

Safety and efficacy of endoscopic mucosal resection for the treatment of early gastric cancer: A systematic study and meta-analysis

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ABSTRACT

Objective: Both gastrectomy and Endoscopic Resection (ER) are recognized as curative procedures for early-stage stomach cancer. Through this systematic review, we aimed to assess patient security, both early gastric cancer survivorship overall and disease-free cancer between ER and gastrectomy therapies.

Materials and methods: The databases PubMed, Embase and Cochrane Library were used to perform a literature search. This meta-analysis includes studies that contrasted early gastric cancer treated with ER and gastrectomy. Before March 2019, we looked for clinical trials. We conducted a systematic analysis using Stata 12.0 software.

Results: In this comprehensive review, nine papers were analysed. ER, therapy was linked to fewer surgical complications (OR=0.47, 95% CI 0.34-0.65) and a shorter hospital stay (WMD=8.53, 95% CI 11.56 to 5.49). ER is carried out safely, reducing hospitalization and after-surgery issues instead of a gastropasty. Recurrence rates were more significant with ER therapy than gastrectomy (HR=3.56, 95% CI 1.86-6.84), primarily for only ER therapy, resulting in the development of metachronous gastric cancers. However, ER may once more be used to effectively treat most metachronous stomach cancers and adverse effects on early-stage gastric cancer patients' overall survival. ER and gastrectomy, overall survival rate remained constant (HR=0.84, 95% CI 0.63-1.13).

Conclusion: Early gastric cancer curative treatment is acceptable with an ER or a gastrectomy. ER is superior to early gastric cancer treatment with gastrectomy patients that meet the requirements of ER therapy. However, overall survival rates are comparable, there are fewer postoperative problems, and the period of stay is shorter.

Keywords: gastric cancer, endoscopic mucosal resection, recurrence, systematic review, overall survival, otolaryngology, public health

INTRODUCTION

The 5th largest cause of mortality globally a 3rd leading contributor to cancer related mortality is death from cancer is gastric cancer and frequent malignant tumours. The percentage of Early Gastric Cancer (EGC) patients dated rising as endoscopic screening technology has advanced and public awareness of early diagnosis has improved, particularly in Japan and Korea. Regardless of incidence about lymph node metastases, EGC describes gastric cancer only in mucosa or submucosa. The recommended course for therapy for EGC had lymph node dissection and a radical gastrectomy, which had an acceptable oncological outcome and a low chance of recurrence [1]. Early Gastric Cancer (EGC) with poor prognoses for lymph node metastases is frequently treated with procedures for endoscopic resection, such as Endoscopic Submucosal Dissection (ESD) and Endoscopic Mucosal Resection (EMR). A lower recurrence rate, the potential for curative resection, and precise histological evaluation of resection margins are only a few of the benefits of ESD versus EMR [2].

Intestinal endoscopy has changed from being a diagnostic tool to now including therapy due to endoscopic diagnostic and treatment technology development. With minimal risk of lymph nodes and distant metastases, early cancers limited to the mucosa and submucosa, such as gastrointestinal adenomas, is treated with Extra Mural Distance (EMD). It is removing tumour tissue effectively and securely while also minimizing patient stress. EMD treating early detection of gastrointestinal cancer leads to fewer traumas, quicker recovery, and fewer problems than surgical resection [3]. ESD is a desirable therapeutic choice in older patients instead of gastrectomy to reduce operational morbidity due to their poor general health state and much additional comorbidity. It is not entirely apparent whether ESD is safe and practical for this population of patients. To recommend resection as a treatment choice is crucial to understand whether the rates for older and non-elderly people are equal [4]. No multicentre trials examined the advantages of ER and gastrectomy regarding survival. Only a few early gastric cancer single-centre studies compared ER with gastrectomy. The outcomes of the investigations, however, varied. A robust and efficient method was systematic evaluation and analysis. It could also achieve a systematic assessment of senior patients to suggest it as a therapy option while overcoming a study's slight sample size restriction [5].

