J Gastric Cancer. 2023 Oct;23(4):535-548
https://doi.org/10.5230/jgc.2023.23.e32
pISSN 2093-582X·eISSN 2093-5641

Journal of Gastric Cancer

Original Article

Real-World Compliance of Surgical Treatment According to the Korean Gastric Cancer Guideline 2018: Evaluation From the Nationwide Survey Data 2019 in Korea

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Received: Apr 1, 2023
Revised: Aug 8, 2023
Accepted: Aug 17, 2023
Published online: Aug 28, 2023

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ABSTRACT

Purpose: This study evaluated real-world compliance with surgical treatment according to Korea's gastric cancer treatment guidelines.
Materials and Methods: The 2018 Korean Gastric Cancer Treatment Guidelines were evaluated using the 2019 national survey data for surgically treated gastric cancer based on postoperative pathological results in Korea. In addition, the changes in surgical treatments in 2019 were compared with those in the 2014 national survey data implemented before the publication of the guidelines in 2018. The compliance rate was evaluated according to the algorithm recommended in the 2018 Korean guidelines.
Results: The overall compliance rates in 2019 were 83% for gastric resection extent, 87% for lymph node dissection, 100% for surgical approach, and 83% for adjuvant chemotherapy, similar to 2014. Among patients with pathologic stages IB, II, and III disease who underwent total gastrectomy, the incidence of splenectomy was 8.08%, a practice not recommended by the guidelines. The survey findings revealed that 48.66% of the patients who underwent gastrectomy had pathological stage IV disease, which was not recommended by the 2019 guidelines. Compared to that in 2014, the rate of gastrectomy in stage IV patients was 54.53% in 2014. Compliance rates were similar across all regions of Korea, except for gastrectomy in patients with stage IV disease.
Conclusions: Real-world compliance with gastric cancer treatment guidelines was relatively high in Korea.

Keywords: Stomach neoplasm; Guideline; Compliance

INTRODUCTION

Gastric cancer is the fifth most common cancer worldwide and the fourth most common cause of cancer-related deaths [1,2]. However, the incidence of gastric cancer is gradually decreasing worldwide, particularly in northeastern Asia [2,3]. This might result from efforts to conduct studies to improve treatment outcomes worldwide and perform screening programs in highly prevalent areas. Gastric cancer guidelines have been published in

Funding
This research was supported by a nationwide survey project of the information committee funded by the Korean Gastric Cancer Association (grant number: KGCA2022IC9).

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

Author Contributions
Conceptualization: R.K.W.; Data curation: P.S.H., E.B.W., Y.H.M., K.Y.W.; Writing - original draft: E.S.S.; Writing - review & editing: R.K.W.

several countries, with evidence levels and recommendation grading determined by clinical data and the specific medical context in each respective nation [4]. The evidence and recommendations were based on a systematic literature review, including prospective multicenter randomized trials and other retrospective studies.

Compliance with gastric cancer treatment guidelines is relatively low, and survival is impaired in non-compliant patients in the Western world [5-7]; however, this is not limited to gastric cancer. The survival rate for many cancers, including ovarian and pancreatic cancers, is significantly lower in patients who do not adhere to these guidelines [8,9]. Moreover, studies have shown differences in survival based on compliance with National Comprehensive Cancer Network (NCCN) guidelines at the patient, regional, and hospital levels in patients with gastric cancer [10,11]. Adherence to the NCCN guidelines differed by region and hospital, and the results were significantly related to survival.

However, such data are not available for Eastern countries. Korea, Japan, and China have their own guidelines; however, no studies have investigated compliance with these guidelines in Eastern countries [12-14]. Evidence-based Korean practice guidelines for gastric cancer were published in 2018 by a panel of clinical experts [12]. Since 1995, a nationwide survey has been conducted every 5 years by the Korean Gastric Cancer Association for patients surgically treated for gastric cancer in Korea. Survey data were collected in 2014 and 2019, before and immediately after the 2018 guidelines were published [15,16].

This study evaluated real-world compliance with surgical treatment according to Korea's gastric cancer treatment guidelines. In addition, compliance before and after the publication of the guidelines was compared.

MATERIALS AND METHODS

Data source

Based on postoperative pathological results in Korea, compliance with the 2018 Korean Gastric Cancer Treatment Guidelines was evaluated using 2019 national survey data for surgically treated gastric cancer. No preoperative data were collected during the 2019 survey period. Data collected from the 2019 national survey included the region of the institution, tumor location, extent of gastric resection, combined organ resection, extent of lymph node dissection (LND), surgical approach, pathological stage (pStage), washing cytology, adjuvant chemotherapy, and preoperative chemotherapy. These institutions were divided into 6 regions (Seoul, Gyeonggi, Gyeongsang, Jeonla, Chungcheong, Gangwon, and Jeju). Data collected from the 2014 national survey included tumor location, extent of gastric resection, surgical approach, and pStage. A total of 14,076 patients who underwent surgery for gastric adenocarcinoma in 2019 and 15,613 patients in 2014 were included in this nationwide survey. This study was approved by the Institutional Review Board of the National Cancer Center (approval No. NCC2022-0297).

