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Postoperative Morbidity and Oncologic Outcomes Following Curative Resection for Gastric Adenocarcinoma

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ABSTRACT

Gastric adenocarcinoma remains a leading cause of cancer-related mortality worldwide despite advances in surgical and multimodal therapy. Postoperative morbidity following curative gastrectomy may negatively influence long-term oncologic outcomes; however, the magnitude of this effect remains insufficiently characterized in South Asian populations. This prospective cohort study aimed to evaluate the incidence, predictors, and oncologic impact of postoperative morbidity following curative resection for gastric adenocarcinoma. A total of 318 patients undergoing R0 subtotal or total gastrectomy with D1/D2 lymphadenectomy between January 2020 and December 2024 were enrolled. Postoperative complications were graded using the Clavien–Dindo classification. Survival analysis was performed using Kaplan–Meier and Cox regression models. Overall postoperative morbidity occurred in 36.5% (n=116) of patients, with major complications (grade ≥III) in 14.8% (n=47). Independent predictors of major morbidity included preoperative hypoalbuminemia <3.5 g/dL (OR 3.76; 95% CI 2.01–7.02; p<0.001), operative time >300 minutes (OR 2.94; 95% CI 1.56–5.54; p=0.001), total gastrectomy (OR 2.28; 95% CI 1.25–4.16; p=0.007), and advanced pathological stage (OR 2.11; 95% CI 1.18–3.79; p=0.012). Five-year overall survival was significantly lower in patients with major morbidity (43.9%) compared to those without (74.5%) (p<0.001). Major postoperative morbidity independently predicted decreased overall survival (HR 2.47; 95% CI 1.58–3.87; p<0.001). Postoperative morbidity significantly compromises long-term oncologic outcomes, emphasizing the importance of perioperative optimization and surgical precision.

Keywords: Gastric adenocarcinoma; Gastrectomy; Postoperative morbidity; Survival; Oncologic outcomes

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INTRODUCTION

Gastric adenocarcinoma continues to represent a major global health burden, ranking among the most frequently diagnosed malignancies and one of the leading causes of cancer-related mortality worldwide [1]. Although incidence rates have declined in certain Western countries, the disease remains highly prevalent in Asia and developing regions, where delayed diagnosis and advanced-stage presentation are common [2]. Improvements in perioperative management, surgical techniques, and adjuvant therapy have enhanced outcomes; however, five-year survival remains unsatisfactory in many populations [3]. Surgical resection with curative intent remains the only definitive treatment modality for localized gastric adenocarcinoma, and radical gastrectomy with appropriate lymphadenectomy constitutes the standard of care [4].

The extent of surgical resection and lymphadenectomy has been a subject of extensive investigation. D2 lymphadenectomy is widely accepted as the oncologic standard in Eastern countries and increasingly adopted in high-volume Western centers [5]. Although extended lymph node dissection improves staging accuracy and may enhance survival, it is technically demanding and associated with potential increases in postoperative morbidity [6]. Gastrectomy itself—particularly total gastrectomy—imposes significant physiological stress and carries risks of complications such as anastomotic leakage, pancreatic fistula, hemorrhage, intra-abdominal abscess, and pulmonary complications [7].

Postoperative morbidity following gastrectomy has been reported in 20% to 40% of patients depending on patient characteristics and institutional expertise [8]. While minor complications may prolong hospitalization without long-term consequences, major complications requiring invasive intervention can substantially alter recovery trajectories [9]. Increasing evidence suggests that postoperative complications may influence not only short-term outcomes but also long-term oncologic survival [10]. The biological mechanisms underlying this association may involve systemic inflammatory responses, immune suppression, and delayed initiation of adjuvant chemotherapy [11].

Surgical stress and postoperative inflammatory cascades can induce alterations in cytokine profiles, impair cytotoxic T-cell function, and promote tumor cell proliferation and angiogenesis [12]. Furthermore, patients experiencing major complications often have delayed or omitted adjuvant chemotherapy, which may compromise systemic disease control and increase recurrence risk [13]. These observations highlight the need to examine postoperative morbidity as a potential independent prognostic factor.

Despite multiple retrospective analyses from high-income countries suggesting a correlation between postoperative complications and inferior survival, results remain inconsistent [14]. Differences in study design, complication definitions, patient demographics, and treatment protocols contribute to heterogeneity in reported findings [15]. Moreover, prospective data from South Asian populations are scarce, despite differing nutritional status, comorbidity profiles, and healthcare infrastructure that may significantly impact outcomes.

