Ann Surg Oncol (2020) 27:802–811
https://doi.org/10.1245/s10434-019-08170-5

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

Check for updates

ORIGINAL ARTICLE – GASTROINTESTINAL ONCOLOGY

Long-Term Survival after Minimally Invasive Versus Open Gastrectomy for Gastric Adenocarcinoma: A Propensity Score-Matched Analysis of Patients in the United States and China

Jun Lu, MD, PhD[1,2], Changhwan Yoon, PhD[2], Binbin Xu, MD[1], Jianwei Xie, MD, PhD[1], Ping Li, MD, PhD[1], Chaohui Zheng, MD, PhD[1], Changming Huang, MD[1], and Sam S. Yoon, MD[2]

[1]Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou, Fujian, China; [2]Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY

ABSTRACT

Background. This study aimed to compare the long-term survival of patients undergoing minimally invasive gastrectomy and those undergoing open gastrectomy for gastric adenocarcinoma (GA) in the United States and China.

Methods. Data on patients with GA who underwent gastrectomy without neoadjuvant therapy were retrieved from prospectively maintained databases at Memorial Sloan Kettering Cancer Center (MSKCC) and Fujian Medical University Union Hospital (FMUUH). Using propensity score-matching (PSM), equally sized cohorts of patients with similar clinical and pathologic characteristics who underwent minimally invasive versus open gastrectomy were selected. The primary end point of the study was 5-year overall survival (OS).

Results. The study identified 479 patients who underwent gastrectomy at MSKCC between 2000 and 2012 and 2935 patients who underwent gastrectomy at FMUUH between 2006 and 2014. Of the total 3432 patients, 1355 underwent minimally invasive gastrectomy, and 2059 underwent open gastrectomy. All the patients had at least 5 years of potential follow-up evaluation. Before PSM, most patient characteristics differed significantly between the patients undergoing the two types of surgery. After PSM, each cohort included 889 matched patients, and the actual 5-year OS did not differ significantly between the two cohorts, with an OS rate of 54% after minimally invasive gastrectomy and 50.4% after open gastrectomy ($p = 0.205$). Subgroup analysis confirmed that survival was similar between surgical cohorts among the patients for each stage of GA and for those undergoing distal versus total/proximal gastrectomy. In the multivariable analysis, surgical approach was not an independent prognostic factor.

Conclusions. After PSM of U.S. and Chinese patients with GA undergoing gastrectomy, long-term survival did not differ significantly between the patients undergoing minimally invasive gastrectomy and those undergoing open gastrectomy.

Although patients with gastric adenocarcinoma (GA) have traditionally undergone surgical resection via an open approach, minimally invasive (laparoscopic or robot-assisted) gastrectomy is increasingly used.[1–4] The potential benefits of minimally invasive gastrectomy for GA include decreased postoperative pain, shorter hospital stay, less blood loss, and better cosmetic results,[1–3,5] whereas its drawbacks include a long learning curve and potentially worse long-term survival if negative margins are not achieved.[4,6]

Prospective clinical trials have demonstrated that laparoscopic distal[5,7] and total gastrectomy[8] have oncologic outcomes similar to those of open surgery for patients with early gastric cancer. Laparoscopic distal gastrectomy

Electronic supplementary material The online version of this article (https://doi.org/10.1245/s10434-019-08170-5) contains supplementary material, which is available to authorized users.

First Received: 7 October 2019;
Published Online: 1 January 2020

S. S. Yoon, MD
e-mail: yoons@mskcc.org

has even been recommended for clinical stage I GA according to the latest Japanese gastric cancer treatment guidelines.[9]

More recently, several multicenter randomized controlled trials have found that laparoscopic gastrectomy is safe and feasible for advanced gastric cancer in terms of short-term outcomes[2,10–12] and 3-year survival.[13] Several studies have shown that robotic gastrectomy is as safe and effective as laparoscopic gastrectomy for treating both early and advanced GA,[4,14,15] yielding similar short-term surgical [1] and long-term oncologic outcomes.[16] This evidence includes a meta-analysis of data on 4576 patients.[17]

Nonetheless, more studies are needed to ensure that long-term outcomes are not being compromised with the use of minimally invasive gastrectomy, especially for advanced GA. In addition, evidence is very limited regarding the survival outcomes after minimally invasive gastrectomy for both Western and Eastern patients with GA.

This study compared 5-year overall survival (OS) between patients undergoing curative-intent gastrectomy for GA by either minimally invasive (laparoscopic or robot-assisted) or open approaches at two high-volume institutions in the United States and China for whom 5 years of follow-up data were available. The two surgical cohorts were matched for clinical and tumor characteristics to eliminate potential bias caused by selection for either approach.

PATIENTS AND METHODS

Patients

We queried the databases of Memorial Sloan Kettering Cancer Center (MSKCC, New York, USA) and Fujian Medical University Union Hospital (FMUUH, Fuzhou, China) for GA patients who underwent curative-intent minimally invasive or open gastrectomy without neoadjuvant therapy at MSKCC between January 2000 and January 2012 and at FMUUH between January 2006 to January 2014. Eligible patients met the following criteria: histologically confirmed diagnosis of GA, tumor located in the gastric or gastroesophageal junction (Siewert type 2 or 3), no other malignancy, no distant metastasis or invasion of adjacent organs, no preoperative therapy (neoadjuvant chemotherapy or chemoradiotherapy), no D3 lymphadenectomy, R0 resection, and complete clinical and follow-up data available.

