

Response to Reviewer ① Comments

Thank you for inviting us to submit a revised draft of our manuscript entitled, “Long-term Outcomes of Postgastrectomy Syndrome After Total Laparoscopic Distal Gastrectomy Using the Augmented Rectangle Technique” to *World Journal of Gastrointestinal Surgery*. We also appreciate the time and effort you and each of the reviewers have dedicated to providing insightful feedback on ways to strengthen our paper. Thus, it is with great pleasure that we resubmit our article for further consideration. We have incorporated changes that reflect the detailed suggestions you have graciously provided. We also hope that our edits and the responses we provide below satisfactorily address all the issues and concerns you and the reviewers have noted.

To facilitate your review of our revisions, the following is a point-by-point response to the questions and comments.

Point 1: The important baseline characteristics of the two cohorts are the major concern. For example, half of the PGSAS group underwent open surgery. I suggest only use the data of those who underwent laparoscopic surgery. Besides, propensity score-matched method is strongly recommended.

Response 1: We wish to express our deep appreciation to the reviewer for his insightful comment on this point. We agree that additional information on propensity matched analysis as the reviewer suggested would be valuable. Regrettably, the PGSAS database does not present individual data, so it is not possible to perform stratification, multivariate analysis, or propensity score matching to adjust for the influence of background factors. Although we are unable to meet the expectations of the reviewers this time, If the national data of the PGSAS study, such as the reference values of clinical laboratory tests and the national standard values of SF-36, are accepted as a standard for comparison and control, we believe that many studies evaluating surgical techniques and procedures at our own institution using the PGSAS statistical kit will be published, and we can expect the evolution of surgical techniques. In this study, the content was described in the limitation. (p 12, lines 18-26)

Additionally, we extracted ART cases using the eligibility criteria adopted in the PGSAS as part of a larger national database and showed the analysis results in the supplement Table S1, S2. (p 28-30)

Patient eligibility criteria were: (1) pathologically confirmed stage IA or IB gastric cancer; (2) first-time gastrectomy; (3) age ≥ 20 and ≤ 75 years; (4) no history of chemotherapy; (5) no known recurrence or distant metastasis; (6) gastrectomy conducted one or more years prior to the enrollment date; (7) performance status (PS) ≤ 1 on the Eastern Cooperative Oncology Group (ECOG) scale; (8) full capacity to understand and respond to the questionnaire; (9) no history of other diseases or operations that might influence the responses to the questionnaire; and (10) no organ failure or mental illness.

Forty-seven of 94 patients in the ART group met the eligibility criteria for the PGSAS. Even if the patient backgrounds between the two groups are aligned and analyzed, almost the same results are obtained. (Supplement Table S1, S2)

Point 2: Postoperative period in months also results in heterogeneity.

Response 2: We thank the reviewer for this comment. We apologize that our interpretation of this comment is very difficult and could be wrong. If our interpretation is wrong, we will correct it immediately. Most of the recent reports^[1-6] on PGS and quality of life in gastrectomy for gastric cancer use months for the postoperative observation period, and we believe that it is acceptable to use that unit in this study.

We agree that the postoperative period influences the results. The postoperative observation period was significantly longer in the PGSAS group than in the ART group (40.7 ± 30.7 mo vs 27.1 ± 12.2 mo, respectively; $P < 0.001$) in this study. Kobayashi *et al*^[7] reported that patients rarely had any subsequent changes in their QOL more than 1 year after gastrectomy. We believe the average observation period in our study is, by definition, appropriate, so we would like to adopt the current text for the present study. Of course, it would be desirable to compare the results by aligning the postoperative observation period, and we will consider this as an additional study in the future.

