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# A meta-analysis of the impact on gastrectomy versus endoscopic submucosal dissection for early stomach cancer

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**Abstract**

Background:
We conducted a meta-analysis to assess the impact of gastrectomy versus endoscopic submucosal dissection for early stomach cancer.
There are-now-a-variety-of-viewpoints-on-gastrectomy-versus-endoscopic-submucosal-dissection-for-early-stomach-cancer,-and-there-are-not-many-thorough-assessments-that-are-pertinent.
Methods:
A-systematic-literature-search-up-to-July-2022-was-performed-and-2456-related-studies-were-evaluated.-The-chosen-studies-comprised-15461-early-stomach-cancer-subjects-who-participated-in-the-selected-studies'-baseline-trials;-6503-of-them-used-the-endoscopic-submucosal-dissection, while 8958 used gastrectomy. Odds ratio (OR), and mean difference (MD) with 95% confidence intervals (CIs) were calculated to assess the effect of the gastrectomy versus endoscopic submucosal dissection for early stomach cancer by the dichotomous, and contentious methods with a random or fixed effect model.
Results:
The use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survivals (OR, 0.59; 95% CI, 0.45-0.77, p<0.001), lower the 5-year overall survival in propensity score-matched patients (OR, 0.49; 95% CI, 0.41-0.59, p<0.001), higher recurrences (OR, 6.99; 95% CI, 5,03-9.70, p<0.001), and higher synchronous lesion (OR, 7.24; 95% CI, 2.78-18.83, p<0.001), and higher metachronous lesion (OR,10.05; 95% CI, 6.44-15.67, p<0.001) compared to the gastrectomy for early stomach cancer.
However, no significant difference was found between submucosal dissection and gastrectomy for early stomach cancer in recurrence-free survival (OR, 0.74; 95% CI, 0.54-1.00, p=0.05), disease-free survival (OR, 0.43; 95% CI, 0.16-1.16, p=0.10), and disease-specific survival (OR, 1.05; 95% CI, 0.38-2.89, p=0.92).
Conclusions:
The use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survival, lower 5-year overall survival in propensity score-matched patients, higher recurrences, higher-synchronous lesion, and higher metachronous lesion, however, no significant difference was found in recurrence-free survival, disease-free survival, and disease-specific survival compared to the gastrectomy for early stomach cancer. The small number of studies in several comparisons calls for care when analyzing the results.

**Keywords:** synchronous lesion; endoscopic submucosal dissection; 5-year overall survival; disease-free survival; disease-specific survival; recurrence; recurrence-free survival; and metachronous lesion

## Introduction

The third most common cancer fatality (10%) and the fifth most prevalent malignancy are stomach cancers. [1, 2] Regardless of lymph node involvement, early stomach cancer is described as carcinoma that is restricted to the mucosa or submucosa. Historically, the sole curative method for treating early stomach cancer was a radical surgical gastrectomy with lymph node dissection. [3] Radical surgery, however, has been linked to increased morbidity and mortality as well as a decline in quality of life. [4, 5] Endoscopic mucosal resection and endoscopic submucosal dissection are two components of endoscopic resection. For early stomach cancer that was less than 15mm in size, endoscopic mucosal excision was initially advised. [6] The accepted criteria for endoscopic mucosal excision currently include less than 2 cm of well-differentiated or moderately differentiated adenocarcinoma that is restricted to the mucosa and shows no signs of ulceration or lymphovascular invasion. [7] The potential for a limited histological examination, particularly if en-bloc resection was not completed, would be the greatest barrier to the widespread adoption of endoscopic mucosal resection in early stomach cancer. To get over the constraints of endoscopic mucosal resection, endoscopic submucosal dissection was developed. By dissecting the submucosal layer with a needle knife during an endoscopic submucosal dissection, a bigger en-bloc resection can be accomplished. When compared to endoscopic mucosal resection, endoscopic submucosal dissection raised the rates of en bloc, histologically complete, and curative resection while decreasing recurrence. [8] The proposed enlarged indication for endoscopic submucosal dissection was put forth by Gotoda et al. in 2001. [9] Four distinct criteria make up the Japanese Stomach cancer Association's enlarged indication: (a) differentiated intramucosal cancer, without ulcerative findings, larger than 2 cm; (b) differentiated intramucosal cancer, with ulcerative findings, larger than 3 cm; (c) undifferentiated intramucosal cancer, without ulcerative findings, smaller than 2 cm; and (d) minimal (500 m from the muscularis mucosa) submucosal invasive cancer, differentiated type, larger than 3 cm. [10-14] Though numerous studies have compared the effects of endoscopic submucosal dissection with those of surgical treatment for early stomach cancer, their findings have been inconsistent and their patient populations for both procedures have been heterogeneous. [10-14] To compare the 5-year overall survival rate, disease-specific survival rate, disease-free survival rate, and recurrence-free survival rate of endoscopic submucosal dissection compared to gastrectomy in the treatment of early stomach cancer, a systematic review and meta-analysis were carried out. The study's objective was to determine how endoscopic submucosal dissection versus gastrectomy might affect early stomach cancer.

## Method

### Eligibility criteria

To create a summary, the study of the endoscopic submucosal dissection in comparison to gastrectomy was selected. The analysis of the impact of gastrectomy versus endoscopic submucosal dissection for early stomach cancer was the major goal of the study. [15]

### Information sources

The main goals of the current meta-analysis were to evaluate the influence of various outcomes of gastrectomy versus endoscopic submucosal dissection for early stomach cancer. Every selected study involved humans and in any language. Inclusion was unaffected by study size. The publications list was purged of review articles, comments, and research that didn't offer a way to quantify a connotation. The complete course of the study is shown in Figure 1. The following publications were encompassed in the meta-analysis when the inclusion criteria were encountered:

1. The study was either a controlled trial, observational, prospective, or retrospective study.
2. Early stomach cancer topics made up the intended subjects.
3. The intervention program included gastrectomy with an endoscopic submucosal dissection.
4. The study contrasted the gastrectomy versus endoscopic submucosal dissection for early stomach cancer.

