

We sincerely thank the reviewers for their interest in our work and for their helpful comments that will greatly improve our manuscript. We have tried our best to respond to all points raised and have made necessary changes to the manuscript.

Anonymous reviewer #1

1. The safe length of PRM is a very meaningful topic. There is still some controversy about the optimal standard of PRM. There were only 20 cases with the length of PRM \leq 1.0 cm. In these cases, partly because the tumor was too large, the length of PRM was forced to be controlled within 1 cm, so the conclusion was prone to statistical bias.

We appreciate the reviewer's constructive comments. There was indeed a statistical difference in tumor size between the different PRM groups, as shown in Table 2. We have carried out a multivariate analysis as shown in Table 5 in an attempt to adjust such confounding factors. There may potentially be an issue of multicollinearity, so we ran a test to verify Variance Inflation Factor (VIF), and all values were <2 . Therefore, we cautiously suggest that we have tried our best to minimize statistical bias.

2. Older age ($p=0.028$), linitis plastica ($p<0.001$) and the presence of lymphovascular invasion ($p=0.013$) were also associated with worse RFS (Table 5). linitis plastica is a special diffuse infiltrating tumor, how to evaluate the length of PRM at this time?

In this study, we used the proximal resection margin as confirmed by the final pathology report. There is a difference between the actual length of the margin from freshly resected specimens due to shrinkage from formalin fixation. However, in this manner, we could decrease any observational errors operators may make, particularly in cases where tumor infiltration is not grossly distinguishable, as the reviewer mentioned above.

3. Billroth II ($p=0.004$) and RYGB ($p=0.004$) reconstructions resulted in worse RFS than Billroth I reconstruction (Table 4). This conclusion seems to be different from that reported in most of the literature. Could you analyze the specific reasons?

We thank the reviewer for their thorough review. We totally agree that the information that

different types of reconstructions can result in different RFS or OS is not general knowledge.

Billroth I (B-I) was the most preferred method of anastomosis for distal gastric cancer at our institution. When the tumor involved pylorus or the stomach stump was too short for gastroduodenostomy, Billroth II (B-II) or RYGB was applied. Therefore, there exists a possibility that cases with B-II and RYGB anastomosis were associated with larger and more progressed tumors. However, when we tested RFS in patients who went through distal gastrectomy stratified by TNM stage, the reconstruction method still showed a significant difference.

In addition, surgeons' preferences are included when deciding the reconstruction method. This study involves data from >10 different surgeons. Although the gastrectomy procedure is standardized, surgical skills and procedures may have differed between surgeons as we have added in the discussion section as a limitation of our study. We added the operator as a variable in our survival analysis but it turned out to have no significant impact on OS or RFS.

Another reason we considered is that because B-I is the most preferred method in our institution, surgeons were more comfortable with it, resulting in better outcomes.

Although there is no consensus, several studies revealed more gastric stump cancer in patients who underwent B-II reconstruction rather than B-I after gastrectomy either due to carcinoma or benign lesions (1–3). In addition, an RCT from Japan showed more hematogenous recurrence in B-II than B-I (4).

We consider this an important issue that warrants further investigation, taking many factors such as patterns of recurrences, recurrence time after surgery, histology of the initial tumor, and many others into consideration. We have added descriptions of this issue in the discussion section because readers may be similarly curious about the results.

Anonymous reviewer #2

In this study, the authors aimed to investigate the effects of the proximal resection margin distance on the prognosis of patients having undergone gastrectomy for advanced gastric cancer. They concluded that the proximal resection margin distance was not a prognostic factor, where they pointed out that if a negative margin was confirmed from the intraoperative frozen section biopsy, wider excision was not

required. The study is well-designed, the results are adequately interpreted in the discussion and the manuscript is suitably written. I congratulate the authors for their successful work.

We appreciate this encouraging reviewer feedback.

Anonymous reviewer #3

1. Surgical treatment is the cornerstone of gastric cancer. Surgical treatment includes D2 lymphadenectomy with total or subtotal gastrectomy for potentially curable T2-T4 tumors and lymph node positive patients. Other resection and lymphadenectomy options should be for only palliative interventions for tumors in these stages. Chemotherapy and targeted therapies are only adjunctive therapies. Adequate resection margin (RM) must be provided for curative surgery in gastric cancers. For T1tumors 2 cm gross PRM should be provided. At least 3 cm proximal margin (PRM) for T2-T4tumors with expansive growth pattern (Type 1-2), and at least 5 cm PM for tumors with infiltrative growth pattern (Type 3-4) is recommended. Frozen section examination of the proximal margin is recommended when safe surgical margin cannot be obtained. For tumors infiltrating the esophagus, a 5 cm margin is not required, but frozen section examination of the PRM is recommended (Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1–19). RM plays an important role in prognosis. -Type of lymphadenectomy should be noted and analyzed (as D0,D1, D1+, D2, ...)

