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# Efficacy and safety of esophageal stenting for esophageal perforation: a systematic review and meta-analysis

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## Abstract

**Background** Esophageal perforations are managed with endoscopic stenting. However, surgical repair is still employed in many centers, if they lack endoscopic services, or for complex perforations.

**Methods** We searched PubMed, Scopus, and Web of Science for relevant clinical trials and observational studies. Quality assessment was evaluated according to GRADE. The studies included were assessed based on the National Heart, Lung, and Blood Institute criteria. We included the following outcomes: leak after primary repair, operative repair after endoscopic therapy, stent migration, length of hospital stay (days), and mortality. We analyzed continuous data using mean differences and 95% confidence intervals (CI), while dichotomous data were analyzed using odds ratios and 95%CI. Statistical heterogeneity was assessed using the $I^2$ statistic.

**Results** Eight studies were analyzed and found to include 95 patients with esophageal perforation. Mortality rates decreased over time from 16.3% (Abbas, 2009) to 6.7% (Heel, 2020). Re-operative procedures were highest at 51.4%(D'Cunha, 2011) and lower in later studies. Stent migration rates varied from 16.2-22.3%. Leakage rates ranged from 8.8-16.2%. Hospital stays ranged from 5.0 days (D'Cunha, 2011) to 15.3 days (Law, 2017), with significant variability across studies.

**Conclusion** Esophageal stenting is considered an efficient and well-tolerated method for managing esophageal perforation.

**Keywords** Esophageal rupture, perforation, esophageal stenting

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Conflict of Interest: None

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## Introduction

Esophageal perforation is a severe, life-threatening condition that is most commonly associated with iatrogenic causes, such as surgery or endoscopic procedures, while spontaneous perforations also occasionally occur [1,2]. Boerhaave syndrome is a spontaneous longitudinal esophageal wall tear due to high intra-abdominal pressure combined with low intra-thoracic pressure, as in retching, trauma, seizures and defecation [3]. This tear usually occurs above the diaphragmatic esophageal hiatus, most commonly on the left side [4-6]. Rarely, malignancy can lead to esophageal perforation, often secondary to chemotherapy and/or radiation therapy. Law *et al* reported spontaneous rupture as the main cause of perforation, with one-third of cases related to malignant etiologies receiving chemotherapy.

Esophageal stenting has been used to treat patients with esophageal perforation to good effect, especially patients who are poor candidates for surgery [7-10]. However, esophagectomy or primary surgical repair for esophageal

perforation are still performed in many institutions, despite their high mortality and morbidity [11,12]. We performed a systematic review and meta-analysis to evaluate the efficacy and safety of esophageal stent placement to manage esophageal perforation.

## Materials and methods

Our study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13].

### Search strategy

We searched various electronic databases using the following strategy: ("esophageal rupture" OR "esophageal perforation" OR "Boerhaave's Syndrome") AND (stent).

### Study selection

We screened in the subsequent steps. First, we imported the data from research databases to a Microsoft Excel sheet using EndNote software. Then, we screened the articles' titles and abstracts in our Excel sheet. Finally, we screened the included studies from the second step in full text.

### Eligibility criteria

The inclusion criteria for study selection were:

- Study design: we included observational studies and randomized clinical trials, and we excluded other study designs, conference abstracts, meta-analyses, all animal studies, and reviews.
- Participants: patients with esophageal perforation.
- Intervention: esophageal stent placement.
- Outcomes: leak after primary surgical repair, need for surgery, stent migration, length of hospital stay (days), and mortality.

### Data collection

We searched Scopus, PubMed and Web of Science databases up to April 2024 for articles that matched our inclusion criteria. We collected baseline and demographic characteristics of the included participants, including author, year, age, sex, diagnosis of sepsis, and time from perforation to treatment (measured in h). The main outcomes for analysis included leak after primary repair, operative repair after endoscopic therapy, stent migration, length of hospital stay (days), morbidity and mortality. The data collection process was done using Microsoft Excel.

### Risk of bias assessment

We used the quality assessment tools from the National Heart, Lung, and Blood Institute (NHLBI) to assess the risk of bias in observational studies [14]. We followed The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Guidelines for assessing the quality of this study.

