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Research Article

Is the Resection Margin Distance Associated with Survival after Resection for Neoadjuvantly treated Gastric and Gastroesophageal Junction Cancer?

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Abstract

Background: The optimal resection margin in neoadjuvantly treated gastroesophageal cancer remains poorly defined. While negative margins (R0) are essential, the clinical relevance of specific margin distances is not defined. **Methods:** We retrospectively analyzed 121 patients undergoing gastric or gastroesophageal junction resection for neoadjuvantly treated adenocarcinomas between 2013 and 2022. The minimal pathological margin was defined as the shortest distance between tumor and the proximal or distal resection margin. Patients were stratified using cutoffs of 1 cm and 2 cm. Overall survival (OS) and recurrence-free survival (RFS) were analyzed using Kaplan–Meier methods and stage-stratified log-rank tests. Patients who died within 30 days after surgery were excluded from survival analyses to reduce perioperative bias. **Results:** The median minimal margin was 2.35 cm. No significant differences in OS or RFS were observed for margins ≥2 cm versus <2 cm or ≥1 cm versus <1 cm (all $p > 0.05$). These findings remained consistent after stage-adjusted analyses. Tumor stage was the dominant prognostic factor. **Conclusion:** Resection margin distance was not associated with survival outcomes after surgery for adenocarcinoma of the stomach or gastroesophageal junction. Achieving an pR0 resection appears oncologically sufficient, and wider margins do not appear to confer additional benefit.

Keywords: Resection Margin; Survival in Gastric Cancer; Gastroesophageal Junction Cancer.

Introduction

Gastric cancer (GC) remains a major global health burden, and surgical resection is the cornerstone of curative treatment [1]. Achieving negative pathological resection margins (pR0) is widely accepted as a fundamental oncologic principle [2, 3]. However, the optimal extent of the resection margin remains controversial [4], particularly in neoadjuvantly treated GCs.

Current guideline recommendations for proximal and distal margins are largely based on historical surgical series and expert consensus rather than high-level prospective clinical trials [5, 6]. Early randomized trials primarily focused on the extent of lymphadenectomy rather than margin distance, yet highlighted the importance of surgical quality for long-term outcomes [2].

Concerns regarding submucosal tumor spread — particularly in diffuse-type gastric cancer — have traditionally supported the concept of wider margins. However, more recent data suggest that once an pR0 resection is achieved, the absolute margin distance may have limited impact on survival [7, 8].

At the same time, advances in multimodal therapy, including perioperative chemotherapy, have shifted the paradigm toward a more biology-driven understanding of GC outcomes [9]. In parallel, minimally invasive and robotic approaches have demonstrated comparable oncologic outcomes to open surgery [10].

These developments raise the question whether traditional concepts of margin width remain clinically relevant in the modern treatment era.

The aim of this study was therefore to evaluate the association between pathological resection margin distance and survival outcomes in a contemporary single-center cohort of patients undergoing surgery for neoadjuvantly treated adenocarcinomas of the stomach or gastroesophageal junction.

Methods

Study Design

This was a retrospective cohort study of consecutive patients undergoing surgery for cancer of the stomach or gastroesophageal junction between 2013 and 2022 at a tertiary referral center. Data was collected from a prospectively led in-clinic database. All patients gave informed written consent for scientific use of their data. This study complies with Helsinki Declaration and good scientific practice guidelines. Follow-up was defined from the date of surgery until death or last contact.

Patients

A total of 229 patients undergoing curative-intent gastrectomy or resection of the gastroesophageal junction for histologically confirmed adenocarcinoma were screened. Patients with metastatic disease at diagnosis or incomplete (pR1, R2) resection were excluded such as patients who died within 30 days after surgery. Surgical approaches included conventional and robotic resection of the distal esophagus/GEJ and gastric resection.

Collected variables included age, sex, tumor stage, tumor localization, neoadjuvant therapy, surgical approach, type and year of surgery.

The minimal margin was defined as the shortest pathological distance between tumor and either the proximal or distal resection margin.

Primary outcomes were overall survival (OS) and recurrence-free survival (RFS). Recurrence-free survival was defined as time from surgery to documented recurrence or tumor-related death.