Method

All statistical analyses were performed using R software version 4.1.2 (R Core Team [2021], R: Language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria). Treatment recommendations were divided into 5 groups: strongly recommended, weakly recommended, not recommended, inclusive, and without recommendation. We defined the compliance rate as the ratio of surgical treatment following a

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strong or weak recommendation among the indicated patients. Treatment recommendations are available for each stage of gastric cancer. Compliance was evaluated according to the treatment algorithm recommended in the 2018 Korean guidelines, with a recommendation grade at each stage. Finally, the overall compliance rate was evaluated by combining all stages regarding the extent of gastric resection, LND, surgical approach, and adjuvant chemotherapy. In the subgroup analysis, the Mann–Whitney U test was used to compare the means. Statistical significance was set at $P<0.05$. Regional compliance variations were analyzed, along with treatment rates, including those not recommended (e.g., prophylactic splenectomy, total gastrectomy, stage IV curative gastrectomy). Additionally, 2019 compliance rates were compared to 2014.

The treatment recommended by the 2018 Korean gastric cancer guidelines is listed below.

Stage T1a gastric cancer

1. If the tumor is located in the upper third, TG (strongly for) or proximal gastrectomy (PG) (weakly for) is recommended.
2. If the tumor is located in the middle third, distal gastrectomy (DG) (strongly for) or pylorus-preserving gastrectomy (PPG) (weekly for) is recommended.
3. If the tumor location is lower-third, DG (strongly for) is recommended.
4. D1+ LND (strongly) or D2 LND (weekly) is recommended.
5. Laparoscopic approach (strongly for) or open approach (weekly for) is recommended.

Stages IB, II, and III of gastric cancer

1. If the tumor location is upper-third, TG (strongly for) is recommended.
2. If the tumor is located in the middle third, TG (strong for) or DG (strong for) is recommended.
3. If tumor location is lower-third, DG (strongly for) is recommended.
4. D2 LND (strongly for) is recommended.
5. Prophylactic splenectomy for hilar LND is not recommended (strongly against).
6. Open approach (strongly for) or laparoscopic approach (weekly for) is recommended.

Gastric cancer with distant metastases

1. Curative intended gastrectomy is not recommended for metastatic gastric cancer except for palliation of symptoms (strongly against).

For adjuvant chemotherapy

1. Patients with pathological stage I do not require adjuvant chemotherapy; observation is sufficient (strongly for).
2. Adjuvant chemotherapy is recommended in patients with pathologic stage II and III gastric cancer (strongly for).

For neoadjuvant chemotherapy

1. Neoadjuvant chemotherapy for potentially resectable gastric cancer is not conclusive if D2 LND is considered (inconclusive).

RESULTS

2019 Guideline compliance

Of the 14,076 patients who underwent surgery for gastric cancer in 2019, 7703 (54.72%)

https://doi.org/10.5230/jgc.2023.23.e32

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were pathologic pStage IA, 5308 (37.71%) had pStage IB, II, III, and 771 (5.05%) had pStage IV (**Fig. 1**). The treatment recommendations for patients with stage IA gastric cancer for the extent of gastric resection, LND, and surgical approach are summarized in **Fig. 2**. The treatment recommendations for patients with pStage IB, II, and III gastric cancer are summarized in **Fig. 3** regarding the extent of gastric resection, LND, and surgical approach. Splenectomy was performed in 2.63% of pStage IB, II, and III patients, which is not recommended by the guidelines. Among the patients with pStage IB, II, and III disease who underwent TG, splenectomy was performed in 8.08%. However, the reasons for splenectomy, whether therapeutic, prophylactic, or other, were not collected from the survey data. The treatment recommendations for patients with stage IV advanced gastric cancer are summarized in **Fig. 4**. In pStage IV patients undergoing surgical treatment, gastrectomy was performed in 346 patients (48.66%) in 2019, not recommended in the guidelines except for the palliation of symptoms. The reasons for gastric resection in pStage IV patients, whether with curative intent or symptom palliation, were not collected from the survey data. Adjuvant chemotherapy has different recommendations depending on the pStage and is divided into stages I, II, and III (**Fig. 5**). Of the pStage I patients, 1.5% received adjuvant chemotherapy, while 24.8% of patients with pStage II and III disease did not receive adjuvant chemotherapy. Reasons for receiving or not receiving adjuvant chemotherapy were not mentioned. In the subgroup analysis, among the 136 patients who underwent adjuvant chemotherapy, 52 (38.23%) were in stage IA, and 84 (61.76%) were in stage IB. Patients who did not receive adjuvant chemotherapy were significantly older than those who did receive adjuvant chemotherapy in stage II (68.2±13.7 vs. 62.3±12.1, P<0.001). In stage III, the age was significantly higher in the group that did not receive adjuvant chemotherapy (67.1±12.4 vs. 63.3±11.6, P<0.001). Of the 14,076 patients, 587 (4.17%) received preoperative chemotherapy, 489 (3.82%) underwent neoadjuvant chemotherapy, and 98 (0.35%) underwent conversion surgery after palliative chemotherapy. After neoadjuvant chemotherapy, 460 patients underwent gastrectomy, and 29 underwent non-gastrectomy, including bypass surgery or biopsy. After palliative chemotherapy, 78 patients underwent gastrectomy, and 20 underwent non-gastrectomy. In 2019, strongly recommended compliance rates were 80% for the gastric resection extent, 61% for LND, 69% for the surgical approach, and 83% for adjuvant chemotherapy. Weakly recommended compliance rates were 3% for the gastric resection extent, 26% for LND, and 30% for the surgical approach. Preoperative chemotherapy before surgery for gastric cancer was described in **Fig. 6**. The overall compliance rates were 83% for the gastric resection extent, 87% for LND, 100% for the surgical approach, and 83% for adjuvant, respectively (**Fig. 7**).

