

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2017 December 16; 9(12): 561-593



ORIGINAL ARTICLE

Retrospective Study

- 561 Gastric endoscopic submucosal dissection as a treatment for early neoplasia and for accurate staging of early cancers in a United Kingdom Caucasian population

Sooltongos A, Davenport M, McGrath S, Vickers J, Senapati S, Akhtar K, George R, Ang Y

Observational Study

- 571 Lumen-apposing metal stents for benign gastrointestinal tract strictures: An international multicenter experience

Santos-Fernandez J, Paiji C, Shakhathreh M, Becerro-Gonzalez I, Sanchez-Ocana R, Yeaton P, Samarasena J, Perez-Miranda M

CASE REPORT

- 579 Retroperitoneal epithelioid sarcoma: A case report

Coronado JA, Chávez MA, Manrique MA, Cerna J, Trejo AL

- 583 Endoscopic ultrasound-guided fine-needle aspiration for diagnosing a rare extraluminal duodenal gastrointestinal tumor

Hayashi K, Kamimura K, Hosaka K, Ikarashi S, Kohisa J, Takahashi K, Tominaga K, Mizuno K, Hashimoto S, Yokoyama J, Yamagiwa S, Takizawa K, Wakai T, Umezu H, Terai S

- 590 Deanxit relieves symptoms in a patient with jackhammer esophagus: A case report

Li JY, Zhang WH, Huang CL, Huang D, Zuo GW, Liang LX

Contents

World Journal of Gastrointestinal Endoscopy
Volume 9 Number 12 December 16, 2017

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Endoscopy*, Gelu Osian, MD, PhD, Doctor, Head, Surgeon, Multi Organ Transplant Center, Department of Transplant Surgery, King Fahad Specialist Hospital-Dammam, Dammam 31444, Eastern Province, Saudi Arabia

AIM AND SCOPE

World Journal of Gastrointestinal Endoscopy (*World J Gastrointest Endosc*, *WJGE*, online ISSN 1948-5190, DOI: 10.4253) is a peer-reviewed open access (OA) academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJGE covers topics concerning gastroscopy, intestinal endoscopy, colonoscopy, capsule endoscopy, laparoscopy, interventional diagnosis and therapy, as well as advances in technology. Emphasis is placed on the clinical practice of treating gastrointestinal diseases with or under endoscopy.

We encourage authors to submit their manuscripts to *WJGE*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great clinical significance.

INDEXING/ABSTRACTING

World Journal of Gastrointestinal Endoscopy is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, and PubMed Central.

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Li-Jun Cui*
Proofing Editorial Office Director: *Xiu-Xia Song*

NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Atsushi Imagawa, PhD, Director, Doctor, Department of Gastroenterology, Mitoyo General Hospital, Kan-onji, Kagawa 769-1695, Japan

Juan Manuel Herrerias Gutierrez, PhD, Academic Fellow, Chief Doctor, Professor, Unidad de Gestión Clínica de Aparato Digestivo, Hospital Universitario Virgen Macarena, Sevilla 41009, Spain

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjnet.com>

www.wjnet.com/1948-5190/editorialboard.htm

EDITORIAL OFFICE
Xiu-Xia Song, Director
World Journal of Gastrointestinal Endoscopy
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLICATION DATE
December 16, 2017

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Retrospective Study

Gastric endoscopic submucosal dissection as a treatment for early neoplasia and for accurate staging of early cancers in a United Kingdom Caucasian population

Aisha Sooltangos, Matthew Davenport, Stephen McGrath, Jonathan Vickers, Siba Senapati, Kurshid Akhtar, Regi George, Yeng Ang

Aisha Sooltangos, Faculty of Biology, Medicine and Health, University of Manchester, Manchester M13 9PL, United Kingdom

Aisha Sooltangos, Matthew Davenport, Regi George, Yeng Ang, Department of Gastroenterology, Salford Royal NHS Foundation Trust, Salford M6 8HD, United Kingdom

Stephen McGrath, Department of Pathology, Salford Royal NHS Foundation Trust, Salford M6 8HD, United Kingdom

Jonathan Vickers, Siba Senapati, Kurshid Akhtar, Department of Upper Gastrointestinal Surgery, Salford Royal NHS Foundation Trust, Salford M6 8HD, United Kingdom

Regi George, Department of Gastroenterology, Pennine Acute NHS Trust, Rochdale Old Rd, Bury BL9 7TD, United Kingdom

Yeng Ang, Gastrointestinal Science, University of Manchester, Manchester M13 9PL, United Kingdom

ORCID number: Aisha Sooltangos (0000-0001-5675-1709); Matthew Davenport (0000-0003-1341-562X); Stephen McGrath (0000-0001-8301-9644); Jonathan Vickers (0000-0001-6973-4828); Siba Senapati (0000-0003-4926-7497); Kurshid Akhtar (0000-0002-2858-1551); Regi George (0000-0001-5761-5215); Yeng Ang (0000-0003-0496-6710).

Author contributions: Ang Y designed the study, supervised the project, obtained the data and wrote the manuscript; Sooltangos A coordinated the study, obtained and analysed the data, and wrote the manuscript; McGrath S reviewed all pathology reports and contributed to data analysis; George R and Ang Y performed the ESD and analysed the data; Vickers J, Senapati S and Akhtar K performed surgery and analysed the data.

Informed consent statement: All the data used in this study have been anonymised.

Conflict-of-interest statement: None to declare.

Data sharing statement: All data are under the control of the

gastroenterology team at Salford Royal NHS Foundation Trust.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Yeng Ang, MD, Doctor, Full Professor, Department of Gastroenterology, Salford Royal NHS Foundation Trust, Stott Lane, Salford M6 8HD, United Kingdom. yeng.ang@srft.nhs.uk
Telephone: +44-0161-2065798
Fax: +44-0161-2065798

Received: September 7, 2017

Peer-review started: September 8, 2017

First decision: September 26, 2017

Revised: October 18, 2017

Accepted: November 15, 2017

Article in press: November 15, 2017

Published online: December 16, 2017

Abstract**AIM**

To investigate the efficacy of endoscopic submucosal dissection (ESD) at diagnosing and treating superficial neoplastic lesions of the stomach in a United Kingdom Caucasian population.

METHODS

Data of patients treated with or considered for ESD at

a tertiary referral center in the United Kingdom were retrieved for a period of 2 years (May 2015 to June 2017) from the electronic patient records of the hospital. Only Caucasian patients were included. Primary outcomes were curative resection (CR) and were defined as ESD resections with clear horizontal and vertical margin and an absence of lympho-vascular invasion, poor differentiation and submucosal involvement on histological evaluation of the resected specimen. Secondary end-points were reversal of dysplasia at 12 mo endoscopic follow-up and/or at the latest follow up. Change in histological diagnosis pre and post ESD was also analysed.

RESULTS

Twenty-four patients were initially identified with intention to treat. 19 patients were eligible after mapping gastroscopy and ESD was attempted on a total of 25 ESD lesions, 4 of which failed and had to be aborted mid-procedure. Out of 21 ESD performed, en-bloc resection was achieved in 71.4% of cases. Resection was considered complete on endoscopy in 90.5% of cases compared to only 38.1% on histology. A total of 6 resections were considered curative (28%), 5 non-curative (24%) and 10 indefinite for CR or non-CR (24%). ESD changed the histological diagnosis in 66.6% of cases post ESD. Endoscopic follow-up in the "indefinite" group and CR group showed that 50% and 80% of patients were clear of dysplasia at the latest follow-up respectively; 2 cases of recurrence were observed in the "indefinite" group. Survival rate for the entire cohort was 91.7%.

