Endoscopic diagnosis and treatment of gastric dysplasia and early cancer: Current evidence and what the future may hold

Edward Young, Hamish Philpott, Rajvinder Singh

Abstract

Gastric cancer accounts for a significant proportion of worldwide cancer-related morbidity and mortality. The well documented precancerous cascade provides an opportunity for clinicians to detect and treat gastric cancers at an endoscopically curable stage. In high prevalence regions such as Japan and Korea, this has led to the implementation of population screening programs. However, guidelines remain ambiguous in lower prevalence regions. In recent years, there have been many advances in the endoscopic diagnosis and treatment of early gastric cancer and precancerous lesions. More advanced endoscopic imaging has led to improved detection and characterization of gastric lesions as well as superior accuracy for delineation of margins prior to resection. In addition, promising early data on artificial intelligence in gastroscopy suggests a future role for this technology in maximizing the yield of advanced endoscopic imaging. Data on endoscopic resection (ER) are particularly robust in Japan and Korea, with high rates of curative ER and markedly reduced procedural morbidity. However, there is a shortage of data in other regions to support the applicability of protocols from these high prevalence countries. Future advances in endoscopic therapeutics will likely lead to further expansion of the current indications for ER, as both technology and proceduralist expertise continue to grow.

Key Words: Gastric cancer; Endoscopy; Endoscopic imaging; Endoscopic mucosal resection; Endoscopic submucosal dissection

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.
Unsurprisingly, low disease prevalence combined with variable guidelines leads to anaemia, family history in first degree relative, citing low-grade evidence patients with multiple risk factors for gastric cancer (male, smoker, pernicious). The British Society of Gastroenterology (BSG) recommends endoscopic screening in screening, only surveillance for patients with gastric intestinal metaplasia (GIM), while the American Gastroenterology Association does not recommend population screening programs as an evidence based, cost effective measure for preventing gastric cancer-related mortality and morbidity. Rates of gastric cancer in Eastern Asia (particularly Japan and Korea) are markedly higher than Western regions, which has resulted in implementation of population screening programs per capita. Accumulating evidence suggests that endoscopic submucosal dissection results in at least equivalent disease-related outcomes with a marked reduction in morbidity compared to gastrectomy. Supportive data are robust in regions with high gastric cancer prevalence, however a paucity of western data results in inconsistencies in clinical practice in these regions. This article serves to review existing evidence regarding endoscopic imaging and therapeutics in gastric cancer, as well as identify future areas for research and development.

**INTRODUCTION**

Gastric cancer remains a leading cause of cancer-related morbidity and mortality, accounting for 780,000 deaths and more than 1 million new diagnoses worldwide in 2020 alone[1,2]. Conventional surgical management with gastrectomy is associated with significant morbidity and mortality[3]. Countries with a high prevalence of gastric cancer have implemented systematic screening programs and demonstrated the benefit of early detection and endoscopic resection (ER) of precancerous gastric lesions and early gastric cancers (EGCs), offering curative treatment with considerably less morbidity[4,5]. Future challenges and opportunities remain, including the judicious surveillance of gastric metaplasia in lower prevalence communities, utilising improvements in endoscopic imaging and further refining existing ER techniques, while at all times accumulating high-quality collaborative data sets to inform and shape future management algorithms.

**ENDOSCOPIC DIAGNOSIS OF GASTRIC NEOPLASIA**

*Endoscopic gastric cancer screening*

Rates of gastric cancer in Eastern Asia (particularly Japan and Korea) are markedly higher than Western regions, which has resulted in implementation of population screening programs as an evidence based, cost effective measure for preventing gastric cancer-related mortality and morbidity[4-6]. Screening programs facilitate the detection of precancerous lesions and EGCs at an endoscopically resectable stage. Japanese guidelines suggest biennial or triennial endoscopic screening for those over the age of 50. This approach could prevent up to 63% of gastric cancer-related mortality, resulting in 27.2 quality-adjusted life years gained per 1000 individuals[4]. In Korea, guidelines similarly suggest biennial screening but commencing at age 40. This is supported by data showing a 38% reduction in age-standardised mortality rate in the screening group at large, at a cost of less than the average gross expenditure product per capita[5].

In Western regions including North America and Australasia, the age-standardised incidence of gastric cancer is 6.5-8.8/100000 population, four-times lower than East Asia[6]. The lower incidence may be attributable to a combination of reduced *Helicobacter pylori* prevalence as well as environmental, lifestyle (diet, smoking) and genetic factors[6]. Given this comparatively low gastric cancer incidence, Western countries are yet to adopt population screening. Instead, guidelines in these regions are varied. The American Gastroenterology Association does not recommend population screening, only surveillance for patients with gastric intestinal metaplasia (GIM), while the British Society of Gastroenterology (BSG) recommends endoscopic screening in patients with multiple risk factors for gastric cancer (male, smoker, pernicious anaemia, family history in first degree relative), citing low-grade evidence[7,8]. Unsurprisingly, low disease prevalence combined with variable guidelines leads to...
White light endoscopy: White light endoscopy (WLE) is the conventional endoscopic imaging modality. It is sufficient for detecting some features of carcinomatous transformation of gastric lesions, including red discolouration of the mucosal surface, depressed-type lesions and mucosal ulceration[30,31]. However, the sensitivity for WLE in detecting GIM, LGD/HGD and EGC has been reported to be as low as 29%-59.1%, 51%-74% and 48%-72% respectively[32-36]. As a result, more advanced endoscopic imaging techniques are now used for lesion detection and characterisation.
**Chromoendoscopy:** Traditional chromoendoscopy requires the topical application of stains or dyes (usually methylene blue, indigo carmine and/or acetic acid) in an effort to enhance tissue characterisation[37,38]. Studies have demonstrated the superiority of chromoendoscopy in the detection of EGCs and precancerous gastric lesions, with a 2016 meta-analysis demonstrating pooled sensitivity of 90% and specificity of 82% [38]. However, the requirement for local dye application has limited its use in the context of the wide field required for gastric lesion detection, particularly following the development of virtual chromoendoscopy.

**Narrow-band imaging:** Narrow-band imaging (NBI) is the most commonly used form of virtual chromoendoscopy; utilising a rotating optical interference filter to restrict incident light into two narrow bands of different wavelengths (Figure 1). This enhances the definition of the surface mucosa, while emphasising the contrast of the vascular network[39]. NBI is superior to WLE in detection of early precancerous gastric lesions, with pooled sensitivity of 69% and specificity of 91% for GIM[40]. Prospective trials have demonstrated a 40% increase in detection of all focal gastric lesions and more than twice the detection rates for GIM using NBI compared to WLE [32,41].

**High-magnification NBI:** High-magnification endoscopy (Figure 2) uses a movable lens in the tip of the endoscope to allow up to 150 times optical zoom without any degradation of image quality[42]. This is usually combined with the use of a translucent cap to stabilise the focal length between the lens and the target tissue, as well as near-focus imaging that allows the endoscope to be positioned closer to the mucosal surface[42]. High-magnification endoscopy has been combined with NBI (ME-NBI) to facilitate detailed assessment of the mucosa and enhance lesion detection and characterisation.

Uedo et al[42] first described the ‘light blue crest’ seen on ME-NBI (Figure 2) which has been demonstrated to detect GIM with a sensitivity of 80%-89% and a specificity of 93%-96%[36,43,44]. In regard to characterisation of dysplasia, a prospective multicentre study in 2016 showed an improvement in sensitivity from 74% to 92% with the use of ME-NBI over WLE[36]. Detailed assessment of surface microvascular patterns on polypoid lesions using ME-NBI results in sensitivity of up to 86.2% and specificity of up to 97% for the presence of dysplasia[45].

In the assessment of EGCs, there have been a number of classification systems using ME-NBI. Yao et al[45] first described the ‘VS’ system in 2008, which has a sensitivity of 86%-97% for EGCs[46-49]. This system requires detailed assessment of the microvascular and surface mucosal pattern to ascertain features of irregularity, which in the presence of a demarcation line is suggestive of carcinoma[46]. The VS classification was further simplified by Yamada et al[49] in 2014, who demonstrated that the presence of a demarcation line with an irregular microvascular pattern was 95% sensitive and 96% specific for EGC[49].

The accuracy of ME-NBE was confirmed in a 2015 meta-analysis of a combined 2171 patients, demonstrating 86% sensitivity and 96% specificity for the diagnosis of EGC [50,51]. Direct comparator studies of ME-NBI vs WLE have also shown up to twice the rate of EGC detection with ME-NBI[52-54].

In addition, ME-NBI is valuable in determining tumour margins at the time of ER, resulting in 97.4%-98.1% accuracy of endoscopic markings[55-57]. Comparator studies have demonstrated the superior precision of ME-NBI vs chromoendoscopy in this context, with 17%-20% higher rates of accurate endoscopic markings[55,57]. The use of ME-NBI is also beneficial when lesion margins are unclear on chromoendoscopy, as demonstrated by Nagahama et al[57] who found that 72.6% of lesions with an unclear margin on chromoendoscopy were able to be clearly delineated using ME-NBI[57].

**Blue laser imaging:** Blue laser imaging (BLI) uses laser to create a highly narrowed blue band, enhancing vascular structures without using a filter as is required for NBI, thereby resulting in a higher light intensity[58,59]. There is a paucity of evidence regarding BLI in comparison to other endoscopic imaging, however recent studies have demonstrated superior sensitivity (93%-94%) in detection of EGCs compared to WLE (46%-50%)[60,61]. While direct comparator studies are limited, Kaneko et al[61] compared BLI and NBI in 39 patients with gastrointestinal neoplasia and found that BLI maintained sufficient brightness and contrast up to 40 mm while NBI deteriorated beyond 20 mm. This could be of relevance in detection of EGCs where endoscopists may benefit from increased field of view, however further studies in this area are required.
Figure 1 White light endoscopy compared to narrow-band imaging in gastric lesions, demonstrating clear demarcation lines and irregular microvascular/microsurface patterns on narrow-band imaging. A: Early gastric cancer at the incisura seen on white light endoscopy (WLE); B: The same lesion seen on narrow-band imaging (NBI) (blue arrows); C: Early gastric cancer in the antrum seen on WLE; D: The same lesion seen on NBI (blue arrows).

Figure 2 Narrow-band imaging demonstrating the ‘light blue crest’ (orange arrows) consistent with intestinal metaplasia.

Confocal laser endomicroscopy: Confocal laser endomicroscopy (CLE) uses a low-power laser to illuminate tissue, detecting reflected fluorescent light and allowing high-resolution endoscopic histological assessment\cite{62,63}. CLE was first assessed in precancerous gastric lesions by Guo et al\cite{63} who reported sensitivity and specificity of 98% and 95% for the detection of GIM\cite{63}. A more recent meta-analysis demonstrated the accuracy of CLE for the diagnosis of all stages of precancerous gastric lesions and
EGCs, with pooled sensitivity of 92% for GIM, 81% for LGD/HGD and 91% for EGC [64,65]. However, its use is limited by the equipment required (either a dedicated endoscopic system or a probe-based system inserted via the therapeutic channel), the time required for image acquisition, as well as the learning curve of image interpretation[63].

Future prospects
Artificial intelligence (AI) has demonstrated efficacy in detection and classification of multiple gastrointestinal lesions[66]. Real-time AI gastric lesion detection has not yet been studied, however convolutional neural networks have been generated from endoscopic images with a sensitivity of 92% using WLE and 97% using ME-NBI[67-69]. This could be of particular benefit for improving lesion detection and characterisation for endoscopists without expertise in advanced imaging interpretation.

Texture and colour enhancement imaging (TXI) is a recently developed technology aiming to improve lesion detection by enhancing texture, brightness and colour tone (Figure 3) using stacked images, while maintaining a similar colour spectrum to WLE [70]. By improving lesion detection within WLE, TXI may facilitate superior detection rates during endoscopic screening, although studies are required to investigate this.

Whilst WLE remains the mainstay for the majority of endoscopists, accumulating evidence as presented above points to a significant additive benefit in repeat interrogation of suspicious areas with chromoendoscopy. The trade-off between time, cost, availability and feasibility means that most proceduralists employ virtual chroendoendoscopy with ME-NBI.

Assessment of invasion depth and nodal metastases
Endoscopic ultrasound: While computed tomography (CT) and positron emission tomography/CT are endorsed by guidelines for the assessment of distant metastases and locally advanced gastric cancers, endoscopic ultrasound (EUS) has been recommended for EGCs, in particular for distinction of T1 and T2 lesions[71]. However, data on the utility of EUS in assessment of EGC depth of invasion have been varied. Han et al[72] reported under-staging in 16.7% of T2 gastric cancers with EUS, and Choi et al[71] reported no advantage of EUS over conventional endoscopic assessment using surface nodularity and fold convergence[71]. In comparison, Mouri et al[73] reported that lesions classified by EUS as being intramucosal or submucosal border lesions were histologically either intramucosal or invading < 500 μm into the submucosal space (SM1) in 99% and 87% of cases[73]. A 2015 Cochrane review also demonstrated 87% sensitivity for submucosal invasion[74,75]. Regarding specific EUS characteristics, Kim et al[76] reported that an arch-shaped submucosal deformity on EUS was associated with a negative predictive value for SM2 (> 500 μm submucosal invasion) or greater of 94.4%, with a sensitivity and specificity of 84% and 83%[76]. More recently, EUS miniature probes have been demonstrated to have higher resolution but less penetration compared to conventional EUS[77]. Miniature probes have demonstrated superiority for assessment of submucosal invasion, with an overall accuracy of 84.5% vs 61.6% using conventional EUS when assessing lesions less than 2 cm in diameter without endoscopic features of submucosal invasion[78]. While the role of conventional EUS in the confirmation of suitability for ER remains unclear, miniature probe EUS may have a role in < 2 cm lesions which are indeterminate endoscopically.

