

# World Journal of *Gastrointestinal Endoscopy*

*World J Gastrointest Endosc* 2024 February 16; 16(2): 51-97



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The WJGE is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJGE as 2.0; IF without journal self cites: 1.9; 5-year IF: 3.3; Journal Citation Indicator: 0.28.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yi-Xuan Cai; Production Department Director: Xu Guo; Editorial Office Director: Jia-Ping Yan.

**NAME OF JOURNAL**

*World Journal of Gastrointestinal Endoscopy*

**ISSN**

ISSN 1948-5190 (online)

**LAUNCH DATE**

October 15, 2009

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Anastasios Koulaouzidis, Bing Hu, Sang Chul Lee, JooYoung Cho

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/1948-5190/editorialboard.htm>

**PUBLICATION DATE**

February 16, 2024

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**PUBLISHING PARTNER**

Digestive Endoscopy Center of West China Hospital, SCU

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<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

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## Editorial article to: Animal experimental study on magnetic anchor technique-assisted endoscopic submucosal dissection of early gastric cancer

Enrico Fiori, Antonietta Lamazza, Daniele Crocetti, Antonio V Sterpetti

**Specialty type:** Gastroenterology and hepatology

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B  
Grade C (Good): C  
Grade D (Fair): 0  
Grade E (Poor): 0

**P-Reviewer:** Batyrbekov K, Kazakhstan; Wang LH, China

**Received:** November 13, 2023

**Peer-review started:** November 13, 2023

**First decision:** December 7, 2023

**Revised:** December 7, 2023

**Accepted:** January 11, 2024

**Article in press:** January 11, 2024

**Published online:** February 16, 2024



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### Abstract

In this editorial we comment on the article published in the recent issue of the *World Journal of Gastrointestinal Endoscopy* 2023; 15 (11): 634-680. Gastric cancer (GC) remains the fifth most common malignancy and the fourth leading cause of cancer-related death worldwide. The overall prevalence of GC has declined, although that of proximal GC has increased over time. Thus, a significant proportion of GC cases and deaths can be avoided if preventive interventions are taken. Early GC (EGC) is defined as GC confined to the mucosa or submucosa. Endoscopic resection is considered the most appropriate treatment for precancerous gastrointestinal lesions improving patient quality of life, with reduced rates of complications, shorter hospitalization period, and lower costs when compared to surgical resection. Endoscopic mucosal resection (EMR) and endoscopic sub-mucosal dissection (ESD) are representative endoscopic treatments for EGC and precancerous gastric lesions. Standard EMR implies injection of a saline solution into the sub-mucosal space, followed by excision of the lesion using a snare. Complete resection rates vary depending on the size and severity of the lesion. When using conventional EMR methods for lesions less than 1 cm in size, the complete resection rate is approximately 60%, whereas for lesions larger than 2 cm, the complete resection rate is low (20%-30%). ESD can be used to remove tumors exceeding 2 cm in diameter and lesions associated with ulcers or submucosal fibrosis. Compared with EMR, ESD has higher en bloc resection rates (90.2% vs 51.7%), higher complete resection rates (82.1 vs 42.2%), and lower recurrence rates (0.65% vs 6.05%). Thus, innovative techniques have been introduced.

**Key Words:** Gastric cancer; Early gastric cancer; Endoscopic resection; Endoscopic

mucosal resection; Endoscopic sub-mucosal dissection

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**Core Tip:** Endoscopic resection (ER) is considered the most appropriate treatment for precancerous gastrointestinal lesions improving patient quality of life, with reduced rates of complications, shorter hospitalization period, and lower costs when compared to surgical resection. Complete ER rates and recurrence rates after procedure vary depending on the size and severity of the lesion. Innovative techniques could improve endoscopic rate and clinical outcomes.

**Citation:** Fiori E, Lamazza A, Crocetti D, Sterpetti AV. Editorial article to: Animal experimental study on magnetic anchor technique-assisted endoscopic submucosal dissection of early gastric cancer. *World J Gastrointest Endosc* 2024; 16(2): 51-54

**URL:** <https://www.wjgnet.com/1948-5190/full/v16/i2/51.htm>

**DOI:** <https://dx.doi.org/10.4253/wjge.v16.i2.51>

## INTRODUCTION

Gastric cancer (GC) remains the fifth most common malignancy and the fourth leading cause of cancer-related death worldwide. The overall prevalence of GC has declined, although that of proximal GC has increased over time. There are important differences in epidemiology, pathology, diagnosis, and treatment strategy worldwide: Several factors influence the prevalence, development of GC as well as its recurrence after resection[1-4].

The high prevalence of autoimmune gastritis in low-income populations is the probable reason for the increased prevalence of GC in specific regions and group of patients. The age standardized mortality rates related with GC differ from country to country. The higher survival rates are documented in Korea and in Japan 5-year survival rates of 65%[5,6], whereas in the rest of the world the 5-year survival rate is around 20%. These differences may be the consequence of specific initiatives implemented in East Asia for the higher prevalence of GC, including early detection of GC through screening programs and diffusion of treatments to eradicate *Helicobacter pylori* infection. Eradication of *Helicobacter pylori* infection has been associated with reduction of more than 30% of the prevalence of GC[7-10].

The better survival rates Easy Asia countries after diagnosis of GC support the importance and effectiveness of preventive measures and interventions in this specific clinical setting. Furthermore, the age standardized mortality rate of early-onset GC in China showed a decreasing trend from 2000 to 2019. Early GC (EGC) is defined as GC confined to the mucosa or sub-mucosa. Endoscopic resection (ER) is considered the most appropriate treatment for precancerous gastric lesions[11,12]. The 10-year observed survival rate for patients with EGC rate was similar between ER (81.9%) and surgery (84.9%)[12].