CONCLUSION

This study provides early evidence for the efficacy of ESD as a therapeutic and diagnostic intervention in Caucasian populations and supports its application in the United Kingdom.

Key words: Endoscopic resection; Endoscopic submucosal dissection; Endoscopic mucosal resection; Dysplasia; Early gastric cancer; United Kingdom

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Endoscopic submucosal dissection (ESD) is a minimally invasive technique used to diagnose or treat early neoplastic lesions of the gastrointestinal tract. Imported from Far East countries, where it is extensively used, this intervention has proven to be highly effective in carefully selected patients and to constitute a viable alternative to radical surgery. ESD is relatively new in the West and local evidence to support its use in the United Kingdom lacking. This retrospective study provides early evidence in favour of the use of ESD in the United Kingdom.

Sooltongos A, Davenport M, McGrath S, Vickers J, Senapati S, Akhtar K, George R, Ang Y. Gastric endoscopic submucosal dissection as a treatment for early neoplasia and for accurate staging of early cancers in a United Kingdom Caucasian

population. *World J Gastrointest Endosc* 2017; 9(12): 561-570 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v9/i12/561.htm> DOI: <http://dx.doi.org/10.4253/wjge.v9.i12.561>

INTRODUCTION

Endoscopic resection (ER) is a minimally invasive technique aimed at staging or curing dysplastic lesions and intramucosal cancers of the gastrointestinal tract. ER includes endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), their respective application mainly depending on the size of the tumour^[1]. EMR was the first endoscopic treatment proven to be as effective as gastrectomy at managing early gastric cancers, with curative rates as high as 85%^[1]. However, in lesions larger than 20mm, ESD is preferred as it can achieve higher rates of en-bloc resections and consequently lower recurrence rates^[1-7]. *En-bloc* resections almost constitute a prerequisite for accurate histological evaluation of the resected specimen.

ER is also considered the only definitive method of excluding invasion in otherwise precancerous lesions, where time and again, endoscopic biopsies and endoluminal ultrasound have proven inadequate^[2,8,9]. ER can change the diagnosis in up to 40% of cases, more commonly resulting in an upstaging^[10-12]. It provides vital information about the depth of invasion of the tumour and as the latter constitutes the strongest predictor of lymph node metastasis^[13,14], it is used to guide subsequent management decisions, in particular the indication for surgery. When compared to surgery, ESD appears to have comparable oncologic outcomes with the advantage of shorter operation times, shorter hospital stays and lower complication rates^[15].

Most evidence for the efficacy and safety of ESD comes from Eastern countries, where ESD has been shown to achieve curative resection (CR) rates as high as 97% in lesions that meet the Japanese Gastric Cancer Association (JGCA) guidelines^[16-18]. Despite being a technically challenging procedure and carrying a high risk of adverse events in inexperienced hands^[19], ESD is gradually gaining popularity in Western countries, partly facilitated by technological advancements^[20]. However, evidence for ESD is still scarce in Western populations. One of the few studies carried out in Germany showed promising results with a high rate of en-bloc resections and remarkably low recurrence rates of 1.5%^[21]. In the United Kingdom, the JGCA criteria guidelines are used to select lesions amenable to ESD. However, since the outcomes of ESD are heavily dependent on the level of skills of the endoscopist, more local studies are crucial^[22,23]. The National Institute of Health and Care Excellence in the United Kingdom only take into account United Kingdom studies when formulating local clinical guidelines. No studies have considered the efficacy of gastric ESD in a United Kingdom Caucasian population

up to this date.

MATERIALS AND METHODS

This retrospective study is part of our service development and audit and aims to investigate the efficacy of ESD at treating early neoplastic lesions of the stomach in a Caucasian population at a tertiary referral centre in the United Kingdom and secondly, its application for staging early cancers.

Inclusion criteria: Data was obtained for a period of 2 years from May 2015 to June 2017. Only Caucasian patients with gastric cancers staged at or below T1a N0M0 on the basis of computed tomography (CT) scans (or Positron Emission Tomography-Computed Tomography (PET-CT) in a few cases) and Endoscopic Ultrasound (EUS) were included in this study.

Exclusion criteria: Patients with gastric cancers staged at T1bN0M0 or above were excluded from the study on the basis of CT scans (or PET-CT scans in a few cases) and EUS.

Mapping oesophagogastroduodenoscopy (mapping OGD, a pre-ESD check to evaluate if the case is suitable for ESD) was used to assess the macroscopic appearance of the lesions, the position and size, the presence of ulceration, any field changes and importantly whether the lesions were liftable. The degree of lift of each lesion was graded according to the Kato classification where Kato 1 denotes lifting without any resistance, Kato 2 lifting with some resistance and Kato 3 no lifting^[24]. Endoscopic imaging enhancements used included White Light Imaging, Olympus Narrow Band Imaging (NBI) or Fuji Fluorescent Intelligent Chromoendoscopy, indigo carmine spray and acetic acid spray. Biopsies were taken prior to any intervention to assess or re-assess the type of neoplasia present and the degree of differentiation. Poor differentiation and non-lifting sign (Kato 3) precluded ESD except in one patient whose co-morbidities notably liver cirrhosis Child's Grade A made him unfit for surgery. Endoscopy reports, histology reports and multi-disciplinary team (MDT) meeting letters were retrieved from the electronic patient record of the hospital. The information about each patient's demographic data, pre-ESD endoscopic assessment, index procedure, follow-up endoscopy, surgery and outcome at the latest follow up were recorded. Microsoft Excel has been used to record all data and for all statistical analyses.

Olympus Double Channel Double-Headed Scope or Fuji Dual Channel Endoscope were used in all procedures and the procedures were jointly performed by two experienced interventional gastroenterologists. The ESD procedure was carried out in theatre (operating room) with the patient under general anaesthesia. The patient was intubated with the assistance of an anaesthetist and endoscopy performed using carbon dioxide gas only. The ESD equipment used for dissection included Olympus ITknife2 Electrosurgical Knife (KD-611L), Olympus ITknife nano Electrosurgical Knife (KD-612L/U), Fujifilm Flush Knife, Fujifilm Clutch Clutter and ERBE Hybrid O Knife. A soft transparent hood (D-201-13404; Olympus,

Tokyo, Japan) was attached to the tip of the endoscope to obtain good endoscopic views of the submucosal layer. In some cases, additional image enhancing techniques (as outlined above) had to be used. This was done through a 2-channel scope equipped with multibending and water jet functions attached to the tip of the endoscope. The lesions were lifted with EMR solution and marking dots were placed using argon on the normal mucosa at approximately 5 mm from the tumour margin to provide safety margins. EMR solution (consisting of a small amount of indigo carmine and 0.1% lidocaine) was then injected into the submucosal layer and a mucosal incision made outside the marking dots. In case of poor mucosal elevation due to ulceration of the lesion or extensive fibrosis of the submucosal layer, hyaluronic acid solution was added to the injection solution to achieve better lift. After mucosal incision, dissection of the submucosal layer was performed, thus achieving *en bloc* resection.

