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The Effectiveness of Postoperative Chemotherapy on pT1bN0 and pT2N0 Gastric Cancer Patients with Risk Factors: An International Dual-Center Analysis

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Purpose: This study aimed to investigate the effectiveness of postoperative chemotherapy in pT1bN0 and pT2N0 gastric cancer patients with high risk factors.

Materials and Methods: Clinicopathological data of gastric cancer patients, who had undergone gastrectomy in high volume centers in Korea and China and were finally diagnosed with pT1bN0 and pT2N0 between 2006 and 2010, were analyzed retrospectively. Survival analyses stratified by risk factors and multivariable analyses were performed.

Results: A total of 1509 patients were enrolled, with 41 (2.7%) patients receiving adjuvant chemotherapy after gastrectomy and 1468 (97.3%) patients undergoing surgery alone. The adjuvant chemotherapy group showed higher percentages of tumor with maximal diameter >3 cm (51.2% vs. 25.8%), poor differentiation (68.3% vs. 49.8%), and less harvested lymph nodes (17.1% vs. 5.2%) compared to the surgery alone group. The overall survival rates were 95.1% in the adjuvant chemotherapy group and 93.3% in the surgery alone group, without significant difference. In multivariable analysis, age was found to be an independent prognostic factor. However, there were no difference in the overall survival between patients with risk factors and those without risk factors, even in terms of age. Meanwhile, patients with more than two risk factors who received chemotherapy showed better survival trend, especially for pT2N0 patients, compared to the surgery alone group, although no significant differences were observed.

Conclusion: In pT1bN0 and pT2N0 patients, age was found to be an independent prognostic factor. However, adjuvant chemotherapy seemed to be unnecessary, while postoperative chemotherapy might offer survival benefits to pT2N0 patients with more than two risk factors.

Key Words: Gastric cancer, chemotherapy, T1bN0, T2N0, gastrectomy, survival

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INTRODUCTION

Although the incidence and cancer death rate of gastric cancer have declined dramatically over the past two decades, a significant disease burden still remains in Japan, Korea, and China.[1,2] Due to the improvement in people's health awareness, as well as the popularization of gastroscopy and the implementation of cancer screening program, the proportion of gastric cancer detected at early stage (T1bN0M0 and T2N0M0) is increasing, especially in Korea and Japan.[3]

According to the National Comprehensive Cancer Network Guidelines (version 1. 2019, Gastric Cancer), postoperative chemotherapy is recommended for patients who have T2 or higher, or N+ gastric cancer.[4] However, patients with T1bN0M0 do not require chemotherapy, and patients with T2N0M0 could also be followed up regularly without chemotherapy.[4] Meanwhile, the Japanese Gastric Cancer Treatment Guidelines 2014 (version 4) indicate that no chemotherapy is needed for stage I patients, including those with T1bN0M0 and T2N0M0.[5] The reason why adjuvant chemotherapy is not recommended for these stages is because previous clinical trials failed to show the benefits of adjuvant chemotherapy over surgery alone in 1990s, and recent studies that applied adjuvant chemotherapy for T1bN±/T2N0 gastric cancer patients showed no statistic difference between chemotherapy and surgery alone groups.[6-9] However, some doctors still intend to give empirical chemotherapy to early stage gastric cancer patients with high risk factors, since the high risk factors such as younger age, vessel invasion, poor differentiation, and number of harvested lymph nodes less than 15 have been identified as independent prognostic factors.[10,11] It has been reported that age, submucosal invasion, and differentiation were risk factors of recurrence for T1N0 gastric cancer patients with curative gastrectomy, who therefore might be potential candidates for adjuvant chemotherapy.[12,13] A multicenter retrospective analysis demonstrated significant survival benefits of adjuvant therapy in T2N0 gastric cancer patients with less than 15 harvested lymph nodes.[14] A Chinese retrospective study also found that adjuvant chemotherapy significantly improved the overall survival rate of T2N0 gastric cancer patients with tumor located in the upper third part of the stomach.[15] Therefore, the benefits of adjuvant chemotherapy for these kinds of patients are still uncertain and inconsistent.

Consequently, we conducted an international dual-center retrospective analysis to investigate the survival benefits of postoperative chemotherapy for T1bN0M0 and T2N0M0 gastric cancer patients with high risk factors, and attempted to find the appropriate candidates to receive adjuvant chemotherapy among these patients.