Undifferentiated gastric malignancies behave biologically differently from differentiated gastric cancers. They often exhibit

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more significant rates of lymph node metastases and infiltrative growth. According to published meta-analysis studies, surgical resection of an EGC is not preferable to endoscopic resection [6]. Early oesophageal cancer therapy has significantly improved with the development of gastroscopy. Both Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD) are equally effective therapies as oesophageal cancer in the most recent guidelines from European Society for Medical Oncology Diagnosis, treatment, and Follow-up [7]. Traditional radical gastrectomy has been supplemented by Endoscopic Resection (ER), which comprises Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD) and obtain emerged as a successful method of treating EGC. It aims to complete an en-bloc resection and thorough histological analysis every lesion, while less invasive and more reasonable [8]. Early diagnostic and therapeutic gastrointestinal endoscopy can prevent and treat many gastrointestinal cancers. It has been established that early screening in conjunction with removing precancerous lesions is an efficient way to lower incidence and mortality [9]. A carcinoma that is limited to the stomach mucosa and submucosa is considered to be early gastric cancer. From a pathologist's perspective, the conflict between high-grade dysplasia and intramucosal carcinoma was eventually categorized as high-grade mucosal neoplasm by the updated Vienna Classification, a classification system that unified the diagnosis and therapy of Gastro Intestinal (GI) epithelial neoplasm [10].

The paper explored and focused on distinctions between early-stage and late-stage outcomes, epidemiology, and gastric cancer risk factors. They go into endoscopic development and early detection of gastric cancer and precancerous tumours. The paper compared LECS using just endoscopic and only laparoscopic techniques, assessing the effectiveness also the safety of Laparoscopic and Endoscopic Cooperative Surgery (LECS) in patients with Esophagogastric Junction (EGJ), gastric, and duodenal lesions. The paper evaluated the successes and difficulties of integrating immunotherapeutic techniques with chemotherapeutic medicines to elucidate many elements in patients with metastatic disease of chemotherapy and immunotherapy Gastric Cancer (GC) [11-13]. Laterally Spreading Tumours (LSTs) more significantly above 20 mm in size might be difficult to remove endoscopically through the mucosa. At the initial Surveillance Colonoscopy (SC1), piecemeal EMR of these lesions causes significant risks of adenoma recurrence. A safe and efficient method to stop adenoma recurrence is Snare Tip Soft Coagulation (STSC) to clean up margins followed [14]. The paper assessed the efficiency and security of prophylactic clipping during Endoscopic Submucosal Dissection (ESD) and Endoscopic Mucosal Resection (EMR), which delayed bleeding and perforation [15]. The paper assessed the effectiveness also safety between Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD) in the management of Superficial Esophageal Cancer (SEC) [16]. The paper evaluated acupuncture's effect on gastrointestinal function recovery in postoperative Gastric Cancer (GC) patients [17]. The article followed Endoscopic Resection (ER) to look for early recurrence or metachronous lesions [18]. In treating superficial pharyngeal tumours, the meta-analysis examined effectiveness and safety of Endoscopic Submucosal Dissection (ESD) [19]. The paper proposed safety and viability about Underwater Endoscopic Mucosal Resection (UEMR) [20]. The paper compared Endoscopic Submucosal Excavation (ESE) with

Submucosal Tunnelling Endoscopic Resection (STER) as the removal of esophageal and gastric Submucosal Tumours (SMTs) inside of muscularis propria [21]. The paper used of Polyglycolic Acid (PGA) sheets in decreasing post-ESD bleeding following a submucosal endoscopic dissection for patients with Early-Stage Gastric Cancer (ESGC) that are at risk of bleeding after the procedure was evaluated by a thorough review of literature and meta-analyses [22].

The paper used Artificial Intelligence (AI) methods in stomach cancer to investigate their limitations and possible future applications [23]. The therapy for esophageal, gastric, and colorectal lesions, known as Endoscopic Submucosal Dissection (ESD), is determined [24]. The paper detailed meta-analysis to more accurately the efficiency of second-line Barrett's Esophagus (BE) patients with persisting dysplasia or Intestinal Metaplasia (IM) following Radio Frequency Ablation (RFA) [25]. The paper compared treating small rectal Neuroendocrine Tumours (NETs), the efficacy and safety of suction combined with endoscopic ESD and Endoscopic Mucosal Resection (EMR) [26]. In this meta-analysis, metaplasia, dysplasia, and early neoplasia are conditions in which EMR and ESD's safety and effectiveness are compared [27]. The low incidence of Lymph Node Metastasis (LNM) in Early Gastric Cancer (EGC) patients, further all patients requiring noncurative resection have surgery following Endoscopic Resection (ER) may be inflated [28]. The paper conducted thorough investigation and meta-analysis and evaluated every preventative efficacy of eliminating *Helicobacter (H) pylori* [29]. *Pylori* on growth endoscopic excision of early stomach cancer, metachronous stomach cancer. The paper proposed using an endo-knife and snare during Hybrid Endoscopic Resection (HYB-ER) [30].

