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Total gastrectomy in patients with gastric adenocarcinoma: Is there an advantage to the minimally invasive approach?

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ABSTRACT

Background: Previous evaluations of the oncologic efficacy of minimally invasive approaches to total gastrectomy in gastric adenocarcinoma have been limited by sample size and duration of follow-up.
Methods: We queried the National Cancer Database to identify patients undergoing robotic and laparoscopic or open total gastrectomy for gastric adenocarcinoma between 2010 and 2015. Propensity score matching was used to adjust for patient, tumor, and treating facility factors. Kaplan-Meier survival functions were used to compare overall survival. Secondary outcomes included margin status, lymph node sampling, mortality, readmission, and length of stay.
Results: In the study, 3,213 (72.2%) patients underwent open total gastrectomy; 1,238 (27.8%) minimally invasive total gastrectomy. Patients undergoing minimally invasive total gastrectomy were more likely to be treated at academic (49.5% vs 57.8%, $P < .05$) and high-volume centers (21.6% vs 28.4%, $P < .05$). Propensity score matching yielded 1,238 open and 1,238 minimally invasive well-matched total gastrectomies. Minimally invasive was associated with a decreased median length of stay (10 vs 9 days; $P < .01$). Rates of positive surgical margins, 30-day readmission, 90-day mortality and overall survival were identical between matched cohorts ($P > .1$).
Conclusion: Minimally invasive approaches to total gastrectomy provide perioperative oncologic outcomes and overall survival rates that are identical to those for open total gastrectomy but are associated with reduced length of stay.

Introduction

Consensus treatment recommendations for resectable gastric tumors involves total or partial gastric resection to achieve negative margins and en bloc resection of ≥15 D1 and D2 lymph nodes.[1–3] Patients with advanced disease or proximal tumors often require a total gastrectomy (TG) with Roux-en-Y reconstruction. These operations are associated with significant postoperative morbidity.[4,5] Many have advocated for the application of minimally invasive (MIS) techniques to these procedures in an effort to reduce postoperative morbidity.

Most comparisons of MIS and open approaches to gastrectomy are retrospective reviews of single institutional experiences with subtotal gastrectomy or distal gastrectomy evaluating small numbers of patients during time periods before implementation of robotic approaches. These studies have all varied considerably in their reporting of oncological outcomes including node counts, tumor staging, and resection margin status. Very few evaluate postoperative outcomes for TG and evaluate outcomes for longer than 30 days after the index procedure.[6–9] The limitations on sample size and reporting of perioperative oncologic outcomes and the fact that robotic procedures are not included make it difficult to definitively assess the efficacy of the MIS approach.

In the present work, we utilize the National Cancer Database (NCDB) to evaluate the independent effect of the MIS approach to TG on short-term perioperative oncologic and clinical outcomes and long-term overall survival (OS) in patients undergoing MIS or open TG for gastric adenocarcinoma between 2010 and 2015.

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Methods

Data source

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society containing Health Insurance Portability and Accountability Act-compliant de-identified patient data.[10] The NCDB is a prospectively maintained hospital-based registry that collects information on >70% of incident malignant diagnoses compiled from 1,500 CoC accredited institutions nationwide. The American College of Surgeons and the CoC have not verified and are not responsible for the analytic or statistical methodology used or the conclusions drawn from these data by the investigators. A Data Use Agreement was obtained, and this project met criteria for exemption from the Loyola University Chicago Institutional Review Board (LU# 211870).