### Statistical analysis

We used Open Meta analyst [15]. Our study included dichotomous and continuous outcomes. We analyzed data using pooled proportion and a 95% confidence interval (CI) for all data. The homogeneous data were analyzed using a fixed-effects model, while heterogeneous data were analyzed using a random-effects model. To measure heterogeneity among the studies, we used the $I^2$ and the P-value of the chi-square tests [16]. Values of $P<0.1$ or $I^2>50\%$ were significant indicators of heterogeneity. We solved the inconsistency of heterogeneous outcomes using subgroup analysis, according to the duration of treatment or Cochrane's leave-one-out method [17].

## Results

### Summary of included studies

Our electronic search strategy is illustrated in Fig. 1. Ninety-five patients with esophageal perforation were evaluated from the 8 studies included in our analysis (Supplementary Table 1&2) [18-25]. All patients underwent esophageal stent placement to manage perforation. Their mean age was 57.65 years. Data from the included studies, patients' demographic data, number of patients with sepsis at diagnosis, and perforation-to-treatment time are presented in Table 1.

## Results of risk of bias

The quality assessment yielded an overall score of 9.5 of 14 according to the NHLBI tool for quality assessment. Supplementary Table 1 shows the quality assessment of the included studies in detail.

### Analysis of outcomes

#### *Leakage after primary repair*

The meta-analysis for leakage after primary repair used a binary fixed-effect model with the inverse variance method. The proportions varied across studies: Law [21] reported a leakage rate of 9.3% (95%CI 0.6-18.0%), while D'Cunha [22] found a higher rate of 20.9% (95%CI