MATERIALS AND METHODS

Search techniques

This systematic evaluation and analysis were executed and published according to a PRISMA statement. The terms that are being retrieved include early stomach cancer, early gastric cancer, endoscopic resection in addition to gastrectomy, "ESD", "EMR" and early gastric cancer, databases from searched PubMed, Embase, and the Cochrane Library. This meta-analysis comprised articles that compared endoscopic retroperitoneal early gastric cancer excision and gastrectomy. Before March 2019, they searched for clinical studies. They looked for pertinent material in clinical study references. After reading each article, experts choose qualified studies. The analysis comprised a total of nine investigations.

Standards to include and remove

Studies were included for systematic review if they satisfied the following criteria:

Research documented a minimum of one among clinical results, such as duration of stay, surgical complications, survival without disease, and overall survival. A comprehensive text on research was released in English. Excluded from consideration were studies with ineffective data extraction or incomplete text availability. Adenocarcinoma restricted a submucosa or mucosa (TNM stage 0-IIIB), newly diagnosed early gastric cancer, and therapy with Gastrectomy and ER were needed for patients to be included.

Patients with a prior gastrectomy met the exclusion criteria. All of the included studies underwent postoperative pathological examination. Pathological analysis indicated a clean surgical margin. Patients need other ER and gastrectomy if a clean surgical margin cannot be obtained. The research also eliminated individuals who required further gastrectomy.

Extraction of data

Two reviewers (Haidong Cheng and Liangliang An) independently extracted the data from every study included and agreed on all the data. The following information was taken out of their research, a list of authors, the year it was published, the study's location, the number of participants, the duration of their stay, postoperative problems, and their overall survival. Overall rates of disease-free survival were calculated using HR and a 95% confidence interval. This meta-analysis's papers that explicitly gave HR and 95% CI were some. If those included did not expressly give 95% CI and HR, they assessed that HR and 95% CI in previous trials. In addition, they calculated an average and variance if initial research contained the median, range, and patient count.

Evaluation quality of included studies

Two reviewers independently peer-reviewed their evaluation (Liangliang An and Haidong Cheng). The effectiveness used to assess a Methodological Index for Nonrandomized Studies (MINORS) clinical research combined and rate. Evaluating 12 factors, they determined a study's overall quality. The systematic review only included high-quality studies, those with 18 ratings.

Analytical statistics

A specific measure for non-randomized studies (the quality rating scale for Newcastle and Ottawa) is employed to evaluate the caliber of the study. A total of nine factors were evaluated for each research, covering three primary domains: comparability,

selection, and results. The overall Newcastle-Ottawa Score (NOS) varied from 0 (poor) to 9 (outstanding), with an NOS of ≥ 6 rating given to a high-caliber study.

Statistical analysis

The Stata 12.0 is statistics software used to conduct a systematic review [22, 23]. Statistics and the Q-test statistic were employed to assess for heterogeneity. They selected a perfect technique according to an integrated test for heterogeneity. They utilized a homogeneous ($p=0.1$); a fixed effects data consolidation model would be appropriate. All study's results are heterogeneous ($p=0.1$) and a random effect usage of a data analysis model. Subgroup analysis by ER treatment indication and Endoscopic Technique (ESD or EMR) permitted to further investigation the causes of interstudy heterogeneity. Sensitivity research was done to assess the stability of a result, excluding individual papers. With the use of Begg's test, publication bias was evaluated. Significant data were those with a p-value of 0.05.

RESULTS

Assessment and study selection and quality

The results of this search method produced 423 possible articles. 323 reports were disregarded after title and abstract screening. 70 papers were ignored after reviewing the study because they were reviews, editorials, or case reports. The lack of a control group led to an exclusion of 11 pieces after reading an entire text. 7 were disqualified for failing to produce needed results. Due to identical patients being included in several investigations, 3 reports were disregarded. Figure 1 shows a process for choosing this research. 9 articles regarded as being of good quality were included in an analysis. Tables 1 and 2 show the significant attributes and study quality ratings.