Study design

Adult patients with histologically confirmed pTis-T4a, N (any), M0 gastric adenocarcinoma diagnosed between January 1, 2010 to December 31, 2015 who underwent total gastrectomy as definitive surgical treatment of their primary tumor were selected for analysis. Total gastrectomy was defined as a near-total or total gastrectomy with or without removal of a portion of esophagus using the NCDB variable "surgical procedure of the primary site" (Supplemental Digital Content Table I). Patients with distant metastases, other tumor histology types, or tumors invading surrounding structures (pT4b) were excluded. In addition, patients with missing data regarding pathologic staging, surgical resection margin, regional lymph nodes sampled, postoperative length of stay (LOS), and tumor size were excluded from analysis. Cohorts were stratified by operative approach into open and MIS gastrectomy groups based on initial intended approach. Owing to potential confounding related to converted cases (including diagnostic laparoscopy with planned conversion to open TG), a sensitivity analysis was performed in which converted cases were excluded before the propensity match. The results obtained from this sensitivity analysis were no different than those obtained from our intent to treat analysis. Therefore, the results reported here are those for the intent to treat analysis in which MIS cases include those labeled by the NCDB as laparoscopic, laparoscopic converted to open, robotic, or robotic converted to open.

Our primary oncologic outcome was OS. Secondary short-term outcomes included positive resection margin (as evidenced by presence of microscopic or macroscopic disease at the excised specimen margin), median number of lymph nodes sampled, performance of at least a 15-node regional lymphadenectomy, median postoperative LOS, rates of 30-day inpatient readmission, 30-day mortality, and 90-day mortality.

Statistical analysis

To account for confounding in the selection of TG operative approach, we developed propensity scores for each patient using logistic modeling with a caliper set at 0.1. Propensity scores (PSM), defined as the conditional probability of undergoing a MIS TG versus an open TG, were used to match patients based on patient, tumor, and hospital level factors using a 1:1 nearest neighbor algorithm.[11] Owing to an absence of available survival data for patients diagnosed in 2015, a separate PSM analysis was performed for 30-day mortality, 90-day mortality, and OS including only patients diagnosed from 2010 to 2014. This PSM developed matched cohorts of 980 open and 980 MIS TG patients with no differences in age, sex, race, insurance, year of diagnosis, Charlson-Deyo comorbidity score, tumor size and location, pT stage, pN stage, treating facility type and TG volume, use of neoadjuvant chemotherapy, use of neoadjuvant radiation, and chemotherapy schedule on univariate analysis ($P > .2$). Reported cohort characteristics represent data from the PSM from all available diagnosis years (2010–2015). Survival statistics represent data from the PSM for years 2010 to 2014.

Primary and secondary outcomes were assessed among matched cohorts. Survival functions were developed using the Kaplan-Meier method in matched cohorts and equality of survivor functions were assessed with the log-rank test. A multivariable cox proportional hazards regression model was also used to assess factor independent associations with risk of death, adjusting for patient, facility, tumor, and operative characteristics.

Unadjusted comparisons of continuous variables were performed using independent Student *t* tests and Wilcoxon rank-sum (Mann-Whitney) tests, as appropriate, and comparisons of proportions between cohorts were performed using Pearson χ^2. Data are presented as means ± standard deviation, median with interquartile range (IQR), or counts with percentages, as appropriate. Adjusted hazard ratios (HR) are represented with the 95% confidence interval (CI). All statistical analyses were performed using Stata software (version 14.2; StataCorp LLC; College Station, TX).

Results

Cohort characteristics

We identified 3,213 patients (72.2%) who underwent open TG, 1,031 patients (23.2%) who underwent laparoscopic TG, and 207 patients (4.7%) who underwent robotic TG during the study period. Conversion to open was observed in 181 (18.5%) planned laparoscopic procedures, and 20 (9.7%) robotic procedures, leading to an overall 17.0% conversion rate in the MIS cohort. Patient and treating facility characteristics before and after PSM are summarized in Table I. Patients who underwent MIS (laparoscopic or robotic) TG were more likely to be white, privately insured, had more limited comorbid disease, and were more likely to be treated at high-volume academic centers than those undergoing the open approach ($P < .05$). PSM developed a 1:1 population of 1,238 open and 1,238 MIS patients that were well matched with no notable differences in age, gender, race, insurance, comorbidity score, diagnosis year, facility type or volume.

