

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2024 April 15; 16(4): 1091-1675



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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (WJGO, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

INDEXING/ABSTRACTING

The WJGO is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, 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 WJGO as 3.0; IF without journal self cites: 2.9; 5-year IF: 3.0; Journal Citation Indicator: 0.49; Ranking: 157 among 241 journals in oncology; Quartile category: Q3; Ranking: 58 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO's CiteScore for 2022 is 4.1 and Scopus CiteScore rank 2022: Gastroenterology is 71/149; Oncology is 197/366.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Xiang-Di Zhang; Production Department Director: Xiang Li; Cover Editor: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Oncology

ISSN

ISSN 1948-5204 (online)

LAUNCH DATE

February 15, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

PUBLICATION DATE

April 15, 2024

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

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

STEPS FOR SUBMITTING MANUSCRIPTS

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

ONLINE SUBMISSION

<https://www.f6publishing.com>



Present situation of minimally invasive surgical treatment for early gastric cancer

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Specialty type: Oncology

Provenance and peer review:

Unsolicited 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, B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Kinami S, Japan;

Yildirim M, Turkey

Received: September 20, 2023

Peer-review started: September 20, 2023

First decision: November 22, 2023

Revised: December 5, 2023

Accepted: February 2, 2024

Article in press: February 2, 2024

Published online: April 15, 2024



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Abstract

Minimally invasive surgery is a kind of surgical operation, which is performed by using professional surgical instruments and equipment to inactivate, resect, repair or reconstruct the pathological changes, deformities and wounds in human body through micro-trauma or micro-approach, in order to achieve the goal of treatment, its surgical effect is equivalent to the traditional open surgery, while avoiding the morbidity of conventional surgical wounds. In addition, it also has the advantages of less trauma, less blood loss during operation, less psychological burden and quick recovery on patients, and these minimally invasive techniques provide unique value for the examination and treatment of gastric cancer patients. Surgical minimally invasive surgical techniques have developed rapidly and offer numerous options for the treatment of early gastric cancer (EGC): endoscopic mucosal resection (EMR), underwater EMR (UEMR), endoscopic submucosal dissection (ESD), endoscopic full-thickness resection (EFTR), endoscopic submu-

cosal excavation (ESE), submucosal tunnel endoscopic resection), laparoscopic and endoscopic cooperative surgery (LECS); Among them, EMR, EFTR and LECS technologies have a wide range of applications and different modifications have been derived from their respective surgical operations, such as band-assisted EMR (BA-EMR), conventional EMR (CEMR), over-the-scope clip-assisted EFTR, no-touch EFTR, the inverted LECS, closed LECS, and so on. These new and improved minimally invasive surgeries are more precise, specific and effective in treating different types of EGC.

Key Words: Minimally invasive surgery; Early gastric cancer; Endoscopic mucosal resection; Endoscopic full-thickness resection; Laparoscopic and endoscopic cooperative surgery

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Core Tip: In this article the authors provide an overview of the surgical forms of minimally invasive surgical treatment performed for early gastric cancer in recent years, adding newly popular surgical procedures such as band-assisted endoscopic mucosal resection (EMR), EMR with circumferential precutting, modified cap-assisted EMR, underwater EMR, ligation-assisted endoscopic full-thickness resection (EFTR), over-the-scope clip-assisted EFTR, no-touch EFTR, non-exposure simple suturing EFTR, exposed EFTR, and so on.

Citation: Li CY, Wang YF, Luo LK, Yang XJ. Present situation of minimally invasive surgical treatment for early gastric cancer. *World J Gastrointest Oncol* 2024; 16(4): 1154-1165