This search identified 3414 patients (479 treated at MSKCC and 2935 treated at FMUUH). Of the 3414 patients, 2059 underwent laparoscopic or robotic gastrectomy, and 1355 underwent open gastrectomy.

All surgeries were performed by highly experienced surgeons. The extent of resection (distal or proximal/total gastrectomy) was decided according to the tumor location. The extent of lymph node dissection was performed according to the Japanese Gastric Cancer Association definitions in the second English Edition (1998)[18] and the third English edition (2010).[19]

The surgical approach (laparoscopic vs open) was agreed upon by the patient and surgeon after thorough discussion.[6,20–22] Written informed consent was obtained from all the patients before surgery.

Differentiated types included papillary and tubular adenocarcinomas, whereas undifferentiated types included poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous adenocarcinoma.[23] Tumor stage was assigned according to the 8th edition of Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) staging system for gastric cancer[24] or the Japanese Gastric Cancer Association.[19,25] Patients with stage II or higher disease were routinely recommended to receive adjuvant chemotherapy with 5-fluororacil-containing regimens for 4–6 months.

Follow-Up Evaluation

The primary outcome was 5-year OS, calculated from the date of surgery to the date of death from any cause or the last follow-up evaluation (July 2017 at MSKCC and January 2019 at FMUUH). The patients were followed every 3 months during the first 2 years after surgery and then every 6 months during the following 3 years. The median follow-up time was 60.2 months (range, 0.2–138.8 months). The Institutional Review Boards of the participating hospitals approved this study.

Statistical Analysis

The Chi square test was used to compare categorical variables between the two groups, and the independent sample *t* test was used to compare continuous variables. To minimize bias in this retrospective study, the cohorts of patients undergoing minimally invasive or open gastrectomy were propensity score-matched at a 1:1 ratio as previously reported.[26] Propensity scores were based on age, sex, tumor differentiation, tumor location, pathologic T stage, and pathologic N stage. The two cohorts were matched using a greedy approach with a caliper width of 0.1 standard deviation of the logit of the propensity score.

Overall survival was estimated using the Kaplan–Meier method and analyzed by the log-rank test. Factors deemed to have potential importance in the univariate analysis were included in the multivariate analysis, which used a Cox proportional hazards model. Hazard ratios (HRs) are presented with 95% confidence intervals (CIs). The HRs associated with minimally invasive surgery after refitting of separate propensity score–weighted survival models for each subgroup were analyzed and illustrated by forest plot.[27] All p values are two-tailed, and those lower than 0.05 were considered significant. All statistical analyses were performed in SPSS version 22.0 (IBM, Chicago, IL, USA) and R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient Characteristics

The clinicopathologic characteristics of the patients from MSKCC and FMUUH are shown in Table S1. The differences between these patients are consistent with previous reports of patients with GA in the United States and China.[28–30]

Using combined data (n = 3432), the patients were stratified into cohorts based on whether they underwent minimally invasive (n = 1355) or open (n = 2059) gastrectomy (Fig. S1). The MSKCC group had 412 open gastrectomy patients and 67 minimally invasive gastrectomy patients before matching, whereas it had 290 open gastrectromy patients and 55 minimally invasive gastrectomy patients after matching.

Before matching, the cohort undergoing minimally invasive gastrectomy was significantly younger (mean age, 61.1 vs 62.3 years; p = 0.003), included more male patients (74.6% vs 70.6%; p = 0.010), and included more patients with well- or moderately differentiated tumors (43.1% vs 33.3%; $p < 0.001$) than the cohort undergoing open gastrectomy (Table 1). Furthermore, the patients undergoing open surgery had more upper third tumors (30.9% vs 24.8%; $p < 0.001$) and more pT4 stage tumors (44.5% vs 35.2%; $p < 0.001$). However, the two groups did not differ significantly in terms of tumor size, type of gastrectomy, number of metastatic lymph nodes, number of harvested lymph nodes, pN stage, or pathologic tumor-node-metastasis (pTNM) stage.

Propensity score-matching (PSM) narrowed the cohorts to 889 patients each. As shown in Table 1, none of the clinical or pathologic variables of the matched samples differed significantly.

Survival Outcomes

Before matching, Kaplan–Meier survival analysis showed that the 5-year OS for the cohort who underwent minimally invasive gastrectomy was significantly longer than for those undergoing open gastrectomy ($p < 0.001$; Fig. 1a). After PSM, the patients undergoing minimally invasive did not differ significantly from those undergoing open gastrectomy (p = 0.205; Fig. 1b). The 5-year OS similarly did not differ between the matched cohorts of patients undergoing gastrectomy by minimally invasive versus open gastrectomy within stage-specific groups as defined by the UICC/AJCC (stage 1: p = 0.893; stage 2: p = 0.352; stage 3: p = 0.054; Fig. 2) or the Japanese Gastric Cancer Association (early GA: p = 0.848; advanced GA: p = 0.745; Fig. S2). Overall survival also did not differ with surgical approaches, between the patients undergoing distal gastrectomy and those undergoing total gastrectomy (Fig. S3).

We further examined whether risk of death differed between the patients undergoing minimally invasive versus open gastrectomy within subgroups divided by mean age (< 65 vs ≥ 65 years), gender, tumor size (< 5 vs ≥ 5 cm), type of gastrectomy (distal gastrectomy vs total or proximal gastrectomy), histologic type (differentiated vs undifferentiated or unknown), and number of examined lymph nodes (≤ 15 vs > 15). The two types of surgery were associated with comparable risk of death in all subgroups (Fig. 3).