Moreover, ER implies a significant reduced operative trauma in comparison with surgical resection, with shorter hospital stay and complications rates: These factors lead to better early and late patient quality of life. ER is associated with reduced costs in comparison with surgical resection, which is an important factor to be considered, namely in regions with high prevalence of the disease.

Extensive clinical experience has brought to specific guidelines: High grade dysplasia is better treated with ER, considering that the lesion has a high probability for degeneration in carcinoma. ER should be extended also to low-grade dysplasia for patients who present specific risk factors for progression of low-grade dysplasia to high grade dysplasia and carcinoma. Recognized risk factors which support ER also in patients with low grade dysplasia are tobacco and alcohol abuse, and presence of *Helicobacter pylori* infection. These conditions favor local inflammation, acidosis, hypoxia with consequent production of growth factors and inflammatory cytokine which trigger cell proliferation and differentiation. Other anatomic and pathological factors which seem to determine progression and degeneration of low-grade dysplasia include larger lesions (lesions with dimension more than 10 mm), presence of ulceration, located in the distal portion of the stomach.

This evidence has brought to a steady trend to extend indications for ER even to more advanced lesions. The Japanese Gastric Cancer Association[13] has extended the use of ER, analyzing the absence of lymph node metastases in patients who underwent gastrectomy with extended lymph node removal for patients with differentiated carcinoma, with dimension inferior to 2 cm, absence of ulceration and cancer confined to the mucosa. A retrospective study of more than 5000 patients who underwent gastrectomy showed absence of lymph node metastases in case of intra-mucosal differentiated carcinoma, less than 2 cm in size and no ulceration.

## ENDOSCOPIC SUBMUCOSAL DISSECTION OF EGC

The most common methods for removal of high degree dysplasia and EGC are endoscopic mucosal resection (EMR) and endoscopic sub-mucosal dissection (ESD). Standard EMR implies injection of a saline solution into the sub-mucosal space, followed by excision of the lesion using a snare. Standard EMR seems to be appropriate and valid for lesions less than 1

cm in dimension. EMR allows a complete resection in about 60%-70% of patients with lesions 1 cm or less in dimension; however, standard EMR fails to achieve complete resection in almost 70%-80% of patients with lesions 2 cm in size. Thus, several effective innovative techniques have been introduced. One of these is cap-mounted pan-endoscopic EMR[14]. The endoscope is provided with a cap mounted at its end. The lesion is aspirated into the plastic cap. The operator can cut the lesion under direct vision with a snare. Another widely used technique implies to circumferential cutting the lesion as first step; then, EMR completes a detailed dissection of the regions surrounding the removed lesion. These endoscopic techniques are very effective, with improved rates of complete resection for lesions less than 2 cm in size. They have resulted less valid for patients with larger lesions and presence of mucosal ulceration. For this reason, there has been a significant interest in developing ESD, using several type of technical details and knives.

ESD implies removal also of the sub-mucosa. ESD is effective in anatomic conditions where the accepted EMR methods commonly fail to achieve complete resection, like lesions with more than 2 cm in size, and tumors with ulceration and high degree of inflammation. Compared with EMR, ESD has higher en bloc resection rates (90.2% *vs* 51.7%), higher complete resection rates (82.1% *vs* 42.2%), and lower recurrence rates (0.65% *vs* 6.05%)[12]. However, often it is difficult to obtain sufficient tension and good field, with possibility for of adverse events, bleeding, and perforation[15]. The improved techniques for ER have brought to important results: The 5-year survival rate for patients with EGC meeting expanded criteria was similar to the 5-year survival rate of patients with standard indications for ER (94.8%-99.5%). A recent prospective study confirmed the effectiveness of ER in EGC with an overall 5-year survival rate of 89.0%[16,17]. Thus, ER should be considered a valid form of treatment for patients with EGC. *Helicobacter pylori* eradication therapy should be performed after ER.

## EXPERIMENTAL STUDY

In this *ex vivo* animal experimental prospective controlled group study, Pan *et al*[18] introduce an innovative technique to perform a more extended ESR. Conceptually, their proposed technique allows a more precise and extended sub-mucosal resection, applying traction on the gastric mucosa, with a good visualization of the area to excise. Bleeding can be more easily prevented and controlled. This is a very important advantage of the proposed technique considering the high percentage of patients taking anti-platelets drugs. The study is at its initial step, and a more extensive applications on patients are required, also considering the difference between the healthy mucosa and healthy muscle layer of the stomach of the experimental animals and the mucosa and muscle layer surrounding an EGC, often associated with inflammation and easier tendency for bleeding. The authors used explanted stomach to experiment their technique. Inevitably, in this condition, every form of experiment is easier to be performed, and the probable difficulties to perform a delicate endoscopic technique like the one proposed by the authors are less evident.

## CONCLUSION

We encourage the authors to continue their studies addressing several important points: (1) To perform the experiments *in vivo*, without sacrificing the experimental animals to be able to determine the difficulties to perform the technique and to ascertain the possibilities of early and medium-term complications; (2) To perform the technique in experimental animals treated with anti-platelets agents, considering that most patients who require ER are taking anti-platelets agents; and (3) The obvious final step is to assess the feasibility and appropriateness of the technique in patients. The technique described by the authors can be extended to treat also colorectal lesions[19-21].

## FOOTNOTES

**Author contributions:** Fiori E, Lamazza A, Crocetti D, and Sterpetti AV contributed to this paper; Fiori E designed the overall concept and outline of the manuscript; Lamazza A and Crocetti D contributed to the discussion and design of the manuscript; Sterpetti AV contributed to the writing, editing the manuscript, and review of literature.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

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**S-Editor:** Wang JJ

**L-Editor:** A

**P-Editor:** Xu ZH

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