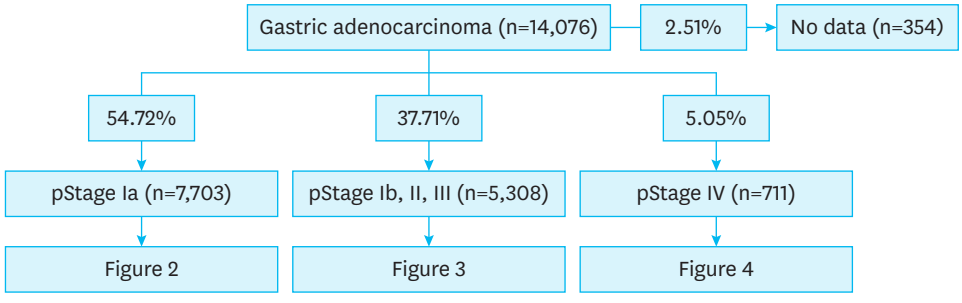

Fig. 1. pStage of surgically treated gastric cancer in 2019.
pStage = pathological stage.

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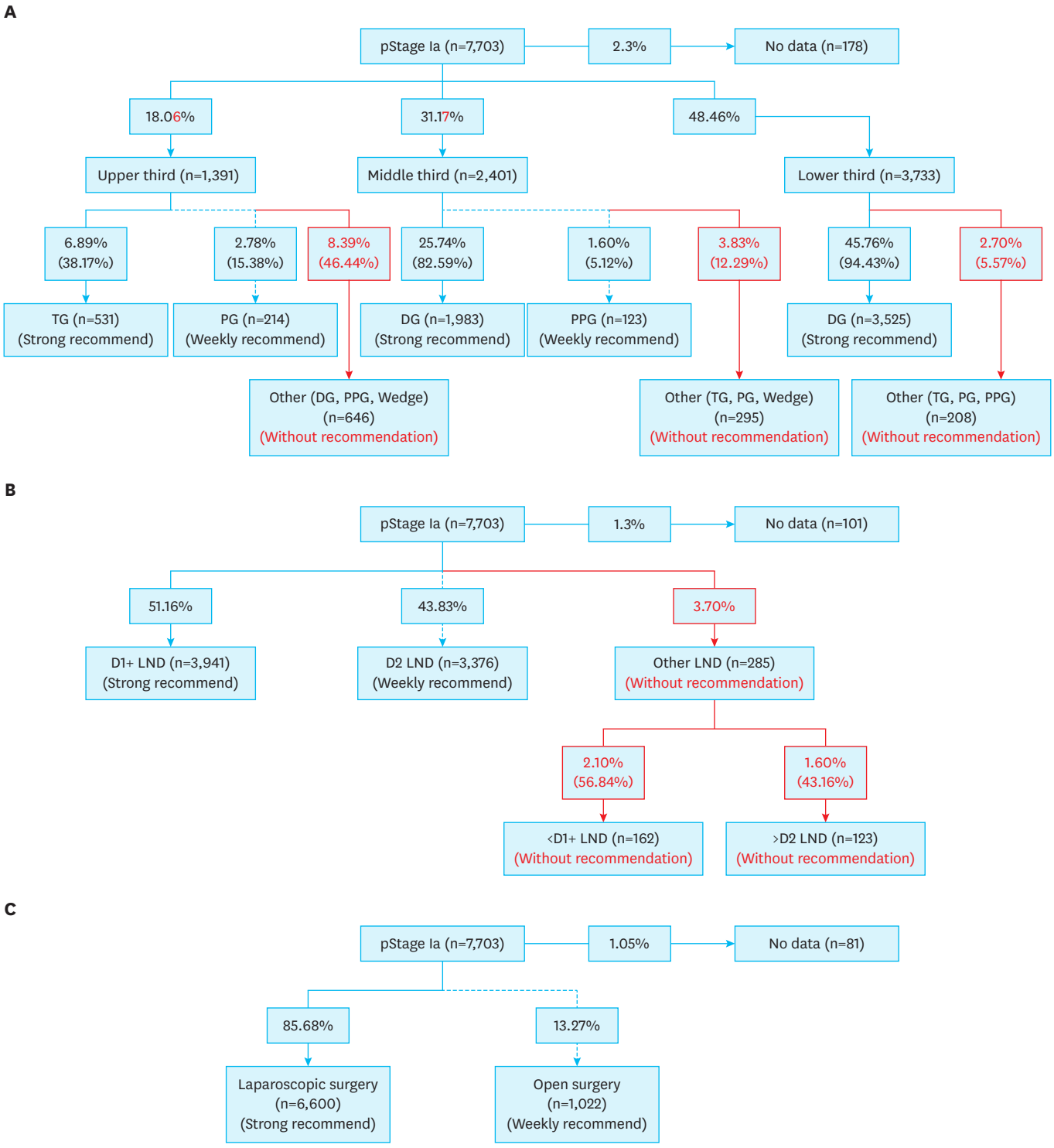

Fig. 2. Guideline compliance in pStage Ia. (A) Gastric resection in pStage Ia, (B) LND in pStage Ia. Percentages in parentheses are the proportions of subgroups. (C) Surgical approach in pStage Ia. Laparoscopic surgery include robot surgery.
pStage = pathological stage; DG = distal gastrectomy; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; PG = proximal gastrectomy; LND = lymph node dissection.