Unmatched and PSM tumor and treatment characteristics are displayed in Table II. Tumors were most commonly found in the gastric cardia for the unmatched (open: 45.8%, MIS: 56.5%; $P < .05$) and matched cohorts (open: 57.3%, MIS: 56.5%; $P = .99$). In the unmatched cohort, when compared to the MIS approach, open TGs were more likely to be performed on tumors >50 mm in size (open: 41.6%, vs MIS: 36.7%, $P < .05$), with more advanced pathologic T (T3-4 open: 59.8%, vs MIS: 51.4%; $P < .05$) and N stages (N1-3 open: 55.7%, vs MIS: 47.9%; $P < .05$). After PSM, cohorts were again well matched with no notable differences in tumor location, size, pathologic T stage, N stage, use of chemotherapy, or use of radiotherapy ($P > .2$).

Short-term postoperative outcomes

Short-term outcomes following TG are summarized in Table III. After PSM, there was no difference between cohorts in rates of positive surgical margins (open: 11.6%, vs MIS: 9.9%; $P = .19$) or median number of lymph nodes sampled (open: 18, IQR [12–25] vs MIS: 18, IQR [12–26]; $P = .08$). The MIS approach demonstrated a reduced median postoperative LOS (open: 10 days, IQR [8–14] vs MIS: 9 days, IQR [7–13]; $P < .01$). Rates of 30-day readmission, 30-day mortality, and 90-day mortality ($P > .7$) were also identical between matched cohorts. When compared with the laparoscopic approach, patients

Table I
Patient and treating facility characteristics

	All patients					Propensity-score matched patients				
	Open		MIS		*P* value	Open		MIS		*P* value
	n = 3,213		n = 1,238			n = 1,238		n = 1,238		
Age (y), mean (SD)	64.4	12.0	63.9	12.3	.18	63.9	12	63.9	12.3	.92
Male, *n* (%)	2,233	69.5%	895	72.3%	.07	877	70.8%	895	72.3%	.42
Race, *n* (%)					<.05					.98
White	2,532	78.8%	995	80.4%		987	79.7%	995	80.4%	
Black	382	11.9%	112	9.0%		115	9.3%	112	9.0%	
Asian/PI	221	6.9%	94	7.6%		98	7.9%	94	7.6%	
Other	78	2.4%	37	3.0%		38	3.1%	37	3.0%	
Insurance, *n* (%)					.16					.86
Uninsured	92	2.9%	24	1.9%		31	2.5%	24	1.9%	
Private	1,224	38.1%	508	41.0%		492	39.7%	508	41.0%	
Medicaid	221	6.9%	91	7.4%		95	7.7%	91	7.4%	
Medicare	1,595	49.6%	589	47.6%		592	47.8%	589	47.6%	
Other	81	2.5%	26	2.1%		28	2.3%	26	2.1%	
Charlson-Deyo, *n* (%)					.16					.68
0	2,102	65.4%	854	69.0%		827	66.8%	854	69.0%	
1	831	25.9%	290	23.4%		308	24.9%	290	23.4%	
2	201	6.3%	69	5.6%		78	6.3%	69	5.6%	
3+	79	2.5%	25	2.0%		25	2.0%	52	4.2%	
Year of diagnosis, *n* (%)					<.05					.84
2010	597	18.6%	134	10.8%		119	9.6%	134	10.8%	
2011	553	17.2%	177	14.3%		173	14.0%	177	14.3%	
2012	523	16.3%	185	14.9%		193	15.6%	185	14.9%	
2013	518	16.1%	209	16.9%		229	18.5%	209	16.9%	
2014	505	16.1%	275	22.2%		269	21.7%	275	22.2%	
2015	517	15.7%	258	20.8%		255	20.6%	258	20.8%	
Facility type, *n* (%)					<.05					.56
Community	119	3.7%	22	1.8%		26	2.1%	22	1.8%	
Comp community	1,038	32.3%	311	25.1%		298	24.1%	311	25.1%	
Academic	1,589	49.5%	716	57.8%		700	56.5%	716	57.8%	
Integrated Network	379	11.8%	143	11.6%		169	13.7%	143	11.6%	
Unknown	88	2.7%	46	3.7%		45	3.6%	46	3.7%	
Facility TG volume, *n* (%)					<.05					.62
1–4 cases	943	29.3%	247	20.0%		259	20.9%	247	20.0%	
5–12 cases	825	25.7%	317	25.6%		294	23.7%	317	25.6%	
13–21 cases	752	23.4%	323	26.1%		342	27.6%	323	26.1%	
22–144 cases	693	21.6%	351	28.4%		343	27.7%	351	28.4%	
Facility location, *n* (%)					<.05					<.05
Northeast	666	20.7%	373	30.1%		264	21.3%	373	30.1%	
Southeast	728	22.7%	238	19.2%		299	24.2%	238	19.2%	
North Central	707	22.0%	247	20.0%		277	22.4%	247	20.0%	
South Central	578	18.0%	119	9.6%		178	14.4%	119	9.6%	
West	446	13.9%	215	17.4%		175	14.1%	215	17.4%	
Unknown	88	2.7%	46	3.7%		45	3.6%	46	3.7%	

