Endoscopic closure of acute perforations of the GI tract: a systematic review of the literature

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Background: Surgical repair of endoscopic perforations of the GI tract used to be the standard, but immediate, secure endoscopic closure has become an attractive alternative treatment with the potential to reduce morbidity and mortality.

Objective: We aimed to perform a systematic review of the medical literature on endoscopic closure of acute iatrogenic perforations of the GI tract.

Design: A systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.

Setting: Available medical literature from 1966 through November 2013.

Patients: Patients with an acute perforation after an endoscopic procedure that was closed endoscopically.

Interventions: Endoscopic closure of an acute perforation of the GI tract.

Main Outcome Measurements: Clinically successful endoscopic closure.

Results: In our search, we identified 726 studies, 702 of which had to be excluded. Twenty-four cohort studies (21 retrospective, 3 prospective) were included in the analysis. No randomized trials were identified. Overall, the methodological quality was low. The 24 studies included described 466 acute perforations in which endoscopic closure was attempted. Successful endoscopic closure was achieved in 419 cases (89.9%; 95% CI, 87%-93%). Successful closure was achieved in 90.2% (n = 359; 95% CI, 87%-93%) of cases by using endoclips, in 87.8% (n = 58; 95% CI, 78%-95%) by using the over-the-scope-clip, and in 100% (n = 2) by using a metal stent.

Limitations: Low methodological quality of included studies.

Conclusion: This systematic review suggests that endoscopic perforation closure is a safe and effective alternative for surgical intervention in selected cases; however, the overall methodological quality was low. Prospective, true consecutive studies are needed to define the definitive role of endoscopic closure of perforations. (Gastrointest Endosc 2015;82:618-28.)

Iatrogenic GI perforations are rare adverse events of endoscopy. The incidence of acute perforations varies in diagnostic and therapeutic endoscopy and ranges from 0.01% to 4%.[1-5] Over the years, the absolute number of diagnostic and especially therapeutic endoscopies has grown tremendously.[6] Therapeutic endoscopy has pushed its boundaries, and widespread resections of the mucosa are now commonly performed. Consequently, the incidence of GI adverse events such as perforations has increased and is expected to increase further. These changes call for an effective per-procedure endoscopic closure modality.

The criterion standard for acute endoscopic perforations has long been surgical repair. Surgical treatment of perforations is, however, relatively invasive and associated with high morbidity and mortality rates. Two recent relatively large retrospective studies on the surgical repair of

Abbreviations: CI, confidence interval; ESD, endoscopic submucosal dissection; OTSC, over-the-scope clip; SD, standard deviation; SEMS, self-expandable metal stent.

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endoscopic perforations revealed morbidity rates of 25% to 36% and mortality rates of 7% to 10%.[7,8] Immediate endoscopic closure is less invasive, does not require anesthesia, and minimizes leakage of GI contents. As a result, it will potentially reduce morbidity and mortality.

Over the past years, various studies have described endoscopic closure of acute iatrogenic perforations. However, to our knowledge, no systematic reviews have been performed regarding endoscopic closure of GI perforations. We aimed to perform a systematic review of the literature on endoscopic closure of acute iatrogenic perforations of the GI tract.

METHODS

Literature search

A systematic review of literature was performed according to the PRISMA guidelines.[9] With the assistance of a clinical librarian, the Cochrane, MEDLINE (January 1966 through November 2013), and Embase libraries were searched from 1966 through November 2013 by using the MeSH terms "Endoscopy, Digestive System" and "Intestinal perforation" and key words oesophagogastroduodenoscopy, oesophagoscopy, gastroscopy, duodenoscopy, colonoscopy, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, perforation, endoscopic closure, endoscopic repair, endoscopic treatment, endoscopic therapy, endoscopic management, endoscopic technique, endoscopic approach, endoscopic intervention, endoscopic surgery, and transluminal were used along with their synonyms. The search terms are provided in Appendix 1, available online at www.giejournal.org. Titles and abstracts of the search results were reviewed by 2 authors (T.V., R.V.). Duplicate references were excluded. All full-text articles were retrieved for further analysis. All cross-references were screened for potentially relevant studies not identified by the initial literature search.

Criteria for inclusion and exclusion

The reviewers responsible for screening the search results (T.V., R.V.) independently checked the retrieved articles with regard to inclusion criteria. Studies were selected when all inclusion criteria were met.

Studies reporting original data in which acute iatrogenic perforations of a GI organ were closed with an endoscopic closure modality were included. An acute perforation was defined as detection and closure within 24 hours after initial endoscopic procedure. Essential outcomes had to be reported: successful closure that was defined as adequate closure of an endoluminal defect without signs of persistent leakage. Only studies reported in English were included. Series with fewer than 3 cases described were excluded. Perforations due to tumor perforation are nonacute, noniatrogenic perforations and were therefore excluded as well. Because perforations after ampullectomy include pancreatic and bile duct perforations after dilation of strictures without the ability for endoscopic closure, these perforations were also excluded.

Outcome parameters

The primary outcome was clinically successful endoscopic closure defined as adequate closure of the perforation with the absence of persistent leakage and mortality within 30 days. Persistent leakage was defined as need for additional endoscopic or surgical intervention for perforation closure. Secondary outcomes included adverse events of endoscopic closure, mortality, and hospital stay.

Data extraction

The following data were extracted from each study: method of data collection (prospective or retrospective), number of acute perforations, type of initial endoscopic procedure, location of perforation, and the endoscopic closure method used. In addition, the number of successfully closed perforations and the number of adverse events was scored. Finally, if available, data on follow-up imaging after closure and hospital stay were scored.

Statistical analyses

Continuous data are presented as mean ± standard deviation (SD) or as median and interquartile range according to distribution. Normally distributed data were tested by using a t test. The Mann-Whitney U test was used for continuous, not normally distributed data. A P value $< .05$ was considered to be statistically significant. Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp, Armonk, NY).

A meta-analysis of the proportions of acute perforations closed endoscopically was performed. However, in 13 of 24 studies, all acute perforations could be closed endoscopically (100% closure rate), causing problems with computation of estimates and standard error.[10] To prevent these problems, it was decided to add 0.5 to the absolute number of closed acute perforations and to the absolute number of acute perforations that could not be closed endoscopically before calculating the proportion of closed acute perforations for each study.

The meta-analysis was performed in Review Manager 5.3. Proportions (p) were entered after logit transformation by $\ln(p/1-p)$, and studies were weighted following the inverse variance approach. Heterogeneity was assessed by significance of the Cochran Q test statistic and the percentage of total variability that is attributable to heterogeneity instead of chance (I^2).

The logit values are presented in Forest and funnel plots and were used in the statistical analyses, but back-transformation to proportions by $\exp(\text{logit})/[1+\exp(\text{logit})]$ was done to ease subsequent interpretation. The logit transformation and back-transformation prevent upper 95% confidence limits of proportions to exceed the value of 1.