Concurrent to these improvements in EUS, the addition of technologies such as CT with multiplanar reformations and virtual gastroscopy has led to overall accuracy as high as 94% for the diagnosis of EGC[79]. In addition, high-speed magnetic resonance imaging (MRI) and diffusion-weighted imaging have also addressed many of the limitations of MRI for the assessment of T-stage, though this remains infrequently used in the assessment of EGCs[80,81]. While a detailed comparison of radiological methods for staging gastric cancers is beyond the scope of this review, improvements in these technologies may facilitate accurate non-invasive assessment of EGCs in the future.

With respect to exclusion of nodal disease prior to ER for EGC, the use of EUS has again been associated with variable accuracy. In a 2008 meta-analysis, the pooled sensitivity of EUS for N1 disease was as low as 58.2%[82]. More recent data have shown an improved sensitivity and specificity of 74%-83% and 67%-70% in detecting nodal positivity[75,83,84]. However, this improved accuracy still remains inadequate to guide consideration of endoscopic management of disease with metastatic potential. Despite technological advances, CT also remains inaccurate for the detection of nodal metastases, with sensitivity between 62.5%-91.9%[85]. Accordingly, gastric cancers
with a significant potential for lymph node metastasis based on lesion characteristics are generally managed surgically with lymphadenectomy to evaluate for lymphatic involvement, as reliable non-invasive exclusion of lymph node metastases (LNM) remains elusive.

ENDOSCOPIC TREATMENT OF GASTRIC NEOPLASIA

ER is indicated for all discrete gastric lesions with histological evidence of dysplasia given the risk of concurrent or future EGC. In addition, data supports ER for lesions histologically indefinite for dysplasia, as the rate of true dysplasia or EGC in resected specimens is as high as 90.8%, particularly in males; lesions > 5 mm in diameter; or lesions with erosions[86]. For gastric mucosal lesions < 1 cm in diameter with LGD, either endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) can be performed, however ESD is preferred in larger lesions and those demonstrating HGD/EGC[87].

Indications for ESD

In the context of histologically confirmed carcinoma, ESD was initially indicated only for the resection of macroscopically intramucosal (T1a) differentiated gastric carcinomas < 2 cm in diameter without ulcer or scar[87]. These have subsequently been labelled ‘absolute criteria’, as data now support the efficacy of ESD for the resection of a broader range of EGCs termed ‘expanded criteria’. In the 2015 JGES guidelines, expanded criteria lesions include all differentiated T1a EGCs > 2 cm without ulcer/scar, differentiated T1a lesions < 3 cm with ulcer/scar, and undifferentiated EGCs < 2 cm in diameter, while the 2015 European Society of Gastrointestinal Endoscopy (ESGE) guidelines also include differentiated lesions < 3 cm with superficial submucosal invasion (SM1 ≤ 500 μm)[87,88].
Another evolving potential indication for ESD is for the resection of submucosal gastric tumours. He et al[88] first demonstrated the efficacy and safety of ESD for gastrointestinal stromal tumours (GIST) in 2013, when they reported successful ESD in 25 large gastric GISTs with a mean diameter of 2.7 cm[88]. More recently, An et al[89] published data on 168 cases of ESD for gastric GISTs, with complete and en bloc resection in 100% of lesions[89]. Delayed bleeding occurred in only 1.2% and there were no other significant complications. While additional data are required before recommending ESD as a standard of care option for GIST management, early data support this as a potential future indication.

**Efficacy of ESD**

Data on the efficacy of ESD (Table 1) are particularly robust in East Asian countries where the incidence of gastric cancer is significantly higher than it is in Western countries. Studies in Japan and South Korea have demonstrated en bloc resection in 95.3%-99.2%, complete resection in 87.7%-95.5% and curative resection in 81.7%-84.1% [90-94]. In Western countries however, data are more limited and results are variable. En bloc resection rates are between 92%-97.8%, with complete resection in 75.6%-89% and curative resection in 72.2%-79.2%[95-100].

One contributing factor to this discrepancy is the differing incidence of gastric cancer, resulting in comparatively limited experience in Western centres. This was supported by a 2020 Italian survey where only 41% of included interventionists had performed more than 80 ESDs and 31% had performed < 40[98]. This study also demonstrated that rates of en bloc resection were higher and rates of perforation lower in more experienced proceduralists. However, there are multiple other contributing factors. Firstly, there are differences in lesion classification, as the Japanese classification of gastric carcinoma includes EGCs which would by European guidelines be classified as HGD[101]. The non-aggressive and non-invasive nature of HGD would result in bias in favour of Japanese outcomes. Further to this, there appear to be differences in disease behaviour in East Asian compared to Western populations. Studies in Korea reviewing rates of LNM in surgical specimens at gastrectomy have reported LNM in 0.3% of absolute criteria lesions and 0.4% in expanded criteria, while marginally higher at 3.2% in undifferentiated carcinomas[102-104]. In contrast, American studies report LNM in 7.5%-13.6% of expanded criteria lesions at gastrectomy[105,106]. Guidelines developed based on data from East Asian populations should therefore be used with caution in Western populations until further evidence is able to clarify this.

**EMR vs ESD:** ESD is associated with longer procedure times and an almost three times higher perforation rate compared to EMR, however multiple meta-analyses have established the superiority of ESD over EMR in regard to en bloc resection rates (OR 9-10 for ESD), complete resection rates (OR 5.7-8.4) and curative resection rates (OR 2.9 [38,107,108]). Tao et al[107] also reported a reduction in local recurrence (OR 0.18), likely resulting from the aforementioned superior rates of en bloc, complete and curative resection[107].

**ESD vs surgery:** Increasing evidence suggests that ESD is associated with equivalent overall survival compared to gastrectomy, while reducing procedural complications. A 2015 retrospective Chinese study used propensity score matching to compare outcomes for surgery and ESD in 176 patients with a median follow up of 77 mo[109]. There was no significant difference in overall survival, and while local recurrence occurred in 1.7% of ESD, all but one of the recurrent lesions were treated endoscopically. There was no difference in early complication rates, but late complications were significantly more common in the surgical group (6.8% vs 0%). A similar 2017 Korean study found no difference in 5-year survival between groups, with a complication rate of 15% in gastrectomy vs 5.1% in ESD[110]. In regard to expanded criteria lesions, data have also reported equivalent survival with a reduction in complications using ESD, with a 2017 study actually demonstrating improved 5-year survival after propensity score matching in the ESD group (97.1% vs 89.8%)[109,111,112]. Unsurprisingly, a recent meta-analysis reported higher rates of locoregional recurrence and metachronous cancer in the ESD group, resulting in lower disease-free survival (HR 4.58)[113]. However, the majority of recurrence is able to be treated with repeat ESD and thus lower disease-free survival is not reflected in any difference in disease-specific survival [109,113]. Further to this, the same meta-analysis reported a mean 128 min shorter operation time, 7 d shorter hospital stay, lower procedure-related death and fewer complications[113].
In regard to complications of surgical management, gastrectomy is associated with significant post-operative complication rates of 9.6%-18.1% for laparoscopic and 17.4%-29.3% for open gastrectomy, as well as a 30-d mortality rate of 2%-4.1%[3,114-116]. In addition, Yu et al[116] assessed quality of life scores after gastrectomy and found that fatigue, diarrhoea, reflux, dysphagia and eating restriction scores all remained persistently worse at 5-year follow-up after surgery[116].

A 2015 study demonstrated the lower overall medical costs of ESD compared to surgery for EGC, with ESD costing a median $2374 USD compared to $4954 USD for surgery (P < 0.001)[117,118]. This was confirmed by Shin et al[109] who reported approximate total hospital stay costs averaging $1871 USD for ESD vs $5925 USD for subtotal gastrectomy and $6476 for total gastrectomy[109].

Long-term outcomes: Long-term data on ESD for EGCs has been extensively reported in Japan and South Korea, where studies including up to 5-9 years of follow-up have documented local recurrence rates of 0%-1.8% in absolute criteria lesions and 0.6%-7.0% in expanded criteria lesions[119-123]. In these same cohorts there were no cases of LNM in absolute criteria lesions, and LNM rates were between 0%-0.48% in expanded criteria lesions. Min et al[123] reported long-term outcomes (48 mo follow-up) for only lesions meeting criteria for curative resection, in whom 0.3% of absolute and no expanded criteria lesions had local recurrence[123]. In a study by Suzuki et al[124] in 2015 (again reporting only on curative resections), despite overall 5-year overall survival being as low as 92.2% due to other comorbidities, the 5-year disease-specific survival was 99.9% in both absolute and expanded criteria lesions[124]. In Western populations, long-term data are limited, but studies have reported local recurrence rates of 4.8%-7% for expanded criteria lesions[125-127].

ESD in ‘outside of criteria’ lesions: ESD is often also employed for the treatment of lesions outside of even the expanded criteria when patients are unsuitable for major surgery. Abe et al[127] followed 14 patients who had ESD for undifferentiated non-curatively resected lesions who were not suitable for or had declined further surgery[127]. Over a median of 76.4 mo follow-up, there was only one case of local recurrence which was managed with repeat ESD. A 2013 Japanese study reviewed 104 patients who undergone ESD despite being outside of criteria in regard to lesion characteristics, who had declined or been deemed unsuitable for surgical management[128,129]. Patients were followed-up for a median of 47 mo after resection, with 5-year overall survival of 70% but disease-specific survival of 91.5%. In patients with comorbidities precluding them from major surgery, ESD may therefore be beneficial even in lesions outside of the expanded criteria.

Approach to incomplete and non-curative resection
Incomplete resection: The limited available evidence supports repeat ESD where possible for lesions with positive horizontal margins after initial resection. Jung et al[129] reported 28 patients with a positive horizontal margin after initial ESD, in whom the curative resection rate of repeat ESD was 89.3%[129]. In a 2018 study, Jeon et al[130] also reported improved disease-free survival following repeat ESD for non-completed resections.
curative resections due to positive lateral margins (89.2% vs 69.1%) [130].

**Non-curative resection**: The management of lesions determined to be beyond the expanded criteria histologically after ER (non-curative resection) remains controversial. A large 2019 meta-analysis demonstrated improved 5-year overall and disease-specific survival (OR 3.5 and 3.99 respectively) following additional surgery after non-curative resection [131,132]. However, these data are retrospective and are therefore susceptible to bias associated with the selection of less systemically unwell and comorbid patients in the additional surgery group. Other studies have reported rates of LNM or residual tumour as low as 5.1%, with differences in overall survival but no difference in disease-specific survival between those treated with additional gastrectomy and those managed with surveillance [133,134]. These studies have hypothesised that further data may delineate a group in whom surveillance after non-curative resection is associated with equivalent long-term outcomes.

Multiple studies have addressed factors to stratify the risk of LNM or residual tumour in patients who have had non-curative ESD. In regard to LNM, lymphovascular invasion (LVI) and depth of submucosal invasion histologically are reported to be the most consistent predictors [135,136]. Goto *et al* [134] reported that the presence of depth of invasion > SM1 or LVI was 100% sensitive and 86% specific for the presence of LNM [135]. For predicting the presence of residual tumour, a 2020 meta-analysis reported significant risk factors to be tumour size > 30 mm and the presence of positive horizontal margins [137]. Although additional data are required to guide decision making, patients who have non-curative resections may not warrant additional surgery provided the invasion depth is ≤ SM1 without evidence of LVI, while patients with tumour size > 30 mm or positive horizontal margin may be appropriate for repeat ESD.

This concept led to a 2017 study by Hatta *et al* [137], who developed the eCura scoring system for predicting the risk of LNM using data from 1101 patients who underwent radical surgery after non-curative ESD [137]. The presence of a positive vertical margin, submucosal invasion > SM1, tumour size > 30 mm and vascular invasion were each assigned 1 point, while lymphatic invasion was assigned 3 points. Patients scoring 0-1 points were classified as low-risk (2.5% risk of LNM), 2-4 points intermediate-risk (6.7% risk of LNM) and 5-7 points high-risk (22.7% risk of LNM). The scoring system was then validated on 905 patients with non-curative ESD who declined surgery. 5-year cancer-specific survival was 99.6% in the low-risk group (60.4% of patients), 96% in the intermediate risk group (27.6% of patients) and 90% in the high-risk group (11.9% of patients), suggesting that ESD without additional surgical management may be sufficient in low-risk patients according to the eCura system [138].