URL: <https://www.wjgnet.com/1948-5204/full/v16/i4/1154.htm>

DOI: <https://dx.doi.org/10.4251/wjgo.v16.i4.1154>

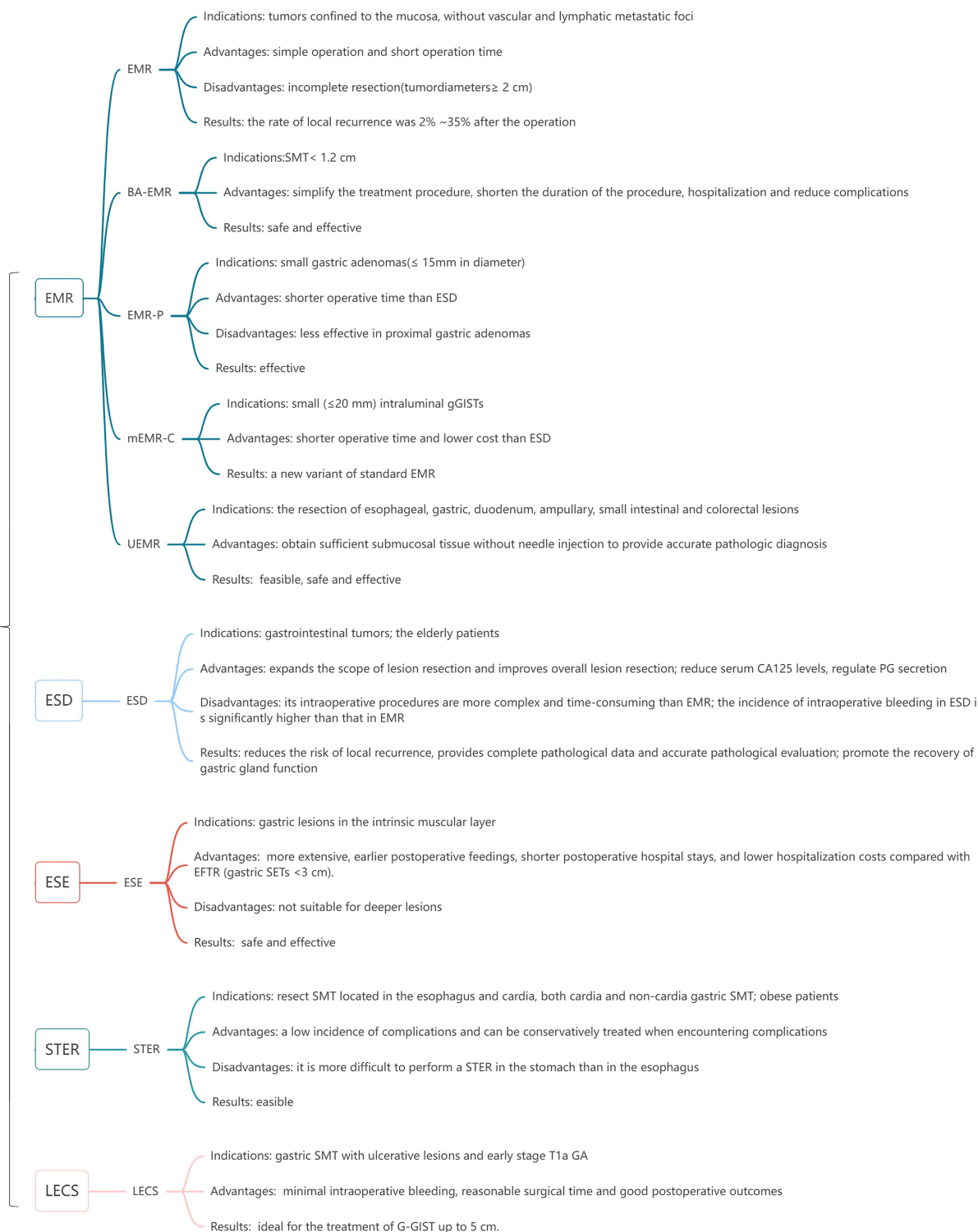
INTRODUCTION

Minimally invasive surgery is a kind of surgical operation, which is performed by using professional surgical instruments and equipment to inactivate, resect, repair or reconstruct the pathological changes, deformities and wounds in human body through micro-trauma or micro-approach, in order to achieve the goal of treatment, its surgical effect is equivalent to the traditional open surgery, while avoiding the morbidity of conventional surgical wounds[1]. In addition, it also has the advantages of less trauma, less blood loss during operation, less psychological burden and quick recovery on patients, and these minimally invasive techniques provide unique value for the examination and treatment of gastric cancer (GC) patients. GC is one of the most common malignant tumors of digestive tract in the world. It is the fifth largest cancer after lung cancer, breast cancer, colorectal cancer and prostate cancer[2], in the meantime, GC is the third most common cause of cancer-related death due to the fact that its high mortality rate and its often advanced stage at the time of diagnosis[3]. Early intervention and treatment in the early stage of GC can effectively improve the prognosis of cancer patients. Surgical minimally invasive surgical techniques have developed rapidly and offer numerous options for the treatment of early GC (EGC), such as endoscopic mucosal resection (EMR), underwater EMR (UEMR), endoscopic submucosal dissection (ESD), endoscopic full-thickness resection (EFTR), endoscopic submucosal excavation (ESE), submucosal tunnel endoscopic resection (STER), laparoscopic and endoscopic cooperative surgery (LECS) *etc.*; The purpose of this review is to discuss the utility of current minimally invasive surgical modalities in the management of EGC by weighing the benefits and limitations of minimally invasive surgical treatments for EGC. In addition, we aim to update the advances in minimally invasive treatment of EGC by considering the latest innovations in the field of minimally invasive surgical treatment of EGC, further defining any additional evidence of its role in minimally invasive treatment of EGC, complications, limitations of the technique and suggesting areas for further research (Figure 1). We present the following article in accordance with the narrative review reporting checklist.

