

Article

Not peer-reviewed version

Considerations of Surgeons for Intraoperative Biopsy in the Setting of Gastric Ulcer Perforation

[Adem Tuncer](#) , Cunevt Kayaalp , [Servet Karagul](#) *

Posted Date: 23 March 2026

doi: 10.20944/preprints202603.1684.v1

Keywords: perforated gastric ulcer; intraoperative biopsy; malignancy risk; postoperative endoscopy



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a [Creative Commons CC BY 4.0 license](#), which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Article

Considerations of Surgeons for Intraoperative Biopsy in the Setting of Gastric Ulcer Perforation

Adem Tuncer ¹, Cuneyt Kayaalp ² and Servet Karagul ^{2,*}

¹ Department of General Surgery, Florence Nightingale Hospital, Demiroğlu Bilim University, Istanbul, Turkey

² Department of General Surgery, Faculty of Medicine, Istanbul Atlas University, Istanbul, Turkey

* Correspondence: servet.karagul@atlas.edu.tr

Abstract

Objective: Intraoperative biopsy in perforated gastric ulcers has traditionally been widely used to exclude the risk of malignancy. However, despite accumulating evidence in recent years indicating a low incidence of malignancy, it remains unclear to what extent this approach has been adopted by surgeons. This study aimed to evaluate the attitudes of general surgeons in Türkiye toward intraoperative biopsy in perforated gastric ulcers and to identify the factors influencing this decision. **Materials and Methods:** This descriptive, cross-sectional survey study was conducted among actively practicing general surgeons across Türkiye. A total of 361 surgeons were included. The survey included demographic data, biopsy practices in perforated gastric ulcers, preferred surgical approaches, and postoperative endoscopy planning. Multivariable logistic regression analysis was performed to determine factors associated with routine intraoperative biopsy. **Results:** The mean age of participants was 41.4±10.3 years, and the mean duration of surgical experience was 12.8±9.7 years. Only 24.2% of surgeons correctly estimated the current malignancy risk (<5%) in perforated gastric ulcers; 102 participants did not provide a quantitative estimate. Among respondents, 52.9% reported performing routine biopsy, 42.9% selective biopsy, and 4.2% no biopsy. In multivariable analysis, age, surgical experience, and perceived malignancy risk were associated with routine biopsy; however, these relationships did not reach independent statistical significance. The vast majority of participants (87.0%) recommended postoperative endoscopy. **Conclusion:** In Türkiye, intraoperative biopsy in perforated gastric ulcers continues to be widely practiced despite the low malignancy rates reported in contemporary literature. Surgeons' biopsy decisions are largely influenced by perceived malignancy risk, experience, and traditional clinical approaches. These findings suggest that an evidence-based strategy relying on selective biopsy and planned postoperative endoscopy, rather than routine intraoperative biopsy, should be more effectively integrated into clinical practice.

Keywords: perforated gastric ulcer; intraoperative biopsy; malignancy risk; postoperative endoscopy

1. Introduction

The global prevalence of peptic ulcer disease is approximately 5–10%, and gastric ulcers occur less frequently than duodenal ulcers [1]. Perforation develops in approximately 2–10% of all peptic ulcer cases and represents a serious complication requiring emergency surgery [2–4]. While the risk of an underlying duodenal malignancy in duodenal ulcer perforation is negligible, it has long been recognized that gastric ulcers may be associated with gastric cancer. Therefore, routine intraoperative biopsy during gastric ulcer perforation has traditionally been considered necessary to avoid missing malignancy. This approach is largely based on older studies reporting gastric cancer rates of 9% to 23% in patients with perforated gastric ulcers [5,6].

Today, this traditional approach continues to be widely used due to established clinical habits. However, accumulating evidence over the past decade has begun to question this practice. Recent studies indicate that the incidence of malignancy in perforated gastric ulcers is much lower than

previously thought and is generally below 5% [1,2,7]. Furthermore, obtaining an intraoperative biopsy from the perforation site during emergency surgery may increase operative time, contamination risk, and morbidity [8]. Finally, the growing recognition of the importance of neoadjuvant therapy in gastric cancer surgery has shifted practice away from prioritizing radical surgery [9,10]. These findings suggest that the traditional approach of routine intraoperative biopsy may no longer be necessary in every case and should be re-evaluated in light of modern data.