These risk stratification tools are of particular importance when considering patients with radiologically enlarged lymph nodes that may or may not signify the presence of LNM. Lee *et al* [138] reported that the presence of a positive lymph node on CT imaging is associated with a 20% risk of LNM or residual tumour in patients who have had non-curative ESD. Despite 4 lesions having histological LVI, there were no cases of LNM. Lee *et al* [138] described 9 patients who had endoscopic full thickness resection (FTR) with laparoscopic regional lymph node resection [139]. Despite 4 lesions having histological LVI, there were no cases of LNM. There may also be a future role for targeted lymph node resection using sentinel node detection strategies. While data have been inconsistent regarding the accuracy of gastric sentinel node detection, these strategies have been most successful in T1 EGs and thus may be of use following higher-risk ESD [140,141]. Studies using dye have reported a sensitivity of only 75%, however in the context of dual tracer with radiolabelled tin colloid and blue dye, the sensitivity for LNM is up to 93%, with an overall accuracy of 99% [142]. Further studies are therefore required to assess the adequacy of sentinel node guided laparoscopic lymph node resection as a treatment strategy after non-curative ESD.

**Complications of ESD**

While ESD offers the promise of reduced morbidity, both acute (bleeding, perforation)
and chronic (stenosis, recurrence, metachronous lesions) complications can occur[107, 108,113].

**Bleeding**: The risk of delayed bleeding with ESD is equivalent to that in EMR, with most studies reporting rates between 4% and 6%.[143-146]. Nam et al[145] retrospectively reviewed 1,864 cases of ESD, in which post-procedural bleeding occurred in 4.1% of patients, with the majority occurring within 24 h of ESD[145]. In their multivariate analysis, predictors of delayed bleeding were patient age ≤ 65 years, resection size > 30 mm, procedure time > 20 min, lesions located in the lower third of the stomach and the presence of erosions. In regard to treatment, delayed bleeding after ESD is generally amenable to routine endoscopic management[146].

Studies have addressed prevention strategies for post-ESD bleeding, with data supporting post-operative proton-pump inhibitor (PPI) use after ESD with an OR of 0.4-0.49 for delayed bleeding[147,148]. A 2016 meta-analysis on the use of PPI prior to ESD found a reduction in gastric pH at the time of procedure, but no pooled difference in delayed bleeding[149]. Previously, routine re-look endoscopies were performed in many centres after ESD in an attempt to prevent rebleeding; a method extrapolated from data supporting second endoscopy after treatment of bleeding peptic ulcers [150]. However, Goto et al[144] reported no difference in rates of bleeding before or after routine follow-up endoscopy within one week of initial ESD, suggesting limited benefit from this strategy[144].

**Perforation**: Perforation occurs more frequently in ESD than in EMR[107,108]. Rates of perforation are generally reported between 1.5% and 9.6%, with a large meta-analysis by Arezzo et al[150] demonstrating a pooled perforation rate of 4.9%[95,100,151-156]. Risk factors for perforation include lesions located in the upper third of the stomach, the presence of submucosal invasion or fibrosis and longer procedure times[152,153, 157]. Longer procedure times may reflect either more complicated resections or less proceduralist experience, while perforations in upper third gastric lesions likely reflect thinner proximal gastric wall in comparison to the antrum[158].

When macroscopic perforations occur during ESD, more than 97% of cases are able to be treated endoscopically with clip closure[155,156]. Micro-perforations, or suspected perforations that are not endoscopically visible, are usually able to be conservatively managed with fasting and intravenous antibiotics[155].

Delayed perforation, when no intraprocedural perforation occurs but symptoms of peritonism and radiological evidence of perforation develop post-procedure, is a phenomenon that appears to be specific to ESD. It is most common in the thin upper third of the stomach and the majority of cases occur within 24 h[159,160]. Yamamoto et al[158] reported 5 cases of delayed perforation in a 2017 case series, of which 4 out of 5 were able to be managed endoscopically[158].

**Stenosis**: Post-ESD stenosis occurs most commonly following resection of gastric antral (occurring in up to 7% of cases) or cardiac lesions, presenting with either oesophageal or gastric outlet obstruction[161,162]. Sumiyoshi et al[160] analysed predisposing factors, with the only risk factor after multivariate analysis being a > 75% circumferential post-resection defect[160]. In regard to treatment, while data is limited, most patients have improvement in their symptoms following either balloon dilation if severe, or conservative management if mild-moderate symptoms[162,163].

**Local recurrence and metachronous gastric lesions**: Guidelines recommend close ongoing surveillance after ESD for EGC, with ESGE and JGES guidelines suggesting 3-to 6-monthly and 6- to 12-monthly surveillance endoscopy respectively[87,88]. The aim of surveillance after ESD is for early detection of not only local recurrence but also metachronous precancerous gastric lesions. These lesions occur in up to 6.9%-13% of patients after ESD, with a 2019 study reporting a cumulative incidence of metachronous gastric cancer of 33.2 cases per 1000 patient-years[155,164,165]. In regard to treatment of metachronous lesions, Kim et al[165] reported 117 cases of metachronous gastric neoplasms, of which 77% were able to be retreated with curative ESD[165].

**FUTURE DIRECTIONS FOR THE ENDOSCOPIC TREATMENT OF GASTRIC NEOPLASIA**

**Methods for generating counter-traction**

Generating counter-traction during ESD is of benefit in reducing procedural time and
complications\cite{166,167}. Depending on the position of the lesion being resected, gravity may not provide sufficient access to submucosal tissue planes. There have been a number of recent developments with regard to endoscopic equipment and techniques to generate counter-traction.

**Magnetic anchor guided ESD:** Magnetic anchor guided ESD uses a large external electromagnet combined with an internal magnet attached to the lesion \textit{via} a clip (Figure 4). No comparative studies have assessed the advantages of this technique over conventional ESD, however studies have shown feasibility as well as subjective benefit from the point of view of endoscopists\cite{168,169}. The main limitations of this technique are the equipment required and the coupling strength of the magnets relative to the abdominal wall thickness\cite{170}.

**Dual channel endoscope:** This technique requires a dedicated dual working channel endoscope, often employed for the ‘grasp-and-snare’ technique in EMR\cite{171}. Hua \textit{et al} \cite{171} compared conventional ESD (24 patients) with dual channel ESD (22 patients), using one channel for dissection while grasping the lesion \textit{via} the second channel\cite{171}. Mean procedure times were significantly shorter with dual channel ESD (20.5 min \textit{vs} 49.1 min) with no other differences in outcomes or complications. There are two main limitations of dual channel endoscopy: The requirement for a dedicated endoscope and the limited distance between working channels inhibiting angulation of traction.

**Additional working channel:** The use of an attachable additional working channel (Figure 5) aims to overcome some of these limitations of dual channel endoscopy by providing greater distance between working channels as well as allowing the use of a conventional therapeutic endoscope. The additional working channel consists of a flexible attachment, a long shaft and an adaptor for fixation at the endoscope handle \cite{172,173}. This technique has been compared with conventional ESD in porcine stomachs, where it resulted in a reduction in procedure time (24.5 min \textit{vs} 32.5 min) and lower rates of muscularis damage (3.13\% \textit{vs} 18.75\%)\cite{173}. However, minimal data exist in humans apart from feasibility studies reporting successful resection of 8 lesions by ESD and 6 lesions by EMR\cite{174,175}. The main limitation of this method is the inability to generate significant angulation on the grasping forceps, preventing the most effective direction of counter-traction.

**Double endoscopes:** Using two separate endoscopes allows maximal angulation for the grasping forceps, optimising counter-traction. Generally, the first endoscope is inserted and a circumferential incision is made. Following this, a second smaller calibre endoscope is inserted to grasp and lift the edge of the lesion while the procedure proceeds with dissection. In 2017, Ogata \textit{et al} \cite{175} demonstrated the efficacy of this method in 122 patients, with a 97.5\% en bloc resection rate and 86.9\% curative resection rate, with perforation and delayed bleeding in 3.3\% and 2.5\% respectively \cite{175}. While there are no direct comparator trials with conventional ESD, Çolak \textit{et al} \cite{176} employed this method in 6 patients where positioning made conventional ESD difficult\cite{176}. They reported no difference in resection times compared to more straightforward ESDs. There are a number of obvious limitations to this method, including the requirement for two endoscopists, endoscopes and light sources, as well as space limitations in both the oral cavity and within the lumen where one endoscope can obstruct the view of the other\cite{176}. Other groups have reported various methods to overcome some of these limitations. Higuchi \textit{et al} \cite{177} reported double endoscope ESD using a single light source, where the light source from the first endoscope is removed and attached to the second endoscope for insertion until the lesion is grasped \cite{177}. Following this, the light source is reattached to the initial main endoscope. This technique resulted in improved accuracy of dissection compared to historical controls, without any serious intra-procedural complications. Alternatively, Ahn \textit{et al} \cite{178} employed a trans-nasal endoscope for applying traction, maximising space within the oral cavity and within the gastrointestinal tract due to the smaller calibre endoscope \cite{178}.

**Endo-lifter:** The ‘endo-lifter’ (Figure 6) consists of a transparent hood with grasping forceps, mounted on the tip of an endoscope, with the forceps running externally to the endoscope to allow dissection \textit{via} the working channel\cite{179}. The attachment of the forceps to the hood produces an arc that aims to provide superior angulation for countertraction. Minimal data exist using the endo-lifter in animal models, with variable results. Schölvinc \textit{et al} \cite{180} reported shortened procedure times when used by ESD-experienced but not inexperienced endoscopists\cite{180}. Teo \textit{et al} \cite{179} reported increased visualisation of the submucosa and a reduction in subjective procedural
difficulty rating from endoscopists[179].

Spring and loop clip traction (using an S-O clip): This method uses the S-O clip (Figure 7) which is attached to a spring and then a loop of nylon[181,182]. One clip is attached to the edge of the lesion, while the other clip is attached to an area of opposing gastric wall to provide traction. Nagata[181] reported data from 140 patients of which 51 had spring and loop clip traction, with shorter procedure times and no difference in complication rates compared to conventional ESD[181]. The main limitations of this technique are the requirement for specific equipment (i.e., the S-O clip) as well as only allowing one direction of traction once the clips are deployed.

Other clip methods: Various methods have been described employing readily available endoscopic equipment with clips to minimise cost. Yoshida et al.[182] reported the efficacy of the ‘dental floss clip’ (DFC) traction device using dental floss tied to the proximal end of a clip before attaching the clip to the edge of the lesion, with the dental floss running externally to the endoscope[182]. There was no difference in procedure time overall, however in upper and middle greater curvature lesions DFC traction reduced procedure time by approximately 50%. In addition, the
Figure 6 ‘Endo-lifter’ (Olympus-Tokyo, Japan)[192]. Citation: Harlow C, Sivananthan A, Ayaru L, Patel K, Darzi A, Patel N. Endoscopic submucosal dissection: an update on tools and accessories. Ther Adv Gastrointest Endosc 2020; 13: 2631774520957220. ©The Author(s) 2020. Published by Open Access Article.

Figure 7 Spring and loop clip traction[193]. Citation: Nagata M, Fujikawa T, Munakata H. Comparing a conventional and a spring-and-loop with clip traction method of endoscopic submucosal dissection for superficial gastric neoplasms: a randomized controlled trial (with videos). Gastrointest Endosc 2021; 93: 1097-1109. ©The Author(s) 2021. Published by Open Access Article.

use of DFC traction reduced perforation rates compared to conventional ESD (0.3% vs 2.2%)[183]. Noda et al[183] added a polypectomy snare sheath external to the endoscope through which the thread (dental floss) was passed, which was then inserted along with the endoscope. The use of the sheath allows the thread to be moved without interference from the endoscope, as well as allowing both ‘pull’ and ‘push’ motions by advancing the entire sheath. In an 88 patient study comparing polypectomy snare sheath ESD with conventional ESD, this technique resulted in a reduction in procedure time and lower rates of significant bleeding[183]. Yoshida et al[184] also reported a reduction in procedure time by simplifying this technique to their ‘clip and snare’ technique: A snare with its sheath external to the endoscope is attached to the proximal end of a clip, then inserted and attached to the lesion[184]. Zhang et al[185] then modified the clip and snare technique (Figure 8), by using additional clips to attach the snare to the circumference of the lesion, allowing multifocal lifting of the lesion, as well as placing clips attached to the snare on opposing gastric wall mucosa to alter the direction of traction[185].