The significance of comparison outcomes was not highlighted in studies, and studies that did not examine the effects of endoscopic submucosal dissection in early stomach cancer subjects, research on early stomach cancer without endoscopic submucosal dissection or gastrectomy, and research on early stomach cancer without endoscopic submucosal dissection were excluded from consideration.

### Search strategy

A protocol of search approaches was developed following the PICOS concept, and we characterized it as follows: topics for early stomach cancer, P; Endoscopic submucosal dissection technique is the"intervention" or "exposure," whereas the "comparison" was endoscopic submucosal dissection compared to gastrectomy; 5-year overall survival, 5-year overall survival in propensity score-matched patients, synchronous lesion, metachronous lesion, recurrence, recurrence-free survival, disease-free survival, and disease-specific survival were the “outcomes” and finally there are no restrictions on the study's design. [16]

We lead a thorough search of the OVID, Embase, Cochrane Library, PubMed, and Google Scholar databases up until June 2022 using an arrangement of keywords and correlated terms for synchronous lesion, endoscopic submucosal dissection, 5-year overall survival, disease-free survival, disease-specific survival, recurrence, recurrence-free survival, and metachronous lesion as shown in Table 1. To avoid studies that did not show a relationship between the endoscopic submucosal dissection and gastrectomy in early stomach cancer individuals, all the papers that had been used were joined into an EndNote file, replicas were eliminated, and the title and abstracts were reviewed and amended.

### Selection process

A technique was developed following the epidemiological declaration, which was thereafter arranged and examined in the form of a meta-analysis.

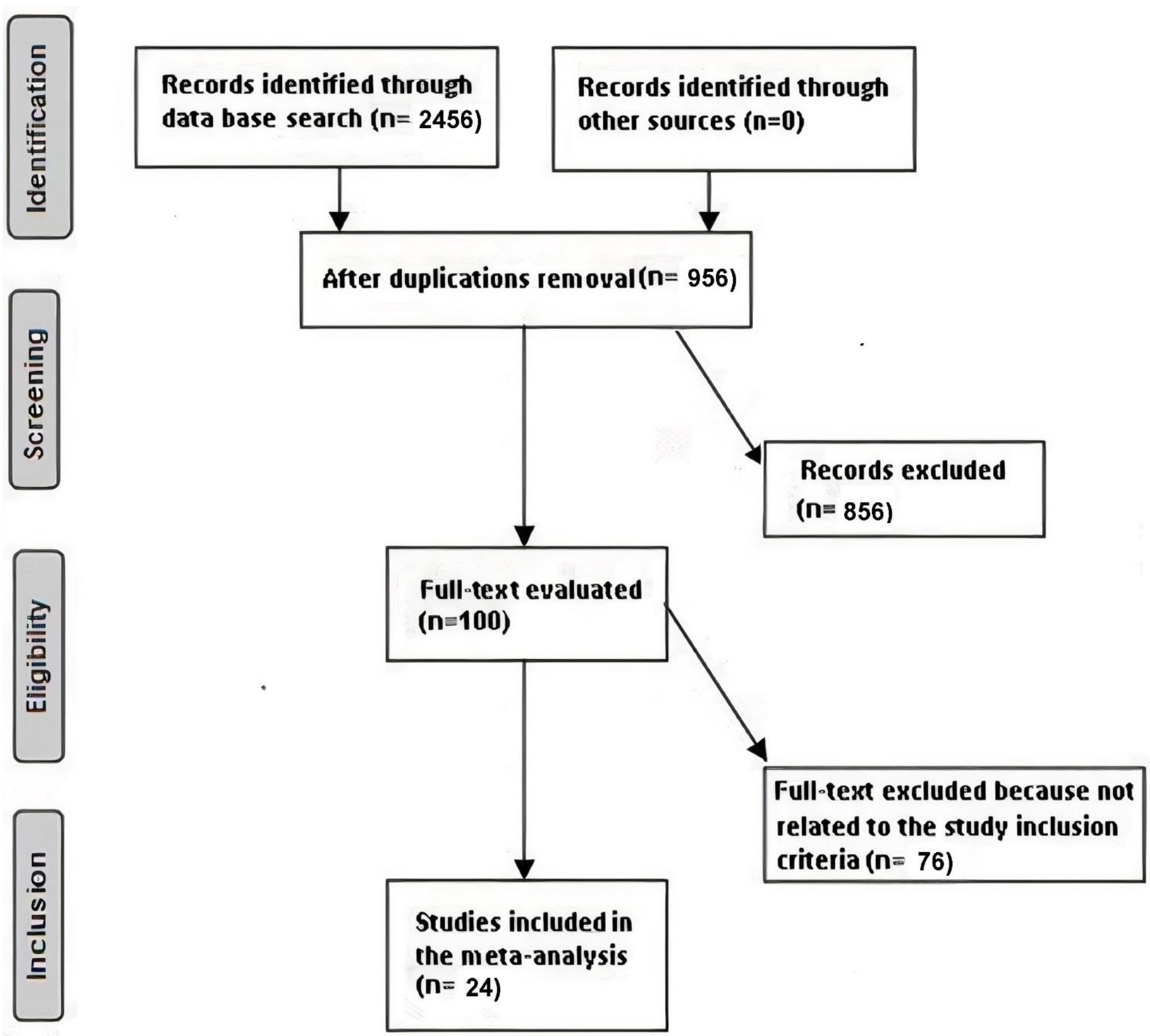


Figure 1 shows a flowchart of the study process.