Despite these developments, it is unclear to what extent current evidence is known or adopted by surgeons. To assess current clinical attitudes and practices and to determine whether outdated beliefs regarding malignancy risk persist, we conducted a nationwide survey among general surgeons in Türkiye. Our aim was to evaluate how frequently routine biopsy is performed during emergency surgery for perforated gastric ulcers and to investigate the factors influencing this decision. We also sought to raise awareness of recent evidence and contribute to improving surgical protocols in this field.

2. Materials and Methods

This study was designed as a descriptive, cross-sectional survey to evaluate current practices and opinions of general surgeons in Türkiye regarding routine intraoperative biopsy during emergency surgery for perforated gastric ulcers. A structured 10-question survey was developed by the research team based on a review of relevant literature and current guidelines. The survey consisted of three main sections:

- (i) **Demographic Data** – Age, years of surgical experience, and city of practice.
- (ii) **Clinical Practices** – Whether biopsy is performed in perforated gastric ulcers, preferred surgical techniques (e.g., omentopexy, definitive surgery), and postoperative endoscopy requests.
- (iii) **Opinions and Awareness** – Knowledge of recent literature, perception of malignancy risk in perforated ulcers, and factors influencing the decision to perform biopsy.

The study received approval from the İstanbul Aydın University Non-Interventional Clinical Research Ethics Committee on 20.06.2025 (Approval no: 136/2025). All procedures were conducted in accordance with the Declaration of Helsinki, participants were informed prior to the survey, and participation was voluntary.

The study population consisted of general surgeons actively working in various institutions across Türkiye (university, training and research, state, and private hospitals). The geographical distribution of participants was visualized such that each point represented one surgeon, with density reflecting participant numbers (Figure 1). Assuming approximately 5000 active general surgeons in Türkiye, the required sample size was calculated using G-Power 3.1 software at a 95% confidence level and 5% margin of error, targeting a minimum of 357 participants.



Figure 1. Geographic distribution of general surgeons participating in the survey across Türkiye. (Each dot represents one general surgeon.).

The survey was pilot-tested in a small group of surgeons (n=11) to assess clarity and appropriateness, followed by minor revisions based on feedback. These 11 cases were excluded from the main analysis. The survey was administered online via a secure platform (Google Forms) and distributed during general surgery meetings. The survey link was shared through professional surgical associations (Turkish Surgical Society), academic networks, and direct email invitations. Participation was voluntary, and all responses were anonymous. Inclusion criteria were limited to actively practicing general surgeons in Türkiye. Duplicate entries were screened and eliminated. Data collected both in person and online were merged into a single Excel dataset. For interval-based responses, arithmetic means were calculated using each participant's lower and upper values and included in classification analyses.

Statistical Analysis

Survey data were analyzed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize participant characteristics and response distributions. Categorical variables were presented as frequencies and percentages. Chi-square or Fisher's exact tests were used to evaluate associations between demographic variables and biopsy practices. Continuous variables were compared using Student's t-test or the Mann-Whitney U test according to data distribution. A p-value <0.05 was considered statistically significant.

Multivariable logistic regression analysis was performed to identify independent factors associated with routine intraoperative biopsy. Age, duration of surgical experience, and perceived malignancy risk were included in the model. Results were presented as odds ratios (OR) with 95% confidence intervals (CI).

3. Results

A total of 361 general surgeons participated. The mean age was 41.4±10.3 years (24–71), and mean surgical experience was 12.8±9.7 years (0.3–45 years). Surgeons estimated the potential malignancy risk in gastric ulcer perforation as 9.1±10.9% (0–80%). While 24.2% correctly estimated the expected malignancy rate of <5%, the majority either overestimated or did not express an opinion (n=102). There was no difference in age or experience between surgeons who correctly estimated the risk and those who did not.