MATERIALS AND METHODS

Patients

Clinicopathological data of 1509 gastric cancer patients, who had undergone curative gastrectomy and were finally diagnosed as pT1bN0 and pT2N0 from 2006 to 2010 at two institutions (West China Hospital, Sichuan University, China and Severance Hospital, Yonsei University Health System, Republic of Korea), were retrieved from the prospectively designed databases and analyzed retrospectively. The diagnosis of gastric adenocarcinoma for all patients was confirmed by upper endoscopy and biopsy. Patients with other gastric tumors, such as lymphoma, gastrointestinal stromal tumor or adenosquamous carcinoma, previous history of malignancies, or remnant gastric cancer were excluded. Those who were treated by endoscopic resection or wedge resection were also excluded. The West China Hospital Research Ethics Committee approved the retrospective analyses of anonymous data from the database [IRB No. 2014(215)]. Signed patient informed consent was waived due to the retrospective nature of the analysis.

Treatments

Curative total or subtotal gastrectomy with D1, D1+, or D2 lymphadenectomy for gastric cancer was performed for all patients according to the Japanese gastric cancer treatment guideline.[5] Fluoropyrimidine alone or a fluoropyrimidine/platinum-based regimen was given to the patients.

Definition of risk factors

The risk factors in the present study were defined as follows, since these factors have been identified as independent prognostic factors in previous studies:[10-15] age <45 years, non-D2 lymphadenectomy, upper third tumor, maximal diameter of the tumor >3 cm, poor differentiation or undifferentiation, number of total harvested lymph nodes <15, vessel or nerve involvement, and with postoperative complications.

Outcomes

Patients underwent follow-ups conducted by telephone calls, letters, or outpatient visits. Survival status for Korean patients was also based on data registered at the Korean National Cancer Center. The follow-up information was updated in December 2014 for Chinese patients and March 2014 for Korean patients. The overall follow-up rate was 98.5% (1509/1532). The overall survival rate was calculated from the date of operations until the date of death or the last follow-up. The mean follow-up duration was 69.3±20.3 months in Chinese patients and 56.2±16.9 months in Korean patients. All terminologies were based on the Japanese Classification of Gastric Carcinoma.[16] The prognostic effect of adjuvant chemotherapy was evaluated by comparing the overall survival of patients with chemotherapy to those without chemotherapy. Subgroup analyses were performed stratified by the risk factors and institutions.

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The survival of patients with more than two risk factors who received chemotherapy was compared to those without chemotherapy as well.

Statistical analysis

Statistical analysis was performed using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY, USA). Data was reported as mean±standard deviation for continuous variables, or frequency (percentage) for categorical variables. Independent two-sample t-test, Pearson's chi-square test (or Fisher's exact test), or Spearman's test was used to compare the differences between the patients with and without chemotherapy, as appropriate. Overall survival curves were analyzed using the Kaplan-Meier method and compared by log-rank test, with the duration of overall survival calculated in months. Multivariable analyses for pT1bN0 and pT2N0 gastric cancer patients were performed using Cox proportional hazards model to identify the independent prognostic factors. Considering the fact that the *p*-value might be affected by the related limited sample size in the chemotherapy group and the clinical significance of the defined risk factors, we included all of the variables to perform the multivariable analysis directly. Two-tailed p-value<0.05 was considered statistically significant. Since correction for multiple testing is recommended when multiple statistical tests are performed on same data, we used the Bonferroni correction to compensate for type I error in survival analyses. An adjusted p-value<0.0028 was considered statistically significant after Bonferroni correction.

RESULTS

Patient characteristics

Among the 1509 patients, only 41 (2.7%) patients received adjuvant chemotherapy after gastrectomy and 1468 (97.3%) patients underwent surgery alone. Clinicopathological characteristics of the adjuvant chemotherapy group and surgery alone group are summarized in Table 1 (while the clinicopathological characteristics of patients according to institutions are also shown in Supplementary Table 1, only online). The adjuvant chemotherapy group showed higher percentages of tumor with maximal diameter >3 cm (51.2% vs. 25.8%), poor differentiation (68.3% vs. 49.8%), and less harvested lymph nodes (17.1% vs. 5.2%) compared to the surgery alone group.

In addition, the adjuvant chemotherapy group had higher percentages of D2 lymphadenectomy in pT1bN0 patients (57.1% vs. 29.3%) and pT2N0 patients (51.9% vs. 25.1%), respectively, compared to the surgery alone group. Also, more patients with harvested lymph nodes <15 could be found in the adjuvant chemotherapy group for pT1bN0 patients (21.4% vs. 5.4%) and pT2N0 patients (14.8% vs. 4.6%), respectively, compared to the surgery alone group.