EMR

In 1984, EMR was first reported in Japan for the treatment of EGC[4]. Due to its simple operation and short operation time, EMR was widely used in clinic. Early EMR was only suitable for early cancers with tumors confined to the mucosa, without vascular and lymphatic metastatic foci, or lesions that were locally not combined with ulcers, and tumors with diameters of more than 2 cm needed to be resected in several parts, slices and layers, which was easy to result in the incomplete resection of the lesions and residual cancerous tissues, and led to local recurrence after the operation, which was reported by Horiki *et al*[5]. The rate of recurrence was 2%-35%. In response to the limitations of conventional EMR (CEMR), several improved EMRs have emerged. A prospective study demonstrated that band-assisted EMR (BA-EMR) is an effective and safe method for small gastric fundus submucosal tumors (SMT) (< 1.2 cm)[6], and that BA-EMR can simplify the treatment procedure, shorten the duration of the procedure, hospitalization, and reduce complications. It was found that EMR with circumferential precutting (EMR-P) was as effective as ESD in the treatment of small gastric

Minimally invasive treatment modalities for EGC



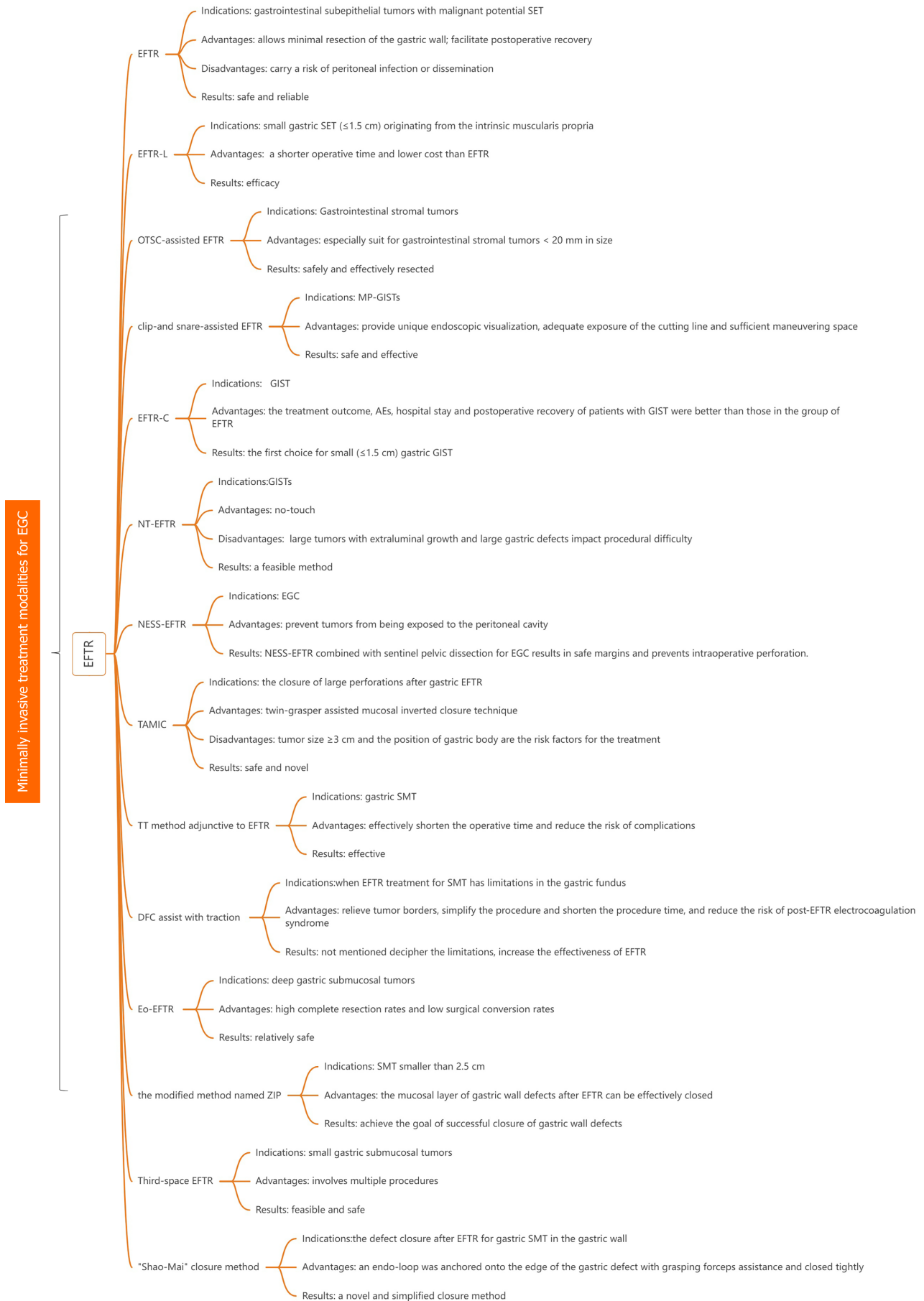


Figure 1 Minimally invasive treatment modalities for early gastric cancer.

adenomas (≤ 15 mm in diameter), with ESD having a significantly longer operative time than EMR-P, but EMR-P was less effective in proximal gastric adenomas[7]. Meng *et al*[8] reported that modified cap-assisted EMR (mEMR-C) is a new variant of standard EMR. The mEMR-C is the technique of choice for small (≤ 20 mm) intraluminal gastric gastrointestinal stromal tumors (gGISTs) with shorter operative time and lower cost than ESD. Meanwhile, on the basis of the EMR and saline solution-assisted snare or endoscopic cap-band mucosal resection technique (which allows for resection of lesions ≤ 14 mm in size in a single session) used by Karaca *et al*[9], the investigators modified the use of a beveled, clear-cap suction to resect small luminal gGISTs, which allows for suctioning of a larger volume of lesion, avoiding tumor remnants as much as possible, and increasing the rate of complete resection.

UEMR

UEMR is a novel developed technique for the resection of esophageal, gastric, duodenum, ampullary, small intestinal and colorectal lesions[10]. In gastric diseases, UEMR can also be used for establishing diagnosis of diffuse infiltrative GC[11]. CEMR can be used to diagnose invasive GC[12], but needle injection into hard tumor tissue is difficult and improper injection can make follow-up operation challenging and inconvenient. UEMR, in