Uni- and Multivariate Survival Analyses of Prognostic Factors

Univariate analysis showed that age of 65 years or older, non-distal tumor location, tumor size of 5 cm or larger, undifferentiated type, proximal or total resection, and pTNM stage II or III were significantly associated with OS (Table 2). However, postoperative chemotherapy and postoperative radiation were not significantly related to OS in the univariate analysis. Multivariate analysis narrowed the list of independent prognostic factors for OS to older age (odds ratio [OR], 1.283; 95% CI 1.124–1.463; p = 0.001), non-distal location (OR, 1.437; 95% CI 1.101–1.875; p = 0.008), large tumor size (OR, 1.693; 95% CI 1.439–1.993; p = 0.001), proximal or total resection (OR, 1.792; 95% CI 1.363–2.355; p = 0.001), stage II disease (OR, 2.896; 95% CI 2.036–4.118; $p < 0.001$), and stage III disease (OR, 6.976; 95% CI 5.030–9.675; $p < 0.001$). Minimally invasive versus open approach was not a significant prognostic variable in the uni- and multivariate analyses.

DISCUSSION

In this retrospective study of prospectively collected data from two high-volume units for gastric cancer surgery in the United States and China, after propensity score-matching, the 5-year OS after minimally invasive

TABLE 1 Characteristics of cohorts defined by surgical approach before and after propensity score-matching[a]

	Before matching			After matching		
	Open (n = 1355) n (%)	MI (n = 2059) n (%)	p Value	Open (n = 889) n (%)	MI (n = 889) n (%)	p Value
Age (years)	62.3 ± 12.1	61.1 ± 11.4	**0.003**	60.6 ± 11.1	60.3 ± 11.2	0.812
Gender			**0.010**			0.382
Male	956 (70.6)	1535 (74.6)		657 (73.9)	674 (75.8)	
Female	399 (29.4)	524 (25.4)		232 (26.1)	215 (24.2)	
Tumor size (cm)	4.8 ± 2.9	4.6 ± 2.7	0.259	5.2 ± 2.8	5.1 ± 2.7	0.230
Differentiation type			< **0.001**			0.474
Differentiated	451 (33.3)	887 (43.1)		398 (44.8)	383 (43.1)	
Undifferentiated/unknown	904 (66.7)	1172 (56.9)		491 (55.2)	506 (56.9)	
Tumor location			< **0.001**			0.053
Lower third	579 (42.7)	877 (42.5)		393 (44.2)	346 (38.9)	
Middle third	230 (17.0)	415 (20.2)		125 (14.1)	178 (20.0)	
Upper third or GE junction	418 (30.9)	510 (24.8)		263 (29.6)	243 (27.4)	
Distributed throughout	128 (9.4)	257 (12.5)		108 (12.1)	122 (13.7)	
Resection extent			0.574			0.388
Distal	619 (45.7)	938 (45.6)		386 (43.4)	367 (41.3)	
Proximal/total	736 (54.3)	1121 (54.4)		503 (56.6)	522 (58.7)	
No. of positive LNs	6.0 ± 9.0	6.3 ± 12.5	0.420	7.5 ± 10.1	7.3 ± 9.1	0.122
No. of LNs examined	26.1 ± 13.2	32.8 ± 13.4	0.409	28.2 ± 14.0	34.2 ± 13.3	0.897
pT stage			< **0.001**			0.123
T1	331 (24.5)	536 (26.0)		154 (17.3)	144 (16.2)	
T2	148 (10.9)	234 (11.4)		98 (11.1)	85 (9.6)	
T3	272 (20.1)	565 (27.4)		170 (19.1)	210 (23.6)	
T4	604 (44.5)	724 (35.2)		467 (52.5)	450 (50.6)	
pN stage			0.652			0.741
N0	511 (37.8)	798 (38.8)		267 (30.0)	250 (28.1)	
N1	205 (15.1)	294 (14.2)		131 (14.7)	127 (14.3)	
N2	205 (15.1)	325 (15.8)		144 (16.3)	159 (17.9)	
N3a	241 (17.8)	354 (17.2)		176 (19.8)	189 (21.3)	
N3b	193 (14.2)	288 (14.0)		171 (19.2)	164 (18.4)	
pTNM stage			0.138			0.471
I	379 (28.0)	632 (30.7)		190 (21.4)	171 (19.2)	
II	286 (21.1)	446 (21.7)		172 (19.3)	185 (20.8)	
III	690 (50.9)	981 (47.6)		527 (59.3)	533 (60.0)	
Postop chemotherapy			0.516			0.739
Yes	646 (47.7)	1005 (48.8)		463 (52.1)	470 (52.9)	
No	709 (52.3)	1054 (51.2)		426 (47.9)	419 (47.1)	
Postop radiation			< **0.001**			0.247
Yes	51 (3.8)	8 (0.4)		8 (0.9)	4 (0.4)	
No	1304 (96.2)	2051 (99.6)		881 (99.1)	885 (99.6)	

Categorical data are presented as n (%) and continuous data as mean ± SD

MI minimally invasive, *GE* gastroesophageal, *LN* lymph node, *TNM* tumor-node-metastasis, *Postop* postoperative

Bold values are statistically significant ($p < 0.05$)