Each patient was given oral Omeprazole 40 mg, twice daily for at least 3 mo (or another equivalent proton pump inhibitor) after the procedure.

The resected specimen was cut into 4-mm-thick slices after formalin fixation. The histological type, size, depth of invasion, horizontal and vertical margins (HM and VM respectively), and lympho-vascular invasion were evaluated in each slice according to the JGCA Japanese Classification of Gastric Carcinoma criteria. To reconcile and allow for the efficacy of ESD to be more accurately investigated in Western populations, a more systematic approach to reporting histological findings such as the Vienna classification was also used^[25]. The measure of efficacy in this study is CR. A resection is considered curative if it achieves clear vertical and horizontal margins and if histological evaluation of the resected specimen shows neither poor differentiation, nor lympho-vascular invasion nor submucosal involvement^[3]. An ESD resection is coded as non-CR if it fails to meet all aforementioned criteria and as "indefinite" if data is inadequate to confirm either CR or non-CR. All resected lesions were coded as "complete resection on endoscopy" unless otherwise specified; a resection was considered to be "complete resection on histology" if the VM and the horizontal margin (HM) were clear on histology. The position of lesion was coded as Upper stomach if it was found in the cardia or fundus, as Mid stomach if in the body and as Lower stomach if in the antrum, pylorus or incisura. The age of the patient was at the time of the index procedure.

The secondary end-point was complete reversal of dysplasia at 12 mo endoscopic follow-up and/or at the latest follow-up and was investigated in the "indefinite" group and the CR group. The schedule for endoscopic surveillance for site check is 3 mo after the procedure and then 6 monthly for first year and then yearly thereafter, for 5 years. This outcome considers a patient as one entity, regardless of the number of ESD resections he/she may have had. The change in histological diagnosis pre and post ESD has also been recorded to assess the ability of ESD to influence diagnosis. The histological diagnosis is recorded as the worst histological

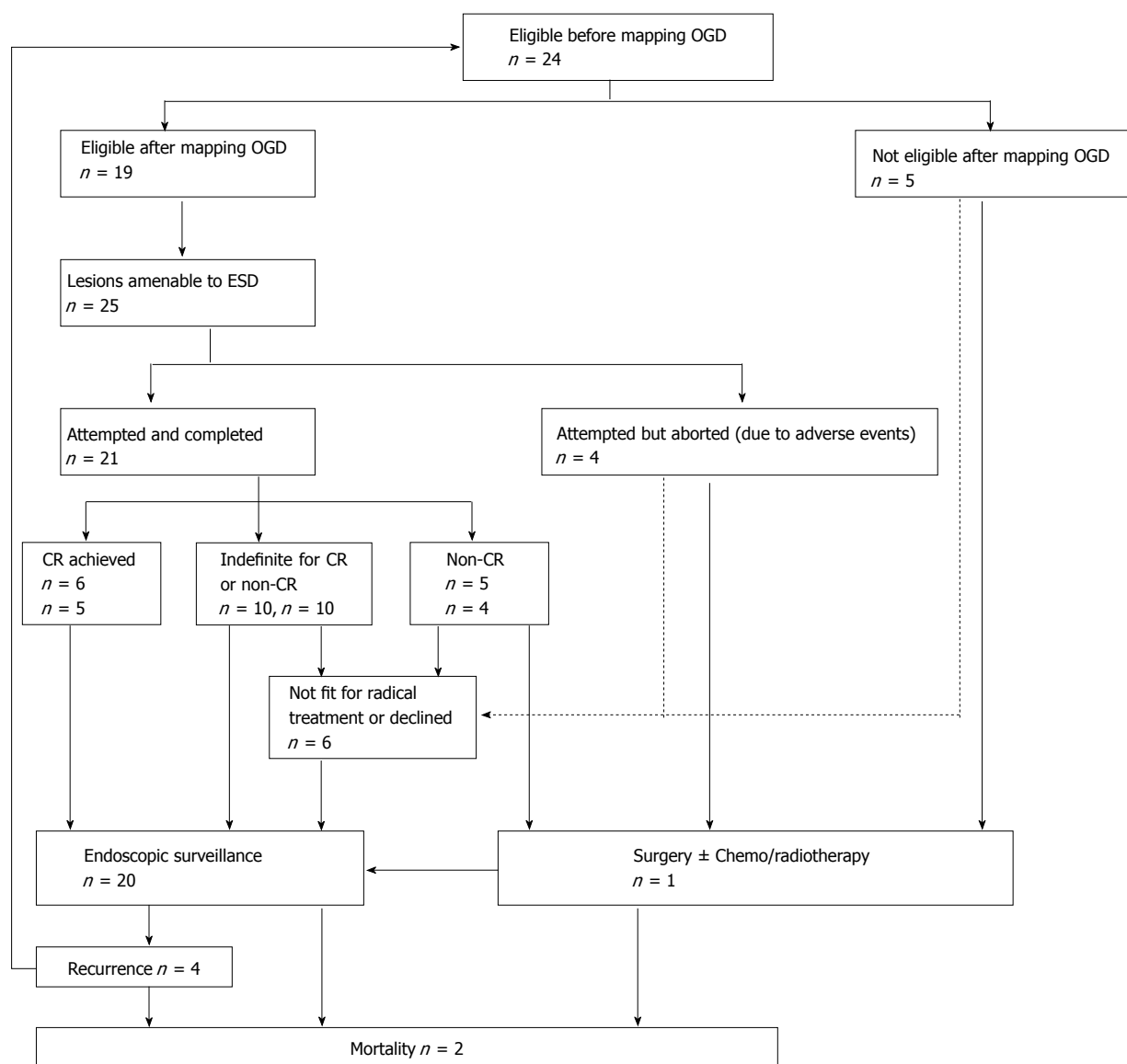


Figure 1 Prisma diagram showing how patients have been selected and their respective outcomes. CR: Curative resection.

grade reported for each lesion.

RESULTS

There were 24 patients with gastric dysplasia and/or neoplasia who were considered for endoscopic treatment using ESD. The demographic data of patients included in the study are shown in Table 1. Out of the 24 patients identified for the study, 19 were deemed suitable for ESD after mapping OGD. ESD was attempted on a total of 25 dysplastic or neoplastic lesions, among which 21 were completed and the patients then followed up or offered further treatment based on histology of the resected specimens, and 4 aborted (Figure 1). There were 5 patients who were found to be unsuitable for ESD after mapping OGD.

Pre-ESD endoscopic assessment

Most lesions were reported as Kato 1, one lesion

as Kato 2 and one as Kato 2 to 3. The mean size of lesions resected was 24.7 mm (standard deviation 11.7 mm; range 10-50 mm). Figure 2 shows a lesion suitable for ESD and the procedure in sequence. The main contraindicative features in lesions unsuitable for ESD were ulceration and poor differentiation. Poor lift, large size and deeper invasion constituted other contraindications (Table 2; Figure 2). In one patient, a severe oesophageal stricture prevented passage of the endoscope to assess the lesion. Features of the lesions deemed suitable for ESD are shown in Table 3.