Statistical Analysis

Patients were stratified by margin cutoffs of ≥1 cm vs. <1 cm and ≥2 cm vs. <2 cm. Kaplan–Meier curves were compared using log-rank tests. Resection margin cutoffs were predefined based on their clinical relevance and previously reported surgical standards rather than data-driven optimization. Historically, margin distances in this range have frequently been discussed in surgical guidelines and retrospective studies evaluating oncologic adequacy in gastric and gastroesophageal junction cancer [6].

The 1 cm cutoff was chosen to assess whether very close but negative margins were associated with impaired outcomes, whereas the 2 cm cutoff was used to reflect a more conservative surgical threshold frequently pursued in clinical practice

To account for confounding by tumor stage, stage-adjusted analyses were performed using stratified log-rank tests with tumor stage as the stratification variable. A p-value < 0.05 was considered statistically significant. Missing data were handled using complete-case analysis. Statistical analysis was performed using JASP (Version 0.16).

Results

Patient Characteristics

A total of 121 patients were included in the analysis. Median age was 64.1 years (IQR 58.2–73.2), and 81.7% of patients were male. The majority of procedures were performed using a robotic approach (79.2%), while 20.8% were performed using an open approach.

With regard to the type of resection, a majority of patients underwent gastroesophageal junction (GEJ)/distal esophageal resections (83%) while a smaller portion underwent gastric resection (83%). Tumor stages were predominantly advanced, with approximately 45% of patients presenting with stage III disease. Detailed baseline characteristics are summarized in Table 1.

Variable	Value
Sex	
Male	98 (≈82%)
Female	22 (≈18%)
Surgical approach	
Robotic	95 (≈79%)
Open	25 (≈21%)
Type of resection	
GEJ[b] resection	100 (≈83%)
Gastric resection[c]	20 (≈17%)
Tumor stage (UICC[d])	
Stage I	20 (≈17%)
Stage II	26 (≈22%)
Stage III	54 (≈45%)
Stage IV	7 (≈6%)

[a]interquartile range
[b]gastroesophageal junction
[c]including partial, total and extended gastrectomy
[d]Union for International Cancer Control

Tabel 1: Patient Characteristics (n=120).

Survival Analysis Patient Characteristics

A total of 121 patients were included in the analysis after exclusion of 30-day mortality. Median age was 64.1 years (IQR 58.2–73.2), and 81.7% of patients were male. The majority of procedures were performed using a robotic approach (79.2%), while 20.8% were performed using an open approach.

With regard to the type of resection, patients were categorized into GEJ/distal esophageal resections and gastric resections. Tumor stages were predominantly advanced, with approximately 45% of patients presenting with stage III disease. Detailed baseline characteristics are summarized in Table 1.

Resection Margin Distribution

The median minimal resection margin was 2.35 cm (IQR 1.38–3.13).

Using a cutoff of 2 cm, 63 patients (52.1%) had margins ≥2 cm, while 58 patients (47.9%) had margins <2 cm.

For the 1 cm cutoff, 97 patients (80.2%) had margins ≥1 cm, whereas 24 patients (19.8%) had margins <1 cm. The distribution of resection margins is illustrated in Figure 4.

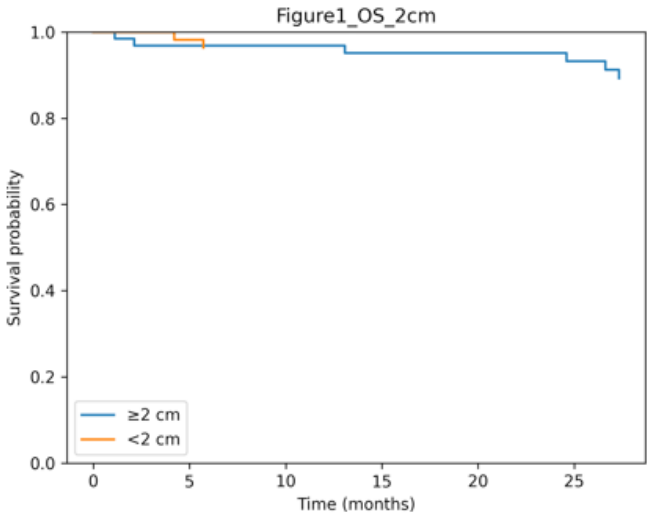

Figure 1: Kaplan–Meier OS (2 cm cutoff).