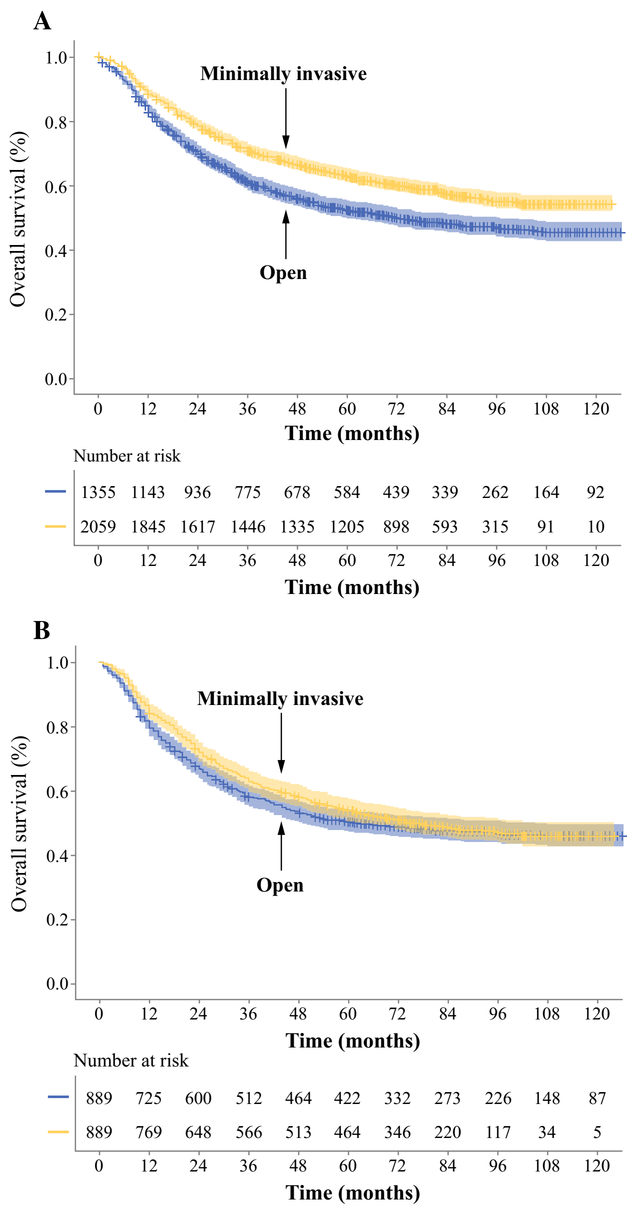

FIG. 1 Comparison of overall survival between patients undergoing minimally invasive and those undergoing open gastrectomy (**A**) before and (**B**) after propensity score-matching. Graphs display the number of patients at risk at different time points. Shaded areas represent 95% confidence intervals

gastrectomy was similar to that after open gastrectomy. To our knowledge, this is the first study to compare long-term survival between patients with GA in a combined Western and Eastern cohort who underwent gastrectomy by the two approaches. Despite differences in patient demographics and perioperative treatment between the East and West, a "real-world study" was indeed necessary to assess fully the oncologic efficacy of minimally invasive gastrectomy, which was one of the advantages of this study. Another major advantage of this study was that all the patients had at least 5 years of potential follow-up evaluation, so that the actual 5-year OS is reported rather than the actuarial 5-year OS.

Laparoscopic and robotic surgeries were considered as a single group in the current study on the basis of prior studies showing them to have equivalent outcomes. A prospective, multicenter comparative study showed that they have similar perioperative surgical outcomes,[1] and retrospective studies have found them to have similar short-term recovery and long-term oncologic outcomes.[14]

We did not compare the short-term outcomes of minimally invasive and open gastrectomy because many studies, including randomized clinical trials, have clearly shown them to have similarly good short-term outcomes. The feasibility and safety of laparoscopic distal and total gastrectomy for stage I GA were confirmed by the KLASS-01[31] and KLASS-03[8] trials, and for advanced GA by the CLASS01,[11] LSSG0901,[12] KLASS-02,[2] and COACT 1001[10] studies. Robotic gastrectomy was shown to be as safe as laparoscopic gastrectomy in a prospective, multicenter comparative study,[1] and a subgroup analysis found that the two approaches have similar surgical outcomes for obese patients.[32] Finally, minimally invasive gastrectomy (both robotic and laparoscopic approaches) was found to have oncologic outcomes equivalent to those for open gastrectomy in a retrospective study using data from the U.S. National Cancer Data Base (NCDB).[33]

Our investigation addressed the need of further evidence for minimally invasive approaches to gastrectomy to be recommended for GA. Whereas several trials have indicated that laparoscopy has 3- to 5-year survival outcomes equivalent to those for open gastrectomy in both stage 1[7] and advanced GA,[13] three additional multicenter randomized controlled trials are ongoing.[8,12,31] To date, no prospective studies have evaluated robotic surgery, nor has survival been analyzed for each stage.