Table 1. Clinicopathological Characteristics of Adjuvant Chemotherapy Group and Surgery Alone Group

	Adjuvant chemotherapy, n (%)	Surgery alone, n (%)	*p* value
Age (yr)	54.85±11.49	58.74±11.29	0.300
Age (yr)			0.156
<45	8 (19.5)	178 (12.1)	
≥45	33 (80.5)	1290 (87.9)	
Lymphadenectomy			0.156
Non-D2	20 (48.8)	878 (59.8)	
D2	21 (51.2)	590 (40.2)	
Tumor location			0.257
Upper	8 (19.5)	224 (15.3)	
Middle	5 (12.2)	380 (25.9)	
Lower	28 (68.3)	863 (58.8)	
Tumor size (cm)			<0.001
>3	21 (51.2)	379 (25.8)	
≤3	20 (48.8)	1089 (74.2)	
Differentiation			0.019
Poor	28 (68.3)	731 (49.8)	
Well and moderate	13 (31.7)	737 (50.2)	
Total number of harvested lymph nodes			0.001
<15	7 (17.1)	76 (5.2)	
≥15	34 (82.9)	1392 (94.8)	
Vessel or nerve involvement			0.155
Positive	5 (12.2)	314 (21.4)	
Negative	36 (87.8)	1154 (78.6)	
Complications			0.251
Yes	3 (7.3)	198 (13.5)	
No	38 (92.7)	1270 (86.5)	
Stage			<0.001
T1b	14 (34.1)	1118 (76.2)	
T2	27 (65.9)	350 (23.8)	
Country			<0.001
China	36 (33.6)	71 (66.4)	
Korea	5 (0.4)	1397 (99.6)	

Multivariable analysis for identifying independent prognostic factors of patients

Results of multivariable analysis for identifying prognostic predictive factors are shown in Table 2, and age was proven to be an independent prognostic factor for T1b and T2 patients. The staging also showed marginal statistical difference (p=0.070) as an independent prognostic factor. When stratified by stage, age was also a significant prognostic factor in either pT1bN0 patients or pT2N0 patients (Table 2). Institution was not an independent prognostic factor.

Effect of adjuvant chemotherapy on overall survival

Overall survival rates were 95.1% (2 deaths) in the adjuvant chemotherapy group and 93.3% (99 deaths) in the surgery alone

Table 2. Multivariable Analysis for Identifying Independent Prognostic Factors of Patients

Variables	T1b+T2 patients			T1b patients			T2 patients		
	HR	95% CI	*p* value	HR	95% CI	*p* value	HR	95% CI	*p* value
Age (yr)	1.064	1.042–1.086	<0.001	1.066	1.038–1.095	<0.001	1.062	1.026–1.100	0.001
Chemotherapy			0.370			0.986			0.250
Yes	0.497	0.108–2.291		1.021	0.107–9.755		0.286	0.034–2.414	
No	1			1			1		
Lymphadenectomy			0.743			0.871			0.342
Non-D2	0.929	0.599–1.442		1.048	0.595–1.845		0.662	0.283–1.551	
D2	1			1			1		
Tumor location			0.707			0.376			0.666
Upper	0.899	0.515–1.569		0.698	0.315–1.547		1.203	0.520–2.781	
Middle and lower third	1			1			1		
Tumor size (cm)			0.245			0.071			0.661
>3	1.284	0.842–1.958		1.617	0.960–2.723		0.858	0.432–1.704	
≤3	1			1			1		
Differentiation			0.234			0.722			0.150
Poor	0.777	0.512–1.177		0.910	0.543–1.527		0.596	0.295–1.207	
Well and moderate	1			1			1		
Number of retrieved nodes			0.235			0.248			0.699
<15	1.522	0.761–3.043		1.649	0.706–3.854		1.285	0.361–4.573	
≥15	1			1			1		
Vessel or nerve invasion			0.239			0.136			0.992
Positive	1.302	0.839–2.020		1.512	0.878–2.604		0.996	0.462–2.147	
Negative	1			1			1		
Complications			0.209			0.315			0.463
Yes	1.365	0.840–2.217		1.375	0.739–2.557		1.349	0.607–2.996	
No	1			1			1		
Stage			0.070						
T1b	0.645	0.401–1.036							
T2	1								
Country			0.388			0.848			0.131
Korea	1.373	0.668–2.822		0.884	0.249–3.133		2.128	0.798–5.674	
China	1			1			1		