**Data collection process**

The criteria used to gather the data included the last name of the primary author, the study period, the publication year, the nation or region, the populace type, the clinical and management physiognomies, the categories, the qualitative and quantitative assessment technique, the information source, the result assessment, and statistical analysis. [17]

**Data items**

When there were disparate findings from a single study founded on the appraisal of the influence of endoscopic submucosal dissection and gastrectomy in early stomach cancer, we independently collected the data.

**Study risk of bias assessment**

The author individually evaluated the methodology of the designated articles to ascertain the possibility of bias in each study. The methodological quality was evaluated using the "risk of bias instrument" from the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. Each study was sorted according to the appraisal criteria and given one of the three risks of bias itemized below: low: A study was rated as having a low risk of bias if all the quality standards were met; if one or more requirements weren't met or weren't encompassed, a study was rated as having a moderate risk of bias. The study was measured to have a high risk of bias in the case that one or more quality criteria were not met at all or were only partially met. The original article was revised to remove any inconsistencies.

**Effect measures**

Only studies that reported and assessed the influence of endoscopic submucosal dissection in comparison to gastrectomy were subjected to sensitivity studies. Sensitivity and subclass analysis was utilized to compare the gastrectomy versus endoscopic submucosal dissection for early stomach cancer.

**Table 1.** Search Strategy for Each Database

| Database | Search strategy |
|---|---|
| Pubmed | #1 "endoscopic submucosal dissection"[MeSH Terms] OR "early stomach cancer"[All Fields] OR "gastrectomy"[All Fields] OR "recurrence"[All Fields]<br>#2 "recurrence-free survival"[MeSH Terms] OR "disease-free survival"[All Fields] OR "5-year overall survival new"[All Fields] OR "disease-specific survival"[All Fields]<br>#3 #1 AND #2 |
| Embase | 'endoscopic submucosal dissection'/exp OR 'early stomach cancer'/exp OR 'gastrectomy'/exp OR 'recurrence'<br>#2 'recurrence-free survival'/exp OR ' 5-year overall survival'/exp OR ' disease-free survival '<br>#3 #1 AND #2 |
| Cochrane library | (endoscopic submucosal dissection):ti,ab,kw (early stomach cancer):ti,ab,kw OR (gastrectomy) :ti,ab,kw (Word variations have been searched)<br>#2 (recurrence):ti,ab,kw OR (recurrence-free survival):ti,ab,kw OR (5-year overall survival) :ti,ab,kw OR (disease-free survival) :ti,ab,kw (Word variations have been searched)<br>#3 #1 AND #2 |

**Synthesis methods**

The current meta-analysis used a random- or fixed-effect model with dichotomous and disputed techniques to compute the odds ratio (OR) and mean difference (MD) with a 95 percent confidence interval (CI). It was decided to calculate the I2 index, with a range of 0 to 100%. The values around 0%, 25%, 50%, and 75%, respectively, showed no, low, moderate, and high heterogeneity. [18] However, additional characteristics that show a high degree of similarity between the included studies were also analyzed to confirm the employment of the correct model. The random effect was considered if I2 was 50% or above; if I2 was less than 50%, the likelihood of employing fixed influence rose. [18] However, additional characteristics that show a high degree of similarity between the included studies were also analyzed to confirm the employment of the correct model. A subclass analysis was completed by stratifying the first evaluation based on the previously specified outcome categories. A p-value of 0.05 was used in the analysis to indicate statistical significance for differences across subcategories.

**Reporting bias assessment**

Publication bias was assessed both qualitatively and statistically using the Egger regression test and funnel plots that display the logarithm of ORs vs their standard errors (publication bias was considered present if p 0.05). [19]

**Certainty assessment**

Two-tailed tests were used to analyze all p-values. The graphs and statistical analysis were created using Reviewer Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

**Results**

From a total of 2456 related research that was examined, 24 articles published between 2012 and 2022 that fit the inclusion criteria and were encompassed in the meta-analysis were selected. [20-43] Table 2 presents the findings from these studies. 15461 early stomach cancer subjects participated in the selected studies' baseline trials; 6503 of them used the endoscopic submucosal dissection, while 8958 used gastrectomy. There were 40 to 3363 subjects present when the trial first began. 21 studies presented data organized by the 5-year overall survivals, 8 studies presented data organized by 5-year overall survival in propensity score-matched patients, 12 studies presented data organized by recurrences, 8 studies presented data organized by synchronous lesion, 14 studies that