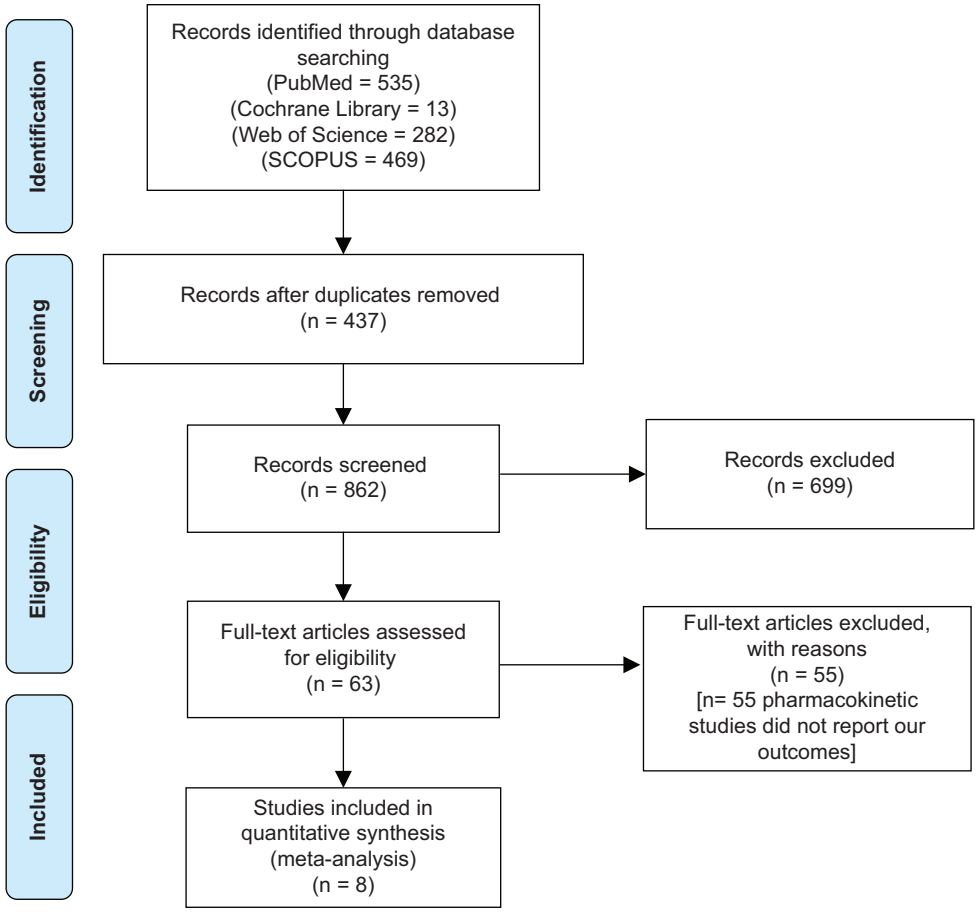


**Figure 1** PRISMA flow diagram of the literature search

**Table 1** Summary of the included studies and patients' demographic data

| Study [ref.] | Age (mean, SD) | Sex (male, female) | Sepsis at diagnosis (N, %) | Perforation to treatment time (mean, SD) |
|---|---|---|---|---|
| Law [19] | Mean: 66 years | Male: 28 (65.1%) | Not reported | Not reported |
| D'Cunha [22] | Mean: 60 years | Male: 26, Female: 11 | Not reported | Overall: median 6 days (range 0-420 days)<br>Leaks: median 7.5 days (range 1-420 days)<br>Perforations: median 2 days (range 0-15 days) |
| Heel [18] | Mean: 57 years<br>range: 13-87 years | Not explicitly stated | 12 of 33 patients (36%) | Median: 1 day (range 0-14 days) |
| Freeman [20] | Mean: 64 years<br>SD: 13 years | Not explicitly provided | 2 out of 29 patients (7%) | Mean: 26 h<br>SD: 39 h |
| Freeman [37] | Mean: 48 years<br>SD: 18 years | Not reported | 3 patients (16%) | Mean: 22 h<br>SD: 33 h |
| Abbas [21] | Mean: 62.1 years | Male: 77% (spontaneous), 41% (iatrogenic) | Not explicitly stated | Median: 12 h (range 1-120 h) |
| Glatz [24] | Mean: 67.4 years<br>SD: 14.2 years | Not explicitly reported | 6 patients (37.5%) | 4 patients (25%) had >48 h |
| Gray [23] | Not mentioned | Not mentioned | Not mentioned | Not mentioned |

*N, number; SD, standard deviation*

13.3-28.5%). Van Heel [18] reported 14.0% (95%CI 8.4-19.5%), Freeman [37] 12.1% (95%CI 7.3-16.9%), Freeman [20] 11.9% (95%CI 7.4-16.4%), and Glatz [24] 13.2% (95%CI 8.7-17.6%). All estimates were statistically significant with P-values <0.001 (Fig. 2).

### *Mortality*

Regarding mortality rates, the binary fixed-effect model analysis revealed diverse outcomes: Law [19] reported a mortality rate of 23.3% (95%CI 10.6-35.9%), whereas D'Cunha [22] showed a rate of 17.7% (95%CI 9.4-26.0%). Van Heel [18] had a rate of 18.6% (95%CI 11.5-25.8%), Freeman [37] 6.6% (95%CI 2.8-10.5%), Freeman [17] 5.6% (95%CI 2.3-9.0%), Abbas [21] 7.6% (95%CI 4.6-10.5%), Glatz [24] 7.7% (95%CI 4.8-10.6%), and Gray [23] 13.4% (95%CI 11.7-15.0%). All estimates were statistically significant with P-values <0.001 (Fig. 3).

### *Re-operative procedures*

The analysis of re-operative procedures, using a binary fixed-effect model, showed proportions ranging from Law [19] at 14.0% (95%CI 3.6-24.3%) to D'Cunha [22] at 24.9% (95%CI 16.2-33.6%). Van Heel [18] reported 17.9% (95%CI 11.4-24.4%), Freeman [37] 14.3% (95%CI 8.9-19.6%), Freeman [20] 13.8% (95%CI 8.8-18.7%), Abbas [21] 10.5% (95%CI 7.1-14.0%), and Glatz [23] 10.9% (95%CI 7.5-14.3%). All proportions were statistically significant with P-values <0.001 (Fig. 4).

### *Stent migration*

For stent migration, the binary fixed-effect model revealed proportions as follows: D'Cunha [22] at 16.2% (95%CI 4.3-28.1%), Van Heel [18] at 22.3% (95%CI 12.7-31.8%), Freeman [37] at 20.6% (95%CI 12.8-28.5%), and Freeman [20] at 20.7% (95%CI 13.5-27.9%). All estimates were statistically significant with P-values <0.001 (Fig. 5).