contrast, can obtain sufficient submucosal tissue without needle injection to provide accurate pathologic diagnosis. It has been shown that UEMR is feasible in gastric tumors of patients with FAP, particularly in elevated lesions and lesions ≤ 20 mm in diameter[13]. Kim *et al*[14] demonstrated that UEMR is a safe and effective treatment for upper gastrointestinal subepithelial tumors (SETs) originating from the deep mucosa and/or submucosa. Kim *et al*[15] reported the results of 4 cases of UEMR for benign mucosal tumors (< 15 mm in diameter) located in the pyloric ring, demonstrating that UEMR is an effective and safe method for the treatment of gastric pyloric ring tumors. During the UEMR procedure, water immersion allowed the lesion to float slightly and be easily identified, and then the whole resection was performed with a loop and an electrosurgical device. All procedures were operated quickly without adverse events (AEs).

The results of a multicenter randomized controlled trial indicated that UEMR, with a cutting plane depth comparable to that of CEMR, which can adequately resect the submucosal layer and is a feasible alternative for the histopathological evaluation of unpredictable submucosal invasive tumors[16].

ESD

ESD was first reported in Japan in 1988[17]. In contrast with EMR, ESD surgery expands the scope of lesion resection and improves overall lesion resection, which reduces the risk of local recurrence[18], provides complete pathological data and accurate pathological evaluation[19]. If there is a postoperative recurrence, it can be re-surgery to achieve the purpose of complete resection of the lesion and improve the cure rate. And ESD is suitable for the elderly patients[20], which has a high degree of safety and reliability. Research has shown that compared to EMR treatment, ESD can not only completely remove cancer lesions, but also reduce serum CA125 levels, regulate PG secretion, promote the recovery of gastric gland function, and reduce the risk of EGC recurrence[21]. However, its intraoperative procedures are more complex and time-consuming than EMR[22], with a larger resection range of tissue and a wider and deeper ulcer base. Therefore, caution should be exercised to reduce complications such as bleeding and perforation. Due to longer surgical time and greater invasiveness, the incidence of intraoperative bleeding in ESD is significantly higher than that in EMR. The review first defines post-ESD bleeding and elaborates on its management, including methods for coagulation of potential bleeding points during surgery, lesion closure, lesion shielding, and the application of gastric acid secretion inhibitors[23].