**Table 2. Characteristics of the selected studies for the meta-analysis**

| **Study** | **Country** | **Total** | **Endoscopic submucosal dissection** | **Gastrectomy** |
|---|---|---|---|---|
| Chiu, 2012 [20] | China | 114 | 74 | 40 |
| Park, 2014 [21] | Korea | 225 | 108 | 117 |
| Kim, 2014 [22] | Korea | 158 | 107 | 51 |
| Choi, 2015 [23] | Korea | 375 | 261 | 114 |
| Ryu, 2016 [24] | Korea | 225 | 81 | 144 |
| Cho, 2016 [25] | Korea | 461 | 288 | 173 |
| Pyo, 2016 [26] | Korea | 2563 | 1290 | 1273 |
| Fukunaga, 2017 [27] | Japan | 308 | 181 | 127 |
| Chang, 2017 [28] | Korea | 153 | 74 | 79 |
| Shin, 2017 [29] | Korea | 275 | 175 | 100 |
| Gong, 2017 [30] | Korea | 79 | 40 | 39 |
| Park, 2018 [31] | Korea | 493 | 111 | 382 |
| Jeon, 2018 [32] | Korea | 617 | 342 | 275 |
| Lee, 2018 [33] | Korea | 1823 | 907 | 916 |
| Hahn, 2018 [34] | Korea | 1988 | 786 | 1202 |
| Bausys, 2019 [35] | Lithuania | 260 | 42 | 218 |
| Hong, 2020 [36] | Taiwan | 127 | 26 | 101 |
| Guo, 2020 [37] | China | 40 | 20 | 20 |
| Pourmousavi, 2020 [38] | USA | 3363 | 786 | 2577 |
| Ahn, 2021 [39] | Korea | 711 | 328 | 383 |
| Quero, 2021 [40] | Italy | 84 | 42 | 42 |
| Hirasawa, 2021 [41] | Japan | 144 | 63 | 81 |
| Lee, 2022 [42] | Korean | 238 | 119 | 119 |
| Kim, 2022 [43] | Korean | 637 | 252 | 385 |
| | **Total** | **15461** | **6503** | **8958** |

presented data organized by metachronous lesion, 10 studies that presented data organized by recurrence-free survival, 9 studies that presented data organized by disease-free survival and 7 studies that presented data organized by the disease-specific survival.

The use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survivals (OR, 0.59; 95% CI, 0.45-0.77, p<0.001) with high heterogeneity ($I^2$ = 75%), lower the 5-year overall survival in propensity score-matched patients (OR, 0.49; 95% CI, 0.41-0.59, p<0.001) with moderate heterogeneity ($I^2$ = 50%), higher recurrences (OR, 6.99; 95% CI, 5,03-9.70, p<0.001) with low heterogeneity ($I^2$ = 38%), and higher synchronous lesion (OR, 7.24; 95% CI, 2.78-18.83, p<0.001) with no heterogeneity ($I^2$ = 0%), and higher metachronous lesion (OR,10.05; 95% CI, 6.44-15.67, p<0.001) with no heterogeneity ($I^2$ = 0%) compared to the gastrectomy for early stomach cancer as shown in Figures 2-6.

However, no significant difference was found between submucosal dissection and gastrectomy for early stomach cancer in recurrence-free survival (OR, 0.74; 95% CI, 0.54-1.00, p=0.05) with low heterogeneity ($I^2$ = 33%), disease-free survival (OR, 0.43; 95% CI, 0.16-1.16, p=0.10) with high heterogeneity ($I^2$ = 86%), and disease-specific survival (OR, 1.05; 95% CI, 0.38-2.89, p=0.92) with high heterogeneity ($I^2$ = 94%) as shown in Figures 7-9.

Stratified models could not be utilized to examine the influence of some factors on comparison outcomes, such as gender, age, and ethnicity, due to the dearth of data on these variables. No indication of publication bias was found (p = 0.87) after visual analysis of the funnel plot and quantitative assessments using the Egger regression test. The bulk of the included randomized controlled trials, however, were found to have subpar methodological quality, no bias in selective reporting, and scant outcome data.

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Chiu, 2012 | 59 | 74 | 36 | 40 | 3.3% | 0.44 [0.13, 1.42] | 2012 |
| Park, 2014 | 105 | 108 | 112 | 117 | 2.5% | 1.56 [0.36, 6.70] | 2014 |
| Kim, 2014 | 100 | 107 | 44 | 51 | 3.6% | 2.27 [0.75, 6.87] | 2014 |
| Choi, 2015 | 250 | 261 | 107 | 114 | 4.2% | 1.49 [0.56, 3.94] | 2015 |
| Ryu, 2016 | 69 | 81 | 140 | 144 | 3.4% | 0.16 [0.05, 0.53] | 2016 |
| Pyo, 2016 | 341 | 1290 | 694 | 1273 | 9.2% | 0.30 [0.25, 0.35] | 2016 |
| Cho, 2016 | 265 | 288 | 156 | 173 | 6.0% | 1.26 [0.65, 2.42] | 2016 |
| Shin, 2017 | 161 | 175 | 93 | 100 | 4.3% | 0.87 [0.34, 2.22] | 2017 |
| Gong, 2017 | 38 | 40 | 38 | 39 | 1.1% | 0.50 [0.04, 5.75] | 2017 |
| Fukunaga, 2017 | 45 | 181 | 78 | 127 | 7.2% | 0.21 [0.13, 0.34] | 2017 |
| Chang, 2017 | 71 | 74 | 76 | 79 | 2.1% | 0.93 [0.18, 4.78] | 2017 |
| Park, 2018 | 111 | 111 | 380 | 382 | 0.7% | 1.47 [0.07, 30.74] | 2018 |
| Jeon, 2018 | 331 | 342 | 270 | 275 | 3.8% | 0.56 [0.19, 1.62] | 2018 |
| Lee, 2018 | 874 | 907 | 894 | 916 | 6.8% | 0.65 [0.38, 1.13] | 2018 |
| Hahn, 2018 | 758 | 786 | 1168 | 1202 | 7.1% | 0.79 [0.47, 1.31] | 2018 |
| Bausys, 2019 | 29 | 42 | 161 | 218 | 5.6% | 0.79 [0.38, 1.62] | 2019 |
| Pourmousavi, 2020 | 448 | 786 | 1959 | 2577 | 9.2% | 0.42 [0.35, 0.49] | 2020 |
| Guo, 2020 | 19 | 20 | 20 | 20 | 0.6% | 0.32 [0.01, 8.26] | 2020 |
| Hirasawa, 2021 | 25 | 63 | 42 | 81 | 6.0% | 0.61 [0.31, 1.19] | 2021 |
| Ahn, 2021 | 232 | 328 | 299 | 383 | 8.3% | 0.68 [0.48, 0.95] | 2021 |
| Kim, 2022 | 237 | 252 | 375 | 385 | 5.0% | 0.42 [0.19, 0.95] | 2022 |
| **Total (95% CI)** | | **6316** | | **8696** | **100.0%** | **0.59 [0.45, 0.77]** | |
| Total events | 4568 | | 7142 | | | | |