### *Hospital stay duration*

The meta-analysis of mean hospital stay duration used a continuous fixed-effect model with the inverse variance method. D'Cunha (2011) reported a mean stay of 5.0 days

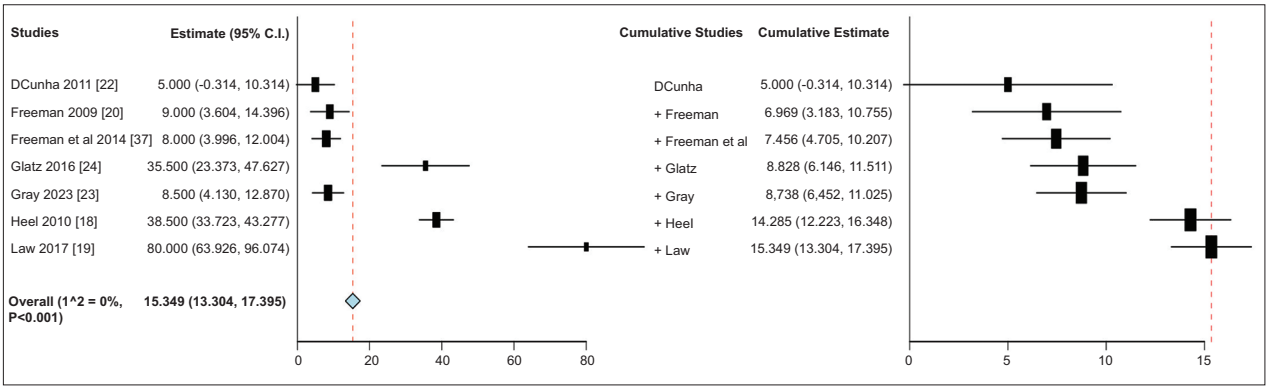


**Figure 2** Forest plot for leakage after primary repair
*C.I., Confidence Interval; Ev, event; Trt, total rate*

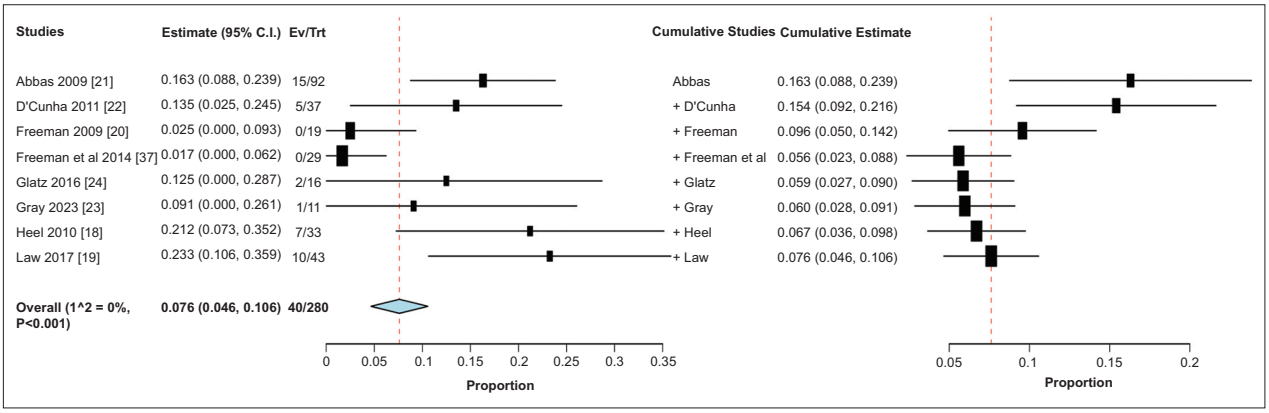


**Figure 3** Forest plot for mortality
*C.I., Confidence Interval; Ev, event; Trt, total rate*

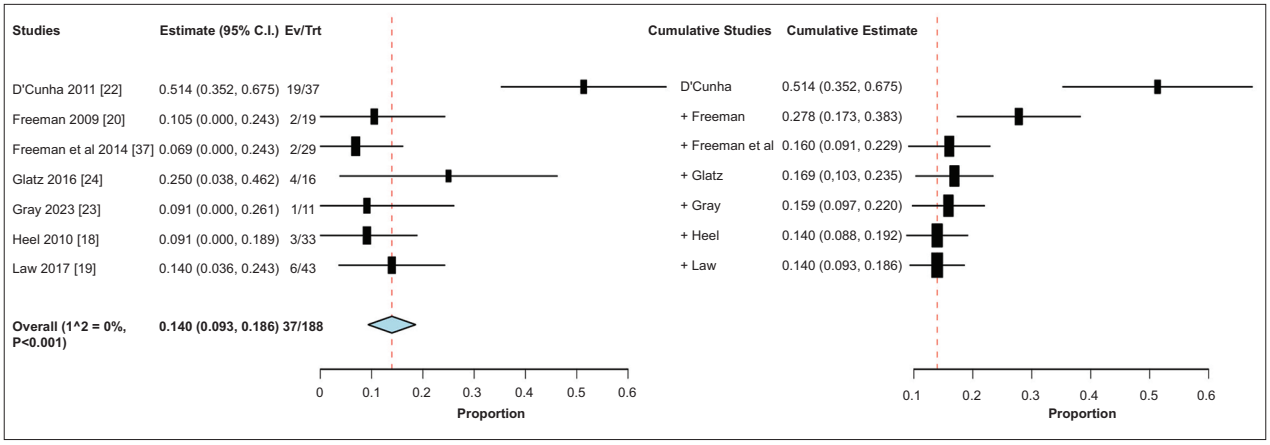


**Figure 4** Forest plot for re-operative repair
*C.I., Confidence Interval; Ev, event; Trt, total rate*

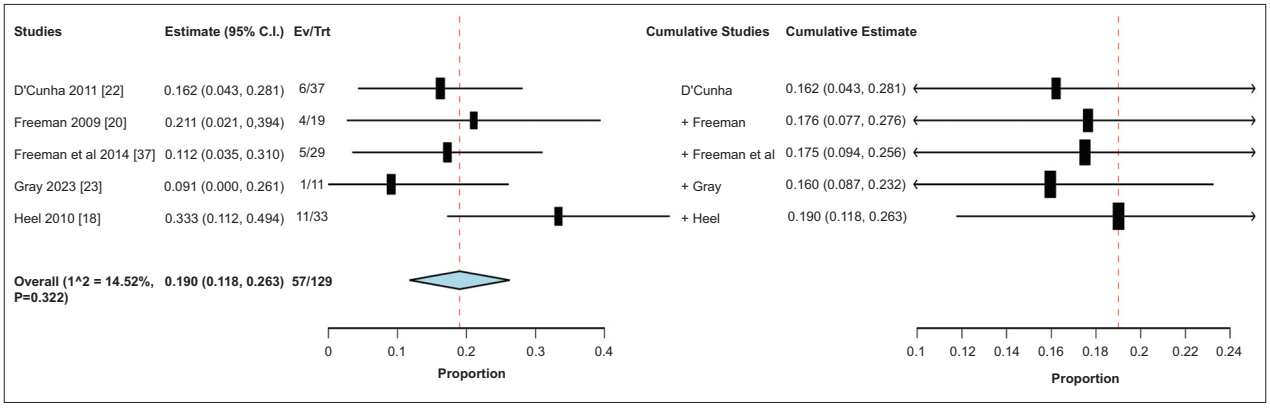


**Figure 5** Forest plot for stent migration
*C.I., Confidence Interval; Ev, event; Trt, total rate*

(95%CI 2.7-7.3). Freeman [20] reported a mean stay of 7.0 days (95%CI 3.2-10.8), Freeman *et al* [37] reported 7.5 days (95%CI 4.7-10.2), Glatz [24] reported 8.8 days (95%CI 6.1-11.5), Gray [23] reported 8.7 days (95%CI 6.5-11.0), Heel [18] reported 14.3 days (95%CI 12.2-16.3), and Law [19] reported 15.3 days (95%CI 13.3-17.4). All studies except D'Cunha had P-values <0.001 (Fig. 6).

## Discussion

Esophageal perforation, whether spontaneous or iatrogenic, is a severe condition traditionally managed by primary surgical repair. With advances in endoscopic techniques, esophageal stenting has emerged as a less invasive alternative, particularly beneficial for patients unsuitable for surgery. This meta-analysis evaluated the efficacy and safety of esophageal stenting for managing esophageal perforation, evaluating 8 studies that met our inclusion criteria.