Surprisingly, differences in 5-year OS between the patients who underwent minimally invasive surgery and those who had open surgery increased with tumor TNM stage. Although no difference was statistically significant in any of the stage subgroups, we unexpectedly found that 5-year survival after minimally invasive gastrectomy tended to be higher than after open gastrectomy, especially for patients with stage III GA. There may be several possible reasons for this phenomenon. First, minimally invasive surgery causes less systemic trauma, which has been shown experimentally to reduce tumor recurrence,[34] induce lower stress responses, and better preserve immune function,[35] whereas conventional open surgery increases serum levels of markers of inflammation such as C-reactive protein

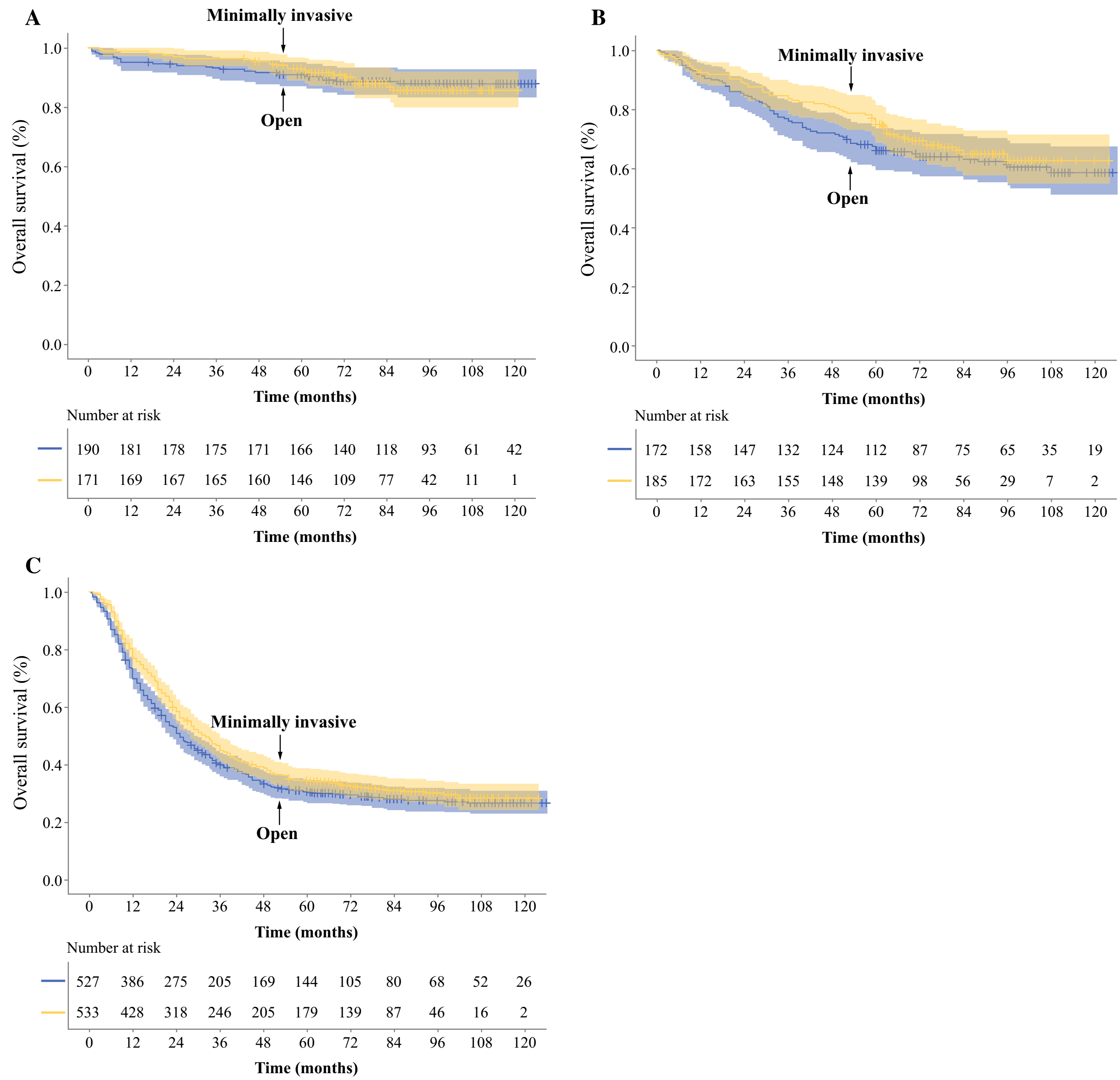

FIG. 2 Comparison of overall survival between patients undergoing minimally invasive and those undergoing open gastrectomy according to pTNM stage in the propensity-matched cohort. **A** Stage I. **B** Stage II. **C** Stage III. Graphs display the number of patients at risk. Shaded areas represent 95% confidence intervals

(CRP) and interleukin-6 (IL-6).[34] This difference in stress and immune impact likely is more important for stage III patients. Second, because faster recovery allows more patients to receive adjuvant systemic chemotherapy,[36] patients with stage III tumors may obtain more survival benefit from earlier postoperative therapy than those with stage II tumors. The small differences also could be explained by selection bias not eliminated by PSM.