Heterogeneity: Tau² = 0.19; Chi² = 79.75, df = 20 (P < 0.00001); I² = 75%
Test for overall effect: Z = 3.89 (P < 0.0001)

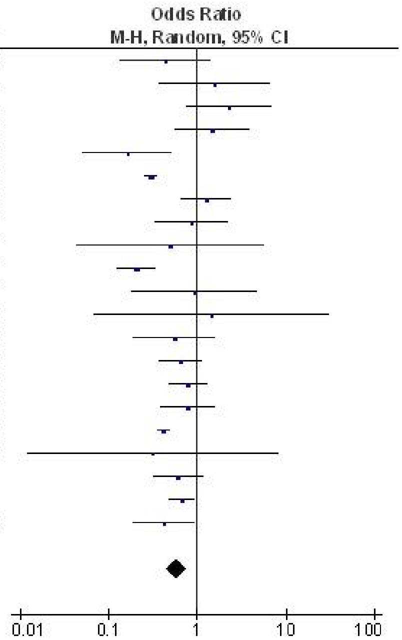


Figure 2. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the 5-year overall survival outcomes in early stomach cancer subjects

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Park, 2014 | 105 | 108 | 112 | 117 | 0.9% | 1.56 [0.36, 6.70] | 2014 |
| Cho, 2016 | 79 | 88 | 80 | 88 | 2.4% | 0.88 [0.32, 2.39] | 2016 |
| Pyo, 2016 | 206 | 611 | 341 | 611 | 66.3% | 0.40 [0.32, 0.51] | 2016 |
| Fukunaga, 2017 | 23 | 74 | 41 | 74 | 8.3% | 0.36 [0.19, 0.71] | 2017 |
| Shin, 2017 | 14 | 175 | 12 | 100 | 4.1% | 0.64 [0.28, 1.44] | 2017 |
| Lee, 2018 | 4 | 117 | 1 | 117 | 0.3% | 4.11 [0.45, 37.30] | 2018 |
| Ahn, 2021 | 157 | 218 | 173 | 218 | 14.2% | 0.67 [0.43, 1.04] | 2021 |
| Quero, 2021 | 18 | 42 | 21 | 42 | 3.5% | 0.75 [0.32, 1.77] | 2021 |
| **Total (95% CI)** | | **1433** | | **1367** | **100.0%** | **0.49 [0.41, 0.59]** | |
| Total events | 606 | | 781 | | | | |

Heterogeneity: Chi² = 14.09, df = 7 (P = 0.05); I² = 50%
Test for overall effect: Z = 7.77 (P < 0.00001)

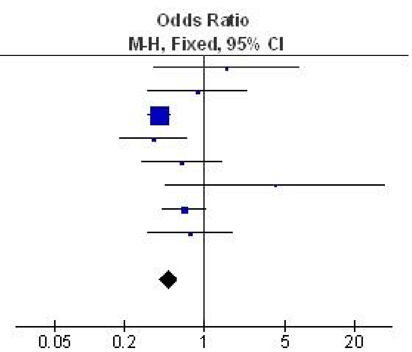


Figure 3. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the 5-year overall survival in propensity score-matched patients outcomes in early stomach cancer subjects

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Kim, 2014 | 5 | 107 | 0 | 51 | 1.8% | 5.53 [0.30, 101.90] | 2014 |
| Ryu, 2016 | 10 | 81 | 3 | 144 | 5.4% | 6.62 [1.77, 24.81] | 2016 |
| Cho, 2016 | 5 | 288 | 1 | 173 | 3.5% | 3.04 [0.35, 26.23] | 2016 |
| Chang, 2017 | 3 | 74 | 0 | 79 | 1.3% | 7.78 [0.40, 153.29] | 2017 |
| Park, 2018 | 13 | 111 | 3 | 382 | 3.4% | 16.76 [4.68, 59.97] | 2018 |
| Hahn, 2018 | 60 | 786 | 9 | 1202 | 18.8% | 10.96 [5.40, 22.21] | 2018 |
| Lee, 2018 | 75 | 907 | 11 | 916 | 28.7% | 7.42 [3.91, 14.06] | 2018 |
| Hong, 2020 | 2 | 26 | 6 | 101 | 6.5% | 1.32 [0.25, 6.95] | 2020 |
| Guo, 2020 | 4 | 20 | 2 | 20 | 4.6% | 2.25 [0.36, 13.97] | 2020 |
| Ahn, 2021 | 22 | 328 | 0 | 383 | 1.2% | 56.31 [3.40, 931.91] | 2021 |
| Lee, 2022 | 7 | 119 | 2 | 119 | 5.4% | 3.66 [0.74, 17.98] | 2022 |
| Kim, 2022 | 14 | 252 | 9 | 385 | 19.3% | 2.46 [1.05, 5.77] | 2022 |
| **Total (95% CI)** | | **3099** | | **3955** | **100.0%** | **6.99 [5.03, 9.70]** | |
| Total events | 220 | | 46 | | | | |

