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Tuncer, A; Kayaalp, C; Karagul, S..

Corresponding author:

Servet Karagul

servet.karagul@atlas.edu.tr

Author Affiliation:

Istanbul Atlas University.

ADMINISTRATIVE INFORMATION**Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202650135**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 May 2026 and was last updated on 25 May 2026.**INTRODUCTION**

Review question / Objective To evaluate the necessity of intraoperative biopsy in gastric ulcer perforations by current biopsy proven malignancy rates and its effect on complications.

Rationale Intraoperative biopsy during surgical repair of gastric ulcer perforation is a subject of debate. Proponents argue that biopsy aids in early detection of malignancy, guiding further oncologic management, while opponents suggest that it may unnecessarily prolong surgery without significantly altering immediate outcomes. Given the potential implications for postoperative treatment and prognosis, determining the necessity of routine intraoperative biopsy is crucial.

This systematic review aims to evaluate the clinical utility, diagnostic yield, and impact on management of intraoperative biopsy in cases of gastric ulcer perforation to determine gastric cancer. By synthesizing available evidence, we

seek to provide evidence-based recommendations on whether routine biopsy should be standard practice or not.

Condition being studied Gastric perforation is a life-threatening surgical emergency that requires prompt intervention to prevent sepsis, peritonitis, and death. The etiology of gastric perforation varies, including peptic ulcer disease, malignancy, trauma, iatrogenic injury, and rare conditions such as infections or vasculitis. While most cases are benign, malignancy remains a critical concern, particularly in regions with a high prevalence of gastric cancer. The necessity of routine intraoperative biopsy in cases of gastric perforation has been a longstanding practice, primarily driven by concerns over missing an underlying malignancy. However, accumulating evidence from recent studies suggests that the risk of malignancy in perforated gastric ulcers is significantly lower than historically reported, and the routine use of intraoperative biopsy may not be justified.

METHODS

Search strategy A comprehensive search was performed in the following databases of PubMed/MEDLINE and Google Scholar on May 2025. Our search terms in title were “gastric” “biopsy” “perforation OR perforations OR perforated”. Search strategy was adapted for each database, and no date restrictions were applied.

Participant or population Adult patients (≥ 18 years) undergoing surgical intervention for gastric ulcer perforation.

Intervention Intraoperative biopsy (frozen section or permanent histopathology) during surgical repair.

Comparator Cases where no intraoperative biopsy was performed.

Study designs to be included Randomized controlled trials (RCTs), cohort studies, case-control studies, and large case series (≥ 10 patients).

Eligibility criteria We searched all articles without any limitation to publication year, country or language. Our eligibility criteria were determined by PICOS as below;

- Population: Adult patients (≥ 18 years) undergoing surgical intervention for gastric ulcer perforation.
- Intervention: Intraoperative biopsy (frozen section or permanent histopathology) during surgical repair.
- Comparator: Cases where no intraoperative biopsy was performed.
- Outcomes: Diagnostic yield of malignancy or other significant pathology. Postoperative morbidity.
- Study Types: Randomized controlled trials (RCTs), cohort studies, case-control studies, and large case series (≥ 10 patients).

Information sources A comprehensive search was performed in the following databases of PubMed/MEDLINE and Google Scholar. Our search terms in title were “gastric” “biopsy” “perforation OR perforations OR perforated”. Search strategy was adapted for each database, and no date restrictions were applied.

Main outcome(s) Diagnostic yield of malignancy or other significant pathology.

Additional outcome(s) Postoperative morbidity.

Data management Two independent reviewers screened titles and abstracts for eligibility, followed by full-text assessment of selected articles. Discrepancies were resolved by consensus.

The following data were collected from included studies: Study characteristics (author, year, country, design, sample size), patient demographics (age, gender), etiology of perforation (benign vs. malignant), postoperative complications.

Quality assessment / Risk of bias analysis Quality Assessment and Risk of Bias: RCTs: Assessed using the Cochrane Risk of Bias Tool, observational studies: Evaluated with the Newcastle-Ottawa Scale (NOS), case series: Assessed using the Joanna Briggs Institute (JBI) checklist.

Strategy of data synthesis Data will be extracted from eligible studies and summarized in tables. Descriptive statistics will be used for study and patient characteristics. The primary outcome will be the malignancy detection rate in intraoperative biopsy specimens. Pooled proportions will be calculated using fixed- and random-effects models. Heterogeneity will be assessed with the I^2 statistic, with $I^2 > 50\%$ considered substantial heterogeneity. Postoperative morbidity will be narratively summarized when comparative data are available.

Subgroup analysis Subgroup analysis may be performed according to study design, country or region, biopsy method, ulcer location when reported, and risk profile such as elderly patients, chronic ulcers, mass-like lesions, or non-prepyloric ulcers. However, subgroup analyses will depend on the availability and consistency of data across included studies.

Sensitivity analysis Sensitivity analysis will be considered by excluding studies with higher risk of bias and by comparing fixed-effect and random-effects pooled estimates. Additional sensitivity analysis may assess the impact of older studies and studies with incomplete complication or biopsy outcome reporting on the pooled malignancy rate.

Language restriction Non-English studies without available translation will be excluded.

Country(ies) involved Turkey.

Other relevant information This systematic review will follow PRISMA guidelines. The review will include adult patients undergoing surgery for

gastric ulcer perforation and will evaluate whether intraoperative biopsy is necessary for detecting malignancy and whether it affects postoperative morbidity. No ethical approval is required because only previously published data will be analyzed.

Keywords gastric cancer; peptic ulcer perforation; gastric ulcer; stomach cancer; intraoperative biopsy; systematic review.

Dissemination plans The findings will be disseminated through submission to a peer-reviewed scientific journal and presentation at relevant national or international surgical meetings.

Contributions of each author

Author 1 - Adem Tuncer - The author collected data and contributed to data analysis and interpretation., drafted the manuscript.

Email: ademtuncer89@hotmail.com

Author 2 - Cuneyt Kayaalp - The author provided statistical expertise, collected data, carried out the analyses and interpretation, conducted the literature review, drafted the manuscript, and critically reviewed and revised the manuscript.

Email: cuneytkayaalp@hotmail.com

Author 3 - Servet Karagul - The author conceptualized and designed the study, drafted the initial manuscript, and critically reviewed and revised the manuscript.

Email: servet.karagul@atlas.edu.tr