Index procedure: Gastric endoscopic submucosal dissection

Of the 21 resections completed successfully, en-bloc resection was achieved in 71.4% of cases. Resection was considered complete on endoscopy in 90.5% of cases compared to only 38.1% on histology (Table 4). 6 achieved a definite CR (5 patients), 5 were confirmed to

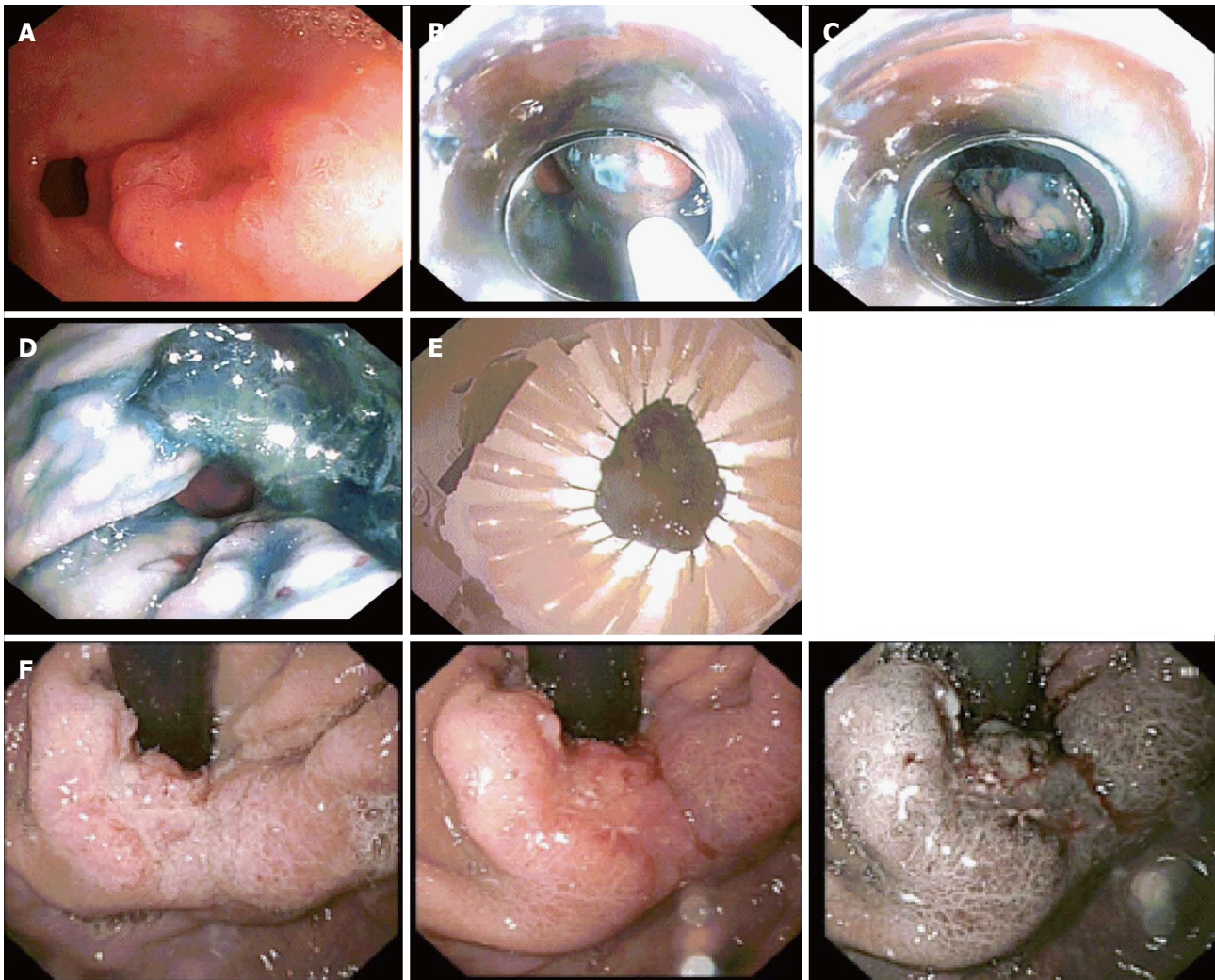


Figure 2 Endoscopic appearance of the gastric lesions considered for resection with endoscopic submucosal dissection. A-E: Macroscopic appearance of lesion with mapping OGD and thus suitable for ESD. This is an area extending from the antrum through to the pyloric ring. The ESD procedure is highlighted here; F: Macroscopic appearance of lesion with suspected sm3 or deeper on mapping OGD and thus unsuitable for ESD. This is an area extending from the cardia through to the upper body. ESD: Endoscopic submucosal dissection.

Table 1 Demographic data of patients included in the study *n* (%)

Variable	Value, <i>n</i> = 24
Number of patients assessed for ESD, <i>n</i>	24
Age, Mean \pm SD, yr	73.0 \pm 10.7
Age, range, yr	44-86
Gender, male	20 (83.3)
Gender, female	4 (16.7)
Caucasian ethnicity	24 (100)

ESD: Endoscopic submucosal dissection.

Table 2 Features found to make endoscopic submucosal dissection unsuitable in 5 patients

Patient	Reasons
A	Ulcerated lesion
B	SM3 or deeper invasion; Poorly differentiated lesion
C	Large size: 4-5 cm; Ulcerated over 3 cm
D	Severe oesophageal stricture prevented passage of scope
E	KATO 3; Deeply ulcerated; Poorly differentiated

Table 3 Features of lesions on which endoscopic submucosal dissection has been attempted *n* (%)

Variable	Value, <i>n</i> = 25
Location of lesion	
Upper stomach	4 (16)
Mid stomach	7 (28)
Lower stomach	14 (56)
Average of longer axis of lesion (mm)	
Mean \pm SD	24.7 \pm 11.7
Range	10-50
Histological grade at baseline	
IMC	13 (52)
HGD	8 (32)
LGD	3 (12)
Invasive	1 (4)

LGD: Low grade dysplasia; HGD: High grade dysplasia; IMC: Intramucosal carcinoma.

be non-curative (4 patients) and 10 were indefinite (10 patients) (Figure 3). In the latter group, only 2 patients were considered potential candidates for surgery. The

Table 4 Results of endoscopic submucosal dissection *n* (%)

Variable	Value, <i>n</i> = 21
Average number of ESD per patient (including failed ESD)	1.3
Number of en-bloc resections	15 (71.4)
Number of pieces in which lesions were resected	
Mean \pm SD	1.5 \pm 1.4
Range	1-7
Unspecified but > 1	2
Rate of complete resection on endoscopy	19 (90.5)
Rate of complete resection on histology	8 (38.1)
Margins clear on histology of ESD specimen	
Both VM and HM	8 (38.1)
VM only	1 (4.8)
HM only	1 (4.8)
Neither VM nor HM	1 (4.8)
Not specified or difficult to interpret specimen due to coagulation effect/poor preservation of tissue	10 (47.6)

ESD: Endoscopic submucosal dissection.