1 Nakada K, Takahashi M, Ikeda M, Kinami S, Yoshida M, Uenosono Y, Kawashima Y, Nakao S, Oshio A, Suzukamo Y, Terashima M, Kodera Y. Factors affecting the quality of life of patients after gastrectomy as assessed using the newly developed PGSAS-45 scale: A nationwide multi-institutional study. *World J Gastroenterol* 2016; **22**(40): 8978-8990 [PMID: 27833389 PMCID: PMC5083803 DOI: 10.3748/wjg.v22.i40.8978]

2 Takiguchi N, Takahashi M, Ikeda M, Inagawa S, Ueda S, Nobuoka T, Ota M, Iwasaki Y, Uchida N, Kodera Y, Nakada K. Long-term quality-of-life comparison of total gastrectomy and proximal gastrectomy by postgastrectomy syndrome assessment scale (PGSAS-45): a nationwide multi-institutional study. *Gastric Cancer* 2015; **18**(2): 407-416 [PMID: 24801198 DOI: 10.1007/s10120-014-0377-8]

3 Kawahira H, Kodera Y, Hiki N, Takahashi M, Itoh S, Mitsumori N, Kawashima Y, Namikawa T, Inada T, Nakada K. Optimal Roux-en-Y reconstruction after distal gastrectomy for early gastric cancer as assessed using the newly developed PGSAS-45 scale. *Surg Today* 2015; **45**(10): 1307-1316 [PMID: 25631461 DOI: 10.1007/s00595-015-1111-9]

4 Kinami S, Takahashi M, Urushihara T, Ikeda M, Yoshida M, Uenosono Y, Oshio A, Suzukamo Y, Terashima M, Kodera Y, Nakada K. Background factors influencing postgastrectomy syndromes after various types of gastrectomy. *World J Clin Cases* 2018; **6**(16): 1111-1120 [PMID: 30613669 PMCID: PMC6306647 DOI: 10.12998/wjcc.v6.i16.1111]

5 Okubo K, Arigami T, Matsushita D, Sasaki K, Kijima T, Noda M, Uenosono Y, Yanagita S, Ishigami S, Maemura K, Natsugoe S. Evaluation of postoperative quality of life by PGSAS-45 following local gastrectomy based on the sentinel lymph node concept in early gastric cancer. *Gastric Cancer* 2020; **23**(4): 746-753 [PMID: 32086650 DOI: 10.1007/s10120-020-01047-7]

6 Yabusaki H, Kodera Y, Fukushima N, Hiki N, Kinami S, Yoshida M, Aoyagi K, Ota S, Hata H, Noro H, Oshio A, Nakada K. Comparison of Postoperative Quality of Life among Three Different Reconstruction Methods After Proximal Gastrectomy: Insights From the PGSAS Study. *World J Surg* 2020; **44**(10): 3433-3440 [PMID: 32506229 PMCID: PMC7458934 DOI: 10.1007/s00268-020-05629-5]

7 Kobayashi D, Kodera Y, Fujiwara M, Koike M, Nakayama G, Nakao A. Assessment of quality of life after gastrectomy using EORTC QLQ-C30 and STO22. *World J Surg* 2011; **35**(2): 357-364 [PMID: 21104250 DOI: 10.1007/s00268-010-0860-2]

Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries. We have worked hard to incorporate your feedback and hope that these revisions persuade you to accept our submission.

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Point 1: The details of ART has not described in the section of methods.

Response 1: Thank you very much for providing important comments. We agree with you. We have added a brief description of the ART technique in the method section. (p 6, lines 21-30, p 7, lines 1-3)

Point 2: The volume of patients in ART group was relative small.

Response 2: Thank you for providing these insights. Since ART is a reconstruction method that we developed ourselves, we can only study it at a single institution where it can be performed. Therefore, unfortunately, it is difficult to increase the number of patients in the ATR group at this time. We hope that the publication of this paper will allow us to study a larger sample of patients by increasing the number of institutions that can perform the procedure.

Point 3: The size of tumor was not provided which might effect the results of Billroth I reconstructions after distal gastrectomies in gastric cancer patients.

Response 3: Thank you for providing these insights. We have added tumor size to the results section. (p 8, lines 27)

Point 4: The section of discussion is redundant, which should only focus on the details and effects of ART on postoperative patients, and explain the reason of beneficial long-term results for postgastrectomy syndrome and quality of life in patients induced by ART.

Response 4: We strongly appreciate the reviewers' comments on this point. We have removed redundant sections and revised the text to be as compact as possible. Thanks for pointing this out, we were able to save about 1000 words and focussed on the impact of ART on PGS and QOL. (Old edit text p 9, lines 21-24, p 9, lines 30-32, p 11, lines 13-19, p 11, lines 22-27)

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