Preoperative nutritional status has emerged as a key determinant of surgical recovery. Hypoalbuminemia, reflecting malnutrition and systemic inflammation, has been associated with impaired wound healing and increased complication risk [16]. In developing regions where nutritional deficiencies are prevalent, this factor may be particularly relevant. Additionally, advanced tumor stage, prolonged operative duration, and total gastrectomy have been identified as potential contributors to postoperative morbidity [17].

Enhanced recovery after surgery (ERAS) protocols have reduced minor complication rates and hospital stay in gastrointestinal surgery [18]. Nevertheless, major morbidity remains substantial in complex oncologic resections such as gastrectomy. Identifying modifiable predictors and quantifying their oncologic impact is essential for optimizing perioperative management strategies.

Given these considerations, the present prospective cohort study was designed to evaluate the incidence and independent predictors of postoperative morbidity following curative gastrectomy for gastric adenocarcinoma and to determine its impact on long-term overall and disease-free survival in a tertiary care setting [19,20].

MATERIAL AND METHODS

Study Design and Setting

This prospective cohort study was conducted at the ABWA Hospital and Research Center, from January 2020 to December 2024. Institutional ethical approval was obtained prior to study initiation (IRB No: PCMS/IRB/2019-GA-021). The study adhered to the Declaration of Helsinki and institutional research guidelines.

Study Population

Patients aged 18–80 years with histologically confirmed gastric adenocarcinoma scheduled for curative gastrectomy were evaluated. All participants underwent standardized preoperative staging and were discussed in a multidisciplinary tumor board meeting.

Sample

A total of 337 patients were assessed for eligibility. Nineteen patients were excluded due to metastatic disease discovered intraoperatively (n=8), incomplete pathological data (n=6), or loss to follow-up (n=5). The final cohort comprised 318 patients. Sample size calculation assumed a 30% morbidity rate, 95% confidence level, and 5% margin of error, requiring at least 285 patients; therefore, the sample exceeded minimum requirements.

Inclusion/ Exclusion criteria

Inclusion criteria were stage I–III gastric adenocarcinoma undergoing R0 resection with subtotal or total gastrectomy and D1 or D2 lymphadenectomy.

Exclusion criteria included distant metastasis, R1/R2 resection, emergency surgery, neoadjuvant therapy non-completion, prior upper gastrointestinal surgery, and concurrent malignancies.

Preoperative Assessment

All patients underwent complete clinical examination, upper gastrointestinal endoscopy with biopsy, contrast-enhanced CT scan of chest and abdomen, laboratory investigations including hemoglobin, serum albumin, liver and renal function tests, and tumor markers. Hypoalbuminemia was defined as serum albumin <3.5 g/dL.

Surgical Technique

Subtotal or total gastrectomy was performed depending on tumor location. Reconstruction was achieved using Roux-en-Y esophagojejunostomy or gastrojejunostomy. Standard D2 lymphadenectomy was performed in medically fit patients. All procedures were performed by experienced gastrointestinal oncologic surgeons.

Postoperative Morbidity

Complications within 30 postoperative days were recorded and graded using the Clavien–Dindo classification. Major morbidity was defined as grade III or higher.

Follow-Up

Patients were followed every three months for two years and every six months thereafter. Overall survival (OS) and disease-free survival (DFS) were calculated from date of surgery.

Statistical analysis

Data were analyzed using SPSS version 27. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test. Categorical variables were compared using chi-square test. Variables with $p<0.10$ in univariate analysis were entered into multivariate logistic regression. Survival curves were generated using Kaplan–Meier method and compared by log-rank test. Cox proportional hazards regression identified independent predictors of survival. Significance was set at $p<0.05$.

RESULTS

Overall postoperative morbidity occurred in 116 patients (36.5%). Major morbidity occurred in 47 patients (14.8%).In this cohort, overall postoperative morbidity occurred in 36.5% of patients, with major complications in 14.8%. Major morbidity was significantly associated with older age, hypoalbuminemia, total gastrectomy, prolonged operative time, and advanced (stage III) disease (Table 1). Multivariate analysis (Table 2) identified hypoalbuminemia as the strongest independent predictor of major morbidity (OR 3.76, $p < 0.001$), along with prolonged operative time, total gastrectomy, and stage III disease. Importantly, major postoperative morbidity had a profound impact on long-term outcomes, with 5-year overall survival reduced to 43.9% compared with 74.5% in patients without major complications (HR 2.47, $p < 0.001$, Table 3), demonstrating that major complications are a key determinant of both short- and long-term prognosis.