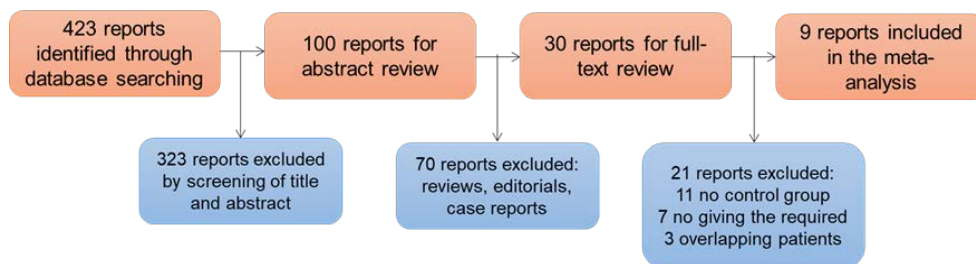


Fig. 1. Flowchart for screening articles

Tab. 1. Meta-analysis included papers' characteristics

Study	Gender (M/F)	Age (Years)	Number	Group	Type of Study	Study Period	ER Indication
Tsuyoshi EtOH	27/17	84.4	49	ER	Retrospective study	1085–1999	Absolute indication
	31/19	82.5	43	Gastrectomy		-	
Philip Chiu	49/27	66(14–88)	77	ER	Retrospective cohort study	1993–2010	Mucosal or submucosal involvement
	23/19	67(33–84)	40	Gastrectomy		-	
Kwi-Sook Choi	127/44	59.3 (9.1)	172	ER	Retrospective Propensity-score matching analysis	1997–2002	Intramucosal Gastric cancer
	286/91	58.4(10.3)	379	Gastrectomy		-	
Takeshi Yamashina	40/14	71.5 (54–89)	45	ER	Retrospective study	1998–2012	Mucosal or submucosal involvement
	12-Nov	69(39–76)	15	Gastrectomy		-	

Dae Yong Kim	94/49	63.0(10.3)	147	ER	Retrospective study	2004–2007	Absolute Criteria (35) Expanded criteria (107)
	54/17	54.7(11.0)	77	Gastrectomy		-	
Chan Park	211/91	64.5 (3.8)	309	ER	Retrospectively analyzed the clinical data	2007–2012	Expanded indication
	13/65	54.1 (3.3)	202	Gastrectomy		-	
Ju Choi	191/61	62(54–68)	265	ER	Retrospective cohort study	2002–2007	Absolute indication
	90 /26	62(54–66)	119	Gastrectomy		-	
Young Kim	122/43	62(54–70)	164	ER	Prospectively	2001–2009	Expanded indication
	217/77	601(52–68)	291	Gastrectomy	Medical data gathered	-	
Sara Na-jmeh	23-May	74(40–86)	35	ER	Prospectively collected database	2007–2014	Expanded Indication
	24/15	71(34–82)	39	Gastrectomy		-	

Tab. 2. Methodological Index for Nonrandomized trials (MINORS) was used to determine the clinical trials' quality scores

Study	M	N	O	P	Q	R	S	T	U	V	W	X	Quality Scores
Tsuyoshi Etoh	1	0	2	0	2	0	1	1	2	2	0	1	21
Kwi-Sook Choi	1	1	2	0	0	2	1	1	1	2	0	2	17
Philip Chiu	1	1	2	0	2	2	1	2	1	2	0	1	22
Dae Yong Kim	1	0	2	0	2	2	1	2	2	2	0	0	20
Takeshi Yamashina	1	1	2	0	2	2	1	2	1	2	0	1	21
Ju Choi	1	1	2	0	0	0	1	2	0	2	1	1	19
Chan Park	1	0	2	0	1	1	1	1	1	2	1	0	23
Young Kin	1	1	2	0	0	1	1	1	0	2	0	0	24
Sara Naimeh	1	2	2	2	0	1	1	2	1	2	2	1	19

(**Note:** M, Clearly Stated Goal; U, A suitable control group; T, Prospective Calculation of Study Size; N, Consecutive Patients Included; O, prospective data gathering P, their intended endpoints; S, Loss to Follow-Up 5%; Q: Objective evaluation of a study's endpoint; V, groups out of modern era; R, a follow-up time according to their objectives; W, Baseline Group Equivalence; X, Sufficient statistical analysis. The responses are given a score of 0 (not reported), 1 (written but inadequately), or 2 (registered and sufficient))

Duration of stay

5 researches, as shown in figure 2, provided information on a duration of stay. Adopting a significant degree of variability requires using a random-effect model ($I^2=91.2\%$, $p=0.000$). Every

duration of stay varied significantly between early gastric cancer therapies with ER and gastrectomy. The length of stay was shorter following ER therapy than following gastrectomy (WMD=8.53, 95% CI 11.56 to 5.49).