Notably, our report differs in several was from prior publications. First, to our knowledge, this is the only such large-scale comparison between minimally invasive and

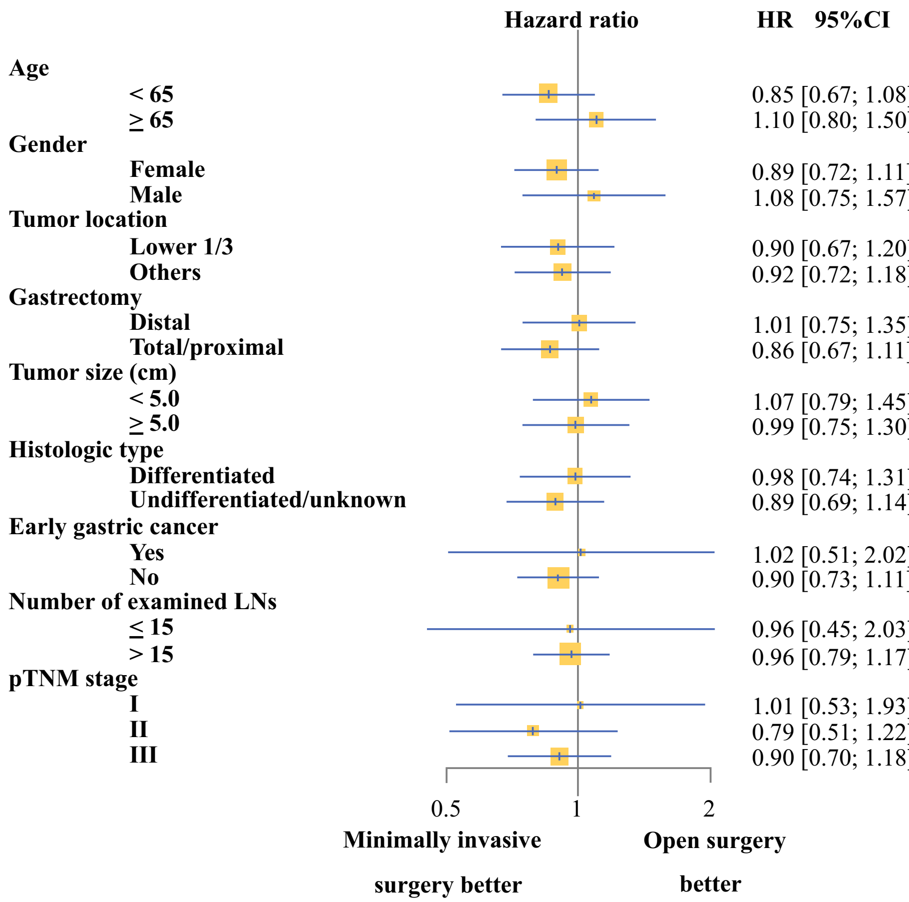

FIG. 3 Forest plot of hazard ratios (HRs) comparing minimally invasive with open gastrectomy in cohort subsets. HRs < 1.0 favor combined-modality therapy. The *p* values are from the subset test of interaction

open surgery for U.S. and Chinese GA patients, although a number of studies that differ fundamentally from the current study have successfully demonstrated differences in patient demographics, treatment policies, and treatment outcomes between the United States and Asia[28–30,37,38] Second, compared with previous studies on long-term survival after minimally invasive surgery and open surgery for GA,[13,39–41] the median follow-up time of this study was longer. Thus, this study provided valuable information that may be used to design future international prospective studies.

The current study had several limitations. First, the study was limited by its retrospective nature and the attendant biases including selection bias. For example, advanced tumors were less often managed with minimally invasive surgery, and advanced tumors at MSKCC usually were treated with neoadjuvant chemotherapy, leading to exclusion of these patients from this study. Additional confounding issues included the following: the patients at the two institutions received different perioperative therapy and had differing durations of follow-up evaluation, and the patients at the two institutions likely had different patient preferences, socioeconomic status, or other patient characteristics. Second, we did not monitor mid- or long-term complications, nutrition status, quality of life, or daily activities. Third, disease-free survival was not investigated in this study. However, a large number of studies have demonstrated that OS is a reliable measure of the prognosis for cancer patients.[42–44] Nevertheless, it should be noted that because our conclusions have not been externally validated, well-designed multicenter randomized trials are needed to definitively compare the long-term outcomes of minimally invasive gastrectomy (including robot-assisted surgery) with those of open gastrectomy for GA patients. Our findings may support the broader use of minimally invasive gastrectomy by other institutions or in other regions. The findings also provide reference data for potential future randomized trials.

TABLE 2 Uni- and multivariable analysis of clinical and pathologic factors associated with overall survival in a matched cohort

Variables	Univariable analysis		Multivariable analysis	
	OS at 5 years	*p* Value	OR (95% CI)	*p* Value
Age (years)		< 0.001		**0.001**
< 65	56.2		1.00 (reference)	
≥65	46.1		1.283 (1.124–1.463)	
Gender		0.953		–
Male	52.3		–	
Female	51.8		–	
Location		< 0.001		**0.008**
Distal	59.8		1.00 (reference)	
Others	47.2		1.437 (1.101–1.875)	
Tumor size (cm)		< 0.001		**0.001**
< 5.0	74.5		1.00 (reference)	
≥5.0	33.4		1.693 (1.439–1.993)	
Differentiation type		< 0.001		0.233
Differentiated	60.4		1.00 (reference)	
Undifferentiated/unknown	45.8		1.087 (0.948–1.247)	
No. of examined LNs		0.446		–
> 15	53.8		–	
≤ 15	51.6		–	
Resection extent		< 0.001		**0.001**
Distal	63.7		1.00 (reference)	
Proximal/total	43.7		1.792 (1.363–2.355)	
TNM stage		< 0.001		< **0.001**
I	91.8		1.00 (reference)	
II	65.7		2.896 (2.036–4.118)	
III	32.4		6.976 (5.030–9.675)	
Surgical approach		0.205		0.115
Open	50.4		1.00 (reference)	
Minimally invasive	54.0		0.900 (0.790–1.026)	
Postop chemotherapy		0.142		
Yes	53.6			
No	51.3			
Postop radiation		0.854		
Yes	53.2			
No	51.9			

OS data are percentages

OS overall survival, *OR* odds ratio, *CI* confidence interval, *LN* lymph node, *TNM* tumor-node-metastasis, *Postop* postoperative

Bold values are statistically significant ($p < 0.05$)

CONCLUSION

In conclusion, our study suggests that minimally invasive gastrectomy is an oncologically safe procedure for both Western and Eastern patients with GA in terms of long-term survival.

