

Letter to the Editor



Reply: Comment on Rethinking Neoadjuvant Therapy: A Critical Evaluation of Exclusion Criteria in Gastric Cancer Surgery Studies

Jawon Hwang ^{1,2}, Woo Jin Hyung ^{1,2,3}

¹Department of Surgery, Yonsei University College of Medicine, Seoul, Korea

²Gastric Cancer Center, Yonsei Cancer Center, Yonsei University Health System, Seoul, Korea

³Department of Faculty Surgery No. 1, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

OPEN ACCESS

► See the letter “Rethinking Neoadjuvant Therapy: A Critical Evaluation of Exclusion Criteria in Gastric Cancer Surgery Studies” in volume 25 on page 523.

Received: Feb 12, 2025

Accepted: Feb 12, 2025

Published online: Mar 10, 2025

Correspondence to

Woo Jin Hyung

Department of Surgery, Yonsei University
College of Medicine, 50-1 Yonsei-ro,
Seodaemun-gu, Seoul 03722, Korea.
Email: wjhyung@yuhs.ac

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ORCID iDs

Jawon Hwang
<https://orcid.org/0009-0008-6759-7426>
Woo Jin Hyung
<https://orcid.org/0000-0002-8593-9214>

Conflict of Interest

No potential conflict of interest relevant to this
article was reported.

We thank Dr. Ilhan et al. [1] for their interest in our study [2]. They mainly addressed 2 issues: 1) the exclusion of patients who underwent neoadjuvant chemotherapy (NAC) and 2) the low rate of patients receiving adjuvant chemotherapy.

Ilhan et al. [1] pointed out that excluding patients who underwent NAC may have made our findings less reflective of real-world practice. This concern likely stems from differences in clinical practice regarding NAC between the East and the West. Western guidelines have recommended NAC since the publication of pivotal trials such as the MAGIC trial (2006) [3]. However, these results have not been widely accepted in the East for several reasons. These include the relatively low completion rates of D2 lymphadenectomy in the studies mentioned above and the lower prevalence of far-advanced gastric cancer in Asia, which reduces the need for tumor shrinkage before surgery [4].

Preoperative treatments did not gain acceptance in the East until the PRODIGY trial in 2021 demonstrated positive outcomes [5]. Even now, the 2023 version of the Japanese Gastric Cancer Treatment Guidelines suggests considering NAC only for cases with bulky nodal metastases, stating, “There is no clear recommendation for NAC for curatively resectable advanced gastric and esophagogastric junctional cancer.” [6]. While the Korean Gastric Cancer Treatment Guidelines recommend considering NAC for locally advanced gastric cancer, these guidelines were only recently introduced in 2023 [7]. Furthermore, the lack of robust evidence regarding patient selection, optimal NAC duration, and appropriate regimens has contributed to its limited adoption in real-world clinical practice in the East [8]. The higher susceptibility of Eastern patients to chemotherapy-related adverse events has also played a role in its restricted use. We acknowledge the need for further research to compare the efficacy of laparoscopic total gastrectomy (LTG) and robotic total gastrectomy (RTG) in the context of NAC. However, it is important to note that during the study period, NAC was not part of the standard treatment protocol in Korea. This is evidenced by the exclusion of only 9 patients who underwent NAC in our study [2].

Second, Ilhan et al. [1] expressed concerns regarding the low proportion of patients who received adjuvant chemotherapy in our study. However, we would like to clarify that the proportion was not as low as suggested. As shown in **Table 2** of the original study, prior to inverse probability of treatment weighting (IPTW), there were 129 and 91 stage II and III patients in the LTG and RTG groups, respectively. Among them, 104 (80.6%) patients in the LTG group and 77 (85.0%) in the RTG group received adjuvant chemotherapy [2]. Some stage IIA patients did not receive adjuvant chemotherapy because, unlike the National Comprehensive Cancer Network [9] or European Society of Medical Oncology [10] guidelines, the Japanese Gastric Cancer Treatment Guidelines classify pT3N0 tumors as ineligible for adjuvant chemotherapy [6]. After IPTW, the total number of stage II and III patients was 140.2 in the LTG group and 102.3 in the RTG group. Of these, 114.9 (82.0%) patients in the LTG group and 82.6 (80.7%) in the RTG group received adjuvant chemotherapy. As mentioned in the letter, the previously cited proportions of 55.7% and 56.2% included stage I patients, which may have led to a misleading interpretation. In previous studies on locally advanced gastric cancer, postoperative adjuvant chemotherapy rates were reported to range from 40% to 60% [11-13]. Thus, the rates observed in our study were not low.

