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Letter to the Editor

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The Necessity of Guidance: Optimizing Adjuvant Therapy for Stage II/III MSI-H Gastric Cancer Through the Interplay of Evidence, Clinical Judgment, and Patient Preferences

Geum Jong Song [1], **Yoon Young Choi** [2]

[1]Department of Surgery, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine, Cheonan, Korea
[2]Department of Surgery, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, Korea

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Correspondence to
Yoon Young Choi
Department of Surgery, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, 170 Jomaru-ro, Wonmi-gu, Bucheon 14584, Korea.
Email: laki98@naver.com

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ORCID iDs
Geum Jong Song
https://orcid.org/0000-0002-1067-8099
Yoon Young Choi
https://orcid.org/0000-0002-2179-7851

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Global variations in the prevalence and treatment of gastric cancer (GC) underscore the need for region-specific clinical guidelines. In response, the Korean Gastric Cancer Association (KGCA) published its first independent guidelines in 2019 and updated in 2023 [1,2]. This guideline is unique in that it prioritizes crucial clinical questions and uses systematic reviews and meta-analyses to establish evidence levels that guide clinical management. We are deeply thankful for these efforts.

Since their publication, these guidelines have been compared to contemporary international GC treatment guidelines [3]. After these comparisons, updates have been notably made to the European Society of Medical Oncology (ESMO) [4] and Chinese Society of Clinical Oncology (CSCO) guidelines [5]. Among these updates, the recommendations for adjuvant chemotherapy in stage II/III microsatellite instability-high (MSI-H) GC are particularly significant.

MSI-H is a unique and representative molecular subtype of GC caused by a deficiency in mismatch repair (dMMR), and accounts for approximately 10% of GC cases [6,7]. The clinical characteristics of dMMR/MSI-H GC have been reported to have a better prognosis than the microsatellite stable one and benefit from additional chemotherapy over surgery alone is questionable [8]. These results were confirmed in a multinational individual patient data meta-analysis [9] of retrospective biomarker studies from four randomized controlled trials (RCTs) (including Korean data, CLASSIC [10], and ARTIST trials [11]). Based on this meta-analysis of RCTs, recent ESMO guideline recommends "Adjuvant (postoperative) chemotherapy should be avoided in resected MSI-H GC" [4]. In addition, updated CSCO guideline recommends "Taking adverse reactions related to chemotherapy and patients' financial implications into account, it is suggested that for dMMR/MSI-H patients, (neo)adjuvant treatments such as immunotherapy in clinical trial settings could be first considered, unless unwillingness from the patient's side, after detailed discussion with the patient and families about the risk and benefits of different treatment strategies, postoperative observation or chemotherapy can be considered." [5].

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Globally, five major guidelines address GC treatment as follows: the KGCA (South Korea) [2], the National Comprehensive Cancer Network (NCCN) [12], ESMO (Europe) [4], Japanese Gastric Cancer Association (JGCA, Japan) [13], and CSCO (China) [5]. The updated ESMO and CSCO guidelines now advise against or at least reconsider adjuvant chemotherapy for patients with stage II/III MSI-H GC. However, others, including KGCA, have not commented on this issue. This discrepancy among the five GC guidelines underscores the complexity of this issue.

Adjuvant chemotherapy is critical for patients with stage II/III GC after curative resection. However, the prognosis of patients with MSI-H GC is comparatively favorable, with no discernible improvement in outcomes attributable to adjuvant chemotherapy. However, the decision-making process remains complex for clinicians as there is still a risk of recurrence among patients with MSI-H, which might be mitigated by adjuvant chemotherapy. While evidence [9] suggests that adjuvant chemotherapy may not be beneficial, the clinical dilemma persists owing to the potential for recurrence prevention. Although administering chemotherapy can reduce the risk of recurrence, subjecting patients to ineffective adjuvant chemotherapy may expose them to unnecessary risks and adverse effects. This dilemma lies between the academic and practical decisions for this patient subset. Thus, guidelines must address this issue and provide clinicians and patients with evidence-based recommendations to assist them in making informed decisions regarding adjuvant chemotherapy for patients with MSI-H GC.

As the KGCA guidelines are planned to be updated, we want to incorporate these findings to aid clinicians in navigating the evidence-based decision-making process while considering individual patient care. These guidelines will enable physicians and patients to discuss and decide on the best treatment strategy. We hope that these updates will allow patients and their doctors to make informed choices regarding adjuvant chemotherapy, based on the latest evidence and considering individual preferences and values.

REFERENCES

1. Guideline Committee of the Korean Gastric Cancer Association (KGCA), Development Working Group & Review Panel. Korean Practice Guideline for gastric cancer 2018: an evidence-based, multi-disciplinary approach. J Gastric Cancer 2019;19:1-48. PUBMED | CROSSREF
2. 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
3. Eom SS, Choi W, Eom BW, Park SH, Kim SJ, Kim YI, et al. A comprehensive and comparative review of global gastric cancer treatment guidelines. J Gastric Cancer 2022;22:3-23. PUBMED | CROSSREF
4. 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
5. Wang FH, Zhang XT, Tang L, Wu Q, Cai MY, Li YF, et al. The Chinese Society of Clinical Oncology (CSCO): clinical guidelines for the diagnosis and treatment of gastric cancer, 2023. Cancer Commun (Lond) 2024;44:127-172. PUBMED | CROSSREF
6. Park YS, Kook MC, Kim Bh, Lee HS, Kang DW, Gu MJ, et al. A standardized pathology report for gastric cancer: 2nd edition. J Gastric Cancer 2023;23:107-145. PUBMED | CROSSREF
7. Park Y, Nam SK, Seo SH, Park KU, Oh HJ, Park YS, et al. Comprehensive study of microsatellite instability testing and its comparison with immunohistochemistry in gastric cancers. J Gastric Cancer 2023;23:264-274. PUBMED | CROSSREF
8. Choi YY, Bae JM, An JY, Kwon IG, Cho I, Shin HB, et al. Is microsatellite instability a prognostic marker in gastric cancer? A systematic review with meta-analysis. J Surg Oncol 2014;110:129-135. PUBMED | CROSSREF

9. Pietrantonio F, Miceli R, Raimondi A, Kim YW, Kang WK, Langley RE, et al. Individual patient data meta-analysis of the value of microsatellite instability as a biomarker in gastric cancer. J Clin Oncol 2019;37:3392-3400. PUBMED | CROSSREF
10. Choi YY, Kim H, Shin SJ, Kim HY, Lee J, Yang HK, et al. Microsatellite instability and programmed cell death-ligand 1 expression in stage II/III gastric cancer: post hoc analysis of the CLASSIC randomized controlled study. Ann Surg 2019;270:309-316. PUBMED | CROSSREF
11. Miceli R, An J, Di Bartolomeo M, Morano F, Kim ST, Park SH, et al. Prognostic impact of microsatellite instability in Asian gastric cancer patients enrolled in the ARTIST trial. Oncology 2019;97:38-43. PUBMED | CROSSREF
12. 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
13. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2021 (6th edition). Gastric Cancer 2023;26:1-25. PUBMED | CROSSREF