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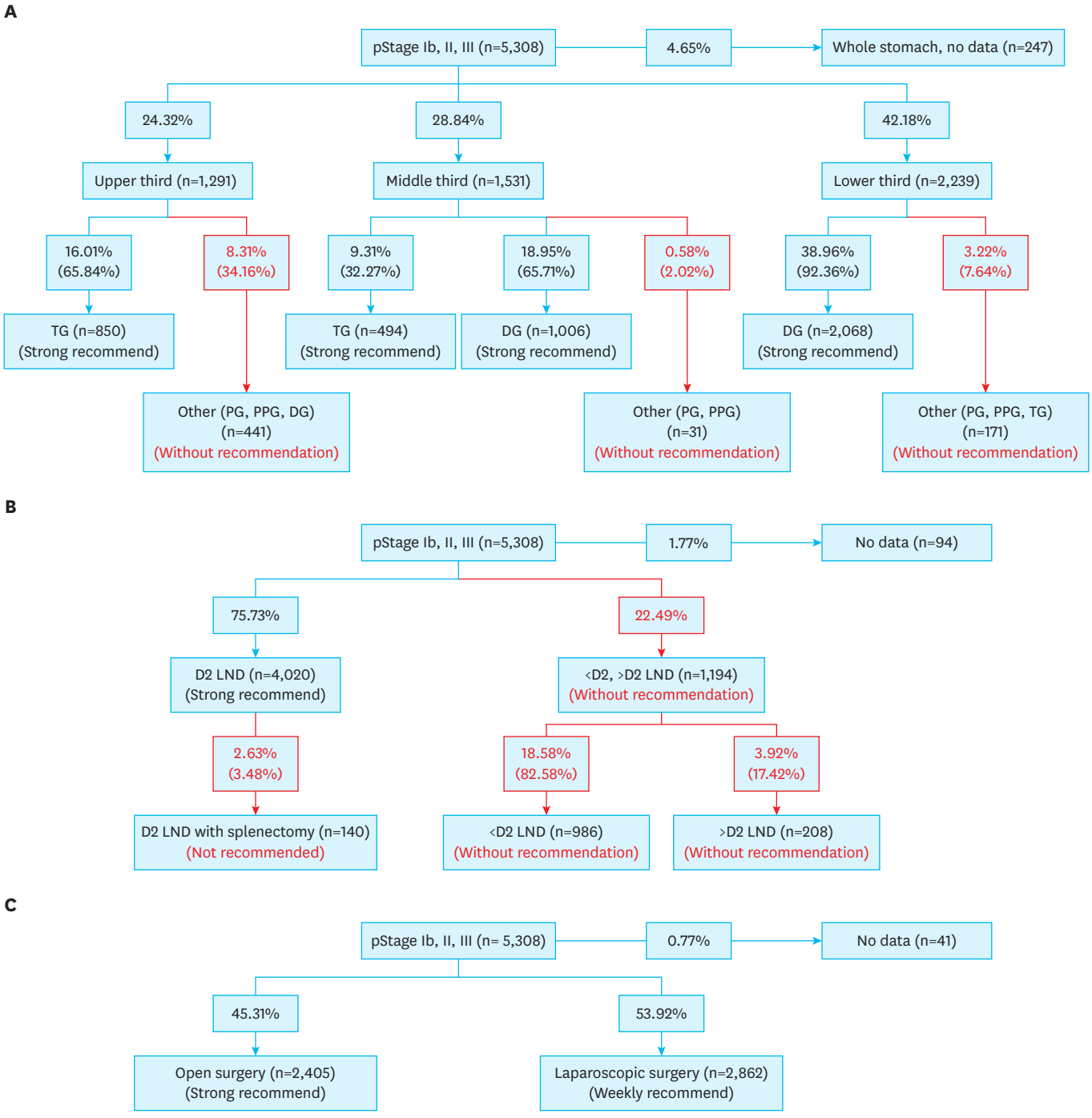

Fig. 3. Guideline compliance in pStage Ib, II, III. (A) Gastric resection in pStage Ib, II, III and (B) LND in pStage Ib, II, III. Percentages in parentheses are the proportions of subgroups. (B) In pStage Ib, II, III, splenectomy was performed in 134 patients (8.08%) among the TG cases (n=1,658). (C) Surgical approach in pStage Ib, II, III. Laparoscopic surgery include robot surgery.
pStage = pathological stage; DG = distal gastrectomy; PPG = pylorus-preserving gastrectomy; TG = total gastrectomy; PG = proximal gastrectomy; LND = lymph node dissection.