We hope this clarifies the issues raised by Dr. Ilhan et al. [1]. Once again, we are sincerely their interest in our work.

REFERENCES

1. Ilhan Y, Guzel HG, Balcik OY. Rethinking neoadjuvant therapy: a critical evaluation of exclusion criteria in gastric cancer surgery studies. *J Gastric Cancer* 2025;25:523-525. [CROSSREF](#)
2. Hwang J, Kim KY, Park SH, Cho M, Kim YM, Kim HI, et al. Long-term oncologic outcomes of robotic total gastrectomy for advanced gastric cancer. *J Gastric Cancer* 2024;24:451-463. [PUBMED](#) | [CROSSREF](#)
3. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med* 2006;355:11-20. [PUBMED](#) | [CROSSREF](#)
4. Ohtsu A. Diverse eastern and Western approaches to the management of gastric cancer. *Gastrointest Cancer Res* 2007;1:S10-S15. [PUBMED](#)
5. Kang YK, Yook JH, Park YK, Lee JS, Kim YW, Kim JY, et al. PRODIGY: a phase III study of neoadjuvant docetaxel, oxaliplatin, and S-1 plus surgery and adjuvant S-1 versus surgery and adjuvant S-1 for resectable advanced gastric cancer. *J Clin Oncol* 2021;39:2903-2913. [PUBMED](#) | [CROSSREF](#)
6. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2021 (6th edition). *Gastric Cancer* 2023;26:1-25. [PUBMED](#) | [CROSSREF](#)
7. Kim TH, Kim IH, Kang SJ, Choi M, Kim BH, Eom BW, et al. Korean practice guidelines for gastric cancer 2022: an evidence-based, multidisciplinary approach. *J Gastric Cancer* 2023;23:3-106. [PUBMED](#) | [CROSSREF](#)
8. Tong X, Zhi P, Lin S. Neoadjuvant chemotherapy in Asian patients with locally advanced gastric cancer. *J Gastric Cancer* 2023;23:182-193. [PUBMED](#) | [CROSSREF](#)
9. Ajani JA, D'Amico TA, Bentrem DJ, Chao J, Cooke D, Corvera C, et al. Gastric cancer, version 2.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2022;20:167-192. [PUBMED](#) | [CROSSREF](#)
10. Lordick F, Carneiro F, Cascinu S, Fleitas T, Haustermans K, Piessen G, et al. Gastric cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol* 2022;33:1005-1020. [PUBMED](#) | [CROSSREF](#)
11. Hyung WJ, Yang HK, Park YK, Lee HJ, An JY, Kim W, et al. Long-term outcomes of laparoscopic distal gastrectomy for locally advanced gastric cancer: the KLASS-02-RCT randomized clinical trial. *J Clin Oncol* 2020;38:3304-3313. [PUBMED](#) | [CROSSREF](#)
12. Huang C, Liu H, Hu Y, Sun Y, Su X, Cao H, et al. Laparoscopic vs open distal gastrectomy for locally advanced gastric cancer: five-year outcomes from the CLASS-01 randomized clinical trial. *JAMA Surg* 2022;157:9-17. [PUBMED](#) | [CROSSREF](#)
13. Kinoshita T, Uyama I, Terashima M, Noshiro H, Nagai E, Obama K, et al. Long-term outcomes of laparoscopic versus open surgery for clinical stage II/III gastric cancer: a multicenter cohort study in Japan (LOC-A study). *Ann Surg* 2019;269:887-894. [PUBMED](#) | [CROSSREF](#)