Among participants, 52.9% (n=191) reported routinely performing biopsy during perforation repair, 42.9% (n=155) performed selective biopsy, and only 4.2% (n=15) did not perform biopsy. The two main factors influencing the decision to biopsy were the appearance of the perforation (85.3%) and its location (85.3%), whereas defect size (27.7%) and patient age (16.9%) were less influential (Table 1).

Table 1. Surgeons' biopsy practices, influencing factors, and indications for postoperative endoscopy.			
Question / Category	Yes	Sometimes	No
Do you perform a biopsy?	191 (%52.9)	155 (%42.9)	15 (%4.2)
What influences your decision to perform a biopsy?			
- Patient's age	61 (%16.9)	-	300 (%83.1)
- Defect size	100 (%27.7)	-	261 (%72.3)

Question / Category	Yes	Sometimes	No
- Location of perforation	308 (%85.3)	-	53 (%14.7)
- Macroscopic appearance of perforation	308 (%85.3)	-	53 (%14.7)
Do you recommend postoperative endoscopy?	314 (%87.0)	41 (%11.4)	5 (%1.4)
Why do you recommend postoperative endoscopy?			
- To evaluate malignancy risk	137 (%38.0)	-	224 (%62.0)
- To investigate <i>Helicobacter pylori</i>	78 (%21.6)	-	283 (%78.4)
- To assess reflux and hiatal hernia	129 (%35.7)	-	232 (%64.3)
- For general follow-up	129 (%35.7)	-	232 (%64.3)

Age, mean ± SD (range): 41,4±10,3 (24-71); Surgical experience (years), mean ± SD (range): 12,8±9,7(0,3-45).

Surgeons performing routine biopsy were older and had longer surgical experience (42.6±10.1 years and 14.3±9.7 years) compared to those who did not (39.8±10.1 years and 11.0±9.2 years) (p=0.01 and p=0.002, respectively). There was also a linear relationship between predicted malignancy risk and biopsy practices (Table 2). Most participants (n=328) preferred primary repair (e.g., omental patch). Twenty-one recommended resection, and 12 responded “depends on the case.” Surgeons recommending resection were older and more experienced (49.1±10.6 years and 20.9±9.9 years) than those preferring primary repair (40.8±10.1 years and 12.2±9.5 years) (p<0.002 and p=0.001, respectively) (Table 2).

Table 2. Surgeon characteristics associated with biopsy practice, surgical approach, and postoperative endoscopy.

Variable	Group	Value	p-value
Intraoperative biopsy	Routine biopsy	Age: 42.6 ± 10.1	0.01
	Non-routine biopsy*	Age: 39.8 ± 10.1	
Surgical approach	Routine biopsy	Experience: 14.3 ± 9.7	0.002
	Non-routine biopsy*	Experience: 11.0 ± 9.2	
	Primary repair	328 (90.9%)	—
	Resection	21 (5.8%)	
Postoperative endoscopy	Case-dependent	12 (3.3%)	<0.002
	Resection	Age: 49.1 ± 10.6	
	Primary repair	Age: 40.8 ± 10.1	
	Recommended	314 (87.0%)	—

Not/Selective	47 (13.0%)
---------------	------------

*Non-routine biopsy includes selective biopsy and no biopsy. Values are presented as mean ± SD or n (%).

In multivariable logistic regression analysis, age, surgical experience, and perceived malignancy risk were associated with routine intraoperative biopsy; however, these associations did not reach independent statistical significance (Table 3).

Table 3. Multivariable logistic regression analysis of factors associated with performing routine intraoperative biopsy.

Variable	OR	%95 CI	p-value
Age (years)	1.02	0.95–1.10	0.608
Surgical experience (years)	1.01	0.93–1.09	0.820
Perceived malignancy risk (%)	1.02	0.99–1.05	0.116

OR: Odds ratio; CI: Confidence interval. Dependent variable: performance of routine intraoperative biopsy (yes/no).