Comp, comprehensive; *PI*, pacific islander; *TG*, total gastrectomy.

undergoing robotic TG demonstrated no statistical difference in rate of margin positivity, median nodes sampled, median LOS, readmission, 30-day mortality, or 90-day mortality ($P > .2$).

Survival analysis in matched cohorts

Kaplan-Meier survivor functions to a mean length of 28.5 months follow-up are shown in Fig 1. Although the MIS approach demonstrated a prolonged median survival after TG when compared with the open approach, this did not reach statistical significance (open: 40.0 months vs MIS: 48.6 months, log rank $P = .079$). Within the MIS cohort, there was no difference between laparoscopic and robotic TG with regard to median survival (laparoscopic: 49 vs robotic: 61 months, log-rank $P = .660$).

Cox proportional hazards model

To identify factors that were independently associated with overall survival, we performed a multivariable Cox Proportional-Hazards regression model within the unmatched cohort (Table IV). In this analysis, MIS approaches to TG were not associated with risk of death when in comparison to open TG (laparoscopic HR 0.95; 95% CI, 0.85–1.07; robotic HR 1.04; 95% CI, 0.79–1.36). Increasing age, Charlson-Deyo index, tumor size, and treatment at a comprehensive community program were each independently associated with increased risk of death ($P < .05$). Protective factors independently associated with reduced risk of death in the unmatched cohort included female sex, Asian or Pacific Islander race, tumors in the gastric body, adequate 15+ node lymphadenectomy, and use of adjuvant or sandwich chemotherapy ($P < .05$).

Discussion

We aimed to determine if MIS approaches to TG independently offer a survival advantage when compared with traditional open TG. In our PSM cohorts, we found no significant difference in 30-day or 90-day mortality, or in OS for patients undergoing MIS approaches to TG relative to those undergoing open approaches to TG. Furthermore, after multivariable Cox modeling, MIS approaches showed identical risk of death in comparison to open TGs. We found the MIS approach to be associated with a reduced postoperative LOS.