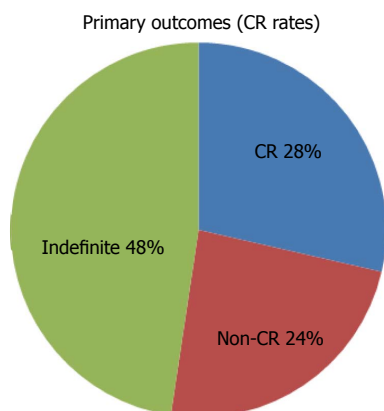


Figure 3 Pie chart showing the rate of primary outcomes: CR (6), non-CR (5) or indefinite (10) when data is inadequate to definitively qualify a resection as CR or non-CR. CR: Curative resection; Non-CR: Non-curative resection.

rest were only offered endoscopic follow-up as complete resection had been achieved on endoscopy and no other poor prognostic features (e.g., poor differentiation) were present. Adjuvant chemo or radio therapy were not given as patients initially selected for this study had no evidence of lymph node involvement or distant metastases on CT and/or PET-CT scans. The histological diagnoses of non-CR patients post ESD are shown in Table 5.

Complications are classified as acute (during the procedure), early (< 48 h after the procedure) or late (> 48 h after the procedure). The most common acute complication reported was oozing small blood vessels (6). In 4 of these cases, bleeding was mild and treated with argon, coagulation forceps or endo-clips. In the other 2, the procedure had to be aborted due to profuse bleeding. Both cases were in the same patient. The patient was on anti-coagulation for atrial fibrillation and had a normal INR after stopping warfarin for 5 d prior to ESD. The marked mucosal friability resulted in bleeding even on mild trauma from the water jet used during endoscopy (Figure 4). A further 2 cases also had

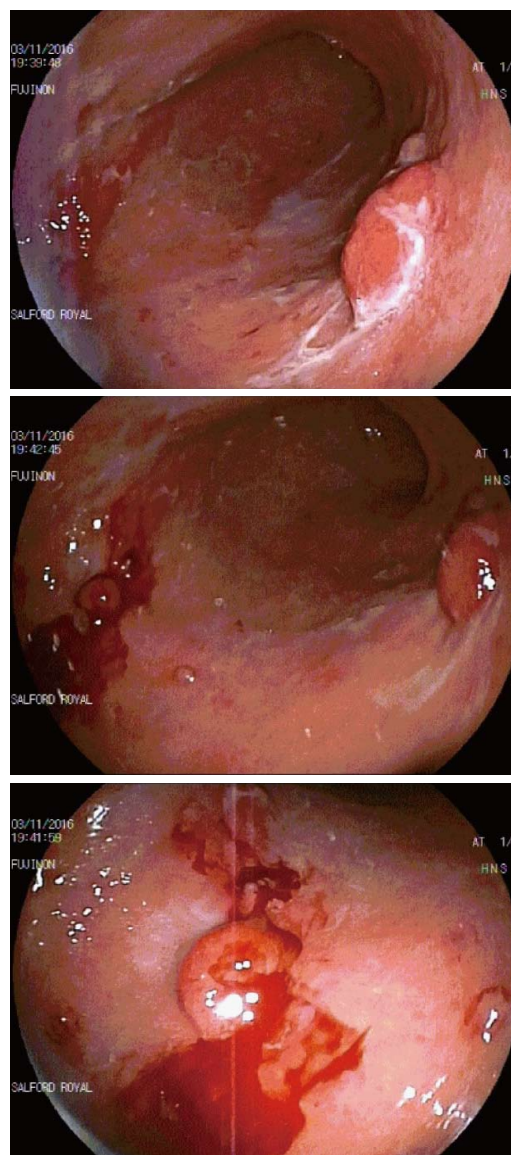


Figure 4 The appearance of the stomach wall on endoscopic follow-up of the patient in which endoscopic submucosal dissection had to be aborted twice due to profuse bleeding. The patient had a high INR and was a poor candidate for ESD at baseline but co-morbidities precluded surgery in his case. Note the 2 metachronous malignant sessile polyps Paris 2a and the marked mucosal friability evident from bleeding. ESD: Endoscopic submucosal dissection.

to be aborted, one due to the location of the lesion, which would have led to gastric outlet obstruction in due course and the other due to extensive scarring secondary to a previous ESD attempt. There was only one case of early complication involving vomiting within 24 h of the procedure. No cases of late complications were reported.

The median duration of the ESD procedures was found to be 120 min (with factors such as the size of the lesion, its location and tissue factors influencing the length of time required to complete the procedure).

Change in histological grade post endoscopic submucosal dissection

Gastric ESD changed the histological grade in 66.6% of the resected lesions (*n* = 21) (Figure 5), equally

Table 5 Histological grade of 5 non- curative resection

Patient	Histological grade at baseline	Histopathologic diagnosis on ESD specimen of non-CR
A	IMC	IMC with lympho-vascular invasion
A	IMC	Invasive adenocarcinoma; Lympho-vascular invasion
B	IMC	Invasive adenocarcinoma; Poorly differentiated; Diffuse (signet ring) type; Tumour extends into submucosa; Further de-differentiation noted at the invasive aspect
C	Highly suspicious of IMC	Adenocarcinoma with deep margin involvement; Moderately to poorly differentiation; Vascular invasion
D	Invasive adenocarcinoma	Invasive adenocarcinoma; Well differentiated; No lympho-vascular invasion

ESD: Endoscopic submucosal dissection; CR: Curative resection; IMC: Intramucosal carcinoma.

Table 6 Secondary outcome in the cohort' indefinite for curative resection or non- curative resection

Variable	Indefinite, <i>n</i> = 10	CR, <i>n</i> = 5
Number of patients under endoscopic follow-up, <i>n</i> (%)	9 (90)	5 (100)
Median follow-up, mo	2	3
Mean follow-up, mo	5.1	8.5
Range, mo	0-19	0-22
Length of time since ESD, mean \pm SD, mo	13.3 \pm 11.3	12.2 \pm 11.1
Length of time since ESD, range, mo	2 - 38	0 - 26
Number of patients with metachronous or synchronous disease post ESD, <i>n</i>	2	0

ESD: Endoscopic submucosal dissection; CR: Curative resection.

downgrading and upgrading the histological diagnoses. Most resected specimens were found to have HGD (5) and IMC (5), compared to the higher proportion of IMC prior to ESD. In addition, as shown in Figure 6, lympho-vascular invasion and invasive cancer were observed in 5 cases compared to only one case pre ESD. Of these 5 cases, 1 resection was found to be completely clear of dysplasia and a further case indefinite for any dysplasia on histology, but with clear evidence of invasion in both cases. LGD was present in 4 cases. In all cases except one, the change in histological grade, if any, was by one stage.

Endoscopic follow-up

In the "indefinite" cohort of 10 patients, one declined further endoscopic follow-up and has been scheduled for a CT scan instead. In addition, 2 patients had not had any follow-up yet at the time of data collection. One passed away 1 mo after his last follow-up endoscopy (the cause of death is unrelated to his gastric diagnosis). The median follow-up period was 2 mo and the mean 5.1 mo for the "indefinite" cohort (Table 6). Complete reversal of dysplasia was observed in 10% and 50% of patients at 12-mo and the latest follow-up respectively in the "indefinite" cohort (Figure 7). Recurrence was observed in 2 patients - both had in fact been considered poor candidates for ESD at baseline due to multiple comorbidities. In the cohort considered to have achieved CR with ESD, 80% were found to be free of dysplasia at their latest endoscopic follow-up at a mean follow-up period of 6.8 mo (Figure 8). Hence, with both cohorts (CR and 'indefinite') combined, 9

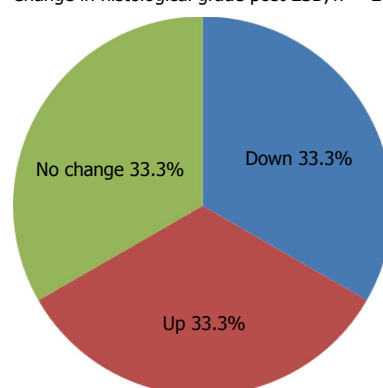
Change in histological grade post ESD, *n* = 21

Figure 5 Pie chart showing how endoscopic submucosal dissection changed the histological grade of the resected lesions. Down: Downstaged; Up: Upstaged; ESD: Endoscopic submucosal dissection.