HR, hazard ratio; CI, confidence interval.

group, without significant difference for the entire patients (p=0.335). Among patients with high risk factors, adjuvant chemotherapy showed no benefit to the 5-year overall survival rates, as well as for patients without high risk factors (Table 3). Even though age was identified as an independent prognostic factor, there were no significant differences in the 5-year overall survival rates between the adjuvant chemotherapy group and the surgery alone group for patients of age <45 years or ≥45 years (Table 3, Fig. 1).

Among pT1bN0 patients and pT2N0 patients, the 5-year overall survival rates were 92.9% (1 deaths) and 96.3% (1 deaths) in the adjuvant chemotherapy group, and 94.3% (64 deaths) and 90.0% (35 deaths) in the surgery alone group, respectively, without significant differences (p=0.762 and p=0.196). Similarly, adjuvant chemotherapy still could not bring any benefits to pT1bN0 patients and pT2N0 patients with risk factors (Table 3). Although we found that the 5-year overall survival rates of Korean pT1bN0 patients who received adjuvant chemotherapy (50.0%) were lower than those without chemotherapy (90.4%), there was no significance after Bonferroni correction. Moreover, there were no statistical differences between the chemotherapy group and the surgery alone group in terms of the 5-year overall survival rates of the entire Chinese and pT2N0 patients after Bonferroni correction.

Although the statistics showed no difference, patients with more than two risk factors who received adjuvant chemotherapy showed notably higher survival rates compared to those in the surgery alone group for the entire pT1bN0 or pT2N0 patients. Especially in the entire Chinese and pT2N0 patients, marginal statistical differences could be observed (p=0.065 and p=0.083, respectively) (Figs. 2–4).

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Table 3. Five-Year Overall Survival of Patients With or Without Risk Factors

Risk factors	T1b+T2 patients (n=1509)			T1b patients (n=1132)			T2 patients (n=377)		
	Adjuvant chemotherapy	Surgery alone	*p* value	Adjuvant chemotherapy	Surgery alone	*p* value	Adjuvant chemotherapy	Surgery alone	*p* value
Age (yr)									
<45	100	98.3 (3)	0.594	100	97.7 (3)	0.723	100	100	-
≥45	93.9 (2)	92.6 (96)	0.496	91.7 (1)	93.8 (61)	0.844	95.2 (1)	88.5 (35)	0.296
Lymphadenectomy									
Non-D2	95 (1)	93.7 (55)	0.572	100	93.9 (48)	0.371	92.9 (1)	92.0 (7)	0.840
D2	95.2 (1)	92.5 (44)	0.416	87.5 (1)	95.1 (16)	0.427	100	89.3 (28)	0.150
Tumor location									
Upper third	100	93.9 (15)	0.415	-	95.5 (7)	-	100	88.1 (8)	0.289
Middle and lower third	93.9 (2)	93.2 (84)	0.511	92.9 (1)	94.1 (57)	0.730	94.7 (1)	90.5 (27)	0.439
Tumor size (cm)									
>3	95.2 (1)	90.8 (35)	0.290	83.3 (1)	91.4 (21)	0.903	100	89.6 (14)	0.164
≤3	95.0 (1)	94.1 (64)	0.660	100	95.1 (43)	0.456	91.7 (1)	90.2 (21)	0.687
Differentiation									
Poor	96.4 (1)	94.5 (40)	0.432	100	95.5 (23)	0.432	94.7 (1)	92.2 (17)	0.542
Well and moderate	92.3 (1)	92.0 (59)	0.754	80.0 (1)	93.2 (41)	0.472	100	86.3 (18)	0.223
Number of retrieved nodes									
<15	100	86.8 (10)	0.282	100	88.3 (7)	0.466	100	81.3 (3)	0.409
≥15	94.1 (2)	93.6 (89)	0.559	90.9 (1)	94.6 (57)	0.990	95.7 (1)	90.4 (32)	0.306
Vessel or nerve invasion									
Positive	100	90.8 (29)	0.270	100	90.9 (19)	0.518	100	90.6 (10)	0.383
Negative	94.4 (2)	93.9 (70)	0.669	91.7 (1)	95.1 (45)	0.924	95.8 (1)	89.8 (25)	0.303
Complications									
Yes	100	88.9 (22)	0.610	100	91.3 (13)	0.792	100	81.3 (9)	0.596
No	94.7 (2)	93.9 (77)	0.446	92.3 (1)	94.7 (51)	0.804	96.0 (1)	91.4 (26)	0.312
Country									
Korea	80.0 (26)	93.7 (88)	0.340	50.0 (1)	94.4 (60)	0.018	100	91.3 (28)	0.600
China	97.2 (1)	84.5 (11)	0.060	100	90.2 (4)	0.237	95.8 (1)	76.7 (7)	0.059

The number in the parenthesis refers to the number of death in each subgroup.