Overall Survival

During follow-up, 8 deaths were observed. Median follow-up was 45.6 months (IQR 28.8–64.4).

Margin Cutoff of 2 cm

No significant difference in overall survival was observed between patients with margins ≥2 cm and those with margins <2 cm (log-rank $p > 0.05$; Figure 2A). Median overall survival was not reached in either group. Perioperative and oncologic outcomes according to the 2 cm margin cutoff are summarized in Table 2. No statistically significant differences were observed between groups with regard to deaths, recurrence, or anastomotic leak. Length of stay was numerically longer in patients with margins ≥2 cm, but this did not reach statistical significance.

Variable	≥2 cm (n = 63)	<2 cm (n = 58)	p-value
Deaths, n (%)	6 (9.5%)	2 (3.4%)	0.276
Recurrence, n (%)	25 (39.7%)	20 (34.5%)	0.578
Anastomotic leak, n (%)	22 (35.5%)*	17 (30.9%)*	0.695
Length of stay, median (IQR), days	22.0 (15.0–35.0)	15.5 (12.3–27.8)	0.078

Table 2: Outcomes according to minimal resection margin (2 cm cutoff).

Margin Cutoff of 1 cm

Similarly, no significant difference in overall survival was observed when applying a 1 cm cutoff (log-rank $p > 0.05$; Figure 2B).

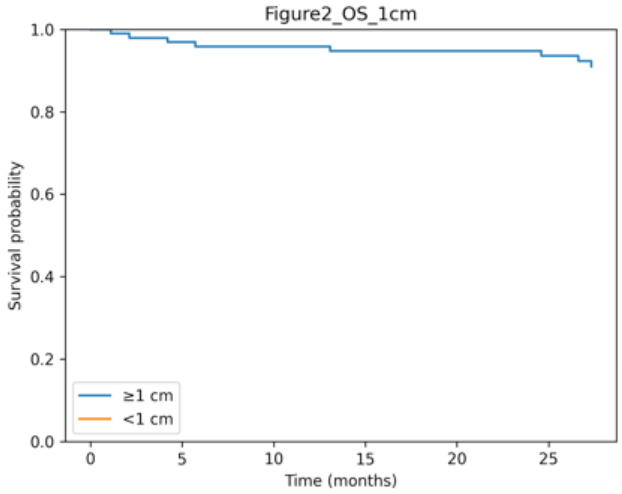

Figure 2: Kaplan–Meier OS (1 cm cutoff).

Recurrence-Free Survival

No significant differences in recurrence-free survival were observed between margin groups, neither for the 2 cm cutoff nor for the 1 cm cutoff (all $p > 0.05$; Figure 3A-B).

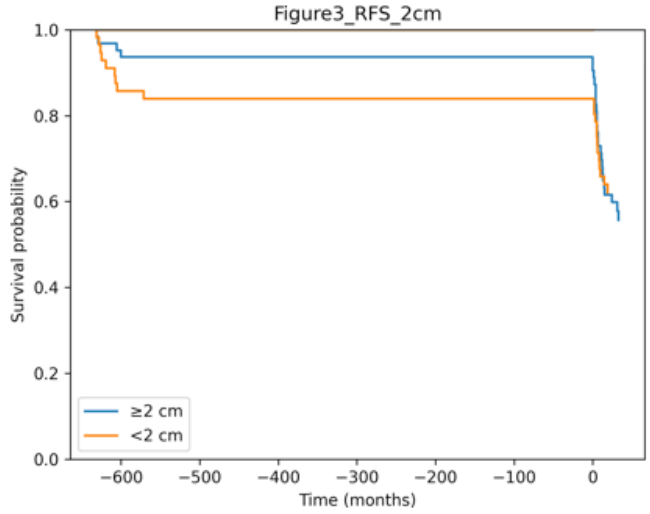

Figure 3: Kaplan–Meier RFS (2 cm cutoff).