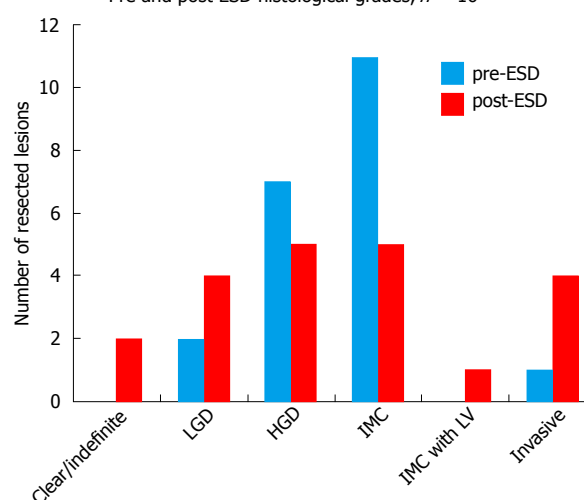
Pre and post ESD histological grades, *n* = 16

Figure 6 Column chart showing the difference between pre-ESD and post-ESD histological grade for all 16 resected lesions. LGD: Low grade dysplasia; HGD: High grade dysplasia; IMC: Intramucosal carcinoma; LV: Lympho-vascular invasion; ESD: Endoscopic submucosal dissection.

of the 11 patients (81.8%) who had had at least one endoscopic follow-up were found to be free of dysplasia on endoscopy at their latest follow-up at a mean follow-up period of 7.7 mo.

Surgery

Overall, 6 patients were considered for surgery after ESD. In the "indefinite" group, the 2 patients with

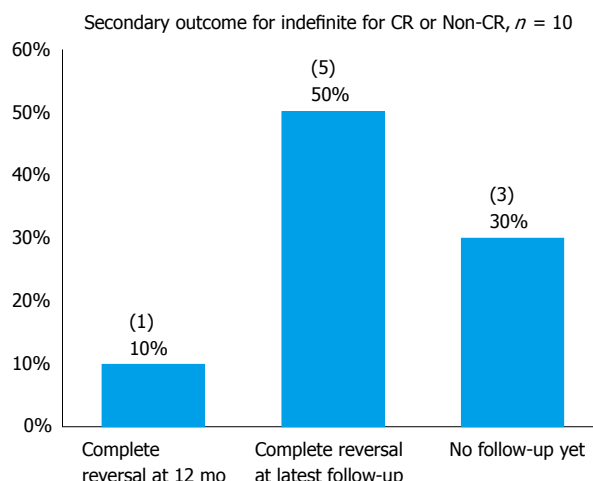


Figure 7 Column chart showing secondary outcomes *i.e.* complete reversal of dysplasia at 12 mo endoscopic follow-up and/or at latest follow-up in the group indefinite for curative resection or non-curative resection post endoscopic submucosal dissection. CR: Curative resection.

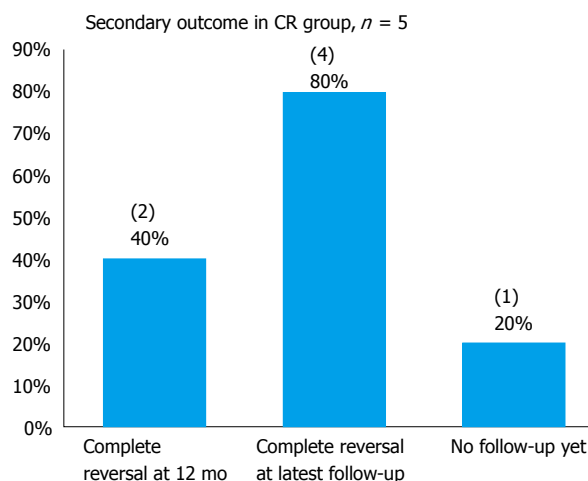


Figure 8 Column chart showing secondary outcomes *i.e.* complete reversal of dysplasia at 12 mo endoscopic follow-up and/or at latest follow-up in the group curative resection post endoscopic submucosal dissection. CR: Curative resection.

recurrence at follow-up were referred for surgery but neither was sufficiently fit to proceed. ESD was attempted again but failed in both patients. They were thus listed for endoscopic surveillance. Metachronous or recurrent polyps were observed at the latest follow-up for both patients at 11 and 19 mo respectively. In the group of 4 patients found to be non-CR, surgery was considered a treatment option in all of them but only one patient was sufficiently fit to proceed with gastrectomy. The rest of non-CR patients were offered either further ESD or endoscopic surveillance or palliative care.

Only 2 of the 5 patients considered unfit for ESD underwent surgery (Patients B and E; Table 2). Post-op staging were pT3N3MxR1 and pT1bN1MxR0 (moderate to poor differentiation) respectively.

Survival rate

One ESD patient died 4 mo after ESD. ESD on this patient was considered curative and endoscopic follow-up at 3 mo post ESD showed no macroscopic recurrence but biopsies could not be taken due to the patient's high INR. Cause of death is unrelated to his primary gastric diagnosis. Survival rate in ESD patients was 94.7% (18 out of 19 patients) at a mean follow-up period of 15 mo.

Another patient in the group found unsuitable for ESD died 5 mo after an attempted mapping OGD. The patient was suffering from a severe oesophageal stricture and was receiving parenteral nutrition. The overall survival rate in the entire cohort was thus 91.7% (22 out of 24 patients).

DISCUSSION

Despite the small sample size, the ability of ESD to achieve CR in carefully selected patients has been demonstrated. Approximately 28% of ESD resections (6) were considered curative. Moreover, 4 of the 5 CR

patients were free of dysplasia at the latest follow-up while the fifth patient had not had any follow-up yet, thus corroborating previous studies that demonstrated the positive long-term outcomes in patients with a CR, as defined by the JGCA criteria.

Positive long-term outcomes were also observed in a large proportion of the "indefinite" patients, despite the inability to confirm CR on histology. In the 2 patients who had recurrence of disease, histological evaluation of the ESD specimens had been particularly challenging due to marked inflammation in one case and very severe distortion of the tissue in the other. The specimen in fact reached the pathology laboratory outside formalin. Non-CR could therefore not be confidently excluded in these 2 patients and was in fact made more likely by a pre-ESD diagnosis of IMC. It was clear however on endoscopic follow-ups that these 2 patients had more advanced disease than suspected prior to ESD, as suggested by the presence of several metachronous and/or synchronous - polyps. Overall, despite the inability to always confirm CR on histology, gastric ESD has proven itself highly effective at clearing neoplastic growth if complete resection can be achieved on endoscopy. It also points to the importance of MDT discussions to avoid unnecessary surgery in patients indefinite for CR or non-CR.