Table II
Tumor and treatment characteristics

	All patients					Propensity-score matched patients				
	Open		MIS		*P* value	Open		MIS		*P* value
	n = 3,213		n = 1,238			n = 1,238		n = 1,238		
Tumor site, *n* (%)					<.05					.99
Antrum	217	6.8%	57	4.6%		62	5.0%	57	4.6%	
Body	739	23.0%	232	18.7%		221	17.9%	232	18.7%	
Cardia	1,470	45.8%	700	56.5%		709	57.3%	700	56.5%	
Fundus	200	6.2%	71	5.7%		66	5.3%	71	5.7%	
Pylorus	16	0.5%	6	0.5%		6	0.5%	6	0.5%	
Overlapping	272	8.5%	91	7.4%		96	7.8%	91	7.4%	
NOS	299	9.3%	81	6.5%		78	6.3%	81	6.5%	
Tumor size, *n* (%)					<.05					.22
<10 mm	238	7.4%	123	9.9%		116	9.4%	123	9.9%	
10–19 mm	305	9.5%	162	13.1%		135	10.9%	162	13.1%	
20–29 mm	470	14.6%	197	15.9%		195	15.8%	197	15.9%	
30–39 mm	452	14.1%	168	13.6%		188	15.2%	168	13.6%	
40–49 mm	411	12.8%	134	10.8%		164	13.2%	134	10.8%	
50 mm+	1,337	41.6%	454	36.7%		440	35.5%	454	36.7%	
pT Stage, *n* (%)					<.05					1.00
In situ	118	3.7%	68	5.5%		66	5.3%	68	5.5%	
T1	701	21.8%	344	27.8%		340	27.5%	344	27.8%	
T2	470	14.6%	190	15.3%		194	15.7%	190	15.3%	
T3	1,406	43.8%	489	39.5%		492	39.7%	489	39.5%	
T4	516	16.1%	147	11.9%		146	11.8%	147	11.9%	
pN Stage, *n* (%)					<.05					.75
N0	1,422	44.3%	645	52.1%		619	50.0%	645	52.1%	
N1	608	18.9%	217	17.5%		233	18.8%	217	17.5%	
N2	526	16.4%	176	14.2%		181	14.6%	176	14.2%	
N3	657	20.4%	200	16.2%		205	16.6%	200	16.2%	
Chemotherapy, *n* (%)					<.05					.63
Adjuvant	677	21.1%	192	15.5%		215	17.4%	192	15.5%	
Neoadjuvant	1,050	32.7%	461	37.2%		451	36.4%	461	37.2%	
Sandwich	291	9.1%	128	10.3%		119	9.6%	128	10.3%	
None	1,195	37.2%	457	36.9%		453	36.6%	457	36.9%	
Radiotherapy, *n* (%)	1,194	37.2%	480	38.8%	.40	487	39.3%	480	38.8%	.51

NOS, not otherwise specified.

Table III
Short-term postoperative outcomes in matched cohorts

Outcome	Open		MIS		*P* value
Positive surgical margin, *n* (%)	143	11.6%	123	9.9%	.19
Lymph nodes sampled, median (IQR)	18	12–25	18	12–26	.08
15+ lymph nodes sampled, *n* (%)	802	64.8%	823	66.5%	.37
Median length of stay, days (IQR)	10	8–14	9	7–13	<.01
30-day readmission, *n* (%)	106	8.6%	111	9.0%	.72
30-day mortality, *n* (%)	28	2.9%	29	3.0%	.89
90-day mortality, *n* (%)	65	6.6%	68	6.9%	.79

The median LOS difference observed was marginal at 1-day. This advantage has questionable significance from the perspective of patient, payer, and provider. Taken broadly, the shorter LOS may translate into substantive cost savings when considered in aggregate across the population of patients undergoing TG in the US annually. On an individual basis, however, a savings of 1 inpatient day may be less significant when the disease process is considered. The most important outcome for the patient by far is clearly recurrence free survival. The underlying reasons for the LOS differential are not able to be identified given limitations of the NCDB dataset. The NCDB does not track postoperative complications including anastomotic leak or stricture. The NCDB does include rates of readmission out to 30 days after the index admission. This variable along with the length of index hospitalization provides some indication of ability to compare incidence of significant postoperative complications between approaches, but that ability is certainly limited by the lack of granularity regarding the reasons for readmission. Our findings would suggest that MIS approaches to TG are safe and provide postoperative recovery profiles comparable to open approaches in selected cases.