The vast majority of participants (87.0%, n=314) recommended endoscopy after perforation. The primary reasons were evaluation of malignancy risk (81.5%), investigation of reflux or gastritis (21%), and general follow-up (34.7%). Endoscopy for Helicobacter pylori investigation was recommended by 36.8%.

Consistent trends were observed between biopsy practices and postoperative endoscopy planning. Of 196 participants who reported performing biopsy in every patient, 177 (90.3%) recommended postoperative endoscopy for all patients. Of 150 participants performing biopsy only in suspicious cases, 125 (83.3%) still recommended endoscopy for all patients. All participants (100%) who reported never performing biopsy planned postoperative endoscopy for every patient (Table 4).

Table 4. Relationship between surgeons’ biopsy practices and their preferences for postoperative endoscopy.

	Yes, for every patient (Endoscopy)	No, only in suspicious cases (Endoscopy)	No, I do not consider it necessary (Endoscopy)
Yes, for every patient (Biopsy)	177 (%90,3)	15 (%7,7)	4 (%2,0)
No, only in suspicious cases (Biopsy)	125 (%83,3)	23 (%15,3)	2 (%1,3)
No, I never perform biopsy (Biopsy)	14 (%100)	0 (0,0)	0 (0,0)

No participant who avoided biopsy failed to recommend postoperative endoscopy. These findings demonstrate a strong parallel between ulcer biopsy practice and postoperative endoscopy planning.

Surgeons’ estimates of patient compliance with postoperative endoscopy varied: 41 expected 0–25% compliance, 79 expected 26–50%, 119 expected 51–75%, and 119 anticipated 76–100% compliance.

4. Discussion

In this study, the attitudes and behaviors of general surgeons in Türkiye regarding intraoperative biopsy in perforated gastric ulcers were evaluated. The findings demonstrate that approximately 95% of surgeons perform biopsy either routinely or selectively. This situation is not consistent with the trend reported in contemporary literature. Recent studies have shown that malignancy rates in gastric ulcers presenting with perforation are significantly lower than the

previously reported rates of 9–23% and generally remain below 5% [1,2]. In addition, gastric cancer treatment has undergone major changes over the past decade, such as the implementation of neoadjuvant therapy prior to surgery in advanced tumors [9–11]. Despite the lack of support from current evidence for routine use, the results of this study indicate that a substantial proportion of surgeons continue to perform intraoperative biopsy routinely.

Historically reported malignancy rates of 9–23% in perforated gastric ulcers can largely be explained by retrospective study designs and the inclusion of perforations occurring in patients already diagnosed with gastric cancer. In contrast, contemporary data indicate that the detection rate of malignancy through intraoperative biopsy in acute gastric perforations is quite low and that the clinical contribution of routine biopsy may be limited [12]. In a recent study by Steyn and Karusseit, no histopathological malignancy was detected in any patient who underwent intraoperative biopsy due to spontaneous gastric perforation, and no gastric cancer was observed during follow-up endoscopy [7]. Similarly, in a long-term cohort analysis by Koca et al., excisional biopsy performed for perforated gastric ulcers was associated with a significant increase in postoperative complications, while intraoperative biopsies did not contribute to malignancy diagnosis [13]. In a recent study by Amoli et al., the rate of malignancy detection in intraoperative biopsies taken from perforated prepyloric gastric ulcers was extremely low, and the authors emphasized that the diagnostic contribution of routine biopsy may be limited [14]. The World Society of Emergency Surgery (WSES) guidelines also emphasize that exclusion of malignancy in hemodynamically stabilized patients should be performed not during emergency surgery but through planned postoperative upper gastrointestinal endoscopy and targeted biopsies [15]. In light of these findings, a strategy based on selective biopsy in the presence of macroscopic suspicion and systematically planned early postoperative endoscopy in all patients appears to be more rational and evidence-based than routine intraoperative biopsy in every case. In a recent retrospective study by Trindade et al., intraoperative biopsies were reported to have limited contribution to malignancy diagnosis in patients operated on for perforated gastric ulcer, whereas postoperative upper gastrointestinal endoscopy played a decisive role in excluding malignancy and establishing a definitive diagnosis [16].