**Endoscopic full-thickness resection**

FTR can either be performed free-hand, attempting to maintain the serosa although often resulting in macroscopic perforation, or device assisted (Figure 9) using an ‘over-the-scope’ clip[186,187]. While some data exist regarding the use of FTR for gastric GIST where successful resection rates are as high as 96.8%, there is no evidence
regarding the use of FTR in EGCs[188]. Theoretical roles for gastric FTR could include treatment of recurrent lesions within EMR/ESD scar limiting repeat resection, or using FTR in combination with laparoscopic nodal resection in non-candidates for gastrectomy with lesions outside of expanded criteria for ESD. Chae et al[188] reported a successful case of FTR for an EGC with a positive horizontal margin after initial ESD which had resulted in severe fibrosis[188]. Cho et al[138] reported a series of 9 patients treated with FTR and laparoscopic lymph node resection who had lesions outside of expanded criteria, in whom lymph nodes were positive in only 1 case[138].
**Robot-assisted ESD**

The ‘Master And Slave Transluminal Endoscopic Robot’ (MASTER) was developed in an attempt to mitigate the technical difficulties commonly encountered in interventional endoscopy\[189-191\]. Initial feasibility studies were performed in 2010 in ex-vivo and in-vivo porcine stomachs, where 20 gastric lesions were successfully resected using MASTER assisted ESD with no difference in procedure time compared to conventional ESD\[190\]. Subsequently, a small case series was reported in 2012, using MASTER assisted ESD in 5 patients, demonstrating clear resection margins in all cases with no major complications\[192\]. More studies are required to further explore the role of robot-assisted ESD, however this technique will clearly be limited by the cost and availability of equipment, while proceduralists already successfully perform more conventional ESD techniques at a fraction of the cost.

**CONCLUSION**

Advances in endoscopic imaging and therapeutics have enhanced the detection, characterisation and treatment of precancerous gastric lesions and EGC, allowing for pre-emptive minimally invasive intervention at an early stage. Endoscopic treatment of precancerous lesions and EGCs not only reduces rates of advanced carcinoma, but also avoids the requirement for high-risk surgical interventions with associated short- and long-term complications. The significant disparity in gastric cancer outcomes between East Asian and Western regions reflects extensive endoscopist experience, and long-term complications. The significant disparity in gastric cancer outcomes also avoids the requirement for high-risk surgical interventions with associated short-term complications and in-vivo porcine stomachs, where 20 gastric lesions were successfully resected using MASTER assisted ESD with no difference in procedure time compared to conventional ESD\[190\]. Subsequently, a small case series was reported in 2012, using MASTER assisted ESD in 5 patients, demonstrating clear resection margins in all cases with no major complications\[192\]. More studies are required to further explore the role of robot-assisted ESD, however this technique will clearly be limited by the cost and availability of equipment, while proceduralists already successfully perform more conventional ESD techniques at a fraction of the cost.

**REFERENCES**

1. International Agency for Research on Cancer. Globocan 2020 - Stomach Cancer. [cited 9 February 2021]. Available from: https://geo.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.pdf
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394-424 [PMID: 30207593 DOI: 10.3322/caac.21492]
3. Papenfuss WA, Kukar M, Ozenberg I, Attwood K, Nurkin S, Malhotra U, Wilkinson NW. Morbidity and mortality associated with gastrectomy for gastric cancer. Ann Surg Oncol 2014; 21: 3008-3014 [PMID: 24700300 DOI: 10.1245/s10434-014-3664-z]
4. Huang HL, Leung CY, Saito E, Katanoda K, Hur C, Kong CY, Nomura S, Shibuya K. Effect and cost-effectiveness of national gastric cancer screening in Japan: a microsimulation modeling study. BMC Med 2020; 18: 257 [PMID: 32921305 DOI: 10.1186/s12916-020-01729-0]
5. Suh YS, Lee J, Woo H, Shin D, Kong SH, Lee HJ, Shin A, Yang HK. National cancer screening program for gastric cancer in Korea: Nationwide treatment benefit and cost. Cancer 2020; 126: 1929-1939 [PMID: 32031687 DOI: 10.1002/cncr.32753]
6. GBD 2017 Stomach Cancer Collaborators. The global, regional, and national burden of stomach cancer in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease study 2017. Lancet Gastroenterol Hepatol 2020; 5: 42-54 [PMID: 31648970 DOI: 10.1016/S2542-5196(19)30328-0]
7. Gupta S, Li D, El Serag HB, Davitkov P, Altayar O, Sultan S, Falck-Ytter Y, Mustafa RA. AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia. Gastroenterology 2020; 158: 693-702 [PMID: 31816298 DOI: 10.1053/j.gastro.2019.12.003]
8. Banks M, Graham D, Jansen M, Gotoda T, Coda S, di Pietro M, Uedo N, Bhandari P, Pritchard DM, Kuipers EJ, Rodriguez-Justo M, Novelli MR, Ragnauth K, Shepherd N, Dinis-Ribeiro M. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. Gut 2019; 68: 1545-1575 [PMID: 31278206 DOI: 10.1136/gutjnl-2018-318126]
9. Vance RB Jr, Kubiliun N, Dunbar KB. How Do We Manage Gastric Intestinal Metaplasia? Dig Dis Sci 2016; 61: 1870-1878 [PMID: 26984230 DOI: 10.1007/s10620-016-4104-1]
10. Maskarinec G, Noh JJ. The effect of migration on cancer incidence among Japanese in Hawaii. Ethn Dis 2004; 14: 431-439 [PMID: 15328946]
11. Kim GH, Liang PS, Bang SJ, Hwang JH. Screening and surveillance for gastric cancer in the United States: Is it needed? Gastrointest Endosc 2016; 84: 18-28 [PMID: 26940296 DOI: 10.1016/j.gi.2015.11.002]
Pimentel-Nunes P, Shue D, Pepper M, Cho D, Laine L. Narrow-band imaging versus white light
endoscopy. World J Gastroenterol 2016; 22: 1311-1320 [PMID: 26811168 DOI: 10.3748/wjg.v22.i3.1311]

Chen HN, Wang Z, Li X, Zhou ZG. Helicobacter pylori eradication cannot reduce the risk of gastric
cancer in patients with intestinal metaplasia and dysplasia: evidence from a meta-analysis. Gastric
Cancer 2016; 19: 166-175 [PMID: 25609452 DOI: 10.1007/s10120-015-0462-7]

Wong BC, Lam SK, Wong WM, Chen JS, Zheng TT, Feng RE, Lai KC, Hu WH, Yuen ST, Leung
SY, Fong DY, Ho J, Ching CK, Chen JS; China Gastric Cancer Study Group. Helicobacter pylori
eradication to prevent gastric cancer in a high-risk region of China: a randomized controlled trial.
JAMA 2004; 291: 187-194 [DOI: 10.1001/jama.291.2.187]

Lash JG, Genta RM. Adherence to the Sydney System guidelines increases the detection of
Helicobacter gastritis and intestinal metaplasia in 400738 sets of gastric biopsies. Aliment Pharmacol
Ther 2013; 38: 424-431 [PMID: 23796212 DOI: 10.1111/apt.12838]

Shichijo S, Hirata Y, Niikura R, Hayakawa Y, Yamada A, Ushiku T, Fukayama M, Koike K.
Histologic intestinal metaplasia and endoscopic atrophy are predictors of gastric cancer development
after Helicobacter pylori eradication. Gastrointest Endosc 2016; 84: 618-624 [PMID: 26995689
DOI: 10.1016/j.gie.2016.03.791]

Capelle LG, de Vries AC, Haringena J, Ter Borg F, de Vries RA, Bruno MJ, van Dekken H, Meijer
J, van Grieken NC, Kuipers EJ. The staging of gastritis with the OLGA system by using intestinal
metaplasia as an accurate alternative for atrophic gastritis. Gastrointest Endosc 2010; 71: 1150-1158
[PMID: 20381801 DOI: 10.1111/j.1468-1377.2009.00209]

You H, Shan L, Bin L. The significance of OLGA and OLGIM staging systems in the risk
assessment of gastric cancer: a systematic review and meta-analysis. Gastric Cancer 2018; 21: 579-
587 [PMID: 29460004 DOI: 10.1007/s10120-018-0812-3]

Pimentel-Nunes P, Libianio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, Garrido M, Kikustie I,
Megraud F, Matsuyak-Budnik T, Annibale B, Dumonceau JM, Barros R, Flejou JF, Carneiro F, van
Hooff JE, Kuipers EJ, Dinis-Ribeiro M. Management of epithelial precancerous conditions and
lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE),
European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology
(ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019.
Endoscopy 2019; 51: 365-388 [DOI: 10.1111/end.13859-1883]

Rugge M, Cassaro M, Di Mario F, Leo G, Leandro G, Russo VM, Pennelli G, Farinati F; Interdisciplinary
Group on Gastric Epithelial Dysplasia (iGGED). The long term outcome of gastric
non-invasive neoplasia. Gut 2003; 52: 1111-1116 [PMID: 12865267 DOI: 10.1136/gut.52.8.1111]

Yamada H, Ikegami M, Shimoda T, Takagi N, Maruyama M. Long-term follow-up study of gastric
adenoma/dysplasia. Endoscopy 2004; 36: 390-396 [PMID: 1500945] DOI: 10.1055/s-2004-814330

de Vries AC, van Grieken NC, Loonman CW, Casparie MK, de Vries E, Meijer GA, Kuipers EJ.
Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the
Netherlands. Gastroenterology 2008; 134: 945-952 [PMID: 18395075 DOI: 10.1013/j.gastro.2008.01.071]

You WC, Li JY, Blot WJ, Chang YS, Jin ML, Gail MH, Zhang L, Liu WD, Ma JL, Hu YR, Mark
SD, Correa P, Fraumeni Jr, Xu GW. Evolution of precancerous lesions in a rural Chinese
population at high risk of gastric cancer. Int J Cancer 1999; 83: 615-619 [PMID: 10521796
DOI: 10.1002/(sici)1097-0215(19990703)83:3<615::aid-ijc8>3.0.co;2-i]

Park SY, Jeon SW, Jung MK, Cho CM, Tak WY, Kweon YO, Kim SK, Choi YH. Long-term
follow-up study of gastric intraepithelial neoplasias: progression from low-grade dysplasia to
invasive carcinoma. Eur J Gastroenterol Hepatol 2008; 20: 966-970 [PMID: 18787462
DOI: 10.1097/MEG.0b013e3282f0313d]

Zhang G, Xue M, Hu Y, Lai S, Chen S, Wang L. How Commonly Is the Diagnosis of Gastric Low
Grade Dysplasia Upgraded Following Endoscopic Resection? PloS One 2015; 10: e0132699
[PMID: 26182344 DOI: 10.1371/journal.pone.0132699]

Yao K, Uedo N, Kamada T, Hirasewa T, Nagahama T, Yoshinaga S, Oka M, Inoue K, Mabe K, Yao
T, Yoshida M, Miyashiro I, Fujimoto K, Tajiri H. Guidelines for endoscopic diagnosis of early
gastric cancer. Dig Endosc 2020; 32: 663-698 [PMID: 32275342 DOI: 10.1111/den.13684]

Jung MK, Jeon SW, Park SY, Cho CM, Tak WY, Kweon YO, Kim SK, Choi YH, Bae HI.
Endoscopic characteristics of gastric adenomas suggesting carcinomatous transformation. Surg
Endosc 2008; 22: 2705-2711 [PMID: 18401651 DOI: 10.1007/s00464-008-9875-2]

Kim JH, Kim JY, An J, Lee JJ, Cho JH, Kim KO, Chung JW, Kwon KA, Park DK, Kim JH.
Endoscopic features suggesting gastric cancer in biopsy-proven gastric adenoma with high-grade
neoplasia. World J Gastroenterol 2014; 20: 12233-12240 [PMID: 25232257
DOI: 10.3748/wjg.v20.i34.12233]

Busbaim JL, Hormodiz D, Dinis-Ribeiro M, Lane C, Dias-Silva D, Sahakian A, Jayaram P,
Pimentel-Nunes P, Shue D, Pepper M, Cho D, Laine L. Narrow-band imaging versus white light
versus mapping biopsy for gastric intestinal metaplasia: a prospective blinded trial. *Gastrointest Endosc* 2017; 86: 857-865 [PMID: 28366441 DOI: 10.1016/j.gie.2017.03.1528]

32 Choi J, Kim SG, Im JP, Kim JS, Jung HC, Song JS. Endoscopic prediction of tumor invasion depth in early gastric cancer. *Gastrointest Endosc* 2011; 73: 917-927 [PMID: 21316050 DOI: 10.1016/j.gie.2010.11.053]

33 Zhang Q, Wang F, Chen ZY, Wang Z, Zhi FC, Liu SD, Bai Y. Comparison of the diagnostic efficacy of white light endoscopy and magnifying endoscopy with narrow band imaging for early gastric cancer: a meta-analysis. *Gastric Cancer* 2016; 19: 543-552 [PMID: 25920126 DOI: 10.1007/s10120-015-0500-5]

34 Capelle LG, Haringsma J, de Vries AC, Steyerberg EW, Biermann K, van Dekken H, Kuipers EJ. Narrow band imaging for the detection of gastric intestinal metaplasia and dysplasia during surveillance endoscopy. *Dig Dis Sci* 2010; 55: 3442-3448 [PMID: 20393882 DOI: 10.1007/s10620-010-1189-2]

