

## Letter to the Editor



# Rethinking Neoadjuvant Therapy: A Critical Evaluation of Exclusion Criteria in Gastric Cancer Surgery Studies

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### Author Contributions

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Dear Editor,

We read with great interest the valuable study by Hwang et al. [1], titled “Long-term Oncologic Outcomes of Robotic Total Gastrectomy for Advanced Gastric Cancer”. The study compares the oncologic outcomes of laparoscopic total gastrectomy (LTG) and robotic total gastrectomy (RTG), which represent cornerstone surgical approaches in the treatment of gastric cancer. In this context, the study makes a significant contribution to the literature. We extend our gratitude to the authors for this intriguing and valuable work. However, from the perspective of medical oncology, we would like to offer some contributions and critiques regarding this study. We believe that addressing the following points in the discussion could further enhance its value to the literature.

In this study, the authors primarily aimed to evaluate the long-term oncologic outcomes of RTG in comparison to LTG in advanced gastric cancer, as stated in the title. The study reported that 5-year relapse-free survival (RFS) and overall survival (OS) were comparable between the RTG and LTG groups, with consistent results observed in both stage II and stage III subgroups. The study was conducted between 2007 and 2020, and it is notable that patients who received neoadjuvant chemotherapy or radiotherapy were excluded. In oncology practice, the MAGIC trial, published in 2006, demonstrated the survival benefit of neoadjuvant chemotherapy with epirubicin, cisplatin, and infusion 5-fluorouracil (ECF) followed by surgery, compared to surgery alone [2]. Subsequently, in 2017, the FLOT regimen, consisting of docetaxel, oxaliplatin, and 5-fluorouracil, was shown to be more effective than ECF and has since become the global standard for neoadjuvant treatment in gastric cancer [3]. In this study, approximately 17% of patients in both groups were classified as cT4a, and more than 50% were cN+, representing a high-risk population for gastric cancer. For such patients, neoadjuvant therapy is currently considered indispensable. Given the study period, when effective neoadjuvant regimens were already well-established, it would have been valuable for the authors to clarify why patients did not receive neoadjuvant therapy or why those who did were excluded from the analysis. Consequently, we believe that the results of this study, which primarily compare OS and RFS, may have limited applicability to real-world practice and could be considered outdated in the context of current oncological

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standards. Furthermore, while the study does not report Eastern Cooperative Oncology Group performance status or the presence of comorbidities—both critical parameters in medical oncology when making treatment decisions—it does provide data on the American Society of Anesthesiologists (ASA) classification. According to this data, over three-quarters of the patients in both groups were classified as ASA-I or ASA-II, suggesting a population generally capable of tolerating neoadjuvant therapy. This observation further underscores the need for a discussion on the exclusion of neoadjuvant treatment in this study.

The comparison of 2 fundamental surgical techniques and the detailed reporting of their outcomes are undoubtedly valuable contributions to oncology practice. In the post-surgical analysis, after the groups were matched, nearly 50% of patients in both groups were pathologically node-positive. The proportions of pathological stage II and stage III patients were reported as 28.3% and 39.7% in the LTG group, and 34.9% and 34.7% in the RTG group, respectively. Overall, the combined proportion of stage II and stage III patients was 67.9% in the LTG group and 69.6% in the RTG group. In contrast, the proportion of patients receiving adjuvant chemotherapy was only 55.7% in the LTG group and 56.2% in the RTG group. Numerous studies and meta-analyses have demonstrated the survival benefit of various adjuvant chemotherapy agents in operable gastric cancer. For instance, a large meta-analysis evaluating 34 randomized trials across East Asian and Western populations showed a 15% absolute reduction in the risk of death with adjuvant systemic chemotherapy compared to surgery alone (hazard ratio, 0.85; 95% confidence interval, 0.80–0.90) [4]. Given the standard recommendation of adjuvant chemotherapy for patients with stage II and higher operable gastric cancer, it is noteworthy that the majority of patients in this study would be candidates for such treatment. The relatively low proportion of patients receiving adjuvant therapy raises concerns. Moreover, key details such as the specific adjuvant chemotherapy agents used and the median number of cycles received are not clearly stated. This omission is significant, as it could potentially influence the survival outcomes between the groups.

In conclusion, the study by Hwang et al. [1] makes a valuable contribution to the literature by demonstrating that RTG is a viable alternative to LTG in terms of oncological safety for gastric cancer surgery. However, the exclusion of neoadjuvant therapy and the lack of details regarding adjuvant treatment limit the study's ability to reflect real-world data. The omission of standard treatment approaches, particularly for high-risk populations, makes it challenging to align survival analyses with contemporary oncology practice. Despite these limitations, the study is noteworthy for demonstrating no significant differences between the two surgical techniques, offering an important reference point in the selection of surgical methods. We commend the authors for addressing a critical gap in the literature and hope that this study will pave the way for future research that incorporates broader and more up-to-date treatment approaches.

## REFERENCES

1. 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](#)
2. 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](#)

3. Al-Batran SE, Homann N, Pauligk C, Illerhaus G, Martens UM, Stoecklacher J, et al. Effect of neoadjuvant chemotherapy followed by surgical resection on survival in patients with limited metastatic gastric or gastroesophageal junction cancer: the AIO-FLOT3 trial. *JAMA Oncol* 2017;3:1237-1244. [PUBMED](#) | [CROSSREF](#)
4. Diaz-Nieto R, Orti-Rodríguez R, Winslet M. Post-surgical chemotherapy versus surgery alone for resectable gastric cancer. *Cochrane Database Syst Rev* 2013;CD008415. [PUBMED](#) | [CROSSREF](#)