Heterogeneity: Chi² = 17.87, df = 11 (P = 0.08); I² = 38%
Test for overall effect: Z = 11.60 (P < 0.00001)

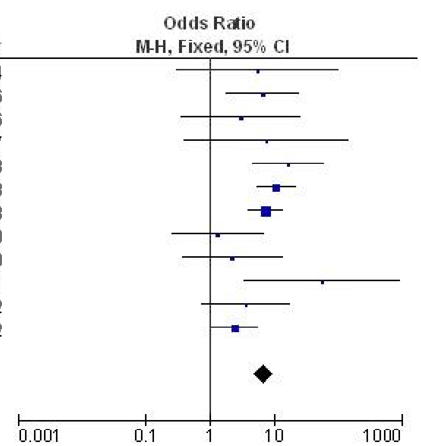


Figure 4. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the recurrence outcomes in early stomach cancer subjects

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Ryu, 2016 | 1 | 81 | 0 | 144 | 8.1% | 5.39 [0.22, 133.73] | 2016 |
| Gong, 2017 | 1 | 40 | 0 | 39 | 11.1% | 3.00 [0.12, 75.90] | 2017 |
| Shin, 2017 | 6 | 175 | 1 | 100 | 28.0% | 3.51 [0.42, 29.62] | 2017 |
| Park, 2018 | 2 | 111 | 0 | 382 | 5.0% | 17.47 [0.83, 366.51] | 2018 |
| Hahn, 2018 | 8 | 786 | 0 | 1202 | 8.9% | 26.26 [1.51, 455.59] | 2018 |
| Guo, 2020 | 1 | 20 | 0 | 20 | 10.6% | 3.15 [0.12, 82.16] | 2020 |
| Ahn, 2021 | 4 | 328 | 0 | 383 | 10.4% | 10.64 [0.57, 198.30] | 2021 |
| Kim, 2022 | 3 | 252 | 1 | 385 | 17.8% | 4.63 [0.48, 44.73] | 2022 |
| **Total (95% CI)** | | **1793** | | **2655** | **100.0%** | **7.24 [2.78, 18.83]** | |
| Total events | 26 | | 2 | | | | |

Heterogeneity: Chi² = 2.33, df = 7 (P = 0.94); I² = 0%
Test for overall effect: Z = 4.06 (P < 0.0001)

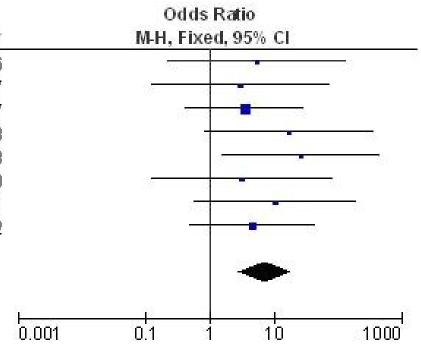


Figure 5. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the synchronous lesion outcomes in early stomach cancer subjects

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Park, 2014 | 12 | 108 | 2 | 117 | 8.6% | 7.19 [1.57, 32.90] | 2014 |
| Kim, 2014 | 10 | 107 | 1 | 51 | 6.2% | 5.15 [0.64, 41.42] | 2014 |
| Choi, 2015 | 16 | 261 | 1 | 114 | 6.6% | 7.38 [0.97, 56.33] | 2015 |
| Ryu, 2016 | 5 | 81 | 1 | 144 | 3.4% | 9.41 [1.08, 81.98] | 2016 |
| Gong, 2017 | 3 | 40 | 0 | 39 | 2.3% | 7.37 [0.37, 147.61] | 2017 |
| Chang, 2017 | 2 | 74 | 0 | 79 | 2.4% | 5.48 [0.26, 116.12] | 2017 |
| Shin, 2017 | 9 | 175 | 0 | 100 | 3.0% | 11.47 [0.66, 199.17] | 2017 |
| Lee, 2018 | 63 | 907 | 4 | 916 | 18.6% | 17.02 [6.17, 46.96] | 2018 |
| Park, 2018 | 1 | 111 | 2 | 382 | 4.5% | 1.73 [0.16, 19.23] | 2018 |
| Jeon, 2018 | 31 | 342 | 0 | 275 | 2.5% | 55.72 [3.39, 914.83] | 2018 |
| Hahn, 2018 | 27 | 786 | 5 | 1202 | 19.2% | 8.52 [3.27, 22.21] | 2018 |
| Guo, 2020 | 2 | 20 | 2 | 20 | 9.1% | 1.00 [0.13, 7.89] | 2020 |
| Ahn, 2021 | 12 | 328 | 0 | 383 | 2.2% | 30.29 [1.79, 513.63] | 2021 |
| Kim, 2022 | 10 | 252 | 3 | 385 | 11.5% | 5.26 [1.43, 19.31] | 2022 |
| **Total (95% CI)** | | **3592** | | **4207** | **100.0%** | **10.05 [6.44, 15.67]** | |
| Total events | 203 | | 21 | | | | |

Heterogeneity: Chi² = 11.84, df = 13 (P = 0.54); I² = 0%
Test for overall effect: Z = 10.17 (P < 0.00001)