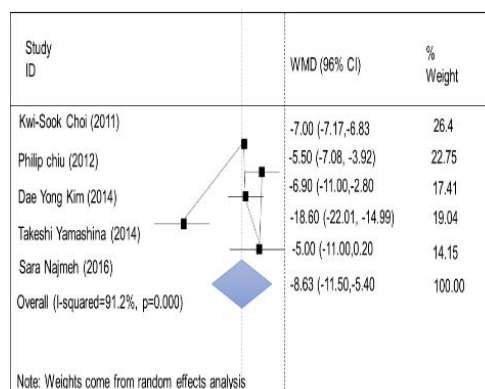


Fig. 2. Meta-analysis the duration of stays, ER, and gastrectomy therapies resulted a significantly shorter length of stay

Complications following surgery

All nine studies included postoperative complications, as shown in figure 3. Utilizing a fixed-effects model, is no discernible heterogeneity ($I^2=91.2\%$, $p=0.058$). Gastrectomy treatment had a

greater incidence of postoperative complications than ER therapy. Complications differed significantly, with increased indication and ESD in the subgroup.

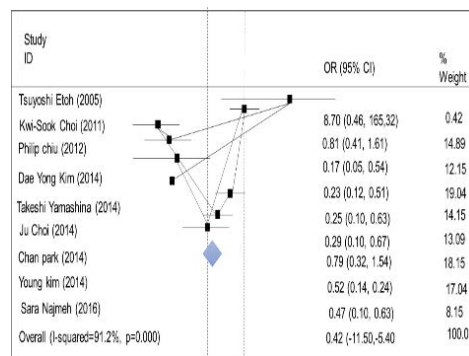


Fig. 3. Meta-analysis of postoperative complications, gastrectomy therapy resulted in more problems than ER treatment

Disease-free survivability

Disease-free survival was examined in five trials for this meta-analysis. Since no heterogeneity was found, using a fixed-effect model

was detected ($I^2=45.1\%$, $p=0.122$). Patients with ER therapy had a greater recurrence incidence than those who underwent gastrectomy treatment, as shown in figure 4.

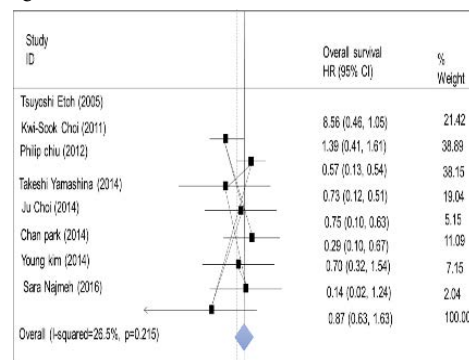


Fig. 4. Meta-analysis of patients that survived disease-free ER therapy had a higher recurrence rate than gastrectomy therapy

The findings showed ER therapy had a considerably greater recurrence rate than gastrectomy surgery. It was probably caused by a layer of stomach mucosa still there, which may include regions where metachronous developing stomach cancer increased. After ER, patients with early gastric cancer should consider additional treatments for recurrence lesions; ER and gastrectomy had similar early gastric cancer overall survival rates, according to recent research, and there were no adverse effects following subsequent metachronous lesions and endoscopic procedures. Every disease-free survival rate after ER and gastrectomy varied significantly into

subgroups of enlarged indication and ESD.

General survival

The overall survival statistics were published in eight investigations, as shown in figure 5. The model was a fixed-effect model because an absence about considerable heterogeneity ($I^2=26.5\%$, $p=0.215$). Gastrectomy and ER showed comparable overall survival rates (HR=0.87, 95% CI 0.63-1.63). There was no noticeable variation in overall survival across each subgroup in these analyses.

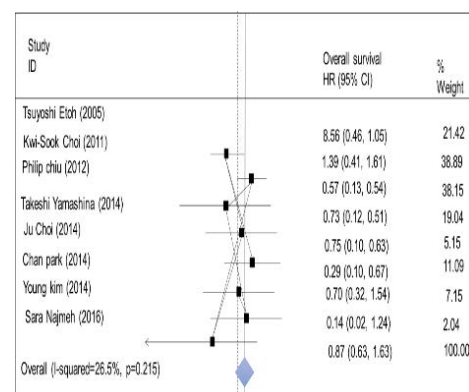


Fig. 5. Overall survival in a meta-analysis of ER and gastrectomy procedures was identical

Bias in publications

Using Begg's test, publication bias was assessed in light of postoperative complications. Nine papers in this meta-analysis showed no publication bias ($p=0.835$). Figure 6 shows their studies' fun-

nel plot analysis. Sensitivity analysis further revealed this pooled overall survival HR was not considerably impacted by leaving out any particular research (Figure 7).