Prior studies of MIS approaches to gastrectomy for gastric cancer have demonstrated a postoperative LOS advantage for the MIS approach and otherwise equivalent long-term outcomes. These studies have largely included partial and subtotal gastrectomies in study periods with nearly absent robotic utilization.[11–15] For example, the group from Memorial Sloan-Kettering Cancer Center retrospectively examined 60 patients with gastric adenocarcinoma treated with either open or laparoscopic subtotal gastrectomy and found that laparoscopically treated patients had equivalent 30-day complication rates and significantly reduced median LOS (5 vs 7 days, $P < .01$).[15] A 2013 systematic review and meta-analysis of laparoscopic TGs versus open TGs for cancer including 8 single-institution experiences with <700 total cases found the laparoscopic approach is associated with reduced LOS and short-term complications.[16]

Multiple institutional cohort studies in Asian patient populations examining gastrectomies for gastric cancer have failed to

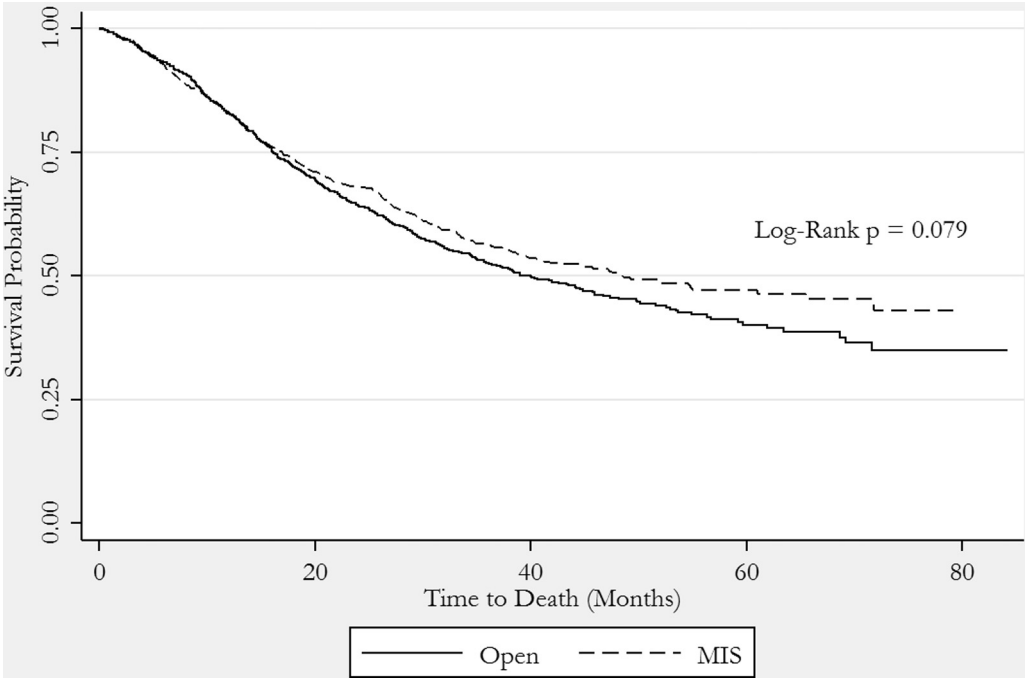

Fig 1. Kaplan-Meier survival analysis by total gastrectomy approach.

demonstrate an MIS survival advantage with up to 5 years of follow-up. There has been some debate regarding whether these results are generalizable to a western patient population.[6,7] In the present study, we find that patients with Asian or Pacific Islander (PI) ethnicities have a reduced risk of overall mortality relative to whites (HR 0.62; 95% CI, 0.50–0.78). This observation has been previously reported in patients with Asian ethnicity being treated in the United States using Surveillance, Epidemiology and End Results data. These findings support the contention that race or genetics are crucial determinants of gastric cancer outcomes but that environmental exposures play an important role as well.[17]