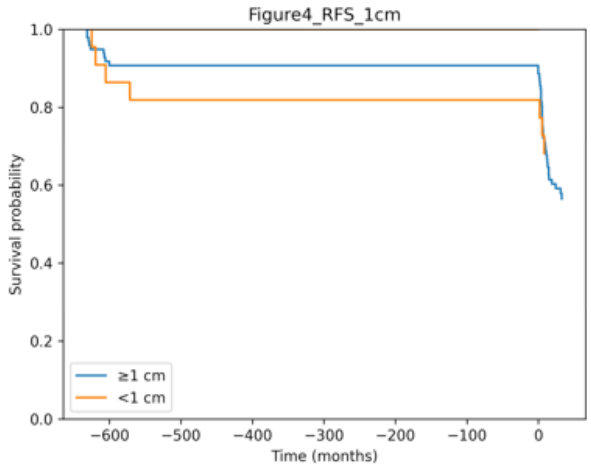

Figure 4: Stage-stratified OS.

Stage-Adjusted Analyses

Stage-adjusted analyses using stratified log-rank tests confirmed the absence of an association between resection margin distance and survival outcomes.

Impact of Tumor Stage

As expected, patients with advanced tumor stages tended to show worse overall and recurrence-free survival compared to patients with early-stage disease.

Additional Analyses

No obvious differences in survival outcomes were observed between patients undergoing GEJ/distal esophageal resections and those undergoing gastric resections.

Discussion

In this study, we found that resection margin distance was not associated with overall or recurrence-free survival following surgical resection of cancer of the stomach or gastroesophageal junction. This finding was consistent across different cutoff values (1 cm and 2 cm) and remained robust after adjustment for tumor stage.

These results challenge the long-standing surgical assumption that wider resection margins translate into improved oncologic outcomes. While achieving a pR0 resection remains essential, our data suggest that the absolute distance to the tumor is not a clinically relevant determinant of survival in neoadjuvantly treated patients.

This observation is consistent with prior studies indicating that tumor biology and response to systemic therapy are the principal determinants of outcome, whereas the extent of surgical resection plays a comparatively limited role. Historically, recommendations for wide margins were based on concerns about microscopic tumor spread, particularly in diffuse-type cancers [6]. However, these concepts were established in an era preceding modern imaging, perioperative chemotherapy, and standardized surgical techniques. Contemporary evidence suggests that these assumptions may overestimate the clinical relevance of margin distance, as large randomized trials and cohort studies have consistently demonstrated that tumor stage and response to systemic therapy are the primary drivers of survival [9, 11, 12].

Current guideline recommendations, including the recent update of the German S3 guideline for gastric cancer, emphasize the importance of achieving an R0 resection, while the exact extent of margin distance remains a subject of ongoing discussion. The guideline revision highlights the need for a nuanced interpretation of resection status, taking into account both tumor biology and anatomical factors [13].

From a clinical perspective, our findings are particularly relevant in situations where wider margins would necessitate more extensive resections, such as higher anastomosis in distal esophageal resection or total gastrectomy instead of subtotal resection. In such cases, the potential increase in morbidity must be carefully balanced against uncertain oncologic benefit, especially in Western patient populations with increasing age and frailty [14].

Importantly, no association between margin distance and survival was observed across different analytical approaches, arguing against the presence of a clinically meaningful threshold effect.

Limitations

This study has several limitations. First, its retrospective design introduces the potential for selection bias and unmeasured confounding. Second, the relatively small sample size and, in particular, the low number of observed events limit statistical power and may obscure small but clinically relevant differences in survival.

Third, while gastric and gastroesophageal junction cancers share biological characteristics, the surgical approach differs substantially, which may introduce heterogeneity in the analysis.

Future studies should more specifically address these technical aspects.

Histological subtypes, such as the distinction between intestinal and diffuse-type tumors, were not systematically analyzed, which may be relevant given differences in tumor spread patterns.

Finally, an important aspect not addressed in the present analysis is the circumferential resection margin (CRM), particularly in tumors of the distal esophagus and gastroesophageal junction. CRM involvement has been shown to be a strong prognostic factor and may in some cases be more relevant than longitudinal margin distance [15, 16]. While pR0 status also applied to the circumferential margin in our cohort, reporting of distance between depth of tumor infiltration and distance to the CRM is not standardized in GC. Thus, potential impact of the latter on survival outcomes could not be assessed and represents an important limitation of the present study. Contemporary guidelines also emphasize the importance of CRM assessment in upper gastrointestinal cancers. Future studies should incorporate both longitudinal and circumferential margin assessment to better define their relative prognostic impact.

Conclusion

Resection margin distance was not associated with survival outcomes in this cohort. Achieving negative margins appears oncologically sufficient, and wider margins do not appear to provide additional benefit.

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