The main reason for uncertainty regarding the completeness of excision on histology was the poor preservation of the resected specimens. In many instances, the specimen had been pinned down too deeply into the polystyrene board thus inflicting substantial trauma to the tissue. Other artefacts such as diathermy changes at the periphery, excision margins not clearly defined and inflammation also hindered accurate interpretation. In one case, the lesion had to be resected piecemeal. Other reasons included missing report and lack of mention of margin clearance. Hence, it is clear that to allow for the efficacy of ESD to be more accurately investigated in the future, ways

to satisfactorily preserve the resected specimen in its original state and implementing a more systematic approach to reporting histological findings are required.

This study also demonstrates the importance of careful selections of patients at baseline. Out of the 5 non-CR resections, 3 already contained poor prognostic features at baseline. However, the MDT consensus was to proceed with ESD given the patients' multiple co-morbidities that made them unfit for surgery. In one case, poor differentiation was seen prior to ESD while in the other two, invasive carcinoma had been identified. In the rest of non-CR cases, deeper invasion would have been left unnoticed had the lesion not been resected by ESD. ESD effectively identified lympho-vascular invasion in these 2 lesions presumed to be IMC only prior to ESD. This observation lends support to the status of ESD as the only definitive tool to exclude invasion. Moreover, ESD changed the histological grade in 66.6% of resected lesions. Unlike more large-scale studies however, ESD equally downgraded and upgraded histological diagnoses. In one exceptional case, the histological grade changed from IMC pre-ESD to clear of any dysplasia or malignancy post ESD. Further investigations into this case revealed observer bias in the interpretation of pre-ESD biopsy specimen at the patient's local hospital. ESD thus enabled the correct diagnosis to be made. This however points to a potential source of error in this study, *i.e.*, bias in interpretation of histology slides.

Only one patient underwent surgery after a non-CR ESD. Interestingly, in this patient, the ESD scar was still present on endoscopic follow-up after the surgery. Deep biopsies taken from this site were all found to be clear of dysplasia, even at the latest endoscopy performed 30 mo post ESD. In this patient, ESD had revealed a well-differentiated invasive adenocarcinoma without any lympho-vascular invasion. This "invasion" constituted the indication for surgery even though the exact depth of invasion was not reported. Hence, it may be possible that ESD patients are being unnecessarily referred for surgery and that ESD alone could be sufficient to treat more advanced diseases with the advantage of shorter hospital stays and fewer complications.

Some of the other limitations of this study include relatively short follow-up periods preventing more accurate assessment of the long-term outcomes and potential bias in letters and endoscopy reports. Hence we plan to study a larger number of patients and have a longer follow-up period in order to reduce bias and truly assess the efficacy of ESD in our Caucasian United Kingdom population.

In conclusion, these results although modest are promising and provide early evidence in favour of the use of ESD in Caucasian populations in the United Kingdom. Despite the wealth of evidence for the efficacy of gastric ESD in Far Eastern countries, the National Institute of Health and Care Excellence (NICE) United Kingdom still views upper GI ESD as a procedure to be applied on a case-by-case basis only with an MDT

approach^[22], thus demonstrating the need for further, larger-scale studies into this technique in the United Kingdom and other Western countries.

ARTICLE HIGHLIGHTS

Research background

Endoscopic submucosal dissection (ESD) is a minimally invasive technique used to treat early superficial lesions of the gastrointestinal tract. It is popular in Far East countries where its outstanding efficacy has been proven by multiple studies. Technological advances have recently made ESD more accessible worldwide. In the United Kingdom, this intervention is still relatively new and local evidence to support its use still scarce.

Research motivation

This study aims to evaluate the application of ESD in Caucasian patients in the United Kingdom and seeks to compensate for the lack of evidence in the literature in favour of its use in this country. Larger scale studies will be required in the future.

Research objectives

This study constitutes a step forward in providing the evidence necessary to support the application of ESD among Caucasian patients in the United Kingdom as well as to help produce standardised clinical guidelines to inform local clinical practice for this relatively new intervention.

Research methods

This retrospective study uses data obtained from the Department of Gastroenterology at Salford Royal NHS Foundation Trust in the United Kingdom, a tertiary centre for gastrointestinal interventions. Data for a period of 2 years has been analysed using Microsoft Excel.

Research results

Of the 21 lesions resected with ESD, 6 achieved curative resection (CR), 10 were "indefinite" for CR or non-CR, and 5 were considered non-CR. A favourable long-term outcome was observed in the CR and "indefinite" groups, with clearance of dysplasia observed overall in 81.8% of patients who had had at least one endoscopic follow-up. ESD also changed the histological diagnoses in 66.6% of cases. These results are promising and provide early evidence in favour of the use of ESD in the United Kingdom.

Research conclusions

ESD as applied to Caucasian patients in the United Kingdom can produce promising results as shown by this study. There have not been similar studies in the United Kingdom in the past and thus larger scale studies are required to fully evaluate the efficacy and safety profile of ESD as applied to upper gastrointestinal cancers.

Research perspectives

To better assess the effectiveness of ESD at clearing early neoplastic lesions of the stomach and other upper gastrointestinal cancers among Caucasian patients in the United Kingdom, a prospective study involving a larger sample of such patients is required.

ACKNOWLEDGMENTS

We acknowledge the hospital coding department for their help in identifying patients for this study. We acknowledge the Upper GI specialist multi-disciplinary team for their contributions to discussions for patient selection for the ESD procedures. We acknowledge the helpful discussions from Mr Ram Chaparala, Ms Rachel Melhedo, our radiology, oncology and pathology colleagues.