Our findings are consistent with previous examinations of the NCDB that have shown MIS partial gastrectomy offers a reduced postoperative LOS when compared with the open approach with no perceived 30-day or 3-year OS benefit.[11,18,19] Our study is the first from the NCDB to evaluate the relationship of laparoscopic and robotic TGs to open TGs on overall survival in patients with gastric adenocarcinoma. Although the difference does not reach statistical significance, the Kaplan-Meier survival curve identifies an actuarial survival advantage for the MIS approach. We are not able to determine the clinical significance or underlying cause of this advantage. Although it is possible that MIS approaches offer a better technical ability to clear a proximal gastric cancer than open approaches, it is more likely that the perceived survival advantage represents a selection bias with patients having less advanced or less aggressive tumor biologies being selected for the MIS approaches. The limitations of the NCDB dataset preclude us from performing a more robust adjustment for tumor biology. Pathologic features such as lymphovascular invasion, histologic subtype, and tumor genetic profiles are not yet consistently captured in the dataset. We recognize this as a limitation of our analysis and understand that, in gastric cancer, tumor biology, not surgical technique, is the most important determinate of disease recurrence and overall survival.

In our study population, adjuvant (HR 0.59; 95% CI, 0.51–0.67) or neoadjuvant + adjuvant (sandwich) systemic chemotherapy (HR 0.67; 95% CI, 0.56–0.81) were both independently associated with a reduced risk of death in our Cox model. However, more than a third of our population (open 37%, MIS 36.9%) received no systemic chemotherapy during their gastric adenocarcinoma treatment, which points to a potential area of undertreatment. As seen in many other studies, we confirmed that a positive resection margin is associated with a significant increased risk of death (HR 1.37; 95% CI, 1.21–1.56), whereas a lymph node sampling of at least 15 lymph nodes offers a protective effect (HR 0.73; 95% CI, 0.66–0.81).

TG is a complex operation requiring a dissection of the esophagus at the diaphragmatic hiatus, a 15+ lymph node sampling, and esophagojejunal reconstruction.[14,20] Our results suggest that MIS approaches to this procedure are oncologically sound and clinically safe. This is evidenced by equivalent rates of margin positivity and adequate lymph node sampling seen in our matched cohorts. Indeed, a small increase in proportion of cases with a 15+ lymph node sampling was observed in our MIS cohort when compared with the open approach (open 64.8% vs MIS 66.5%, $P = .37$), but this did not reach statistical significance. It is possible that experienced cancer treatment centers using contemporary MIS approaches may offer an improved lymph node sampling over low-volume community centers; however, long-term data is lacking.[21] We observed an interesting corollary in our Cox modeling where patients treated at comprehensive community cancer programs showed a higher independent risk of death when compared with academic or research cancer centers (HR 1.36; 95% CI, 1.20–1.54). This topic may be the subject of future studies.

Although the NCDB prospectively collects data on participants, the nature of our retrospective observational study allows for introduction of selection bias. Our intent to treat analysis is limited by the way the NCDB captures cases converted from laparoscopic to open. The NCDB includes cases for which there was a preoperative plan to convert from a diagnostic laparoscopy to an open gastrectomy in the conversion category. For this reason, a true intent to treat comparison of MIS to open total gastrectomy cannot be done using data form the NCDB. To attempt to control for this we repeated our analysis excluding the conversions before the propensity match. The results obtained were no different than the

Table IV
Multivariable Cox proportional hazards regression model for risk of death