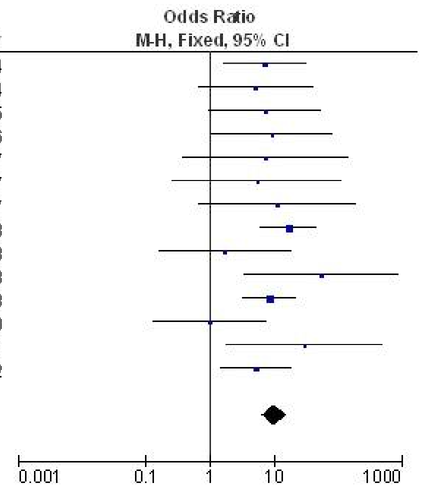


Figure 6. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the metachronous lesion outcomes in early stomach cancer subjects

| Study or Subgroup | Endoscopic submucosal dissection Events | Total | Gastrectomy Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Park, 2014 | 1 | 108 | 0 | 117 | 0.5% | 3.28 [0.13, 81.36] | 2014 |
| Choi, 2015 | 131 | 261 | 74 | 114 | 53.9% | 0.54 [0.35, 0.86] | 2015 |
| Cho, 2016 | 5 | 288 | 0 | 173 | 0.6% | 6.73 [0.37, 122.50] | 2016 |
| Shin, 2017 | 3 | 175 | 1 | 100 | 1.3% | 1.73 [0.18, 16.83] | 2017 |
| Lee, 2018 | 10 | 907 | 7 | 916 | 7.2% | 1.45 [0.55, 3.82] | 2018 |
| Jeon, 2018 | 8 | 342 | 2 | 275 | 2.3% | 3.27 [0.69, 15.52] | 2018 |
| Guo, 2020 | 18 | 20 | 19 | 20 | 2.0% | 0.47 [0.04, 5.69] | 2020 |
| Hong, 2020 | 3 | 26 | 20 | 101 | 7.6% | 0.53 [0.14, 1.94] | 2020 |
| Hirasawa, 2021 | 23 | 63 | 42 | 81 | 24.5% | 0.53 [0.27, 1.05] | 2021 |
| **Total (95% CI)** | | **2190** | | **1897** | **100.0%** | **0.74 [0.54, 1.00]** | |
| Total events | 202 | | 165 | | | | |

Heterogeneity: Chi² = 11.92, df = 8 (P = 0.15); I² = 33%
Test for overall effect: Z = 1.96 (P = 0.05)

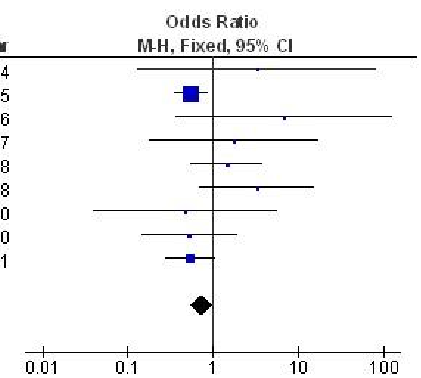


Figure 7. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the recurrence-free survival outcomes in early stomach cancer subjects

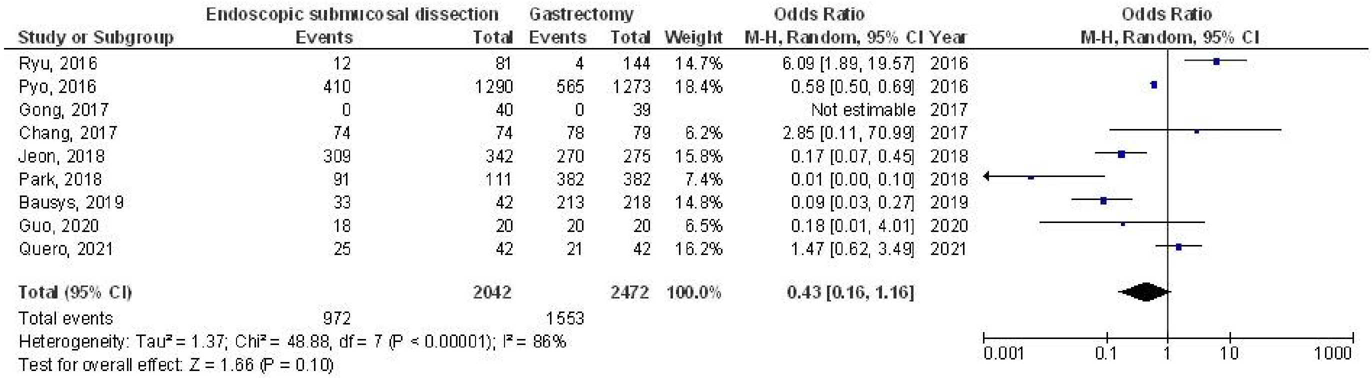


Figure 8. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the disease-free survival outcomes in early stomach cancer subjects

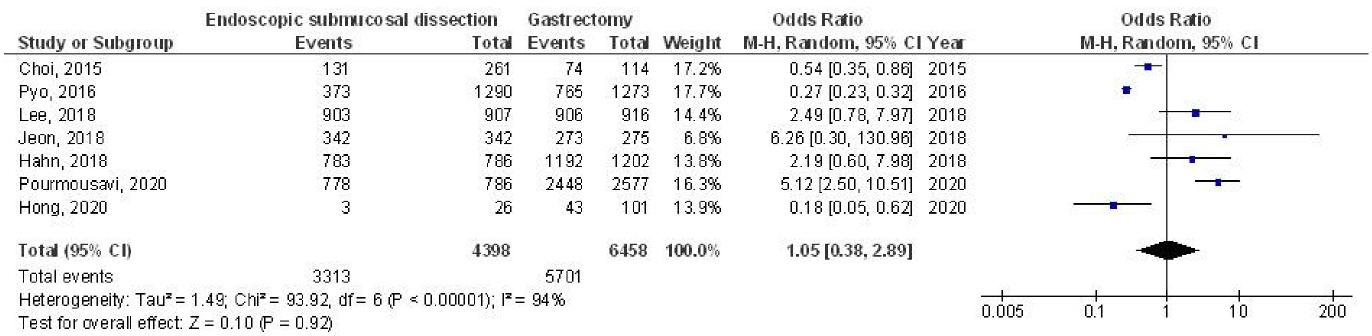


Figure 9. The effect's forest plot of endoscopic submucosal dissection vs gastrectomy on the disease-specific survival outcomes in early stomach cancer subjects