DISCUSSION

Over the last few decades, chemotherapy has been evaluated in an attempt to improve the survival outcomes following surgery.[17] However, the benefits of adjuvant chemotherapy for relatively early gastric cancer (T1bN0M0 and T2N0M0) still remain uncertain. Some high risk factors, such as younger age, poor differentiation, and number of harvested lymph nodes less than 15,[10,11] had independent effects on the gastric cancer patients' prognosis. Chemotherapy, which may improve the survival rates of patients with these risk factors, was often administrated by experience.[12-15] As our results showed, patients receiving adjuvant chemotherapy were more likely to have larger tumors, poor tumor differentiation, and retrieved lymph nodes <15. However, the effectiveness of postoperative chemotherapy for T1bN0M0 and T2N0M0 gastric cancer patients with high risk factors requires more supporting evidence.

In our study, the results of multivariable analysis indicated that age was an independent prognostic factor for patients with T1bN0M0 and T2N0M0 gastric cancer. These results were consistent with previous studies, which also showed that age was a significant independent prognostic factor for gastric cancer.[11,13,18] Some reports indicated that elderly patients had lower survival rates than non-elderly patients.[11,13,18] In our study, early stage patients with younger age (<45 years old) had also shown higher survival rates. That might be because the prognosis was extremely good in T1bN0M0 and T2N0M0 patients, and the deaths caused by age-related comorbidities were more than gastric cancer-related mortality in T1bN0M0 and T2N0M0 patients.[13] However, postoperative chemotherapy offered no significant survival benefit for patients, both of younger age (<45 years) and older age (≥45 years). Similar findings were also shown in the subgroup analysis of pT1bN0 and pT2N0 patients; a possible reason is that, since the survival rates of relative early cancer (pT1bN0 and pT2N0) after curative resection were already very high (exceeding 90%), the negative prognostic effect of age and the benefit of adjuvant chemotherapy could not be reflected. Beside age, the tumor size, dif-

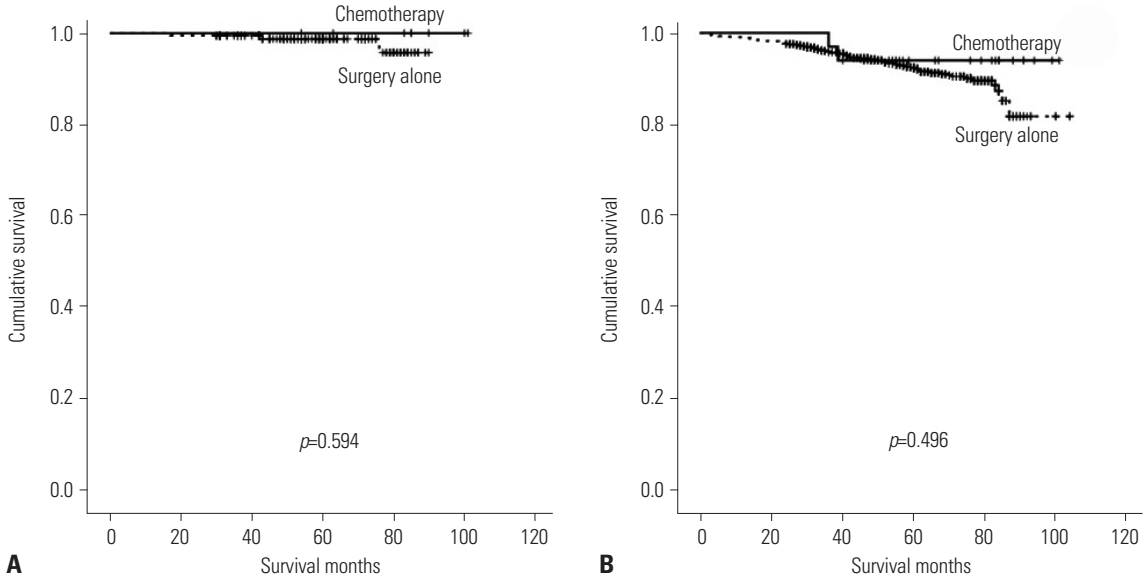

Fig. 1. Survival analyses for patients of age <45 years and age ≥45 years who received postoperative chemotherapy and surgery alone. A: Age <45 years. B: Age ≥45 years.