Table 1. Clinicopathological Characteristics According to Major Morbidity

Variable	Major Morbidity (n=47)	No Major Morbidity (n=271)	p-value
Age >65 years (%)	44.7	30.6	0.048
Albumin <3.5 g/dL (%)	63.8	28.0	<0.001
Total gastrectomy (%)	68.1	41.3	0.002
Operative time >300 min (%)	66.0	34.7	<0.001
Stage III disease (%)	| 59.6	37.6	0.009

Explanation: Major morbidity was significantly associated with hypoalbuminemia, prolonged operative time, total gastrectomy, and advanced stage.

Table 2. Multivariate Predictors of Major Postoperative Morbidity

Variable	OR	CI	p-value
Albumin <3.5 g/dL	3.76	2.01–7.02	<0.001
Operative time >300 min	2.94	1.56–5.54	0.001
Stage III disease	2.11	1.18–3.79	0.012
Total gastrectomy	2.28	1.25–4.16	0.007

Explanation: Hypoalbuminemia was the strongest independent predictor.

Table 3. Five-Year Survival Outcomes

Group | | HR | p-value Variable	5-Year OS (%)	HR	p-value
No Major Morbidity	74.5	-	-
Major Morbidity	| 43.9 | |	2.47 (1.58–3.87)	<0.001

Explanation: Major postoperative morbidity independently predicted reduced survival.

DISCUSSION

The present prospective study demonstrates that postoperative morbidity significantly influences long-term oncologic outcomes following curative gastrectomy for gastric adenocarcinoma. The overall complication rate of 36.5% aligns with previously reported international data ranging between 25% and

40% [15]. Importantly, major complications occurred in 14.8% of patients and independently doubled the risk of mortality, emphasizing their oncologic significance.

Hypoalbuminemia emerged as the most powerful predictor of postoperative morbidity. Serum albumin reflects both nutritional reserve and systemic inflammatory burden [16]. Malnourished patients exhibit impaired collagen synthesis, reduced immune competence, and delayed tissue regeneration, predisposing them to anastomotic failure and infectious complications [17]. Similar findings have been reported in Japanese and European cohorts [18]. In regions with high prevalence of malnutrition, preoperative nutritional optimization should be prioritized.

Operative time exceeding 300 minutes independently increased morbidity risk. Prolonged procedures often reflect technical complexity, extensive lymphadenectomy, or intraoperative difficulties [19]. Extended operative duration may also increase tissue trauma and inflammatory response, contributing to postoperative complications.

Total gastrectomy was associated with higher morbidity compared to subtotal resection. This finding is consistent with prior studies demonstrating increased physiological stress and anastomotic complexity in total gastrectomy [20]. Careful patient selection and meticulous technique are therefore essential.

Advanced pathological stage independently predicted major morbidity. Patients with stage III disease often require more extensive dissection and exhibit compromised nutritional status, potentially explaining this association [21].

The survival analysis revealed a striking reduction in five-year overall survival among patients with major complications (43.9% vs 74.5%). The hazard ratio of 2.47 suggests that postoperative morbidity exerts a substantial independent oncologic effect. Mechanistically, postoperative inflammatory responses may promote tumor growth and micrometastatic progression [22]. Additionally, delayed or omitted adjuvant chemotherapy following complications may compromise systemic disease control [23].

These findings are consistent with multicenter European analyses demonstrating reduced survival in patients experiencing severe postoperative complications [24]. However, some earlier studies failed to demonstrate independent prognostic impact after adjusting for tumor stage [25]. The prospective design and standardized complication grading in our study strengthen the validity of the observed association.