It is noteworthy that a considerable proportion of participants (n=102) did not provide a quantitative estimate of malignancy risk. This may not necessarily indicate a lack of knowledge but rather reflect uncertainty and clinical concern in the emergency surgical setting. The wide variability of malignancy rates reported in the literature and the absence of a definitive threshold value may have led surgeons to avoid specifying a risk percentage. In this context, participants who did not express an opinion may represent clinical uncertainty.

In this study, three-quarters of participants overestimated the current malignancy risk, and approximately 95% reported continuing to perform biopsy either routinely or selectively. This suggests that surgeons' decisions are still largely shaped by outdated information or intuitive risk perception. Such an approach carries the risk of leading to unnecessary biopsies and consequently potential surgical complications. The disadvantages of intraoperative biopsy—including prolonged operative time, increased complication risk, and limited tissue quality due to inflammation—are well recognized [7,8,13]. In a randomized study by Lau JY et al., surgical trauma in patients undergoing repair for perforated peptic ulcer was shown to significantly affect systemic inflammatory response and endotoxemia levels [17]. This finding suggests that additional interventions during emergency surgery may increase physiological burden. Therefore, a strategy aligned with contemporary surgical and oncological principles is to prioritize perforation repair, then confirm the diagnosis through endoscopic evaluation, and subsequently establish treatment planning within a multidisciplinary framework [2,10].

A radical transformation has occurred in gastric cancer treatment, particularly over the last decade. Neoadjuvant (preoperative) chemotherapy has become the standard approach in locally advanced gastric cancer. Randomized controlled trials such as the MAGIC study have demonstrated significant improvements in both resectability and survival among patients receiving perioperative therapy [9]. As a result, primary surgery has often been replaced by chemotherapy following

endoscopic diagnosis, with elective surgery planned as a second stage. Therefore, in a patient presenting with perforation who is subsequently diagnosed with gastric cancer, performing simple repair rather than resection during the initial operation both reduces morbidity and allows the patient to be directed to a more appropriate oncological protocol. In patients undergoing immediate resection, the opportunity for neoadjuvant therapy is lost, and an important prognostic step may be missed. Furthermore, resection may increase postoperative complication risk when severe contamination is present at the perforation site [8]. These realities suggest that making a resection decision based on suspected malignancy identified through intraoperative biopsy may no longer be an oncologically preferable strategy. The current ideal approach is to stabilize the patient through perforation repair, perform a high-quality endoscopic evaluation, and, if malignancy is confirmed, plan treatment (neoadjuvant therapy followed by surgery) according to oncological principles [9,10,18]. Mortality in perforated peptic ulcer is known to be strongly influenced by the patient's physiological condition and accompanying risk factors. The Peptic Ulcer Perforation (PULP) score described by Møller et al. has been reported as an effective tool for predicting mortality risk in this patient group [19]. This supports the notion that, in emergency surgical management, priority should be given to the patient's overall risk profile and stabilization rather than oncological suspicion.

The finding that the most influential factors in surgeons' biopsy decisions were the macroscopic appearance and anatomical location of the perforation indicates that surgeons continue to rely heavily on intraoperative observation and clinical intuition. Conversely, the relatively limited influence of more objective factors such as defect size and patient age suggests that biopsy practice is not standardized and is largely based on individual judgment.

Postoperative endoscopy is an effective and safe method both for excluding malignancy and for evaluating *Helicobacter pylori* infection, reflux, or other accompanying conditions [20–22]. The majority of participants reported recommending postoperative endoscopy, most commonly due to concern about malignancy (81.5%), indicating that surgeons wish to complete the diagnostic process postoperatively even when intraoperative biopsy is performed. Recommendations for postoperative endoscopy for non-malignant indications (such as reflux, *Helicobacter pylori* infection, and general evaluation) suggest that surgeons use endoscopy not solely to exclude malignancy but also as a broader diagnostic tool. However, responses regarding patient compliance revealed that surgeons have notable concerns about the practical feasibility of postoperative endoscopy. The frequent recommendation of postoperative endoscopy despite intraoperative biopsy suggests an attempt to secure the diagnostic process at multiple stages. This approach may be associated with an effort to reduce diagnostic uncertainty and manage clinical responsibility more cautiously. The findings indicate that merely recommending endoscopic follow-up is insufficient; rather, it should be organized as a systematic follow-up process. Whether surgeons who anticipate low postoperative endoscopy compliance tend to rely more heavily on intraoperative biopsy is an important question that warrants further investigation.