## Discussion

In the trials used for this meta-analysis, 15461 early stomach cancer subjects participated in the selected studies' baseline trials; 6503 of them used the endoscopic submucosal dissection, while 8958 used gastrectomy. [20-43] The use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survival, lower 5-year overall survival in propensity score-matched patients, higher recurrences, higher synchronous lesion, and higher metachronous lesion compared to the gastrectomy for early stomach cancer. However, no significant difference was found between submucosal dissection and gastrectomy for early stomach cancer in recurrence-free survival, disease-free survival, and disease-specific survival. The small number of studies in several comparisons calls for care when analyzing the results e.g. recurrence-free survival.

Following endoscopic submucosal dissection, there is a greater prevalence of recurring, synchronous, and metasynchronous lesions. Most typically, the middle or lower portion of the stomach is where primary early gastric malignancies first appear. With a distal gastrectomy, the entire high-risk section of the stomach is removed, leaving just the lower-risk portion. Additionally, endoscopic submucosal dissection enables the persistence of intestinal metaplasia and atrophic gastritis in the remaining mucosa after the procedure. [44] The 5-year overall survival rate would not be negatively impacted by repeating the endoscopic submucosal dissection if metachronous early gastric tumors are discovered after the procedure. In addition, endoscopic submucosal dissection is less intrusive than surgery, leading to a superior quality of life. Therefore, if metachronous lesions are found early and removed, the increased quality of life with endoscopic submucosal dissection over surgery may offset the minor risk of those lesions. Our findings support the earlier meta-analysis's finding that endoscopic resection had a greater recurrence and metachronous cancer rates than gastrectomy. [45, 46] In terms of en-bloc resection and recurrence rates, multiple pieces of evidence show that endoscopic submucosal dissection is preferable to endoscopic mucosal resection. [47, 48] Bleeding and perforation are the primary endoscopic submucosal dissection consequences, and both can be effectively treated intraprocedural in skilled hands. [49] However, anastomotic leakage, intestinal obstruction, and anastomotic stricture are among the surgical complications that frequently have a considerably greater influence on patients' quality of life, length of hospital stay, and mortality. [50, 51] Few studies met the inclusion requirements. Some studies omitted descriptions of the random allocation technique, allocation concealment, or blinding. Due to the significant likelihood of bias and the generally poor quality of the papers, the results were not very strong. The study's general conclusions were unaffected by a sensitivity analysis. To collect pertinent research data more thoroughly, improve the standard of the study, and provide reliable and accurate results, randomized controlled trials should be done precisely following methodological principles going ahead. Furthermore, there is a limited amount of published research on the simultaneous use of studies on endoscopic submucosal dissection and gastrectomy for early stomach cancer. Smaller control and intervention groups were utilized in the majority of the randomized controlled studies included in this study. We believe that these problems could be solved over time and with more research.

This meta-analysis demonstrated how endoscopic submucosal dissection and gastrectomy for early stomach cancer. More research is still needed to clarify these potential connections and compare the impact of endoscopic submucosal dissection and gastrectomy for early stomach cancer on the outcomes under discussion. Larger, more homogeneous samples are required for this investigation. This was also emphasized in a previous study that employed a related meta-analysis technique and found comparable advantageous outcomes for endoscopic submucosal dissection and gastrectomy for early stomach cancer. [52-57] Because our meta-analysis study was unable to determine whether differences in gender, age, and ethnicity are related to the outcomes, well-conducted randomized controlled trials are required to evaluate these factors as well as the combination of different gender, ages, ethnicities, and other variants of subjects.

In conclusion, the use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survival, lower 5-year overall survival in propensity score-matched patients, higher recurrences, higher synchronous lesion, and higher metachronous lesion compared to the gastrectomy for early stomach cancer. However, no significant difference was found between submucosal dissection and gastrectomy for early stomach cancer in recurrence-free survival, disease-free survival, and disease-specific survival.

**Limitations**

Because several of the studies included in this study were not encompassed in the meta-analysis, there may have been selection bias. The removed publications, nevertheless, did not encounter the requirements for inclusion in our meta-analysis. Furthermore, we were unable to determine whether factors such as age, gender, or ethnicity affected the outcomes. The study aims to compare the outcomes of the gastrectomy group and the endoscopic submucosal dissection group for early stomach cancer. The incorporation of data from earlier studies could have added bias due to incomplete or inaccurate data. Potential sources of bias included the nutritional status of the participants as well as their age and gender characteristics. Unfortunately, certain unpublished papers and missing data can bias the effect being studied.

**Conclusions**

The use of endoscopic submucosal dissection resulted in significantly lower 5-year overall survival, lower 5-year overall survival in propensity score-matched patients, higher recurrences, higher synchronous lesion, and higher metachronous lesion compared to the gastrectomy for early stomach cancer. However, no significant difference was found between submucosal dissection and gastrectomy for early stomach cancer in recurrence-free survival, disease-free survival, and disease-specific survival. The small number of studies in several comparisons calls for care when analyzing the results e.g. recurrence-free survival.

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