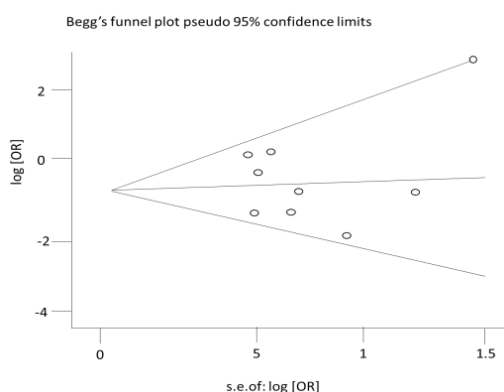


Fig. 6. Standard error by log relative risk is shown in a funnel plot

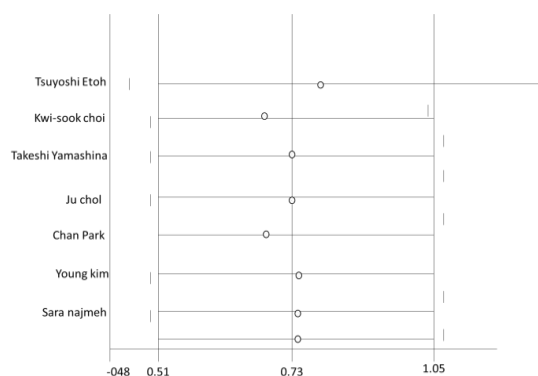


Fig. 7. Analysis of overall survival sensitivity

DISCUSSION

Since the invention of digestive endoscopic procedures, more early cases of stomach cancer without any symptoms are discovered. As a usual course of therapy for early stomach cancer, gastroplasties is performed. But because of its low level of invasiveness and improved post-procedure quality of life, ER is accepted in some early cases of gastric cancer. In recent years, minimum therapy treatment for early gastric cancer has developed into include ER.

Additionally, ulcerative adenocarcinoma of a differentiated type features UL (-), clinically classified as T1a, the depth of invasion has a diameter of less than ≤ 2 cm, is suggested a candidate for ER as a routine therapy. Tumours that have been clinically determined to be T1a are (a) distinct-type, UL (-), but larger than 2 cm in diameter, (b) differed in kind, UL (+), dimension above ≤ 3 cm, and (c) the UL (-) undifferentiated kind, with a diameter of ≤ 2 cm. When early gastric cancer satisfies the criteria, ER is a minimally invasive therapy. Although the clinical effects of ER are still debatable, some new findings indicate that lymph node metastases in early gastric cancer may happen following ER treatment. As a result, the efficacy of ER in treating early stomach cancer is still debatable. This meta-analysis was performed on ER results and included data from several other researches.

There was ER and gastrectomy procedures were investigated in a total of nine experiments and publications in a meta-analysis. According to ER care, this meta-analysis offered certain benefits, including a considerably shorter hospital stay and decreased surgical complication rates. Additionally, overall survival rate was not noticeably different for early gastric cancer gastrectomy and ER treatments: overall survival, surgical complications, and duration

of stay findings aligned with prior meta-analyses. Recurrence rates for ER were 4.7%-11.1%, while those for gastrectomy were 0.0%-1.1%, respectively, demonstrating that ER therapy had a substantially higher recurrence rate than gastrectomy therapy. According to these findings, ER group's chance of tumour recurrence was noticeably more significant than the surgical group's. It was most likely caused by the presence of remaining gastric mucosa, which may include regions that are more susceptible to an occurrence, such as metachronous stomach cancer, those that have intestinal metaplasia, and mucosa with atrophic gastritis. Patients with early gastric cancer should consider additional treatments for recurrence lesions after ER; ER and gastrectomy treatment had similar overall survival rates for early gastric cancer; however, recent trials did not show any adverse outcomes following subsequent metachronous lesions or endoscopic procedures. Additionally, stomach metachronous cancer had no impact on overall survival.

CONCLUSIONS

In conclusion, gastrectomy and ER are suitable curative procedures for early gastric cancer. The similar overall survival, lesser surgical complications, and shorter hospital stay make ER more advantageous than gastrectomy for early-stage gastric cancer patients that satisfy requirements for ER treatment. The scope of this meta-analysis has several restrictions. One potential element that could contribute to outcome heterogeneity was extrapolating the HR of overall survival. And only fully published research was considered in this meta-analysis. Meta-analysis excluded unpublished studies from consideration. This analysis only included English-language research because the study was searched with a language constraint.

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