A North American study mentioned[24] that in Asia, ESD has been proven to be superior to EMR; This large multicenter prospective trial evaluated ESD in North America, demonstrating that ESD can be safely and effectively performed with a low postoperative recurrence rate, further supporting the implementation of ESD treatment for gastrointestinal tumors.

EFTR

The EFTR technique was first introduced in Japan in 1998[25], and subsequently the same team reported that it is safe and reliable for completely closed early gastrointestinal malignancies tumors[26]. The use of commercially available EMR kit devices to assist EFTR has been shown to be a safe and feasible approach for endoscopic resection of gastrointestinal SETs with malignant potential SET[27]. Mucosal resection and limited submucosal dissection to preserve the mucosa prior to tumor resection in SET patients may facilitate postoperative recovery. Ligation-assisted EFTR has been demonstrated efficacy in treating small gastric SETs (≤ 1.5 cm) originating from the intrinsic muscularis propria, with a shorter operative time and lower cost than EFTR[28].

gGISTs can be safely and effectively resected by the over-the-scope clip-assisted EFTR, especially for gGISTs < 20 mm in size[29]. A Novel approach to clip-and snare-assisted EFTR (also named as m-EFTR or chen-EFTR) safely and effectively resects muscularis propria layer GISTs by providing unique endoscopic visualization, adequate exposure of the cutting line and sufficient maneuvering space[30]. It has been shown that[31] double-curved endoscope has an advantage over single-curved endoscopes in the duration of EFTR surgery in gGISTs, especially in the fundus of the stomach. Yang *et al*[32] found that the treatment outcome, AEs, hospital stay and postoperative recovery of patients with

GIST in the group of cap-assisted EFTR were better than those in the group of EFTR, which may be the first choice for small (≤ 1.5 cm) gastric GIST. The new no-touch EFTR technique developed by Chen *et al*[33] is a feasible approach for GIST resection and holds promise for complete radical resection. The growth of large extra-cavity tumor is one of the factors affecting the difficulty of surgery. EFTR locates the tumor endoscopically and carries the risk of peritoneal infection or dissemination while maximizing the resection of the gastric wall. In response to this question, a new EFTR [34] technique has been devised: silicone sheets and gauze are attached to the plasma membrane of the intact porcine stomach using a fibrinogen-thrombin solution to prevent gastric juices from escaping before proceeding to subsequent surgical steps. The experimental results show that the time required to perform a seromuscular incision is significantly shorter with the new EFTR technique, which avoids exposure of the tumor to the peritoneal cavity while incising all layers of the stomach, and that gastric collapse can be prevented using this technique. Non-exposure simple suturing EFTR (NESS-EFTR) can also prevent tumors from being exposed to the peritoneal cavity. Studies have shown[35] that NESS-EFTR combined with sentinel pelvic dissection for EGC results in safe margins and prevents intraoperative perforation. The closure of large perforations after gastric EFTR can be achieved by the safe and novel twin-grasper assisted mucosal inverted closure technique[36]. The study has showed[37] that the tumor size ≥ 3 cm and the position of gastric body are the risk factors for the treatment of SMT with EFTR. When intraoperative tumor exposure is suboptimal, the thread-traction method adjunctive to EFTR for gastric SMT can effectively shorten the operative time and reduce the risk of complications[38]. Exposed EFTR is relatively safe with high complete resection rates and low surgical conversion rates in the treatment of deep gastric SMT[39]. When EFTR treatment for SMT has limitations in the gastric fundus, the use of dental floss and a hemoclip to assist with traction can decipher the limitations, increase the effectiveness of EFTR, relieve tumor borders, simplify the procedure and shorten the procedure time, and reduce the risk of post-EFTR electro-coagulation syndrome[40,41]. To achieve the goal of successful closure of gastric wall defects, for SMT smaller than 2.5 cm, the mucosal layer of gastric wall defects after EFTR can be effectively closed by the modified method named ZIP[42]; Third-space EFTR is one of the minimally invasive endoscopic options for the treatment of small gastric SMT, which involves multiple procedures such as circumferential mucosal incisions, proximal submucosal tunneling, peripheral mucosal endoscopic suturing, circumferential serosal myotomy of the submucosal tunneling, transoral retrieval, and closure of the tunneling entrance site[43]. It is feasible and safe. The endoscopic "Shao-Mai" closure method is a novel and simplified closure method[44]: after successful resection of the tumor *via* the EFTR, a grasping forceps-assisted internal loop ligation device is used to secure the lining to the edge of the gastric defect and close it tightly. The Koreans[45] have also added a sentinel lymph node drainage area clearance at the tumor site to the EFTR procedure, which obtained a good oncologic outcome while providing maximum protection to the patient's postoperative gastric function.