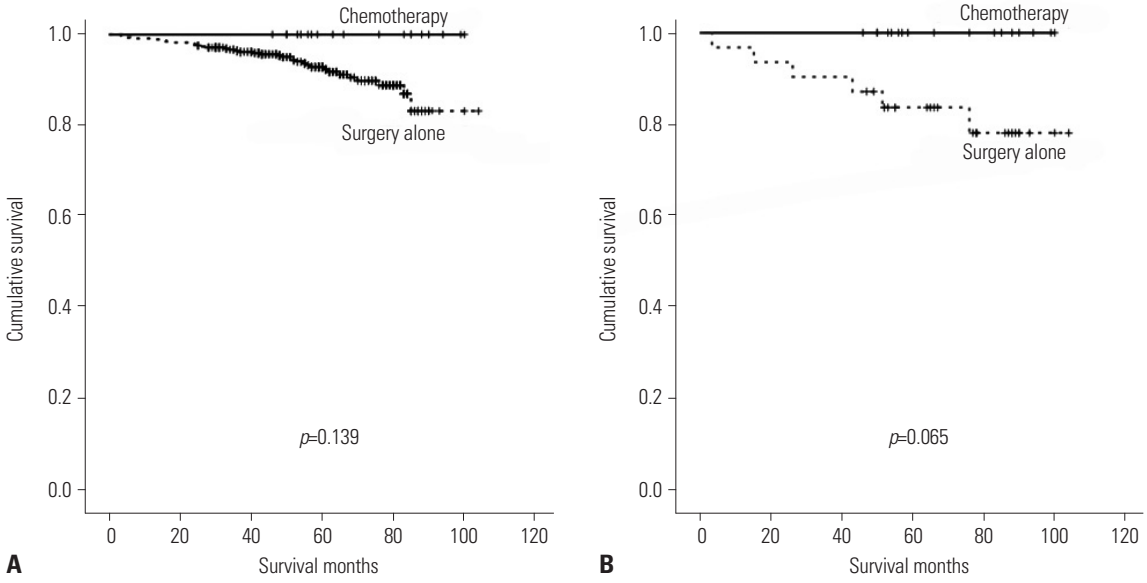

Fig. 2. Survival analyses for pT1bN0 and pT2N0 patients with more than two risk factors who received postoperative chemotherapy and surgery alone. A: All patients. B: Chinese patients.

ferentiation, and vascular invasion were also identified as independent predictive factors in early gastric cancer without lymph nodes metastasis.[13,19,20] However, they were not selected as independent prognostic factors in our study, since curative surgery alone yielded extreme high survival rate.

Regarding the survival benefits of adjuvant chemotherapy for pT1bN0 and pT2N0 patients, adjuvant chemotherapy did not show survival benefits for patients with or without high risk factors in our study. Our results have been supported by other studies. Some studies found that there was no overall survival benefit of perioperative chemotherapy for clinically staged T2N0 gastric adenocarcinoma compared to surgery alone.[7] Therefore, chemotherapy was unnecessary in T2N0 patients after curative gastrectomy for gastric cancer.[9] A large cohort of patients with early stage gastric cancer suggested that adjuvant systemic or locoregional therapies should be avoided in adequately staged node-negative and/or stage IB patients.[21] Even in pT1N1 gastric cancer patients, adjuvant chemotherapy did not show any survival benefits.[8] However, controversy still remained. Liu, et al.[22] reported that adjuvant chemotherapy could significantly improve the overall survival of T2N0 gastric cancer patients. Du, et al.[23] constructed a prognostic risk model of patients with pT2N0 gastric cancer undergoing radical resection, and they recommended adjuvant chemotherapy to