We appreciate your constructive review. For curative-intent surgery for advanced gastric cancer, surgeons always endeavor to achieve D2 lymph node dissection. In this study, we only included cases where R0 resection with D2 or D2+ lymph node dissection was performed and we have excluded cases where proper node dissection was not achieved. However, there is a limitation in that as a retrospective study, we have relied on the surgeons' record on operation notes to determine the type of lymphadenectomy. The number of collected lymph nodes (CLN) is the only objective record we have concerning the lymphadenectomy, so we have presented it as a variable and excluded cases with fewer than 15 CLNs.

2. Although it is not clear that either the resection margin determined during the surgery or by the histopathological examination will be taken into consideration, it is a fact that the final microscopic surgical margin is generally accepted. This leads to some disagreements between surgeons and pathologists. Immediately after resection and after formol fixation, contractility and shrinkage in tissues are well known. May be important difference in the proximal RMs of patients with gastric cancer between measurements before resection and after resection. -In this study; The authors used only the final pathologic report after formalin fixation. Whereas, use of correction factors to predict the shrinkage of surgical margins in curative surgeries will be effective in providing adequate resection margin.

This is an important issue. We agree with comment regarding the shortcoming in our data on proximal resection before formalin fixation. This is a retrospective study based on medical records and we do not have a complete record on proximal resection margins as measured by surgeons on fresh specimens. In addition, among the data we do have, the measurement method differs for each surgeon and the time after resection for measurements is non-uniform; some were measured immediately after resection, some were measured after surgery was completed. Observational errors may increase in cases where tumor infiltration is not grossly distinguishable such as in the linitis plastica. Therefore, we abandoned the proximal resection margin measured by the surgeons and used the final pathologic report for this study. This is described in the conclusion section as a limitation of our study.

3. An important criticism for conclusion section: “Once a negative margin is acquired from the intraoperative frozen section biopsy, it is no longer necessary for surgeons to strive to achieve ‘sufficient’ proximal margins as recommended by conventional guidelines” is an insubstantial sentence for a retrospective study. Should be reevaluated

We agree with the reviewer’s comment. We have deleted the presumption in the sentence and revised the conclusion as follows.

“In conclusion, the distance of PRM is not a prognostic factor for AGC patients; it does not affect the incidence of recurrence or local recurrence. A greater PRM distance was not associated with better survival outcomes and a distance of < 1 cm did not correlate with worse OS or RFS.”

4. In Tables: -TNM stages should be noted and analyzed in tables 1-5

Thank you for your important comment. We have added the TNM stages as variables in Tables 1–3. However, for multivariate analysis on recurrence-free survival (Tables 4-7), we have not added this variable because it may cause a collinearity problem, being a factor closely related the variables T-stage and N-stage.

Anonymous reviewer #4

1. What is the basis of the group dividing? why is <1cm , 1-3cm,3-5cm and >5cm ?

According to the 2014 Japanese Guidelines (ver. 4) at least 3 cm of PRM for T2–T4 tumors with expansive growth pattern type and at least 5 cm PRM for tumors with an infiltrative growth pattern is recommended. We consulted the statistician for a reasonable method to divide the PRM groups and determine that group dividing should be done according to the clinical significance. Therefore, we divided the groups into <3 cm, 3–5 cm and >5 cm in accordance with the Japanese guidelines as quoted above and added a <1 cm group to evaluate cases with very short resection margins.

2. The authors did not conduct a univariate or multivariate analysis of 5-year survival.

We thank you for your constructive review and we have now added a table to show the results of univariate and multivariate analysis of overall survival.

3. The researchers did not record the length of the PRM in living condition, PRM could be longer than measured.

Your comment is absolutely true. We have used the final pathologic report for the length of the PRM, and because there is a formalin fixation step, specimen shrinkage is inevitable. We have described this in the discussion section as a limitation of our study.

4. why the authors excluded the siewert II type AEG tumor?

While Siewert type III is treated as gastric cancer, consensus has yet to be reached regarding the treatment of Siewert type II. Therefore, we excluded Siewert type II gastroesophageal junction cancer in this study.

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3. **Tanigawa N**, Nomura E, Lee S-W, Kaminishi M, Sugiyama M, Aikou T, et al. Current state of gastric stump carcinoma in Japan: based on the results of a nationwide survey. *World J Surg*. 2010; **34**(7): 1540-1547.
4. **Morita M**, Nabeshima K, Nakamura K, Kondoh Y, Ogoshi K. Which is better long-term survival of gastric cancer patients with Billroth I or Billroth II reconstruction after distal gastrectomy?-Impact on 20-year survival rate. *Ann Cancer Res Ther*. 2013; **21**: 20-25.