35 Pimentel-Nunes P, Libânia D, Lage J, Abrantes D, Coimbra M, Esposito G, Hormozdi D, Pepper M, Drasovean S, White JR, Dobru D, Buxbaum J, Ragunath K, Anagnostopoulos GK, Dinis-Ribeiro M. A multicenter prospective study of the real-time use of narrow-band imaging in the diagnosis of premalignant gastric conditions and lesions. *Endoscopy* 2016; 48: 723-730 [PMID: 27280384 DOI: 10.1055/s-0042-106435]

36 ASGE Technology Committee. Wong Kee Song LM, Adler DG, Chand B, Conway JD, Croffie JM, Disario JA, Mishkin DS, Shah RJ, Somogyi L, Tierney WM, Petersen BT. Chromoendoscopy. *Gastrointest Endosc* 2007; 66: 639-649 [PMID: 17643437 DOI: 10.1016/j.gie.2007.05.029]

37 Zhao Z, Yin Z, Wang S, Wang J, Bai B, Qiu Z, Zhao Q. Meta-analysis: The diagnostic efficacy of chromoendoscopy for early gastric cancer and premalignant gastric lesions. *J Gastroenterol Hepatol* 2016; 31: 1539-1545 [PMID: 26860924 DOI: 10.1111/jgh.13313]

38 Larghi A, Lecca PG, Costamagna G. High-resolution narrow band imaging endoscopy. *Gut* 2008; 57: 976-986 [PMID: 18208902 DOI: 10.1136/gut.2007.127845]

39 Song J, Zhang J, Wang J, Guo X, Liu Y, Dong W. Meta-analysis: Narrow band imaging for diagnosis of gastric intestinal metaplasia. *PLoS One* 2014; 9: e94869 [PMID: 24743566 DOI: 10.1371/journal.pone.0094869]

40 Ang TL, Pittayanon R, Lau JY, Rerknimitr R, Ho SH, Singh R, Kwek AB, Ang DS, Chiu PW, Luk S, Goh KL, Ong JP, Tan JY, Teo EK, Fock KM. A multicenter randomized comparison between high-definition white light endoscopy and narrow band imaging for detection of gastric lesions. *Europ J Gastroenterol Hepatol* 2015; 27: 1473-1478 [PMID: 26428636 DOI: 10.1097/MEG.0000000000000978]

41 ASGE Technology Committee. High-definition and high-magnification endoscopes. *Gastrointest Endosc* 2014; 80: 919-927 [PMID: 25442091 DOI: 10.1016/j.gie.2014.06.019]

42 Uedo N, Ishihara R, Iishi H, Yamamoto S, Yamada T, Imanaka K, Takeuchi Y, Higashino K, Ishiguro S, Tatsuta M. A new method of diagnosing gastric intestinal metaplasia: narrow-band imaging with magnifying endoscopy. *Endoscopy* 2006; 38: 819-824 [PMID: 17001572 DOI: 10.1055/s-2006-944632]

43 Savarino E, Corbo M, Dulbecco P, Gemignani L, Giambrauno E, Mastracci L, Grillo F, Savarino V. Narrow-band imaging with magnifying endoscopy is accurate for detecting gastric intestinal metaplasia. *World J Gastroenterol* 2013; 19: 2668-2675 [PMID: 23674874 DOI: 10.3748/wjg.v19.i17.2668]

44 Omori T, Kamiya Y, Tahara T, Shibata T, Nakamura M, Yonemura J, Okubo M, Yoshioka D, Ishizuka T, Maruyama N, Kamano T, Fujita H, Nakagawa Y, Nagasaka M, Iwata M, Arisawa T, Hirata I. Correlation between magnifying narrow band imaging and histopathology in gastric protruding/or polypoid lesions: a pilot feasibility trial. *BMJ Gastroenterol* 2012; 12: 17 [PMID: 22336674 DOI: 10.1186/1471-230X-12-17]

45 Yao K, Takayi Y, Matsu T, Iwashita A, Anagnostopoulos GK, Kaye P, Ragunath K. Clinical application of magnification endoscopy and narrow-band imaging in the upper gastrointestinal tract: new imaging techniques for detecting and characterizing gastrointestinal neoplasia. *Gastrointest Endosc Clin N Am* 2008; 18: 415-433, vii [PMID: 18674694 DOI: 10.1016/j.gi.2008.05.011]

46 Muto M, Yao K, Kaise M, Kato M, Uedo N, Yagi K, Tajiri H. Magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G). *Dig Endosc* 2016; 28: 379-393 [PMID: 26896760 DOI: 10.1111/den.12638]

47 Yao K, Anagnostopoulos GK, Ragunath K. Magnifying endoscopy for diagnosing and delineating early gastric cancer. *Endoscopy* 2009; 41: 462-467 [PMID: 19418401 DOI: 10.1055/s-0029-1214594]

48 Yao K, Doyma H, Gotoda T, Ishikawa H, Nagahama T, Yokoi C, Oda I, Machida H, Uchita K, Tabuchi M. Diagnostic performance and limitations of magnifying narrow-band imaging in screening endoscopy of early gastric cancer: a prospective multicenter feasibility study. *Gastric Cancer* 2014; 17: 669-679 [PMID: 24407989 DOI: 10.1007/s10120-013-0352-0]

49 Yamada S, Doyma H, Yao K, Uedo N, Eozoe Y, Oda I, Kaneko K, Kawahara Y, Yokoi C, Sugira Y, Ishikawa H, Takeuchi Y, Saito Y, Muto M. An efficient diagnostic strategy for small, depressed early gastric cancer with magnifying narrow-band imaging: a post-hoc analysis of a prospective randomized controlled trial. *Gastrointest Endosc* 2014; 79: 55-63 [PMID: 23932092 DOI: 10.1016/j.gie.2013.07.008]

50 Hu YY, Lian QW, Lin ZH, Zhong J, Xue M, Wang LJ. Diagnostic performance of magnifying
narrow-band imaging for early gastric cancer: A meta-analysis. World J Gastroenterol 2015; 21: 7884-7894 [PMID: 26167089 DOI: 10.3748/wjg.v21.i25.7884]

51 Kato M, Kaise M, Yonezawa J, Toyoozumi H, Yoshimura N, Yoshida Y, Kawamura M, Tajiri H. Magnifying endoscopy with narrow-band imaging achieves superior accuracy in the differential diagnosis of superficial gastric lesions identified with white-light endoscopy: a prospective study. Gastrointest Endosc 2010; 72: 523-529 [PMID: 20598685 DOI: 10.1016/j.gie.2010.04.041]

52 Makis S, Yao K, Nagahama T, Beppu T, Hisabe T, Takaki Y, Hirai F, Matsui T, Tanabe H, Iwashita A. Magnifying endoscopy with narrow-band imaging is useful in the differential diagnosis between low-grade adenoma and early cancer of superficial elevated gastric lesions. Gastric Cancer 2013; 16: 140-146 [PMID: 25292604 DOI: 10.1007/s10120-012-0160-7]

53 Eoee Y, Muto M, Uedo N, Doyama H, Yao K, Oda I, Kaneko K, Kawahara Y, Yokoi C, Sugiyura Y, Ishikawa H, Takeuchi Y, Kaneko Y, Saito Y. Magnifying narrow-band imaging is more accurate than conventional white-light imaging in diagnosis of gastric mucosal cancer. Gastroenterology 2011; 141: 2017-2025.e5 [PMID: 21856628 DOI: 10.1053/j.gastro.2011.08.007]

54 Kiyoheki S, Nishikawa J, Satake M, Fukagawa Y, Shirai Y, Hamabe K, Saito M, Okamoto T, Sakaida I. Usefulness of magnifying endoscopy with narrow-band imaging for determining gastric tumor margin. J Gastroenterol Hepatol 2010; 25: 1636-1641 [PMID: 20880172 DOI: 10.1111/j.1440-1746.2010.06379.x]

55 Horii Y, Dohi O, Naito Y, Takayama S, Ogita K, Terasaki N, Nakano T, Majima A, Yoshida N, Kamada K, Uchiyama K, Ishikawa T, Takagi T, Handa O, Konishi H, Yagi N, Yanagisawa A, Itoh Y. Efficacy of Magnifying Narrow Band Imaging for Delineating Horizontal Margins of Early Gastric Cancer. Digestion 2019; 100: 93-99 [PMID: 30423508 DOI: 10.1159/000494653]

56 Uchita K, Yao K, Uedo N, Shimokawa T, Iwasaki T, Kojima K, Kawada A, Nakayama M, Okazaki M, Iwamura S. Highest power magnification with narrow-band imaging is useful for improving diagnostic performance for endoscopic delineation of early gastric cancers. BMC Gastroenterol 2015; 15: 155 [PMID: 26526857 DOI: 10.1186/s12876-015-0385-0]

57 Nagahama T, Yao K, Maki S, Yasaki M, Takaki Y, Matsu T, Tanabe H, Iwashita A, Ota A. Usefulness of magnifying endoscopy with narrow-band imaging for determining the horizontal extent of early gastric cancer when there is an unclear margin by chromoendoscopy (with video). Gastrointest Endosc 2011; 74: 1259-1267 [PMID: 22136775 DOI: 10.1016/j.gie.2011.09.005]

58 Weigt J, Malferttheiner P, Canbay A, Haybaeck J, Bird-Lieberman E, Link A. Blue Light Imaging and Linked Color Imaging for the Characterization of Mucosal Changes in Chronic Gastritis: A Clinicians View and Brief Technical Report. Dig Dis 2020; 38: 9-14 [PMID: 31336369 DOI: 10.1159/0004501265]

59 Dohi O, Yagi N, Naito Y, Fukui A, Gen Y, Iwai N, Ueda T, Yoshida N, Kamada K, Uchiyama K, Takagi T, Konishi H, Yanagisawa A, Itoh Y. Blue laser imaging-bright improves the real-time detection rate of early gastric cancer: a randomized controlled study. Gastrointest Endosc 2019; 89: 47-57 [PMID: 30189197 DOI: 10.1016/j.gie.2018.08.049]

60 Dohi O, Yagi N, Majima A, Horii Y, Kitaichi T, Onozawa Y, Suzuki K, Tomie A, Kimura-Tsuchiya R, Tsuji T, Yamada N, Bito N, Okawama T, Yoshida N, Kamada K, Katada K, Uchiyama K, Ishikawa T, Takagi T, Handa O, Konishi H, Naito Y, Yanagisawa A, Itoh Y. Diagnostic ability of magnifying endoscopy with blue laser imaging for early gastric cancer: a prospective study. Gastrointest Cancer 2017; 20: 297-303 [PMID: 27294430 DOI: 10.1016/j.10120-016-0260-6]

61 Kaneko K, Oono Y, Yano T, Ikematsu H, Odagaki T, Yoda Y, Yagishita A, Sato A, Nomura S. Effect of novel bright image enhanced endoscopy using blue laser imaging (BLI). Endosc Int Open 2014; 2: E212-E219 [PMID: 26135095 DOI: 10.1055-s-0034-1390707]

62 ASGE Technology Committee. Confocal laser endomicroscopy. Gastrointest Endosc 2014; 80: 928-938 [PMID: 25444092 DOI: 10.1016/j.gie.2014.06.021]

63 Guo YT, Li YQ, Yu T, Zhang TG, Zhang JN, Liu H, Liu FG, Xie XJ, Zhu Q, Zhao Y. Diagnosis of gastric intestinal metaplasia with confocal laser endomicroscopy in vivo: a prospective study. Endoscopy 2008; 40: 547-553 [PMID: 18618938 DOI: 10.1055/s-2007-995633]

64 Zhang HP, Yang S, Chen WH, Hu TT, Lin J. The diagnostic value of confocal laser endomicroscopy for gastric cancer and precancerous lesions among Asian population: a system review and meta-analysis. Scand J Gastroenterol 2017; 52: 382-388 [PMID: 28078907 DOI: 10.1080/00365521.2016.1275770]

65 Abadir AF, Ali MF, Karnes W, Samaraseka JB. Artificial Intelligence in Gastrointestinal Endoscopy. Clin Endosc 2020; 53: 132-141 [PMID: 32252506 DOI: 10.5946/ce.2020.038]

66 Kanesaka T, Lee TC, Uedo N, Lin KP, Chen HZ, Lee JY, Wang HP, Chang HT. Computer-aided diagnosis for identifying and delineating early gastric cancers in magnifying narrow-band imaging. Gastrointest Endosc 2018; 87: 1339-1344 [PMID: 29225083 DOI: 10.1016/j.gie.2017.11.029]

67 Hirasawa T, Aoyama K, Tanimoto T, Ishihara S, Shichijo S, Ozawa T, Ohnishi T, Fujishiro M, Matsuo K, Fujisaki J, Tada T. Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. Gastric Cancer 2018; 21: 653-660 [PMID: 29335825 DOI: 10.1007/s10120-018-0793-2]

68 Yu H, Singh R, Shin SH, Ho KY. Artificial intelligence in upper GI endoscopy - current status, challenges and future promise. J Gastroenterol Hepatol 2021; 36: 20-24 [PMID: 33448515 DOI: 10.1111/jgh.15354]