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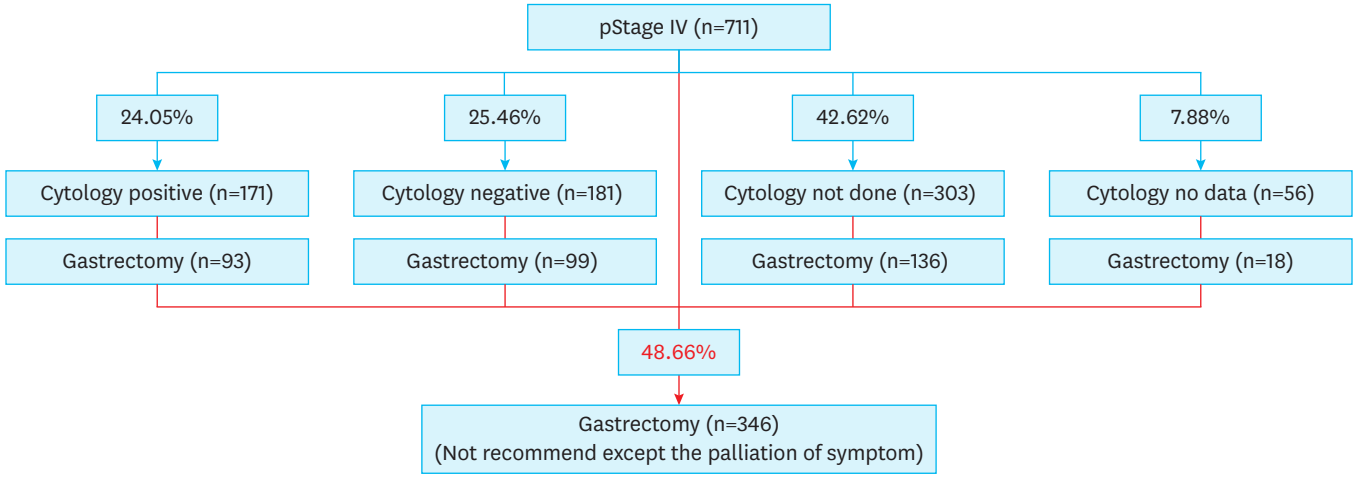

Fig. 4. Surgically treated gastric cancer in pStage IV.
pStage = pathological stage.

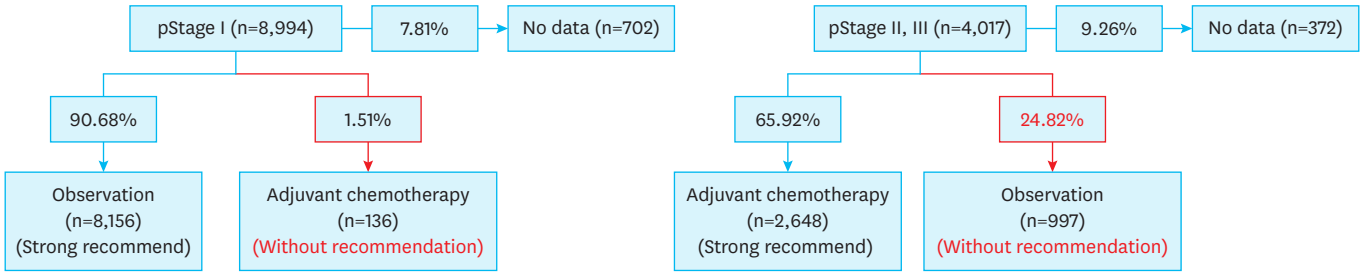

Fig. 5. Adjuvant chemotherapy after surgical resection of gastric cancer.
pStage = pathological stage.

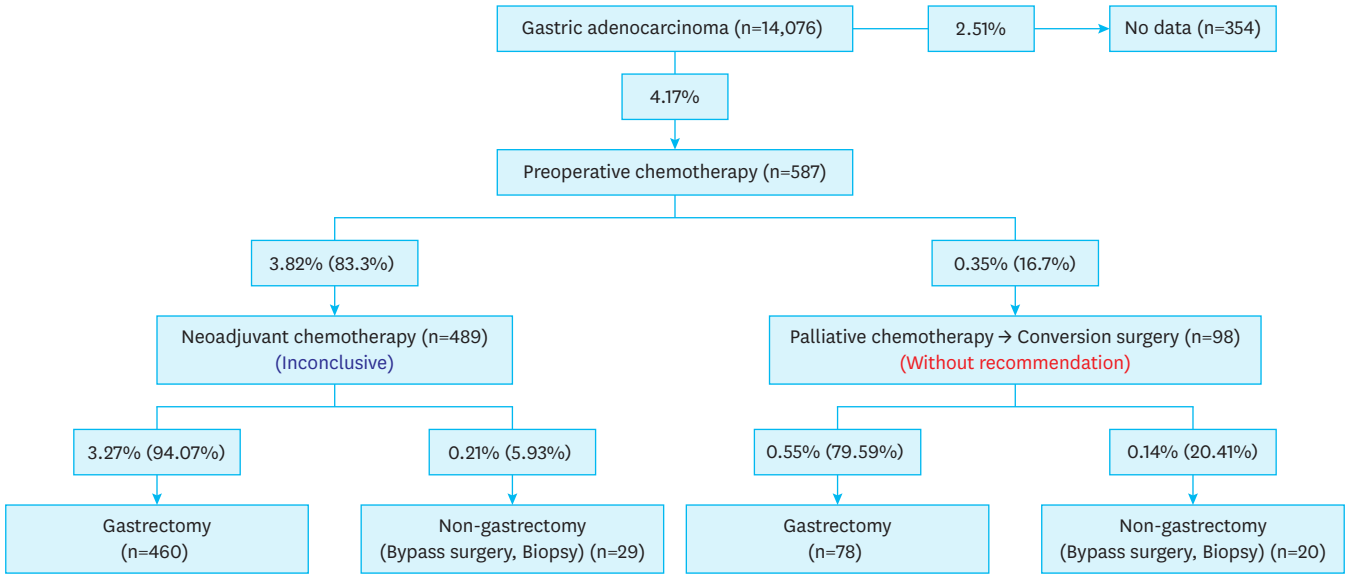

Fig. 6. Preoperative chemotherapy before surgery for gastric cancer. Percentages in parentheses are the proportions of subgroups.