ESE

ESE evolved from ESD technology[46]. ESE involves a longitudinal or circular incision in the mucosa overlying the lesion to resect the lesion, which is more extensive but not suitable for deeper lesions. The literature suggests that the ESE technique is safe and effective for gastric[47,48] lesions in the intrinsic muscular layer.

When treating gastric SETs (< 3 cm), ESE resulted in earlier postoperative feedings, shorter postoperative hospital stays, and lower hospitalization costs compared with EFTR[49]. Compared with STER, the removal time of ESE was shorter but the wound closure time was longer when treating upper gastroenterology SMT originating from the muscularis propria layer[50,51], with no significant difference in total operative time. The operation time of ESE surgery is shorter than that of STER in the treatment of cardiac SMT[52], and the intraoperative risk factor is the irregular tumor shape.

STER

STER was originally used to resect SMT located in the esophagus and cardia, and it is feasible to treat both cardia and non-cardia gastric SMT with comparable efficacy[53]. Because of differences in anatomical and physiological characteristics, it is more difficult to perform a STER in the stomach than in the esophagus. A meta-analysis[54] evaluating the results showed that STER treatment for gastric SMT has a low incidence of complications and can be conservatively treated when encountering complications. A study showed[55] a low incidence of short-term complications in large SMT originating from the muscularis propria of esophagus and gastric cardia, with the most common complication during or after surgery being perforation. A study with a follow-up time of over 1 year showed[56] that STER has a clear therapeutic effect on upper gastrointestinal SMTs, but the incidence of AE is not low. Conservative treatment can be used when AE occurs. STER is a safe and effective procedure for resecting SETs of the gastrointestinal tract[57]. STER is also safe and effective for obese patients awaiting surgical treatment and does not interfere with bariatric surgery[58]. Independent risk factors for postoperative complications after endoscopic treatment of subepithelial lesions were lesion diameter greater over 4 cm and operative time greater than 2 h[59]. All surgical treatments require a high degree of vigilance against the occurrence of postoperative complications.

LECS

It was first performed LECS by Hiki *et al*[60] in 2008 for dissection of gastric SMT (such as GIST) with minimal intraoperative bleeding, reasonable surgical time and good postoperative outcomes. In 2012, the medical team achieved good results in treating EGC with a wide range of lesions with LECS[61]. Initially, the indication for classical LECS was gastric SMT without ulcerative lesions[62]. The indication for LECS was expanded to include gastric SMT with ulcerative lesions and early stage T1a GC without lymph node metastasis[63], with the development and advancement of the technology, a number of improved LECS procedures have gradually emerged, expanding the indications for LECS. The inverted LECS technique involves inverting the tumor into the gastric cavity during surgery, which can avoid contamination with gastric juices as well as direct contact between the surrounding tissues and the tumor[64], removing the tumor and placing it into the gastric cavity. Finally, the tumor was removed from the mouth. A case of successful treatment of GIST near the pyloric ring using the inverted LECS demonstrated that LECS can preserve the function of the cardia and pylorus by minimal resection without blocking the passage or stasis[64]. The CLEAN-NET procedure preserves the mucosa and prevents the flow of gastric contents into the peritoneal cavity[65]; CLEAN-NET can be used in conjunction with lymph node dissection for further treatment of the disease after completion of a total gastric wall resection. CLEAN-NET has been found to be safe and useful in the treatment of gastric GIST with ulceration[66]. Nineteen patients treated with CLEAN-NET were studied[67], all of whom had their tumors removed as a whole with no intraoperative ruptures. It was performed safely within an average operative time of 105.4 minutes and the postoperative course was uneventful. A patient with gastric heterotopic inverted polyp (GHIP)[68], which was difficult to diagnose accurately due to the location of the polyp and difficult to resect the tissue. It was diagnosed and treated with a modified CLEAN-NET. The good postoperative results show that the modified CLEAN-NET can treat SMT while avoiding gastric metaplasia and tumor dissemination, as in the case of GHIP with a central dimple. The researchers performed closed LECS in three cases of EGC after ESD failure[69], by which gastric tumors can be accurately removed without exposing tumor cells to the abdominal cavity. Closed LECS is less invasive in the treatment of EGC.

