lesions within the expanded or outside of criteria group, which included more lesions with ulcer findings. Previous studies of ESD in a whole stomach reported a marked decline in en bloc resection rates, from 92.9% to 19.2% in EGC with ulcer findings compared with EGC without ulcer findings [16]. In the current study, 31% of the lesions had concomitant ulceration, and 47% of the lesions involved the surgical suture line. The influence of fibrosis and deformity due to the previous surgery would be one reason to explain the decrease in the en bloc resection rate.

Although the operative time did not significantly differ among the same indication group (standard or expanded criteria), it was longer for ESD in a remnant stomach or gastric tube than in a whole stomach. The difference of lesion characteristics is that nearly half of the lesions included in the current study were those involving the anastomotic site or stump line. We believe that the anatomical deformity and limited working space due to the anastomosis or stump line are possible reasons for the time-consuming procedure.

A high rate of perforation (18%) was identified in this study. Previous reports of perforation during ESD in a whole stomach have reported rates of 0% to 12% [17]. The presence of ulceration is reported to put the patient at a higher risk of perforation [18]. In the current study, except for one perforation case, all lesions had either ulceration or involved the anastomotic site or stump line. Once perforation occurs in a remnant stomach or a gastric tube, not only is pneumoperitoneum likely to occur but also pneumomediastinum, which may cause peritonitis or mediastinitis. Therefore, measures to avoid perforation should be taken, and rapid treatment is essential for minimizing complications. In the current study, all patients who experienced perforation were successfully treated by immediate closure with endoclips and subsequent nasogastric suction. Although no cases of delayed perforation occurred, we should always be aware of this possibility at low blood flow areas or fibrotic areas that have been subjected to too much electrocauterization [13].

In a large consecutive series, a 3-year overall survival rate of 98.4% and a 3-year disease-specific survival rate of 100% have been reported for patients who underwent ESD for an EGC in a whole stomach [19]. Although the numbers of patients in the current study are limited, results showed a 3-year overall survival rate of 85%, and no deaths from gastric cancer were observed during the follow-up period.

In conclusion, this study represents the largest experience of ESD for EGC in a remnant stomach or gastric tube, with a high en bloc resection rate. However, this method is still a technically demanding treatment due to the high complication rate of perforation.

Competing interests: None.

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