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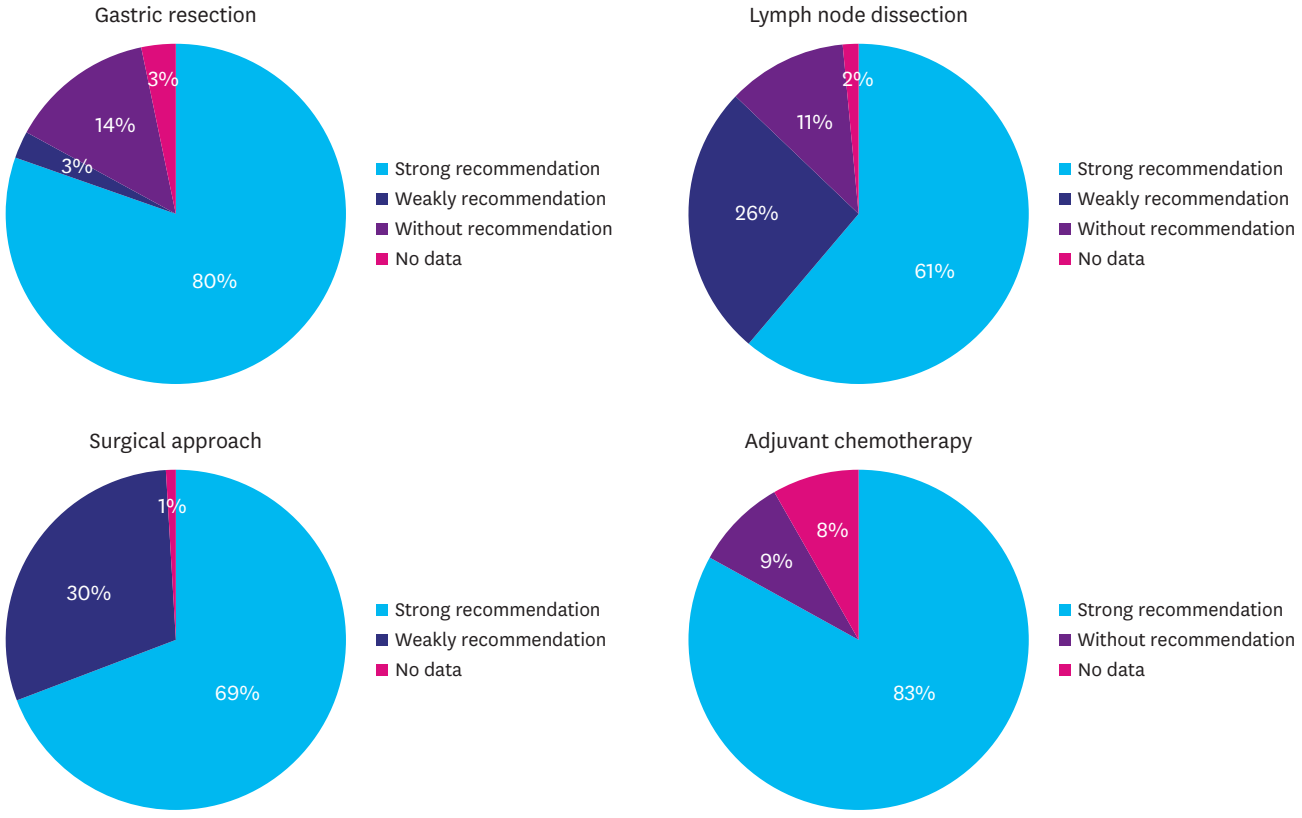

Fig. 7. Compliance rate in 2019.

2014 Guideline compliance

Of the 15,613 patients who underwent surgery for gastric cancer in 2014, 8,051 (51.57%) had pStage IA, 6,350 (40.68%) had pStages IB, II, and III; and 684 (4.38%) had pStage IV. In 2014, the strongly recommended compliance rates were 87% for gastric resection extent and 70% for surgical approach. Weakly recommended compliance rates were 1% for gastric resection extent and 30% for the surgical approach. The overall compliance rates were 88% for gastric resection extent and 100% for the surgical approach, similar to those in 2019 (**Fig. 8**). The gastrectomy rate in patients surgically treated for stage IV disease was 54.53%. Compliance with LND, adjuvant chemotherapy, and splenectomy compared with 2019 could not be evaluated because there were no data on those in the 2014 survey.