CONCLUSION

Surgical minimally invasive procedures are increasingly being used for the treatment and resection of EGC, thanks to their flexibility in removing tumors in anatomically challenging areas while providing precision to minimize the removal of undiseased tissue margins. Within this already widely used technique, researchers have explored a number of different improved and innovative surgical approaches based on tumor factors and surgeon selection, allowing for dynamic optimization of tailoring the appropriate surgical technique for different patients in different situations (Table 1). EMR, EFTR and LECS are a few of the more widely used surgical techniques for treating early stage, and the most derived and innovative measures based on them are likely to become more widespread and indispensable in the future for treating EGC.

Table 1 Summary of minimally invasive treatment modalities for early gastric cancer					
Initial	Upgrade	Indications	Advantages	Disadvantages	Results
EMR	EMR	Tumors confined to the mucosa, without vascular and lymphatic metastatic foci	Simple operation and short operation time	Incomplete resection (tumor diameters ≥ 2 cm)	The rate of local recurrence was 2%-35% after the operation[5]
	BA-EMR	SMT (< 1.2 cm)[6]	Simplify the treatment procedure, shorten the duration of the procedure, hospitalization and reduce complications	Not mentioned	Safe and effective
	EMR-P	Small gastric adenomas (≤ 15 mm in diameter)	Shorter operative time than ESD	Less effective in proximal gastric adenomas[7]	Effective
	mEMR-C	Small (≤ 20 mm) intraluminal gGISTs	Shorter operative time and lower cost than ESD	Not mentioned	A new variant of standard EMR
UEMR	UEMR	The resection of esophageal, gastric, duodenum, ampullary, small intestinal and colorectal lesions[10]	Obtain sufficient submucosal tissue without needle injection to provide accurate pathologic diagnosis	Not mentioned	Feasible, safe and effective
ESD	ESD	Gastrointestinal tumors; the elderly patients[20]	Expands the scope of lesion resection and improves overall lesion resection; reduce serum CA125 levels, regulate PG secretion	Its intraoperative procedures are more complex and time-consuming than EMR[22]; the incidence of intraoperative bleeding in ESD is	Reduces the risk of local recurrence[18], provides complete pathological data and accurate pathological evaluation[19]; promote the

				significantly higher than that in EMR	recovery of gastric gland function[21]
EFTR	EFTR	Gastrointestinal subepithelial tumors with malignant potential SET [27]	Allows minimal resection of the gastric wall; facilitate postoperative recovery	Carry a risk of peritoneal infection or dissemination	Safe and reliable
	EFTR-L	Small gastric SET (≤ 1.5 cm) originating from the intrinsic muscularis propria	A shorter operative time and lower cost than EFTR[28]	Not mentioned	Efficacy
	OTSC-assisted EFTR	Gastrointestinal stromal tumors	Especially suit for gastrointestinal stromal tumors < 20 mm in size[29]	Not mentioned	Safely and effectively resected
	Clip-and snare-assisted EFTR	MP-GISTs	Provide unique endoscopic visualization, adequate exposure of the cutting line and sufficient maneuvering space [30]	Not mentioned	Safe and effective
	EFTR-C	GIST	The treatment outcome, AEs, hospital stay and postoperative recovery of patients with GIST were better than those in the group of EFTR	Not mentioned	The first choice for small (≤ 1.5 cm) gastric GIST
	NT-EFTR	GISTs	No-touch	Large tumors with extraluminal growth and large gastric defects impact procedural difficulty	A feasible method
	NESS-EFTR	EGC	Prevent tumors from being exposed to the peritoneal cavity	Not mentioned	NESS-EFTR combined with sentinel pelvic dissection for EGC results in safe margins and prevents intraoperative perforation
	TAMIC	The closure of large perforations after gastric EFTR	Twin-grasper assisted mucosal inverted closure technique[36]	Tumor size ≥ 3 cm and the position of gastric body are the risk factors for the treatment	Safe and novel
	TT method adjunctive to EFTR	Gastric SMT	Effectively shorten the operative time and reduce the risk of complications[38]	Not mentioned	Effective
	Eo-EFTR	Deep gastric submucosal tumors	High complete resection rates and low surgical conversion rates	Not mentioned	Relatively safe
	DFC assist with traction	When EFTR treatment for SMT has limitations in the gastric fundus	Relieve tumor borders, simplify the procedure and shorten the procedure time, and reduce the risk of post-EFTR electrocoagulation syndrome[40,41]	Not mentioned	Decipher the limitations, increase the effectiveness of EFTR
	The modified method named ZIP	SMT smaller than 2.5 cm	The mucosal layer of gastric wall defects after EFTR can be effectively closed	Not mentioned	Achieve the goal of successful closure of gastric wall defects
	Third-space EFTR	Small gastric submucosal tumors	Involves multiple procedures [43]	Not mentioned	Feasible and safe
	"Shao-Mai" closure method	The defect closure after EFTR for gastric SMT in the gastric wall	An endo-loop was anchored onto the edge of the gastric defect with grasping forceps assistance and closed tightly	Not mentioned	A novel and simplified closure method[44]
ESE	ESE	Gastric lesions in the intrinsic muscular layer	More extensive, earlier postoperative feedings, shorter postoperative hospital stays, and lower hospitalization costs compared with EFTR[49] (gastric SETs < 3 cm)	Not suitable for deeper lesions	Safe and effective
STER	STER	Resect SMT located in the esophagus and cardia, both cardia and non-cardia gastric SMT; obese patients	A low incidence of complications and can be conservatively treated when encountering complications	It is more difficult to perform a STER in the stomach than in the esophagus	Easible