Our analysis revealed a mortality rate associated with stenting of approximately 6.7% (95%CI 3.6-9.8%), which is lower compared to earlier studies. Stent migration was observed in 16.2-22.3% of patients, showing a consistent issue but with variability in reported rates. Leakage after primary repair ranged from 8.8% (95%CI 3.0-14.6%) to 16.2% (95%CI 12.1-20.3%), indicating a persistent challenge across studies. The mean hospital stay varied from 5.0 days (D'Cunha [22]) to 15.3 days (Law [19]), a notable variability, but generally reflecting a trend towards longer stays compared to earlier studies.

Primary repair in delayed diagnosis can be very challenging, because of severe tissue necrosis, and has a higher risk of leakage with mediastinal contamination [25]. Keeling *et al* reported a postoperative leak rate of approximately 30% [5]. Heel *et al* described a single-center prospective trial that reported the short-term effect of esophageal stenting in treating benign perforations [18]. The investigators suggested that the use of a temporary stent in benign esophageal perforation was effective and well-tolerated, and could provide an alternative option to operation. Freeman *et al* found that esophageal stenting in patients with acute esophageal perforation is as effective as surgical repair, compared to propensity-matched

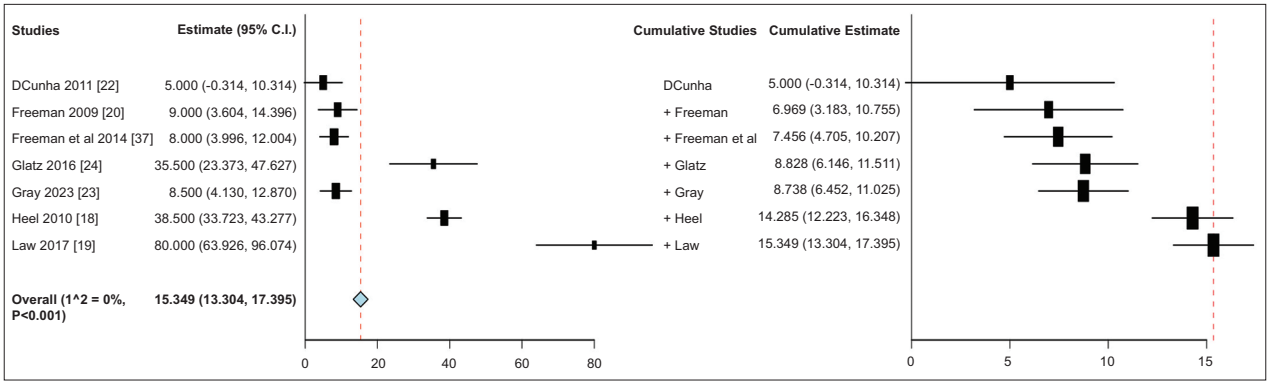


**Figure 6** Forest plot for duration of hospital stay
*C.I., Confidence Interval*

patients, with no difference in persistent leaks after initial repair [17].

Fischer *et al* reported that 15 patients with benign esophageal perforations treated using a self-expandable metal stent had a 7% mortality rate [26]. Another retrospective study of 27 patients reported that early diagnosis and management (within 24 h) led to a significant decrease in mortality rate (6.2% vs. 40%, P=0.047) [25]. Deng *et al* reported higher perioperative mortality in abdominal esophageal perforation (11%) and malignant thoracic esophageal perforation (63%), cervical esophageal perforation (8%), and benign esophageal perforation (13%) [27]. Co-existing hepatic and pulmonary diseases increase hospital-related morbidity and mortality significantly [19]. Some studies report a better response with palliative metallic stenting for spontaneous esophageal perforation in elderly patients with advanced cancer [28,29]. However, our analysis was limited to reporting the mechanism, site and etiology of perforation in included patients.

Dumonceau *et al* reported stent migration as the most common etiology for treatment failure in 33% of patients [30-35]. Benign lesions, distal esophageal perforations and partially covered self-expanding metal stents are reported risk factors for stent migration [36].

Freeman *et al* reported leak occlusion in 93% of cases with esophageal stent placement, as opposed to 6.8% of cases requiring postoperative repair for persistent leak, mostly due to delayed (>24 h) primary intervention [27]. Post-primary repair stent placement provided an opportunity for early oral nutrition, while decreasing the length of hospital stay and the risk for repeat surgical repair [20,37]. The main limitation of this paper is the heterogeneity in one outcome, which weakens the certainty of evidence, according to GRADE [38]. Another limitation is the lack of a placebo or comparator and the observational nature of some studies.