ACKNOWLEDGMENTS This research was funded in part by a National Institutes of Health/National Cancer Institute Cancer Center Support Grant (P30 CA008748), the National Nature Science Foundation of China (No. 81871899), the Construction Project of Fujian Province Minimally Invasive Medical Centre (No. [2017] 171), and the Natural Science Foundation of Fujian Province (2019J01155). The authors thank Jessica Moore, senior editor at MSKCC, for editing the manuscript.

DISCLOSURES There are no conflicts of interest.

REFERENCES

1. Kim HI, Han SU, Yang HK, et al. Multicenter prospective comparative study of robotic versus laparoscopic gastrectomy for gastric adenocarcinoma. *Ann Surg*. 2016;1:103–9.
2. Lee HJ, Hyung WJ, Yang HK, et al. Short-term outcomes of a multicenter randomized controlled trial comparing laparoscopic distal gastrectomy with d2 lymphadenectomy to open distal gastrectomy for locally advanced gastric cancer (KLASS-02-RCT). *Ann Surg*. 2019; 270:983–91.
3. Herrera-Almario G, Strong VE. Minimally invasive gastric surgery. *Ann Surg Oncol*. 2016;12:3792–7.
4. Chang KK, Park DJ, Yoon SS. Laparoscopic versus open surgery for gastric adenocarcinoma: innovation continues to challenge tradition. *Ann Surg*. 2016;2:223–5.
5. Honda M, Hiki N, Kinoshita T, et al. Long-term outcomes of laparoscopic versus open surgery for clinical stage I gastric cancer: the LOC-1 study. *Ann Surg*. 2016;2:214–22.
6. Yang SY, Roh KH, Kim YN, et al. Surgical outcomes after open, laparoscopic, and robotic gastrectomy for gastric cancer. *Ann Surg Oncol*. 2017;7:1770–7.
7. Kim HH, Han SU, Kim MC, et al. Effect of laparoscopic distal gastrectomy vs open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. *JAMA Oncol*. 2019; 5:506–13.
8. Hyung WJ, Yang HK, Han SU, et al. A feasibility study of laparoscopic total gastrectomy for clinical stage I gastric cancer: a prospective multi-center phase II clinical trial, KLASS 03. *Gastric Cancer*. 2019;1:214–22.
9. Japanese Gastric Cancer Treatment Guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;1:1–19.
10. Park YK, Yoon HM, Kim YW, et al. Laparoscopy-assisted versus open D2 distal gastrectomy for advanced gastric cancer: results from a randomized phase II multicenter clinical trial (COACT 1001). *Ann Surg*. 2018;4:638–45.
11. Hu Y, Huang C, Sun Y, et al. Morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer: a randomized controlled trial. *J Clin Oncol*. 2016;12:1350–7.
12. Inaki N, Etoh T, Ohyama T, et al. A multi-institutional, prospective, phase II feasibility study of laparoscopy-assisted distal gastrectomy with D2 lymph node dissection for locally advanced gastric cancer (JLSSG0901). *World J Surg*. 2015;11:2734–41.
13. Yu J, Huang C, Sun Y, et al. Effect of laparoscopic vs open distal gastrectomy on 3-year disease-free survival in patients with locally advanced gastric cancer: the CLASS-01 randomized clinical trial. *JAMA*. 2019;20:1983–92.
14. Gao Y, Xi H, Qiao Z, et al. Comparison of robotic- and laparoscopic-assisted gastrectomy in advanced gastric cancer: updated short- and long-term results. *Surg Endosc*. 2019;2:528–34.
15. Lu J, Zheng HL, Li P, et al. A propensity score-matched comparison of robotic versus laparoscopic gastrectomy for gastric cancer: oncological, cost, and surgical stress analysis. *J Gastrointest Surg*. 2018;7:1152–62.
16. Obama K, Kim YM, Kang DR, et al. Long-term oncologic outcomes of robotic gastrectomy for gastric cancer compared with laparoscopic gastrectomy. *Gastric Cancer*. 2018;2:285–95.
17. Bobo Z, Xin W, Jiang L, et al. Robotic gastrectomy versus laparoscopic gastrectomy for gastric cancer: meta-analysis and trial sequential analysis of prospective observational studies. *Surg Endosc*. 2019;4:1033–48.
18. Japanese GCA. Japanese Classification of Gastric Carcinoma. 2nd English edition. *Gastric Cancer*. 1998;1:10–24.
19. Japanese Classification of Gastric Carcinoma: 3rd English edition. *Gastric Cancer*. 2011;2:101–12.
20. Li P, Lin JX, Tu RH, et al. Early unplanned reoperations after gastrectomy for gastric cancer are different between laparoscopic surgery and open surgery. *Surg Endosc*. 2019;12:4133–42.
21. Xu Y, Hua J, Li J, et al. Long-term outcomes of laparoscopic versus open gastrectomy for advanced gastric cancer: a large cohort study. *Am J Surg*. 2019;4:750–6.
22. Xu BB, Lu J, Zheng ZF, et al. Comparison of short-term and long-term efficacy of laparoscopic and open gastrectomy in high-risk patients with gastric cancer: a propensity score-matching analysis. *Surg Endosc*. 2019;1:58–70.
23. Kano Y, Ohashi M, Ida S, et al. Oncological feasibility of laparoscopic subtotal gastrectomy compared with laparoscopic proximal or total gastrectomy for cT1N0M0 gastric cancer in the upper gastric body. *Gastric Cancer*. 2019;22:1060–8.
24. Lu J, Zheng CH, Cao LL, et al. The effectiveness of the 8th American Joint Committee on Cancer TNM classification in the prognosis evaluation of gastric cancer patients: a comparative study between the 7th and 8th editions. *Eur J Surg Oncol*. 2017;12:2349–56.
25. Japanese Classification of Gastric Carcinoma. 2nd English edition. Response assessment of chemotherapy and radiotherapy for gastric carcinoma: clinical criteria. *Gastric Cancer*. 2001;1:1–8.
26. Tian S, Zhang X, Jiang R, et al. Survival outcomes with thoracic radiotherapy in extensive-stage small-cell lung cancer: a propensity score-matched analysis of the National Cancer Database. *Clin Lung Cancer*. 2019; 20:484–93.
27. Melamed A, Margul DJ, Chen L, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N Engl J Med*. 2018;20:1905–14.
28. Strong VE, Russo A, Yoon SS, et al. Comparison of young patients with gastric cancer in the United States and China. *Ann Surg Oncol*. 2017;13:3964–71.
29. Strong VE, Wu AW, Selby LV, et al. Differences in gastric cancer survival between the US and China. *J Surg Oncol*. 2015;1:31–7.
30. Lin JX, Yi BC, Yoon C, et al. Comparison of outcomes for elderly gastric cancer patients at least 80 years of age following gastrectomy in the United States and China. *Ann Surg Oncol*. 2018;12:3629–38.
31. Kim W, Kim HH, Han SU, et al. Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage I gastric cancer: short-term outcomes from a multicenter randomized controlled trial (KLASS-01). *Ann Surg*. 2016;1:28–35.
32. Park JM, Kim HI, Han SU, et al. Who may benefit from robotic gastrectomy? A subgroup analysis of multicenter prospective comparative study data on robotic versus laparoscopic gastrectomy. *Eur J Surg Oncol*. 2016;12:1944–9.
33. Leung K, Sun Z, Nussbaum DP, Adam MA, Worni M, Blazer DR. Minimally invasive gastrectomy for gastric cancer: a national perspective on oncologic outcomes and overall survival. *Surg Oncol*. 2017;3:324–30.
34. Agalar F, Daphan C, Hayran M, Sayek I. Laparoscopic surgery is associated with less tumour growth stimulation than conventional surgery: an experimental study. *Br J Surg*. 1997;10:1480.
35. Veenhof AA, Vlug MS, van der Pas MH, et al. Surgical stress response and postoperative immune function after laparoscopy or open surgery with fast track or standard perioperative care: a randomized trial. *Ann Surg*. 2012;2:216–21.
36. Kelly KJ, Selby L, Chou JF, et al. Laparoscopic versus open gastrectomy for gastric adenocarcinoma in the West: a case-control study. *Ann Surg Oncol*. 2015;11:3590–6.