2019 Regional guideline compliance

Surgeries were performed primarily in Seoul (47.58%), followed by Gyeonggi (19.39%), Gyeongsang (19.38%), Jeonla (6.94%), Chungcheong (5.55%), and Gangwon and Jeju (1.16%) (**Fig. 9**). The compliance rates of the 6 regions were all over 80% and were similar in terms of gastric resection extent, LND, surgical approach, and adjuvant chemotherapy. In addition, the rate of prophylactic splenectomy was less than 4% in all 6 regions. Gastrectomy in pStage IV was the highest in Chungcheong (74.42%) and the lowest in Gangwon and Jeju (11.1%). The regional compliance data are summarized in **Fig. 9**.

https://doi.org/10.5230/jgc.2023.23.e32

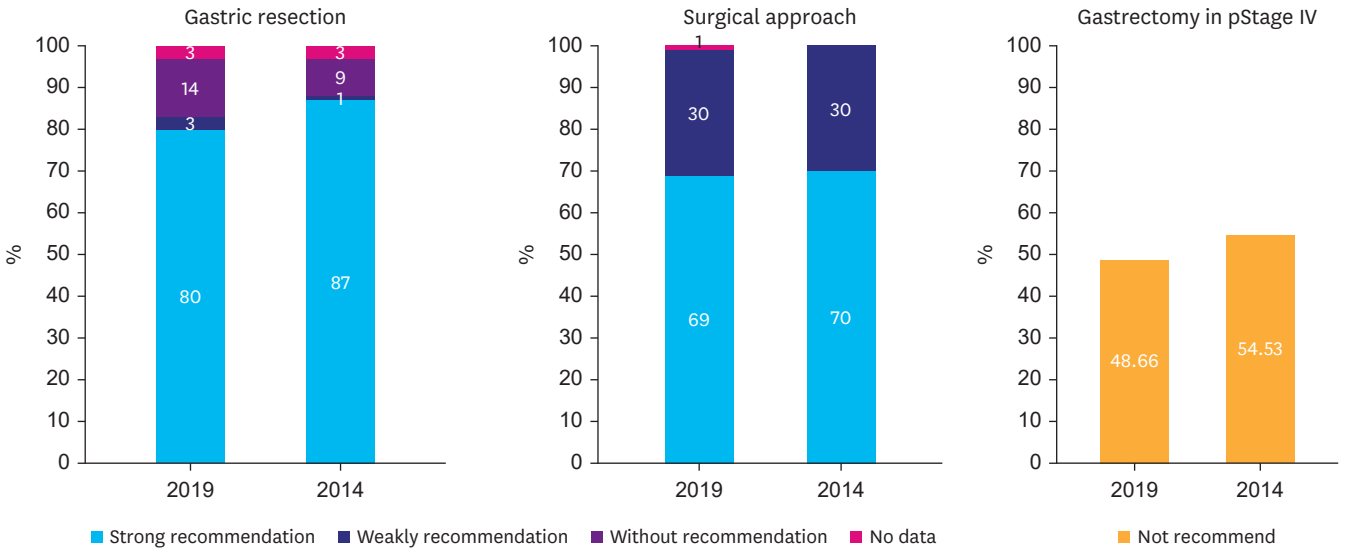

Fig. 8. Comparison of compliance rates between 2019 and 2014.
pStage = pathological stage.

DISCUSSION

In our study, overall compliance to guideline was over 80% in all aspects of the 2019 and 2014, before and after the 2018 guidelines in Korea. In addition, there was no significant difference in the overall compliance rate based on regional data. Compared with previously reported compliance rates in Western countries, the compliance rate in Korea is quite high. Because the recommendation guidelines were based on evidence of improved survival, one of the critical factors for the high cure rate of gastric cancer in Korea may be the high compliance rate with the recommendations in the guidelines and the national screening program [17]. So far, this study is the first report concerning compliance with guidelines in Eastern countries in the literature.

According to the results of a study analyzing guideline compliance between 2004 and 2014 in patients with gastric cancer based on the NCCN guidelines, only 36.5% of stage 0/I and 41.8% of stage II/III patients met the minimum standard of at least 16 lymph nodes examined and R0 resection [7]. In that study, guideline adherence was defined as satisfying 5 operative standards, including gastric resection extent, surgical method, and LND. However, it is a looser definition than that used in our study. Another study investigating NCCN guideline adherence based on data from 2004 to 2015 in patients with gastric cancer reported that only 32% followed the guidelines [10]. In this study, guideline adherence was satisfied if only one of the NCCN guidelines was followed. In both studies, the survival rate was low in the nonadherent patient group.

Compared with the 2019 data, the overall compliance rate in 2014 was similar regarding the extent of gastric resection (83% and 89%, respectively). Several inferences can be made regarding why 2014 was slightly higher than 2019 before the publication of the guidelines. In the subgroup analysis, the majority of noncompliance was when the DG was in the upper third portion. Guidelines recommend TG or PG in the upper third portion; however, this bias may occur because surgeons prefer near-TG to TG when it is possible to preserve the stomach, even if the remnant stomach is very small. Most surgeons prefer DG because

https://doi.org/10.5230/jgc.2023.23.e32

Fig. 9. Regional compliance rate. (A) Regional distribution of enrolled patients, (B) Extent of gastric resection in each regions, (C) Lymph node dissection in each regions, (D) Surgical approach in each regions, (E) Adjuvant chemotherapy in each regions, (F) Splenectomy in each regions, and (G) Gastrectomy of stage IV in each regions.

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it is technically easier [18,19]. Second, the number of surgical options, such as PG and PPG, increased in 2019 (4.5%) compared with 2014 (2.6%) as clinical interest in function-preserving surgery increased. In the recently updated 2022 guidelines, the recommendations to decide whether to perform TG or DG change depending on whether the fundus should be preserved [20].