69 Olympus. News Release: Olympus launches EVIS X1, its most advanced endoscopy system to date [Internet]. Olympus Global 2020; 1-4. [cited 9 February 2021]. Available from: https://www.wjgnet.com
An W, Sun PB, Gao J, Jiang F, Liu F, Chen J, Wang D, Li ZS, Shi XG. Endoscopic submucosal dissection for gastric gastrointestinal stromal tumors: a retrospective cohort study. *Surg Endosc* 2017; 31: 4522-4531 DOI: 10.1007/s00464-017-5511-3

He Z, Sun C, Zheng Z, Yu Q, Wang T, Chen X, Cao H, Liu W, Wang B. Endoscopic submucosal dissection of large gastrointestinal stromal tumors in the esophagus and stomach. *J Gastroenterol Hepatol* 2013; 28: 262-267 DOI: 10.1111/j.1440-1789.2012.06163.x

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, Mouri R, Nam HS, Ono H, Pasquali S, Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D; ESMO Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016; 27: v38-v49 DOI: 10.1093/annonc/mdw350

Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D; ESMO Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016; 27: v38-v49 DOI: 10.1093/annonc/mdw350

Choi J, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Comparison of endoscopic ultrasonography and conventional endoscopy for prediction of depth of tumor invasion in early gastric cancer. *Endoscopy* 2010; 42: 705-713 DOI: 10.1055/s-0030-1255617

Hase C, Nie C, Chen X, Xu T, Liu J, Ding Z, Hou X. Exploration of an effective training system for the diagnosis of pancreateobiliary diseases with EUS: A prospective study. *Endosc Ultrasound* 2020; 9: 308-318 DOI: 10.4103/ceuces.ceucess.47.20

Mocellin S, Pasquali S. Diagnostic accuracy of endoscopic ultrasonography (EUS) for the preoperative locoregional staging of primary gastric cancer. *Cochrane Database Syst Rev* 2015; CD009944 DOI: 10.1007/14651858.CD009944.pub2

Takamaru H, Yoshinaga S, Takasawa H, Oda I, Katai H, Sekine S, Taniguchi K, Saito Y. Endoscopic Ultrasonography Miniature Probe Performance for Depth Diagnosis of Early Gastric Cancer with Suspected Submucosal Invasion. *Gut Liver* 2020; 14: 381-388 DOI: 10.5009/gnl19243

Kim SJ, Choi CW, Kang DH. Endoscopic features of submucosal invasion in undifferentiated type early gastric cancer sized less than 2 cm without ulceration. *JCO* 2019; 47: 76 DOI: 10.1200/JCO.2019.37.4_suppl.76

Kim J, Kim SG, Chung H, Lim JH, Choi JM, Park JY, Yang HJ, Han SJ, Oh S, Kim MS, Kim HJ, Hong H, Lee HJ, Kim JL, Lee E, Jung HC. Clinical efficacy of endoscopic ultrasonography for decision of treatment strategy of gastric cancer. *Surg Endosc* 2018; 32: 3789-3797 DOI: 10.1007/s00464-018-6104-5

Wani AH, Parry AH, Feroz I, Choh NA. Preoperative Staging of Gastric Cancer Using Computed Tomography and Its Correlation with Histopathology with Emphasis on Multi-planar Reformatations and Virtual Gastroscopy. *J Gastrointest Cancer* 2021; 52: 606-615 DOI: 32535756 DOI: 10.1007/s12029-020-00436-6

De Vuysere S, Van de Cauwe V, De Bruecker Y, Carton S, Vermeiren K, Tollens T, De Keyzer F, Dresen RC. Accuracy of whole-body diffusion-weighted MRI (WB-DWI/MRI) in diagnosis, staging and follow-up of gastric cancer, in comparison to CT: a pilot study. *BMC Med Imaging* 2021; 21: 18 DOI: 33546626 DOI: 10.1186/s12880-021-00550-2

Choi JI, Lee JH, Park JH, Min JW, Kim YM, Kim YM, Oh SH, Park JY, Yang HJ, Park SH, Kim MS, Kim HJ, Hong H, Lee HJ, Kim JL, Lee E, Jung HC. Clinical efficacy of endoscopic ultrasonography for decision of treatment strategy of gastric cancer. *Surg Endosc* 2013; 27: 3976-3983 DOI: 10.1007/s00464-018-6104-5

Choi J, Sun PB, Gao J, Jiang F, Liu F, Chen J, Wang D, Li ZS, Shi XG. Endoscopic submucosal dissection for gastric indefinite for neoplasia: which lesions should be resected? *Endoscopy* 2019; 51 Suppl 1: S19-S26 DOI: 10.1055/s-0030-1255617

Choi J, Sun PB, Gao J, Jiang F, Liu F, Chen J, Wang D, Li ZS, Shi XG. Endoscopic submucosal dissection of large gastrointestinal stromal tumors in the esophagus and stomach. *J Gastroenterol Hepatol* 2013; 28: 262-267 DOI: 10.1111/j.1440-1789.2012.06163.x

He Z, Sun C, Zheng Z, Yu Q, Wang T, Chen X, Cao H, Liu W, Wang B. Endoscopic submucosal dissection for gastric gastrointestinal stromal tumors: a retrospective cohort study. *Surg Endosc* 2017; 31: 4522-4531 DOI: 10.1007/s00464-017-5511-3
Endoscopy in gastric neoplasia

Young E et al.

Suzuki H, Takizawa K, Hirasawa T, Takeuchi Y, Ishido K, Hoteya S, Yano T, Tanaka S, Endo M, Nakagawa M, Toyonaga T, Doyama H, Hirasawa K, Matsuda M, Yamamoto H, Fujiishiro M, Hashimoto S, Maeda Y, Oyama T, Takenaka R, Yamamoto Y, Naito Y, Michida T, Kobayashi N, Kawahara Y, Hirano M, Jin M, Hori S, Niwa Y, Hikichi T, Shimazu T, Ono H, Tanabe S, Kondo H, Ishii H, Ninomiya M, Ichiro Oda for J-WEB/EGC group. Short-term outcomes of multicenter prospective cohort study of gastric endoscopic resection: ‘Real-world evidence’ in Japan. Dig Endosc 2019; 31: 30-39 [PMID: 30058258 DOI: 10.1111/den.13246]

Ryu DG, Choi CW, Kang DH, Kim HW, Park SB, Kim SI, Nam HS. Pathologic outcomes of endoscopic submucosal dissection for gastric epithelial neoplasia. Medicine (Baltimore) 2018; 97: e11802 [PMID: 30113468 DOI: 10.1097/MD.0000000000011802]

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]

Watanabe K, Hikichi T, Nakamura J, Takagi T, Suzuki R, Sugimoto M Md, Waragai Y, Kikuchi H, Kono N, Asama H, Takasumi M, Obara K, Ohira H. Endoscopic submucosal dissection for early gastric cancer in very elderly patients age 85 or older. Endosc Int Open 2017; 5: E17-E24 [PMID: 28191493 DOI: 10.1055/s-0042-122960]

Ngamruengphong S, Ferri L, Alhara H, Draganov PV, Yang DJ, Perbtani YB, Yue TL, Munroe CA, Boparai ES, Mehta NA, Bhatt A, Kumta NA, Othman MO, Mercado M, Javad H, Aadam AA, Siegel A, James TW; Grimm IS, DeWitt JM, Novikov A, Schlachterman A, Kowalski T, Samarasa J, Hashimoto R, Chehade NEH, Lee J, Chang K, Su B, Ujiki MB, Mehta A, Shahariah RZ, Carr-Loock DL, Chen A, Chen M, Yi PJ, Pourmousavi Khoshknab M, Wang R, Kersdriechairat T, Tomizawa Y, von Renteln D, Kumbhari V, Karasik M, Patel NJ, Fukarini N, Nishimura M, Hamada Y, Song YK, Wong Kee Song LM, Lazekowska M, Wang AY, Gh H, Friedman S, Sethi A, Kallool AN. Efficacy of Endoscopic Submucosal Dissection for Superficial Gastric Neoplasia in a Large Cohort in North America. Clin Gastroenterol Hepatol 2021; 19: 1611-1619.e1 [PMID: 32565290 DOI: 10.1016/j.cgh.2020.06.023]

Manta R, Galloro G, Pugliese F, Angeletti S, Caruso A, Zito FP, Mangiafico S, Marmo R, Zullo A, Esposito G, Annibale B, Mutignani M, Conigliaro R. Endoscopic Submucosal Dissection of Gastric Neoplastic Lesions: An Italian, Multicenter Study. J Clin Med 2020; 9 [PMID: 32182894 DOI: 10.3390/jcm9030737]

Abdelrahim M, Kandiah K, Masselli R, Invernizzi M, Vartyminidi L, Al-Kandari A, Hossain E, Seewald S, Repici A, Bhandari P, Arndtz S. Endoscopic submucosal dissection of early gastric neoplasia: experience from three european tertiary centres. Gut 2019; A146-A147 [DOI: 10.1136/gutjnl-2019-BSGAbstracts.275]

Maselli R, Iacopini F, Azzolini F, Petruzzello L, Manno M, De Luca L, Cincinato P, Fiori G, Siaiano T, Rosa Rizzotto E, Angeletti S, Caruso A, Coppola F, Andrisani G, Viale E, Missale G, Panarese A, Mazzeo F, Cesarop M, Campanale M, Occhipinti P, Tirantino O, Crosta C, Bresolo P, Serraszza S, Rondonotissi E, Aomoto A, Fuccio L, Costamagna G, Repici A. Endoscopic submucosal dissection: Italian national survey on current practices, training and outcomes. Dig Liver Dis 2020; 52: 64-71 [PMID: 31629705 DOI: 10.1016/j.dld.2019.09.009]

Pagano N, Frazzoni L, La Porta M, Fuccio L, Bazzoli F, Zagari RM. Endoscopic submucosal dissection for superficial premalignant and malignant epithelial neoplasms of the digestive tract: a real-life experience in Italy. Eur Rev Med Pharmacol Sci 2019; 23: 8354-8359 [PMID: 31646565 DOI: 10.26355/eurrev_201910_19146]

Tate DJ, Klein A, Sidhu M, Desomer L, Awadie H, Lee EYT, Mahajan H, McLeod D, Bourke MJ. Endoscopic submucosal dissection for suspected early gastric cancer: absolute versus expanded criteria in a large Western cohort (with video). Gastrointest Endosc 2019; 90: 474-479.e4 [PMID: 31077699 DOI: 10.1016/j.gie.2019.04.024]

Sano T, Aiko T. New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. Gastric Cancer 2011; 14: 97-100 [PMID: 21573921 DOI: 10.1007/s10120-011-0040-6]

Oh SY, Lee KG, Suh YS, Kim MA, Kong SH, Lee HJ, Kim WH, Yang HK. Lymph Node Metastasis in Mucosal Gastric Cancer: Reappraisal of Expanded Indication of Endoscopic Submucosal Dissection. Ann Surg 2017; 265: 137-142 [PMID: 28009738 DOI: 10.1097/SLA.0000000000001649]

Park YD, Chung YJ, Chung HY, Yu W, Bae HJ, Jeon SW, Cho CM, Tak WY, Kweon YO. Factors related to lymph node metastasis and the feasibility of endoscopic mucosal resection for treating poorly differentiated adenocarcinoma of the stomach. Endoscopy 2008; 40: 7-10 [PMID: 18210339 DOI: 10.1055/s-2007-966750]

Choi KK, Bae JM, Kim SM, Sohn TS, Noh JH, Lee JH, Choi MG, Kim S. The risk of lymph node metastases in 3951 surgically resected mucosal gastric cancers: implications for endoscopic resection. Gastrointest Endosc 2016; 83: 896-901 [PMID: 26344882 DOI: 10.1016/j.gie.2015.08.051]

Hanada Y, Choi AY, Hwang JH, Draganov PV, Khanna L, Sethi A, Bartel MJ, Goel N, Abe S, De Latour RA, Park K, Melis M, Newman E, Hatzaras I, Reddy SS, Farma JM, Liu X, Schlachterman A, Kresak J, Trapp G, Ansari N, Schrope B, Lee JY, Dhal D, Lo S, Jamiil LH, Burch M, Gaddam S, Gong Y, Del Portillo A, Tomizawa Y, Traong CD, Brewer Gutierrez Ol, Montgomery E, Johnston
FM, Duncan M, Canto M, Ahuja N, Lennon AM, Ngamuraengphong S. Low Frequency of Lymph Node Metastases in Patients in the United States With Early-stage Gastric Cancers That Fulfill Japanese Endoscopic Resection Criteria. *Clin Gastroenterol Hepatol* 2019; 17: 1763-1769 [PMID: 30471457 DOI: 10.1016/j.cgh.2018.11.031]

Pereira MA, Ramos MFKP, Dias AR, Faraj SF, Yagi OK, Safatle-Ribeiro AV, Maluf-Filho F, Zilberstein B, Ccecconello I, de Mello ES, Ribeiro U Jr. Risk Factors for Lymph Node Metastasis in Western Early Gastric Cancer After Optimal Surgical Treatment. *J Gastrointest Surg* 2018; 22: 23-31 [PMID: 28755085 DOI: 10.1007/s11605-017-3517-8]