REFERENCES

- 1 **Takekoshi T**, Baba Y, Ota H, Kato Y, Yanagisawa A, Takagi K, Noguchi Y. Endoscopic resection of early gastric carcinoma: results of a retrospective analysis of 308 cases. *Endoscopy* 1994; **26**: 352-358 [PMID: 8076567 DOI: 10.1055/s-2007-1008990]
- 2 **Pimentel-Nunes P**, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, Amato A, Berr F, Bhandari P, Bialek A, Conio M, Haringsma J, Langner C, Meisner S, Messmann H, Morino M, Neuhaus H, Piessevaux H, Rugge M, Saunders B, Robaszkiewicz M, Seewald S, Kashin S, Dumonceau J, Hassan C, Deprez P. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015; **47**: 829-854 [DOI: 10.1055/s-0034-1392882]
- 3 **Uedo N**, Takeuchi Y, Ishihara R. Endoscopic management of early gastric cancer: endoscopic mucosal resection or endoscopic submucosal dissection: data from a Japanese high-volume center and literature review. *Ann Gastroenterol* 2012; **25**: 281-290 [PMID: 24714247]
- 4 **Cao Y**, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. *Endoscopy* 2009; **41**: 751-757 [PMID: 19693750 DOI: 10.1055/s-0029-1215053]
- 5 **Takeuchi Y**, Uedo N, Iishi H, Yamamoto S, Yamamoto S, Yamada T, Higashino K, Ishihara R, Tatsuta M, Ishiguro S. Endoscopic submucosal dissection with insulated-tip knife for large mucosal early gastric cancer: a feasibility study (with videos). *Gastrointest Endosc* 2007; **66**: 186-193 [PMID: 17591498 DOI: 10.1016/j.gie.2007.03.1059]
- 6 **Gotoda T**. A large endoscopic resection by endoscopic submucosal dissection procedure for early gastric cancer. *Clin Gastroenterol Hepatol* 2005; **3**: S71-S73 [PMID: 16013003 DOI: 10.1016/S1542-3565(05)00251-X]
- 7 **Park YM**, Cho E, Kang HY, Kim JM. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. *Surg Endosc* 2011; **25**: 2666-2677 [PMID: 21424201 DOI: 10.1007/s00464-011-1627-z]
- 8 **Hull MJ**, Mino-Kenudson M, Nishioka NS, Ban S, Sepehr A, Puricelli W, Nakatsuka L, Ota S, Shimizu M, Brugge WR, Lauwers GY. Endoscopic mucosal resection: an improved diagnostic procedure for early gastroesophageal epithelial neoplasms. *Am J Surg Pathol* 2006; **30**: 114-118 [PMID: 16330950 DOI: 10.1097/01.pas.0000180438.56528.a0]
- 9 **Yoshinaga S**, Oda I, Nonaka S, Kushima R, Saito Y. Endoscopic ultrasound using ultrasound probes for the diagnosis of early esophageal and gastric cancers. *World J Gastrointest Endosc* 2012; **4**: 218-226 [PMID: 22720122 DOI: 10.4253/wjge.v4.i6.218]
- 10 **Pech O**, May A, Manner H, Behrens A, Pohl J, Weferling M, Hartmann U, Manner N, Huijsmans J, Gossner L, Rabenstein T, Vieth M, Stolte M, Ell C. Long-term efficacy and safety of endoscopic resection for patients with mucosal adenocarcinoma of the esophagus. *Gastroenterology* 2014; **146**: 652-660.e1 [PMID: 24269290 DOI: 10.1053/j.gastro.2013.11.006]
- 11 **Peters F**, Brakenhoff K, Curvers W, Rosmolen W, Fockens P, ten Kate F, Krishnadath K, Bergman J. Histologic evaluation of resection specimens obtained at 293 endoscopic resections in Barrett's esophagus. *Gastrointest Endosc* 2008; **67**: 604-609 [DOI: 10.1016/j.gie.2007.08.039]
- 12 **Pech O**, Gossner L, Manner H, May A, Rabenstein T, Behrens A, Berres M, Huijsmans J, Vieth M, Stolte M, Ell C. Prospective evaluation of the macroscopic types and location of early Barrett's neoplasia in 380 lesions. *Endoscopy* 2007; **39**: 588-593 [PMID: 17611912 DOI: 10.1055/s-2007-966363]
- 13 **Merkow R**, Bilimoria K, Keswani R, Chung J, Sherman K, Knab L, Posner M, Bentrem D. Treatment trends, risk of lymph node metastasis, and outcomes for localized esophageal cancer. *J Natl Cancer Inst* 2014; **106** [DOI: 10.1093/jnci/dju133]
- 14 **Buskens C**, Westerterp M, Lagarde S, Bergman J, ten Kate F, van Lanschoot J. Prediction of appropriateness of local endoscopic treatment for high-grade dysplasia and early adenocarcinoma by EUS and histopathologic features. *Gastrointest Endosc* 2004; **60**: 703 [PMID: 25031273 DOI: 10.1093/jnci/dju133]
- 15 **Chiu PW**, Teoh AY, To KF, Wong SK, Liu SY, Lam CC, Yung MY, Chan FK, Lau JY, Ng EK. Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: a retrospective cohort study. *Surg Endosc* 2012; **26**: 3584-3591 [PMID: 22678176 DOI: 10.1007/s00464-012-2371-8]
- 16 **Ono H**, Yao K, Fujishiro M, Oda I, Nimura S, Yahagi N, Iishi H, Oka M, Ajioka Y, Ichinose M, Matsui T. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc* 2016; **28**: 3-15 [PMID: 26234303 DOI: 10.1111/den.12518]
- 17 **Japanese Gastric Cancer Association**. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer* 2017; **20**: 1-19 [PMID: 27342689 DOI: 10.1007/s10120-016-0622-4]
- 18 **Toyonaga T**, Man-i M, East JE, Nishino E, Ono W, Hirooka T, Ueda C, Iwata Y, Sugiyama T, Dozaiku T, Hirooka T, Fujita T, Inokuchi H, Azuma T. 1,635 Endoscopic submucosal dissection cases in the esophagus, stomach, and colorectum: complication rates and long-term outcomes. *Surg Endosc* 2013; **27**: 1000-1008 [PMID: 23052530 DOI: 10.1007/s00464-012-2555-2]
- 19 **Oda I**, Suzuki H, Nonaka S, Yoshinaga S. Complications of gastric endoscopic submucosal dissection. *Dig Endosc* 2013; **25** Suppl 1: 71-78 [PMID: 23368986 DOI: 10.1111/j.1443-1661.2012.01376.x]
- 20 **Chiu PW**. Novel endoscopic therapeutics for early gastric cancer. *Clin Gastroenterol Hepatol* 2014; **12**: 120-125 [DOI: 10.1016/j.cgh.2013.07.037]
- 21 **Probst A**, Pommer B, Golger D, Anthuber M, Arnoldt H, Messmann H. Endoscopic submucosal dissection in gastric neoplasia - experience from a European center. *Endoscopy* 2010; **42**: 1037-1044 [PMID: 20972955 DOI: 10.1055/s-0030-1255668]
- 22 **National institute for health and clinical excellence, N.I.C.E.** 2015. Interventional procedures programme interventional procedure overview of endoscopic submucosal dissection of gastric lesions. Available from: URL: <https://www.nice.org.uk/guidance/ipg360/evidence/overview-pdf-495581293>
- 23 **Chung IK**, Lee JH, Lee SH, Kim SJ, Cho JY, Cho WY, Hwangbo Y, Keum BR, Park JJ, Chun HJ, Kim HJ, Kim JJ, Ji SR, Seol SY. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. *Gastrointest Endosc* 2009; **69**: 1228-1235 [PMID: 19249769 DOI: 10.1016/j.gie.2008.09.027]
- 24 **Kato H**, Haga S, Endo S, Hashimoto M, Katsube T, Oi I, Aiba M, Kajiura T. Lifting of lesions during endoscopic mucosal resection (EMR) of early colorectal cancer: implications for the assessment of resectability. *Endoscopy* 2001; **33**: 568-573 [PMID: 11473326 DOI: 10.1055/s-2001-15308]
- 25 **Schlemper RJ**, Riddell RH, Kato Y, Borchard F, Cooper HS, Dawsey SM, Dixon MF, Fenoglio-Preiser CM, Fléjou JF, Geboes K, Hattori T, Hirota T, Itabashi M, Iwafuchi M, Iwashita A, Kim YI, Kirchner T, Klimpfinger M, Koike M, Lauwers GY, Lewin KJ, Oberhuber G, Offner F, Price AB, Rubio CA, Shimizu M, Shimoda T, Sipponen P, Solcia E, Stolte M, Watanabe H, Yamabe H. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000; **47**: 251-255 [PMID: 10896917 DOI: 10.1136/gut.47.2.251]

P- Reviewer: Braden B, Coskun A, Rabago L, Trifan A

S- Editor: Chen K **L- Editor:** A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