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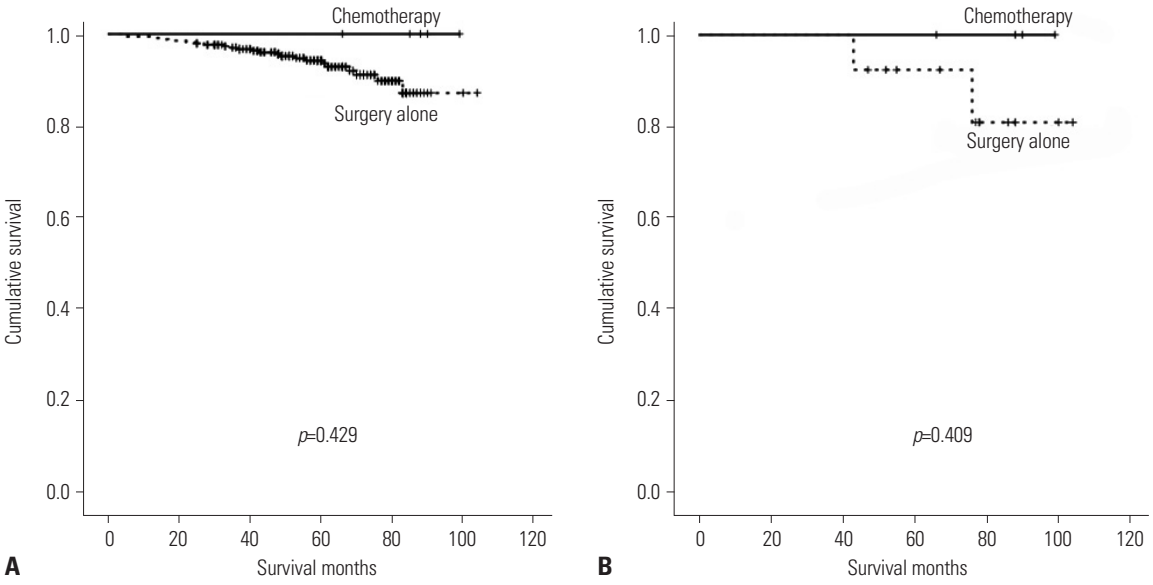

Fig. 3. Survival analyses for pT1bN0 patients with more than two risk factors who received postoperative chemotherapy and surgery alone. A: All patients. B: Chinese patients.

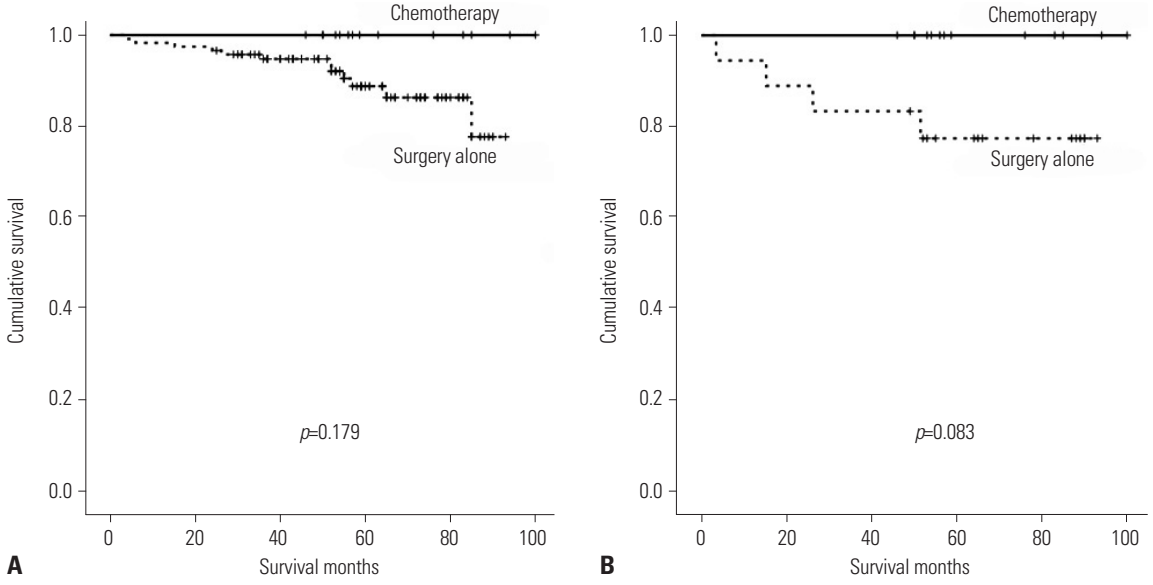

Fig. 4. Survival analyses for pT2N0 patients with more than two risk factors who received postoperative chemotherapy and surgery alone. A: All patients. B: Chinese patients.