In conclusion, we suggest that esophageal stenting is an effective and well-tolerated method for treating esophageal perforation. It can reduce both morbidity and mortality, the need for postoperative surgical leak repair, and the duration of hospitalization.

## Summary Box

### What is already known:

- Esophageal perforation is commonly managed with either endoscopic stenting or surgical repair
- Surgical repair is often preferred in centers without advanced endoscopic services or for complex perforations
- Previous studies have reported variable outcomes regarding the efficacy and safety of esophageal stenting
- Mortality rates, stent migration and hospital stay durations have been reported with differing results across studies

### What the new findings are:

- This systematic review and meta-analysis consolidates data from 8 studies, demonstrating a decreasing trend in mortality rates associated with esophageal stenting over time
- Re-operative procedures were notably high in earlier studies, with lower rates observed in more recent research
- Stent migration occurred in 21.7% of patients, with leakage rates ranging from 8.8-16.2%, providing a clearer picture of stenting complications
- The review highlights significant variations in hospital stay durations across studies, with a range from 5.0-15.3 days, indicating variability in patient outcomes and management practices

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## Supplementary material

**Supplementary Table 1** Prisma Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | TITLE | |
| Title | 1 | Identify the report as a systematic review. | Page 1 |
| | | ABSTRACT | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Page 3 |
| | | INTRODUCTION | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 12 |
| Objectives | 4 | Provide an explicit statement of the objective (s) or question (s) the review addresses. | Page 12 |
| | | METHODS | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page 5 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 6 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 6. |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 4-6 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 4-6 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page7-9 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 7-9 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 6 |
| Effect measures | 12 | Specify for each outcome the effect measure (s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 7-9 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Page 7-9 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Page 5-9 |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Page 5-9 |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice (s). If meta-analysis was performed, describe the model (s), method (s) to identify the presence and extent of statistical heterogeneity, and software package (s) used. | |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 5-9 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 5-9 |

*(Contd...)*

**Supplementary Table 1** *(Continued)*

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 5-9 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 5-9 |
| | | RESULTS | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page7-9 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Supplementary table |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Page7-9 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Page 5-9 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Page7-9 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Page7-9 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page7-9 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Page7-9 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Page7-9 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Page7-9 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Page7-9 |
| | | DISCUSSION | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 8-11 |
| | 23b | Discuss any limitations of the evidence included in the review. | Page 8-11 |
| | 23c | Discuss any limitations of the review processes used. | Page 8-11 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Page 8-11 |
| | | OTHER INFORMATION | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | N/A |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | N/A |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | N/A |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | N/A |
| Competing interests | 26 | Declare any competing interests of review authors. | None |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | On request |

*From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71*

**Supplementary Table 2** showing quality assessment for included retrospective studies

| | Freeman, 2010[20] | Freeman, 2015[17] | Heel, 2009[18] | Law, 2017[19] | Abbas, 2009[21] | D'Cunha, 2011[22] | Glatz, 2016[24] | Gray, 2023[23] |
|---|---|---|---|---|---|---|---|---|
| 1. Was the research question or objective in this paper clearly stated? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2. Was the study population clearly specified and defined? | 1 | 1 | 1 | * | 1 | 1 | 1 | 1 |
| 3. Was the participation rate of eligible persons at least 50%? | 1 | 1 | 1 | * | 1 | 1 | 1 | 1 |
| 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 5. Was a sample size justification, power description, or variance and effect estimates | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6. For the analyses in this paper, were the exposure (s) of interest measured prior to the outcome (s) being measured? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? | N\A | N\A | N\A | N\A | N\A | N\A | N\A | N\A |
| 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | 1 | 0 | 0 | * | 1 | 0 | 1 | 0 |
| 10. Was the exposure (s) assessed more than once over time? | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 12. Were the outcome assessors blinded to the exposure status of participants? | * | * | * | * | * | * | * | * |
| 13. Was loss to follow-up after baseline 20% or less? | 1 | 1 | 1 | * | 1 | 1 | 1 | 1 |
| 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure (s) and outcome (s)? | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Total score (out of 14) | 11/14 | 10/14 | 10/14 | 7/14 | 11/14 | 10/14 | 11/14 | 10/14 |

*Key: 1=Yes, 0=No, * = Not reported, N/A=Not applicable*