Compared with 2014, the compliance rate was similar in 2019, both before and after the guidelines were published. In 2010, a study comparing guideline adherence before and after guidelines was published in the Netherlands (6). In this study, the overall compliance was relatively low (42.5%–78.0%); differences before and after publication of the guidelines did not show significant changes, and they concluded that the recommendations were already well implemented. In Korea, the difference before and after the implementation of the guidelines was not large; however, the relatively high compliance rate indicates that appropriate treatment has been administered. Among the data investigated in the 2019 and 2014 national surveys, we evaluated the changes in compliance related to LND, adjuvant chemotherapy, and splenectomy, which were not surveyed in 2014.

The 2018 guideline included two "not recommended" negative recommendations. The first procedure was splenectomy. Among patients with pStage IB, II, and III disease, splenectomy was performed in 2.63% of all patients, representing 8.08% of the patients who underwent TG. However, the exact reason for splenectomy for therapeutic or prophylactic LND or other purposes is unknown. Second, gastrectomy in pStage IV patients was performed in 48.66% in 2019 and 54.53% in 2014. However, based on national survey data, the exact cause of noncompliant surgeries was not identified for curative intent or palliation of symptoms in stage IV. Therefore, the actual noncompliance rate may be lower than the survey data.

In 2019, 1.51% of patients with pStage I gastric cancer received adjuvant chemotherapy, whereas 24.82% of patients with stage II or III did not receive adjuvant chemotherapy. However, the cause of noncompliance to adjuvant chemotherapy has not yet been identified. Some guidelines recommend that adjuvant chemotherapy be considered even in pStage I if patients have high-risk factors [21]; however, observation is recommended in the 2018 [12] and 2022 revised Korean guidelines [20]. Among the 997 patients who did not receive adjuvant chemotherapy in stages II and III, 585 (58.67%) were stage II, and 412 (41.32%) were stage III. The survey did not identify why patients did not receive adjuvant chemotherapy. However, it was assumed that old age, poor general condition, and lack of follow-up were the frequent causes in the real world. Some studies also recommend adjuvant chemotherapy for elderly patients, considering their general condition [22]. However, the benefits of adjuvant chemotherapy in elderly patients remain controversial [23]. Based on the age difference between patients compliant and non-compliant with adjuvant chemotherapy, age was probably the most significant reason adjuvant chemotherapy was not administered. Data on adjuvant chemotherapy were not surveyed in 2014, and a comparison was not performed.

Although the efficacy of preoperative chemotherapy remains controversial, research on this topic is actively progressing. In 2019, 587 of 14,077 patients received preoperative chemotherapy. A total of 489 patients underwent neoadjuvant chemotherapy, and 98 patients underwent conversion surgery after palliative chemotherapy. According to the 2018 Korean guidelines, neoadjuvant chemotherapy for potentially resectable gastric cancer is inconclusive if D2 LND is considered. [12]. However, neoadjuvant chemotherapy is conditionally recommended in the 2022 Korean guidelines as part of the perioperative

https://doi.org/10.5230/jgc.2023.23.e32

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chemotherapy for patients with resectable locally advanced gastric cancer. Conversion surgery is recommended for patients with stage IV gastric cancer [20]. As long as the guidelines are updated, changes in compliance must be evaluated.

In our study, the number of surgical cases differed according to region of origin. More than half of the surgeries were performed in Seoul and surrounding metropolitan areas. In contrast, only 1.16% of surgeries were executed in remote areas of Seoul. Nevertheless, there was no significant difference in the regional compliance rate, which implies that gastric cancer treatment is well-standardized nationwide in Korea, except for the rate of gastrectomy in stage IV patients. Regional differences exist; however, the exact reason for gastrectomy is unknown. Disparities in cancer treatment by region have been studied not only for gastric cancer but also for pancreatic, breast, lung, and colorectal cancers [11,24-27]. All these studies were conducted in the United States, and there were regional differences in treatment methods for all types of cancer except breast cancer, which has been reported to be significantly associated with improved survival. One study compared adherence to the NCCN gastric cancer guidelines by region, and the median 2-year overall survival varied significantly by region [11].

Gastric cancer guidelines in each country show little difference but are based on studies that have proven to improve survival [4]. In addition, studies have demonstrated that a high guideline compliance rate improves survival [7,28]. According to a 2020 study on primary gastric cancer, the incidence rate in Korea was the third highest; however, its mortality rate was the lowest among 185 countries [29]. One reason for this may be the high rate of early gastric cancer due to its early detection through national screening endoscopy [30], and another reason may be that compliance with guidelines is higher than that in other countries.

This study has some limitations. First, this study included patients who underwent surgery for gastric cancer but did not include all patients who received endoscopic treatment or systemic therapy. Second, the collected data included pathological rather than clinical stages. Therapeutic strategies are typically based on clinical staging. Therefore, the intended surgical method may differ because of the discrepancy between clinical and pStages. Third, there were no data related to survival, thus proving the effectiveness of these guidelines. Fourth, the exact reason for noncompliance was not identified, which might include several clinical trials that enrolled patients or other causes. These data included patients enrolled in several prospective studies conducted during data collection. These clinical trials may have affected the compliance rates regarding the extent of gastric resection or LND. Therefore, further studies on guideline compliance are required to collect more data and analyze survival.

In conclusion, real-world compliance with gastric cancer treatment guidelines is quite high in Korea compared with other countries. Additionally, there were no significant regional differences in compliance regarding the extent of gastric resection, LND, surgical approach, or adjuvant chemotherapy.

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