LECS	LECS	Gastric SMT with ulcerative lesions and early stage T1a GC[63,64]	Minimal intraoperative bleeding, reasonable surgical time and good postoperative outcomes	Not mentioned	Ideal for the treatment of G-GIST up to 5 cm
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EMR: Endoscopic mucosal resection; BA-EMR: band-assisted endoscopic mucosal resection; ESD: Endoscopic submucosal dissection; SET: Subepithelial tumor; EFTR: Endoscopic full-thickness resection; MP-GISTs: Muscularis propria layer gastrointestinal stromal tumors; OTSC: Over-the-scope clip; EFTR-C: Cap-assisted endoscopic full-thickness resection; AEs: Adverse events; GIST: Gastrointestinal stromal tumor; NT-EFTR: No-touch endoscopic full-thickness resection; NESS-EFTR: Non-exposure simple suturing endoscopic full-thickness resection; TAMIC: Twin-grasper assisted mucosal inverted closure; TT: Thread-traction; Eo-EFTR: Exposed endoscopic full-thickness resection; DFC: Dental floss and a hemoclip; SMT: Submucosal tumor; STER: Submucosal tunnel endoscopic resection; EMR-P: Endoscopic mucosal resection with circumferential precutting; mEMR-C: Modified cap-assisted endoscopic mucosal resection; gGISTs: Gastric gastrointestinal stromal tumors; UEMR: Underwater endoscopic mucosal resection; EFTR-L: Ligation-assisted endoscopic full-thickness resection.

ACKNOWLEDGEMENTS

The authors offered technical support and materials used for experiments.

FOOTNOTES

Co-first authors: Chun-Yan Li and Yi-Feng Wang.

Author contributions: Li CY and Wang YF contributed conceptualization; Li CY and Luo LK contributed methodology; Yang XJ contributed formal analysis, supervision and funding acquisition; Li CY contributed investigation; Wang YF contributed resources; Luo LK contributed data curation and visualization; Li CY contributed original draft preparation; Li CY and Wang YF contributed review and editing; Luo LK and Yang XJ contributed project administration; all authors have read and agreed to the published version of the manuscript.

Supported by Key R&D projects of provincial science and technology plans of Gansu Province, No. 21YF5WA027; Scientific Research Program of Health Industry of Gansu Province, No. GSWSKY2020-45; Gansu Provincial People's Hospital Intramural Research Fund Program, No. 22GSSYD-61; Grants from Innovation Base and Talent Project of Gansu Province, No. 20JR10RA433; and The 2021 Central-Guided Local Science and Technology Development Fund, No. ZYYDDFFZZJ-1.

Conflict-of-interest statement: The authors declare no conflict of interest.

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S-Editor: Gao CC

L-Editor: A

P-Editor: Yu HG

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