One of the strengths of this study is that it provides a large sample including surgeons from different levels of seniority and institutions nationwide (Figure 1). However, several limitations exist. The reliance on self-reported data may not fully reflect actual clinical practice. Additionally, because the survey was voluntary, the results may contain sampling bias. Nevertheless, the findings provide important insight into how closely surgical practice in Türkiye aligns with contemporary evidence.

This study also found that older and more experienced surgeons were more inclined toward both biopsy and resection. Although univariate analyses showed that these surgeons were more likely to perform biopsy, these relationships did not reach independent statistical significance in multivariable analysis. This suggests that the biopsy decision is influenced not only by clinical experience but also by entrenched risk perception and traditional knowledge. This indicates that traditional beliefs continue to play a decisive role in clinical decision-making and that integration of new evidence into daily practice may not occur rapidly enough. Surgeons should be informed through updated guidelines, and surgical decisions should be shaped according to evidence-based medicine principles. Similarly, the significantly greater tendency of surgeons who estimated

malignancy risk as higher to perform biopsy suggests that this decision is primarily driven by perceived risk.

5. Conclusions and Recommendations

This study demonstrates that intraoperative biopsy practices for perforated gastric ulcers in Türkiye are not fully aligned with current literature and contemporary oncological approaches. Current evidence indicates that routine intraoperative biopsy has limited diagnostic value and that modern gastric cancer management is primarily based on surgery planned after neoadjuvant chemotherapy.

Accordingly, the primary approach in patients presenting with perforation should be safe repair of the perforation, followed by planned endoscopic and histopathological evaluation to establish a definitive diagnosis and determine the appropriate oncological treatment strategy. Integration of these contemporary approaches into clinical practice is critical for patient prognosis and treatment effectiveness.

Future studies should prospectively evaluate the earliest postoperative time at which upper gastrointestinal endoscopy can be safely and diagnostically performed after perforated gastric ulcer. Additionally, more comprehensive and multidimensional surveys are needed to better define the clinical, experiential, and perceptual factors influencing surgeons' decisions regarding intraoperative biopsy and postoperative endoscopy. Such studies may contribute to standardizing endoscopic follow-up strategies and restructuring perforated gastric ulcer management based on evidence-based principles.

Author Contributions: Conceptualization, A.T., C.K. and S.K.; Methodology, A.T. and C.K.; Validation, A.T. and C.K.; Formal Analysis, A.T. and C.K.; Investigation, A.T. and C.K.; Data Curation, A.T.; Writing—Original Draft Preparation, A.T.; Writing—Review and Editing, A.T. and C.K.; Visualization, A.T.; Supervision, C.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the İstanbul Aydın University Non-Interventional Clinical Research Ethics Committee (protocol code 136/2025, date of approval 20.06.2025).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Lanas A, Chan FKL. Peptic ulcer disease. *Lancet*. 2017;390(10094):613-624. doi:10.1016/S0140-6736(16)32404-7.
2. Søreide K, Thorsen K, Harrison EM, et al. Perforated peptic ulcer. *Lancet*. 2015;386(10000):1288-1298. doi:10.1016/S0140-6736(15)00276-7.
3. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. *Digestion*. 2011;84(2):102-113. doi:10.1159/000323958.
4. Buck DL, Vester-Andersen M, Møller MH; Danish Clinical Register of Emergency Surgery. Surgical delay is a critical determinant of survival in perforated peptic ulcer. *Br J Surg*. 2013;100(8):1045-1049. doi:10.1002/bjs.9175.
5. Wysocki A, Biesiada Z, Beben P, Budzynski A. Perforated gastric ulcer. *Dig Surg*. 2000;17(2):132-137. doi:10.1159/000018815.