This study provides valuable prospective evidence from a South Asian population, addressing an important gap in literature [26–30]. The results underscore the necessity of integrating perioperative optimization, nutritional assessment, and surgical precision into gastric cancer management. The present study provides compelling evidence that postoperative morbidity, particularly major complications, has a profound and independent impact on long-term survival after curative gastrectomy for gastric adenocarcinoma, reinforcing the concept that perioperative events are not merely transient surgical setbacks but pivotal determinants of oncologic outcomes. The overall complication rate of 36.5% and major morbidity of 14.8% fall within internationally reported ranges, supporting the external validity of our findings. Hypoalbuminemia emerged as the most potent predictor of major complications, reflecting the critical interplay between nutritional status, systemic inflammation, and tissue healing capacity. Malnutrition compromises collagen synthesis, impairs immune function, and delays tissue regeneration, predisposing patients to anastomotic failure, infections, and wound complications, a relationship corroborated in prior Japanese and European cohorts. These results highlight the urgent need for preoperative nutritional optimization, particularly in regions with high malnutrition prevalence, as interventions such as enteral supplementation, immunonutrition, and targeted prehabilitation may mitigate postoperative risk and improve recovery. Prolonged operative time exceeding 300 minutes independently predicted morbidity, likely reflecting procedural complexity, extensive lymphadenectomy, or intraoperative challenges, and contributing to increased tissue trauma, oxidative stress, and systemic inflammatory responses that exacerbate postoperative complications. Similarly, total gastrectomy was associated with higher morbidity compared to subtotal resection, consistent with prior studies showing that total gastrectomy imposes greater physiological stress, more complex anastomoses, and increased risk of leakage or bleeding, underscoring the necessity for meticulous surgical technique and judicious patient selection. Advanced pathological stage, particularly stage III disease, also independently predicted major complications, likely due to the combination of extensive dissection requirements, compromised nutritional reserve, and tumor-related systemic effects, aligning with previous reports linking tumor burden to perioperative risk. Crucially, survival analysis demonstrated a dramatic reduction in five-year overall survival among patients experiencing major morbidity (43.9% vs. 74.5%), with a hazard ratio of 2.47, signifying that postoperative complications are not simply markers of frailty but exert a direct oncologic influence, potentially via multiple mechanisms including postoperative immunosuppression, enhanced inflammatory milieu promoting micrometastatic progression, and delays or omission of adjuvant chemotherapy. This association is reinforced by multicenter European data, though some earlier studies failed to show independent prognostic impact after stage adjustment, highlighting the value of our prospective design and

standardized complication grading in clarifying this relationship. The study further emphasizes that targeted perioperative strategies, including rigorous preoperative assessment, nutritional supplementation, optimization of operative planning to minimize surgical duration and blood loss, and enhanced recovery protocols, are essential not only to reduce morbidity but also to improve long-term survival outcomes. Importantly, these findings fill a significant knowledge gap in South Asian populations, where differences in baseline nutritional status, tumor biology, and healthcare resources may influence both morbidity and survival, thereby providing context-specific guidance for clinical practice. Limitations include the single-center design, which may limit generalizability, and the absence of molecular or genomic tumor profiling, which could refine risk stratification and identify biologically aggressive tumors more susceptible to perioperative stress. Nevertheless, the prospective methodology, adequate sample size, and rigorous data collection strengthen the reliability of our conclusions. Overall, our results support a paradigm in which postoperative morbidity should be considered a modifiable risk factor with direct implications for survival, emphasizing that interventions aimed at improving nutritional status, reducing operative complexity, and optimizing perioperative care can have dual benefits: decreasing immediate postoperative complications and enhancing long-term oncologic outcomes. Future research should focus on integrating prehabilitation, personalized surgical planning, and postoperative monitoring to mitigate complications and facilitate timely initiation of adjuvant therapy, ultimately translating perioperative optimization into tangible survival benefits. In conclusion, major postoperative morbidity following curative gastrectomy is a critical determinant of patient outcomes, and strategies targeting the identified predictors—hypoalbuminemia, prolonged operative time, total gastrectomy, and advanced stage—are imperative to improve both perioperative safety and long-term survival in gastric cancer patients.

Limitations include single-center design and absence of molecular tumor profiling. Nonetheless, the prospective methodology and adequate sample size enhance reliability.

CONCLUSION

Major postoperative morbidity following curative gastrectomy significantly compromises long-term survival in gastric adenocarcinoma. Preoperative nutritional optimization, minimization of operative duration, and careful surgical planning are critical to improving oncologic outcomes. Early identification and aggressive management of complications may enhance survival and reduce recurrence risk.

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ETHICS STATEMENT

Approved by Institutional Review Board (IRB No: PCMS/IRB/2019-GA-021).

INFORMED CONSENT

Written informed consent was obtained from all participants.

COMPETING INTERESTS

The authors declare no competing interests.

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