37. Shim JH, Song KY, Jeon HM, et al. Is gastric cancer different in Korea and the United States? Impact of tumor location on prognosis. *Ann Surg Oncol*. 2014;7:2332–9.
38. Noguchi Y, Yoshikawa T, Tsuburaya A, Motohashi H, Karpeh MS, Brennan MF. Is gastric carcinoma different between Japan and the United States? *Cancer Am Cancer Soc*. 2000;11:2237–46.
39. Shi Y, Xu X, Zhao Y, et al. Long-term oncologic outcomes of a randomized controlled trial comparing laparoscopic versus open gastrectomy with D2 lymph node dissection for advanced gastric cancer. *Surgery*. 2019;165:1211-1216.
40. Li Z, Liu Y, Hao Y, Bai B, Yu D, Zhao Q. Surgical and long-term oncologic outcomes of laparoscopic and open gastrectomy for serosa-positive (pT4a) gastric cancer: a propensity score-matched analysis. *Surg Oncol*. 2019;28:167–73.
41. Solaini L, Bazzocchi F, Pellegrini S, et al. Robotic vs open gastrectomy for gastric cancer: a propensity score-matched analysis on short- and long-term outcomes. *Int J Med Robot*. 2019;5:e2019.
42. Hirabayashi S, Kosugi S, Isobe Y, et al. Development and external validation of a nomogram for overall survival after curative resection in serosa-negative, locally advanced gastric cancer. *Ann Oncol*. 2014;6:1179–84.
43. Han DS, Suh YS, Kong SH, et al. Nomogram predicting long-term survival after D2 gastrectomy for gastric cancer. *J Clin Oncol*. 2012;31:3834–40.
44. Lu J, Zheng ZF, Zhou JF, et al. A novel prognosis prediction model after completion gastrectomy for remnant gastric cancer: development and validation using international multicenter databases. *Surgery*. 2019.;166:314–21.