Facciorusso A, Antonino M, Di Maso M, Muscatiello N. Endoscopic submucosal dissection vs endoscopic mucosal resection for early gastric cancer: A meta-analysis. *World J Gastrointest Endosc* 2014; 6: 555-563 [PMID: 25400870 DOI: 10.4253/wjge.v6.i11.555]

Tao M, Zhou X, Hu M, Pan J. Endoscopic submucosal dissection versus endoscopic resection for patients with early gastric cancer: a meta-analysis. *BMJ Open* 2019; 9: e025803 [PMID: 31874864 DOI: 10.1136/bmjopen-2018-025803]

Cho JH, Cha SW, Kim HG, Lee TH, Cho JY, Ko WJ, Jin SY, Park S. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a comparison study to using propensity score-matched analysis. *Surg Endosc* 2016; 30: 3762-3773 [PMID: 26659226 DOI: 10.1007/s00464-015-4672-1]

Shin DW, Hwang HY, Jeon SW. Comparison of Endoscopic Submucosal Dissection and Surgery for Differentiated Type Early Gastric Cancer within the Expanded Criteria. *Clin Endosc* 2017; 50: 170-178 [PMID: 27157836 DOI: 10.5946/ce.2016.017]

Fukunaga S, Naganami Y, Shiba M, Ominami M, Tanigawa T, Yamagami H, Tanaka H, Muguruma K, Watanabe T, Tominaga K, Fujiiwara Y, Ohira M, Hirakawa K, Arakawa T. Long-term prognosis of expanded-indication differentiated-type early gastric cancer treated with endoscopic submucosal dissection or surgery using propensity score analysis. *Gastrointest Endosc* 2017; 85: 143-152 [PMID: 27362565 DOI: 10.1016/j.gie.2016.06.049]

Ryu SJ, Kim BW, Kim BG, Kim JH, Kim JS, Kim JL, Park JM, Oh JH, Kim TH, Kim JJ, Park SM, Park CH, Song KY, Lee JH, Kim SG, Kim DJ, Kim W. Endoscopic submucosal dissection vs surgical resection for early gastric cancer: a retrospective multicenter study on immediate and long-term outcome over 5 years. *Surg Endosc* 2016; 30: 5283-5289 [PMID: 27338583 DOI: 10.1007/s00464-016-4877-y]

Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: A systematic review and meta-analysis. *Int J Surg* 2020; 73: 28-41 [PMID: 31783166 DOI: 10.1016/j.ijsu.2019.11.027]

Haverkamp L, Wejs TJ, van der Sluis PC, van der Tweel I, Ruurda JP, van Hillegersberg R. Laparoscopic total gastrectomy versus open total gastrectomy for cancer: a systematic review and meta-analysis. *Surg Endosc* 2013; 27: 1509-1520 [PMID: 23263644 DOI: 10.1007/s00464-012-2661-1]

Liu F, Huang C, Xu Z, Su X, Zhao G, Ye J, Du X, Huang H, Hu J, Li G, Yu P, Li Y, Suo J, Zhao N, Zhang W, Li H, He H, Sun Y. Chinese Laparoscopic Gastrointestinal Surgery Study (CLASS): Group Morbidity and Mortality of Laparoscopic vs Open Total Gastrectomy for Clinical Stage I Gastric Cancer: The CLASS02 Multicenter Randomized Clinical Trial. *JAMA Oncol* 2020; 6: 1590-1597 [PMID: 32815991 DOI: 10.1001/jamaoncol.2020.3152]

Li SS, Costantino CL, Mullen JT. Morbidity and Mortality of Total Gastrectomy: A Comprehensive Analysis of 90-Day Outcomes. *J Gastrointest Surg* 2019; 23: 1340-1348 [PMID: 31062268 DOI: 10.1007/s11605-019-04228-7]

Yu W, Park KB, Chung HY, Kwon OK, Lee SS. Chronological Changes of Quality of Life in Long-Term Survivors after Gastrectomy for Gastric Cancer. *Cancer Res Treat* 2016; 48: 1030-1036 [PMID: 27004956 DOI: 10.4143/ct.2015.398]

Soj JS, Kim JK, Lim H, Kang HS, Park JW, Kim SE, Moon SH, Kim JH, Park CK, Cho JW, Lim MS, Kim KO. Comparison of endoscopic submucosal dissection and surgical resection for treating gastric subepithelial tumours. *Scand J Gastroenterol* 2016; 51: 633-638 [PMID: 26673035 DOI: 10.1111/sjg.13445]

Tanabe S, Ishido K, Matsumoto T, Kosaka T, Oda I, Suzuki H, Fujijsaki J, Ono H, Kawata N, Oyama T, Takahashi A, Doyama H, Kobayashi M, Ueno N, Hamada K, Toyonaga T, Kawara F, Tanaka S, Yoshifu ku Y. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a multicenter collaborative study. *Gastric Cancer* 2017; 20: 45-52 [PMID: 27807641 DOI: 10.1007/s10120-016-0066-7]

Choi MK, Kim GH, Park DY, Song GA, Kim DU, Ryu DY, Lee BE, Cheong JH, Cho M. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a single-center experience. *Surg Endosc* 2013; 27: 4250-4258 [PMID: 23765426 DOI: 10.1007/s00464-013-3030-4]

Kosaka T, Endo M, Toya Y, Abiko Y, Kudara N, Inomata M, Chiba T, Takikawa Y, Suzuki K, Sugai T. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a single-center retrospective study. *Dig Endosc* 2014; 26: 183-191 [PMID: 23560494 DOI: 10.1111/den.12099]

Tanabe S, Ishido K, Higuchi K, Sasaki T, Katada C, Azuma M, Naruke A, Kim M, Koizumi W. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a retrospective comparison with conventional endoscopic resection in a single center. *Gastric Cancer* 2014; 17: 130-136 [PMID: 23576197 DOI: 10.1007/s10120-013-0241-2]
Endoscopy in gastric neoplasia

122 Nakamura K, Honda K, Akahoshi K, Ihara E, Matsuoka H, Sumida Y, Yoshimura D, Akiho H, Mortomura Y, Iwasa T, Komori K, Chijiiwa Y, Harada N, Ochiai T, Oya M, Oda Y, Takayanagi R. Suitability of the expanded indication criteria for the treatment of early gastric cancer by endoscopic submucosal dissection: Japanese multicenter large-scale retrospective analysis of short- and long-term outcomes. Scand J Gastroenterol 2015; 50: 413-422 [PMID: 25633366 DOI: 10.1080/00365552.2014.940377]

123 Min BH, Kim KM, Park CK, Lee JH, Rhee PL, Rhee JC, Kim JJ. Outcomes of endoscopic submucosal dissection for differentiated-type early gastric cancer with histological heterogeneity. Gastric Cancer 2015; 18: 618-626 [PMID: 24801199 DOI: 10.1007/s10120-014-0378-7]

124 Suzuki H, Oda I, Abe S, Sekiguchi M, Mori G, Nonaka S, Yoshinaga S, Saito Y. High rate of 5-year survival among patients with early gastric cancer undergoing curative endoscopic submucosal dissection. Gastric Cancer 2016; 19: 198-205 [PMID: 25616808 DOI: 10.1007/s10120-015-0469-0]

125 Pimentel-Nunes P, Mourão F, Veloso N, Afonso LP, Jácome M, Moreira-Dias L, Dinis-Ribeiro M. Long-term follow-up after endoscopic resection of gastric superficial neofiblastic lesions in Portugal. Endoscopy 2014; 46: 933-940 [PMID: 25019970 DOI: 10.1055/s-0034-1377348]

126 Probst A, Schneider A, Schaller T, Anthuber M, Ebigbo A, Messmann H. Endoscopic submucosal dissection for early gastric cancer: are expanded resection criteria safe for Western patients? Endoscopy 2017; 49: 855-865 [PMID: 28564714 DOI: 10.1055/s-0043-116762]

127 Abe S, Oda I, Suzuki H, Nonaka S, Yoshinaga S, Odagaki T, Taniguchi H, Kushima R, Saito Y. Short- and long-term outcomes of endoscopic submucosal dissection for undifferentiated early gastric cancer. Endoscopy 2013; 45: 703-707 [PMID: 23990461 DOI: 10.1055/s-0033-1344396]

128 Kakushima N, Hagiwara T, Tanaka M, Sawah H, Kawata N, Takizawa K, Imai K, Takao T, Hotta K, Yamaguchi Y, Matsubayashi H, Ono H. Endoscopic submucosal dissection for early gastric cancer in cases preoperatively contraindicated for endoscopic treatment. United European Gastroenterol J 2013; 1: 453-460 [PMID: 23417997 DOI: 10.1177/2050641313508550]

129 Jung DH, Youn YH, Kim JH, Park JJ, Park H. Secondary endoscopic submucosal dissection for locally recurrent or incompletely resected gastric neoplasms. World J Gastroenterol 2018; 24: 3776-3785 [PMID: 30197483 DOI: 10.3748/wjg.v24.i33.3776]

130 Jeon MY, Park JC, Hahn KY, Shin SK, Lee SK, Lee YC. Long-term outcomes after noncurative endoscopic resection of early gastric cancer: the optimal time for additional endoscopic treatment. Gastrointest Endosc 2018; 87: 1003-1013.e2 [PMID: 29031882 DOI: 10.1016/j.gie.2017.10.004]

131 Li D, Luan H, Wang S, Zhou Y. Survival benefits of additional surgery after non-curative endoscopic resection in patients with early gastric cancer: a meta-analysis. Surg Endosc 2019; 33: 711-716 [PMID: 30397744 DOI: 10.1007/s00464-018-6570-9]

132 Suzuki H, Oda I, Abe S, Sekiguchi M, Nonaka S, Yoshinaga S, Saito Y, Fukagawa T, Kati H. Clinical outcomes of early gastric cancer patients after noncurative endoscopic submucosal dissection in a large consecutive patient series. Gastric Cancer 2017; 20: 679-689 [PMID: 27722825 DOI: 10.1007/s10120-016-0651-z]

133 Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hitoya S, Nakamura K, Hirano M, Esaki M, Matsuda M, Ohnita K, Shimoda R, Yoshida M, Doi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Hayashi Y, Nakamura T, Shimosegawa T. Is radical surgery necessary in all patients who do not meet the curative criteria for endoscopic submucosal dissection in early gastric cancer? J Gastroenterol 2017; 52: 175-184 [PMID: 27908178 DOI: 10.1007/s00535-016-1210-4]

134 Goto A, Nishikawa J, Hideura E, Ogawa R, Nagao M, Sasaki S, Kawasato R, Hashimoto S, Okamoto T, Ogihara H, Hamamoto Y, Sakaida I. Lymph node metastasis can be determined by just tumor depth and lymphovascular invasion in early gastric cancer patients after endoscopic submucosal dissection. Eur J Gastroenterol Hepatol 2017; 29: 1346-1350 [PMID: 29084076 DOI: 10.1097/MEG.0000000000000987]

135 Sunagawa H, Kinoshita T, Kaito A, Shibasaki H, Kaneko K, Ochiai A, Ohtsu A, Nishida T. Additional surgery for non-curative resection after endoscopic submucosal dissection for gastric cancer: a retrospective analysis of 200 cases. Surg Today 2017; 47: 202-209 [PMID: 27194020 DOI: 10.1007/s00595-016-1535-1]

136 Jiang B, Zhou L, Lu J, Wang Y, Guo J. Predictors of lymph node metastasis and residual tumor in early gastric cancer patients after noncurative endoscopic resection: a systematic review and meta-analysis. Therap Adv Gastroenterol 2020; 13: 1756284820935033 [PMID: 32636929 DOI: 10.1177/1756284820935033]

137 Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hitoya S, Nakagawa M, Hirano M, Esaki M, Matsuda M, Ohnita K, Yamanouchi K, Yoshida M, Doi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Hayashi Y, Nakaya N, Nakamura T, Shimosegawa T. A Scoring System to Stratify Curability after Endoscopic Submucosal Dissection for Early Gastric Cancer: "eCura system". Am J Gastroenterol 2017; 112: 874-881 [PMID: 28397873 DOI: 10.1038/aig.2017.95]

138 Lee DS, Park JK, Lee SJ, Cheon GJ. Clinical significance of regional lymph node enlargement in patients with EGC within the expanded criteria for ESD. BMC Gastroenterol 2020; 20: 51 [PMID: 32138692 DOI: 10.1186/s12877-020-01197-2]

139 Cho WY, Kim YJ, Cho JY, Bok GH, Jin SY, Lee TH, Kim HG, Kim JO, Lee JS. Hybrid natural orifice transluminal endoscopic surgery: endoscopic full-thickness resection of early gastric cancer and laparoscopic regional lymph node resection--14 human cases. Endoscopy 2011; 43: 134-139
Wang Z, Dong ZY, Chen JQ, Liu JL. Diagnostic value of sentinel lymph node biopsy in gastric cancer: a meta-analysis. *Ann Surg Oncol* 2012; 19: 1541-1550 [PMID: 22048632 DOI: 10.1245/s10434-011-1214-2]