patients with vessel invasion, tumor diameter >3 cm, and perineural invasion. In, et al.[14] demonstrated that the overall survival benefits of adjuvant chemoradiation could be found in T2N0 gastric cancer patients with <15 lymph nodes examined, rather than the patients who had ≥15 lymph nodes examined. However, we should consider the fact that the 5-year survival rates of T2N0 patients with risk factors who underwent surgery alone in the aforementioned studies only ranged from 50% to 60%, which might partly explain the benefits of adjuvant chemotherapy for T2N0 gastric cancer patients after curative resection. On the other hand, adjuvant chemotherapy seemed to be unnecessary in our study, as curative surgery alone has already shown very satisfying survival outcomes.[6] Therefore, the status of adjuvant chemotherapy has not been identified as an independent prognostic factor for pT1bN0 and pT2N0 patients in our study. In addition, our survival analyses showed that the survival rates of patients with risk factors were higher compared to those without risk factors, which could also indirectly reflect staging as the most important prognostic determinant that could veil the negative prognostic effect of risk factors and the benefits of adjuvant chemotherapy.

Considering the fact that almost 90% of patients who received chemotherapy were from China in this study, the results may have been affected by the differences between institutions.

Therefore, we included the institutions as a confounding variable while performing Cox regression analysis. However, we found that the institution itself was not an independent prognostic factor, and that it had no impact on the overall survival of patients. In addition, we performed survival analysis stratified by the institutions. Although we found that the 5-year overall survival rates of Korean pT1bN0 patients who received adjuvant chemotherapy were lower compared to those without chemotherapy, there was no significant difference after Bonferroni correction. Also, this result might have been caused by sampling error, since only two patients received chemotherapy. Although there were no statistical difference after Bonferroni correction, the 5-year overall survival rates of the entire Chinese and pT2N0 patients seemed more favorable in the chemotherapy group than in the surgery alone group, corresponding to the better survival trends for the entire Chinese and pT2N0 patients with more than two risk factors who received adjuvant chemotherapy (p=0.065 and p=0.083, respectively). This result might indicate that the adjuvant chemotherapy would bring survival benefits to the patients with more than two risk factors; and this should be confirmed in prospective studies.

This study had some limitations. Firstly, selection bias, detection bias, and performance of analysis bias could exist in any retrospective studies. Therefore, our results might be biased and need to be further confirmed through more research, especially in well-designed prospective controlled trials. Secondly, since our data were collected from only two Asian institutions, they may not well represent Western patients. Therefore, a lot of caution is required when applying our results to Western patients. Thirdly, the number of patients who received chemotherapy in our study was small, and the rate of adjuvant chemotherapy was unexpectedly higher in Chinese patients, which could lead to possible bias. Due to the little evidence supporting the necessity of adjuvant chemotherapy after curative gastrectomy during the study period, as well as the fact that adjuvant chemotherapy was not recommended to the pT1bN0 and pT2N0 patients by the guidelines at that time, only a few patients with curative surgery were given chemotherapy, especially in Korea. On the other hand, an insufficient amount of lymphadenectomy was performed in Chinese hospitals during the study period. Our previous published article indicated that less than 50% of Chinese patients with stages II and III gastric cancer had undergone D2 lymphadenectomy, whereas more than 80% of Korean patients with the same stages underwent this procedure.[24] Similar results were found in the present study, which showed a higher percentage of patients with standardized D2 lymphadenectomy in Korea for T2N0 patients. This was also the reason why the Chinese doctors more actively performed chemotherapy for such patients, especially for those with risk factors. As a result, the rate of adjuvant chemotherapy was unexpectedly higher in Chinese patients than in Korean patients. Considering to the issue, we performed multivariable analysis to adjust the effectiveness of postoperative chemotherapy. In addition, we also performed subgroup analysis stratified by the institutions to investigate the survival benefits of adjuvant chemotherapy in different countries. Lastly, the sample size of patients who received fluoropyrimidine and platinum chemotherapy regimen was only 6, which was too small to be used for survival analysis; therefore, we did not compare the survival differences between different chemotherapy regimens.

In conclusion, age was found to be an independent prognostic factor for pT1bN0 and pT2N0 patients. However, there were no differences in the overall survival between patients with risk factors and patients without risk factors, even in terms of age. Moreover, postoperative chemotherapy might bring survival benefits to pT2N0 patients with more than two risk factors.

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