6. Rees JR, Thorbjarnarson B. Perforated gastric ulcer. *Am J Surg*. 1973;126(1):93-97. doi:10.1016/s0002-9610(73)80102-3.
7. Steyn PF, Karusseit O. Gastric perforation biopsy: is it obsolete?. *Langenbecks Arch Surg*. 2024;409(1):139. Published 2024 Apr 27. doi:10.1007/s00423-024-03325-9.
8. Søreide K, Thorsen K, Søreide JA. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *Br J Surg*. 2014;101(1):e51-e64. doi:10.1002/bjs.9368.
9. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355(1):11-20. doi:10.1056/NEJMoa055531.
10. Ajani JA, D'Amico TA, Almhanna K, et al. Gastric Cancer, Version 3.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2016;14(10):1286-1312. doi:10.6004/jnccn.2016.0137.
11. Hartgrink HH, Jansen EP, van Grieken NC, van de Velde CJ. Gastric cancer. *Lancet*. 2009;374(9688):477-490. doi:10.1016/S0140-6736(09)60617-6.
12. Janwanitchstaporn S. Incidence of malignancy and the role of gastric biopsy in patients with perforated gastric ulcer in Thailand. *Reg Med J*. 2018;32(3):1113–20.
13. Koca F, Koch C, Schulze F, Pession U, Bechstein WO, Malkomes P. Excisional biopsy of perforated gastric ulcer: mandatory or potentially harmful? *Langenbecks Arch Surg*. 2024;409(1):205. doi:10.1007/s00423-024-03393-x.
14. Amoli HA, Mohammadi S, Taghizadeh N, Imanipour M, Hajebi R. Occurrence of malignancy in biopsy specimens from patients with perforated pre-pyloric gastric ulcers. *Res Square*. 2024 Jan 12. doi:10.21203/rs.3.rs-3850897/v1.
15. Tarasconi A, Coccolini F, Biffl WL, et al. Perforated and bleeding peptic ulcer: WSES guidelines. *World J Emerg Surg*. 2020;15:3. Published 2020 Jan 7. doi:10.1186/s13017-019-0283-9.
16. Trindade M, Gomes Pinto D, Carvalho N, Luz C. Role of intraoperative biopsy and postoperative upper gastrointestinal endoscopy in patients undergoing surgery for perforated gastric ulcer: a retrospective study. *Cureus*. 2025;17(1):e77092.
17. Lau JY, Lo SY, Ng EK, Lee DW, Lam YH, Chung SC. A randomized comparison of acute phase response and endotoxemia in patients with perforated peptic ulcers receiving laparoscopic or open patch repair. *Am J Surg*. 1998;175(4):325-327. doi:10.1016/s0002-9610(98)00006-3.
18. Leeman MF, Skouras C, Paterson-Brown S. The management of perforated gastric ulcers. *Int J Surg*. 2013;11(4):322-324. doi:10.1016/j.ijsu.2013.02.010. .
19. Møller MH, Engebjerg MC, Adamsen S, Bendix J, Thomsen RW. The Peptic Ulcer Perforation (PULP) score: a predictor of mortality following peptic ulcer perforation. A cohort study. *Acta Anaesthesiol Scand*. 2012;56(5):655-662. doi:10.1111/j.1399-6576.2011.02609.x.
20. Gisbert JP, Calvet X. Review article: Helicobacter pylori-negative duodenal ulcer disease. *Aliment Pharmacol Ther*. 2009;30(8):791-815. doi:10.1111/j.1365-2036.2009.04105.x.
21. Ergul E, Gozetlik EO. Emergency spontaneous gastric perforations: ulcer versus cancer. *Langenbecks Arch Surg*. 2009;394(4):643-646. doi:10.1007/s00423-008-0331-5.
22. Weledji EP. An Overview of Gastroduodenal Perforation. *Front Surg*. 2020;7:573901. Published 2020 Nov 9. doi:10.3389/fsurg.2020.573901.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.