Kitagawa Y, Takeuchi H, Takagi Y, Natsugoe S, Terashima M, Murakami N, Fujimura T, Tsujimoto H, Hayashi H, Yoshimizu N, Takagane A, Mohri Y, Nabeshima K, Uenosono Y, Kinami S, Sakamoto J, Morita S, Aikou T, Miwa K, Kitajima M. Sentinel node mapping for gastric cancer: a prospective multicenter trial in Japan. *J Clin Oncol* 2013; 31: 3704-3710 [DOI: 10.1200/JCO.2013.50.3789]

Furuhata T, Kaise M, Hoye S, Iizuka T, Yamada A, Nomura K, Kuribayashi Y, Kikuchi D, Matsui A, Ogawa O, Yamashita S, Mitanu T. Postoperative bleeding after gastric endoscopic submucosal dissection in patients receiving antithrombotic therapy. *Gastric Cancer* 2017; 20: 207-214 [PMID: 26754296 DOI: 10.1007/s10120-015-0588-7]

Tsui Y, Ohata K, Ito T, Chiha H, Ohyia T, Gunji T, Matsuhashi N. Risk factors for bleeding after endoscopic submucosal dissection for gastric lesions. *World J Gastroenterol* 2010; 16: 2931-2937 [PMID: 20556838 DOI: 10.3748/wjg.v16.i23.2913]

Goto O, Fujiyoshi M, Kodashima S, Ono S, Niimi K, Hirano K, Yamamichi N, Koike K. A second-look endoscopy after endoscopic submucosal dissection for gastric epithelial neoplasm may be unnecessary: a retrospective analysis of postendoscopic submucosal dissection bleeding. *Gastrointest Endosc* 2010; 71: 241-248 [PMID: 19922919 DOI: 10.1016/j.gie.2009.08.030]

Nam HS, Choi CW, Kim SJ, Kim HW, Kang DH, Park SB, Ryu DG. Risk factors for delayed bleeding by onset time after endoscopic submucosal dissection for gastric neoplasm. *Sci Rep* 2019; 9: 2674 [PMID: 30804386 DOI: 10.1038/s41598-019-39381-1]

Uedo N, Takeuchi Y, Yamada T, Ishihara R, Ogijima Y, Yamamoto S, Kato M, Tatsumi K, Masuda E, Tanai C, Hijashino K, Ishi H, Tatsuta M. Effect of a proton pump inhibitor or an H2-receptor antagonist on prevention of bleeding from ulcer after endoscopic submucosal dissection of early gastric cancer: a prospective randomized controlled trial. *Am J Gastroenterol* 2007; 102: 1610-1616 [PMID: 17403076 DOI: 10.1111/j.1572-0241.2007.01197.x]

Martin J, Kim M, Bainbridge D, Cheng D. Do proton pump inhibitors prevent bleeding from ulcers after endoscopic submucosal dissection or endoscopic mucosal resection? *Gastrointest Endosc* 2009; 69: AB103 [DOI: 10.1016/j.gie.2009.03.061]

Nishizawa T, Suzuki H, Akimoto T, Maehata T, Morizane T, Kanai T, Yahagi N. Effects of preoperative proton pump inhibitor administration on bleeding after gastric endoscopic submucosal dissection: A systematic review and meta-analysis. *United European Gastroenterol J* 2016; 4: 5-10 [PMID: 26966517 DOI: 10.11177/2050640615588023]

Chiu PW, Lam CY, Lee SW, Kwong KH, Lee DT, Kwok SP. Effect of scheduled second therapeutic endoscopy on peptic ulcer rebleeding: a prospective randomised trial. *Gut* 2003; 52: 1403-1407 [PMID: 12970130 DOI: 10.1136/gut.52.10.1403]

Arezzo A, Passera R, Marchese N, Galloro G, Manta R, Cirocchi R. Systematic review and meta-analysis of endoscopic submucosal dissection vs endoscopic mucosal resection for colorectal lesions. *United European Gastroenterol J* 2016; 4: 18-29 [PMID: 26966519 DOI: 10.11177/2050640615585470]

Yoo JH, Shin SJ, Lee KM, Choi JM, Wi JO, Kim DH, Lim SG, Hwang JC, Cheong JY, Yoo BM, Lee KJ, Kim JH, Cho SW. Risk factors for perforations associated with endoscopic submucosal dissection in gastric lesions: emphasis on perforation type. *Surg Endosc* 2012; 26: 2456-2464 [DOI: 23398962 DOI: 10.1007/s00464-012-2211-x]

Toyokawa T, Inaba T, Omote S, Okamoto A, Miyasaka R, Watanabe K, Izumikawa K, Horii J, Fujita I, Ishikawa S, Morikawa T, Murakami T, Tomoda J. Risk factors for perforation and delayed bleeding associated with endoscopic submucosal dissection for early gastric neoplasms: analysis of 1123 lesions. *J Gastroenterol Hepatol* 2012; 27: 907-912 [PMID: 22142449 DOI: 10.1111/j.1440-1746.2011.07039.x]

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.1445-1661.2012.01376.x]

Kim HJ, Chung H, Jung DH, Park JC, Shin SK, Lee SK, Lee YC. Clinical outcomes of and management strategy for perforations associated with endoscopic submucosal dissection of an upper gastrointestinal epithelial neoplasm. *Surg Endosc* 2016; 30: 5059-5067 [PMID: 26983439 DOI: 10.1007/s00464-016-4854-5]

Minami S, Gotoda T, Ono H, Oda I, Hamanaka H. Complete endoscopic closure of gastric perforation induced by endoscopic resection of early gastric cancer using endoclips can prevent surgery (with video). *Gastrointest Endosc* 2006; 63: 596-601 [PMID: 16564858 DOI: 10.1016/j.gie.2005.07.029]

Isomoto H, Nishiyama H, Yamaguchi N, Fukuda E, Ishii H, Ikeda K, Ohnita K, Nakao K, Kohno S, Shikuwa S. Clinicopathological factors associated with clinical outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. *Endoscopy* 2009; 41: 679-683 [PMID: 19670135 DOI: 10.1055/s-0029-1214979]

Pickhardt PJ, Asher DB. Wall thickening of the gastric antrum as a normal finding: multidetector CT with cadaveric comparison. *AJR Am J Roentgenol* 2003; 181: 973-979 [PMID: 14500212 DOI: 10.2214/ajr.181.4.1810973]
Double-endoscope endoscopic submucosal dissection for the treatment of early gastric cancer accompanied by an ulcer scar (with video). *Gastrointest Endosc* 2013; 78: 266-273 [PMID: 23472995 DOI: 10.1016/j.gie.2013.01.010]

178 Ahn JY, Choi KD, Choi JY, Kim MY, Lee JH, Choi KS, Kim DH, Song HJ, Lee GH, Jung HY, Kim JH. Transnasal endoscope-assisted endoscopic submucosal dissection for gastric adenoma and early gastric cancer in the pyloric area: a case series. *Endoscopy* 2011; 43: 233-235 [PMID: 21165828 DOI: 10.1055/s-0030-1256037]

179 Teoh AY, Chia PW, Hon SF, Mak TW, Ng EK, Lau JY. Ex vivo comparative study using the Endolifter® as a traction device for enhancing submucosal visualization during endoscopic submucosal dissection. *Surg Endosc* 2013; 27: 1422-1427 [PMID: 23093235 DOI: 10.1007/s00464-012-2583-v]

180 Schöllwinkel DW, Goto O, Bergman JJ, Yahagi N, Weusten BL. The Efficacy of an Endoscopic Grasp-and-Traction Device for Gastric Endoscopic Submucosal Dissection: An Ex Vivo Comparative Study (with Video). *Clin Endosc* 2015; 48: 221-227 [PMID: 26064822 DOI: 10.5946/ce.2015.48.3.221]

181 Nagata M. Internal traction method using a spring-and-loop with clip (S-O clip) allows countertraction in gastric endoscopic submucosal dissection. *Surg Endosc* 2020; 34: 3722-3733 [PMID: 32350668 DOI: 10.1007/s00464-020-07590-9]

182 Yoshida M, Takizawa K, Suzuki S, Koike Y, Nonaka S, Yamasaki Y, Minagawa T, Sato C, Takeuchi C, Watanabe K, Kanzaki H, Morimoto H, Yano T, Sudo K, Mori K, Gotoda T, Ono H; CONNECT-G Study Group. Conventional versus traction-assisted endoscopic submucosal dissection for gastric neoplasms: a multicenter, randomized controlled trial (with video). *Gastrointest Endosc* 2018; 87: 1231-1240 [PMID: 29233673 DOI: 10.1016/j.gie.2017.11.031]

183 Noda H, Ogasawara N, Koshino A, Fukuta S, Nagoya T, Hoshino H, Nagao K, Sugiya T, Kondo Y, Ito Y, Izawa S, Ebi M, Funaki Y, Sasaki M, Kasugai K. Thread-Traction with a Sheath of Polypectomy Snare Facilitates Endoscopic Submucosal Dissection of Early Gastric Cancers. *Gastroenterol Res Pract* 2016; 2016: 9415497 [PMID: 26843860 DOI: 10.1155/2016/9415497]

184 Yoshida N, Doyama H, Ota R, Takeda Y, Nakashishi H, Tominaga K, Tsuji S, Takemura K. Effectiveness of clip-and-snare method using pre-looping technique for endoscopic gastric submucosal dissection. *World J Gastroenterol* 2016; 8: 451-457 [PMID: 27358671 DOI: 10.4253/wjg.v8.i12.451]

185 Zhang Q, Yao X, Wang Z. A modified method of endoclip-and-snare to assist in endoscopic submucosal dissection with mucosal traction in the upper GI tract. *VideoGIE* 2018; 3: 137-141 [PMID: 29917027 DOI: 10.1016/j.vgie.2018.01.002]

186 Cai MY, Martin Carreras-Presas F, Zhou PH. Endoscopic full-thickness resection for gastrointestinal submucosal tumors. *Dig Endosc* 2018; 30 Suppl 1: 1-24 [PMID: 29658639 DOI: 10.1111/den.13003]

187 Jain D, Mahmood E, Desai A, Singhal S. Endoscopic full thickness resection for gastric tumors originating from muscularis propria. *World J Gastroenterol* 2016; 8: 489-495 [PMID: 27499831 DOI: 10.4253/wjg.v8.i14.489]

188 Chae JM, Jang JY, Hong S, Kim JW, Chang YW. A case of endoscopic full-thickness resection in a patient with gastric high-grade dysplasia unsuitable for endoscopic submucosal dissection. *Clin Endosc* 2014; 47: 353-357 [PMID: 25133125 DOI: 10.5946/ce.2014.47.3.353]

189 Phee SJ, Low SC, Huynh VA, Kencana AP, Sun ZL, Yang K. Master and slave transluminal endoscopic robot (MASTER) for natural orifice transluminal endoscopic surgery (NOTES). *Annu Int Conf IEEE Eng Med Biol Soc* 2009; 2009: 1192-1195 [PMID: 19963992 DOI: 10.1109/EMBS.2009.5333413]

190 Ho KY, Phee SJ, Shabbir A, Low SC, Huynh VA, Kencana AP, Yang K, Lomanto D, So BY, Wong YY, Chung SC. Endoscopic submucosal dissection of gastric lesions by using a Master and Slave Transluminal Endoscopic Robot (MASTER). *Gastrointest Endosc* 2010; 72: 593-599 [PMID: 20646698 DOI: 10.1016/j.gie.2010.04.009]

191 Phee SJ, Reddy N, Chiu PW, Rebala P, Rao GV, Wang Z, Sun Z, Wong JY, Ho KY. Robot-assisted endoscopic submucosal dissection is effective in treating patients with early-stage gastric neoplasia. *Clin Gastroenterol Hepatol* 2012; 10: 1117-1121 [PMID: 22642951 DOI: 10.1016/j.cgh.2012.05.019]

192 Harlow C, Sivananthan A, Ayaru L, Patel K, Darzi A, Patel N. Endoscopic submucosal dissection: an update on tools and accessories. *Ther Adv Gastroenterol* 2020; 13: 2631774520957220 [PMID: 33089213 DOI: 10.1177/2631774520957220]

193 Nagata M, Fujikawa T, Munakata H. Comparing a conventional and a spring-and-loop with clip traction method of endoscopic submucosal dissection for superficial gastric neoplasms: a randomized controlled trial (with videos). *Gastrointest Endosc* 2021; 93: 1097-1109 [PMID: 33058886 DOI: 10.1016/j.gie.2020.09.040]

194 Mão de-Ferro S, Castela J, Pereira D, Chaves P, Dias Pereira A. Endoscopic Full-Thickness Resection of Colorectal Lesions with the New FTRD System: Single-Center Experience. *GE Port J Gastroenterol* 2019; 26: 235-241 [PMID: 31328137 DOI: 10.1159/000493808]