	HR	95% CI			HR	95% CI	
Age (y)	1.02*	1.02	1.03	Tumor location			
Sex				Antrum	0.87	0.70	1.08
Male	Ref			Body	0.73*	0.64	0.83
Female	0.87*	0.78	0.97	Cardia	Ref		
Race				Fundus	0.98	0.79	1.21
White	Ref			Pylorus	0.85	0.38	1.91
Black	0.96	0.82	1.12	Overlapping	0.92	0.77	1.09
Asian/PI	0.62*	0.50	0.78	NOS	0.95	0.79	1.13
Other	0.78	0.55	1.12	pT Stage			
Insurance				Tis	Ref		
Private	Ref			T1	0.88	0.61	1.28
Uninsured	0.79	0.56	1.11	T2	1.28	0.90	1.84
Medicaid	0.94	0.75	1.17	T3	1.62*	1.15	2.29
Medicare	1.03	0.91	1.17	T4a	2.35*	1.63	3.39
Other	1.03	0.74	1.42	pN Stage			
Charlson-Deyo				N0	Ref		
0	Ref			N1	1.73*	1.50	2.00
1	1.00	0.90	1.12	N2	2.18*	1.87	2.53
2	1.23*	1.02	1.47	N3	3.50*	3.01	4.08
3	1.75*	1.31	2.33	Facility TG Volume, *n* (%)			
Diagnosis year				1–4 cases	Ref		
2010	Ref			5–12 cases	0.96	0.84	1.10
2011	1.08	0.94	1.24	13–21 cases	1.03	0.89	1.19
2012	1.01	0.87	1.16	22–144 cases	1.09	0.92	1.28
2013	0.95	0.81	1.11	Approach			
2014	1.07	0.91	1.25	Open	Ref		
Facility type				Laparoscopic	0.95	0.85	1.07
Academic	Ref			Robotic	1.04	0.79	1.36
Community	1.17	0.88	1.55	Lymph nodes Sampled			
Comp community	1.36*	1.20	1.54	<15	Ref		
Integrated	1.15	0.98	1.34	15+	0.73*	0.66	0.81
Missing	1.93*	1.31	2.84	Resection margin			
Tumor size				Negative	Ref		
<10 mm	Ref			Positive	1.37*	1.21	1.56
10–19 mm	1.33	0.97	1.84	Chemotherapy			
20–29 mm	1.36*	1.00	1.85	Adjuvant	0.59*	0.51	0.67
30–39 mm	1.47*	1.08	2.00	Neoadjuvant	0.92	0.81	1.05
40–49 mm	1.47*	1.08	2.01	Sandwich	0.67*	0.56	0.81
50 mm+	1.61*	1.20	2.17	None	Ref		

Comp, comprehensive; *NOS*, not otherwise specified; *PI*, pacific islander; *TG*, total gastrectomy.
* $P < .05$.

results obtained when the propensity match was done including the conversions. Also, although our methods allowed for matching based on total hospital TG volume during the study period, we were not able to control for additional operative factors such as surgeon experience or case complexity. Again, we controlled for cancer treatment facility type in our PSM, but it is possible that outcomes for patients in the MIS cohort may be confounded by an increased proportion of patients treated at designated cancer facilities that offer unaccounted for factors associated with improved overall oncologic care. Unfortunately, owing to the large proportion of patients undergoing resection for gastric cancer that were noted to have missing values for time to chemotherapy, we elected not to use it as a variable in our analysis.

This study provides justification for surgeons offering MIS approaches to total gastrectomy as potentially curative resection of gastric adenocarcinoma. Although we found no increased risk of death for either laparoscopic or robotic approaches when compared with open, we acknowledge that future efforts with larger samples may be able to draw more nuanced conclusions regarding the long-term oncologic efficacy and cost differences associated with these MIS approaches to TG. Additional variable granularity in future versions of these large datasets may allow future investigators to identify specific predictors of improved long-term oncologic outcomes. Given that surgeon and institutional experience with MIS approaches to gastrointestinal cancer resection have been increasing in recent years, outcomes associated with MIS operative approach will likely improve and should continue to be monitored for long-term differences compared to traditional open procedures.[22]

In conclusion, when compared to the traditional open approach, in patients with non-metastatic gastric adenocarcinoma, MIS approaches to TG are oncologically sound with similar short-term risk profiles, a slightly reduced postoperative LOS, and similar long-term overall survival rates.

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Conflict of interest/Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2019.05.041.

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Discussion

Dr Michael G. House (Indianapolis, IN): I would like to congratulate Dr Sweigert for the very easy, organized study and a very beautiful presentation. I think under the mentorship of Dr Marshall Baker, you have done a very nice analysis of patients with invasive gastric adenocarcinoma who were captured by the National Cancer Database. You focused on patients who underwent total gastrectomy. It's a large-scale study. It obviously had appropriate propensity matching between the surgical treatment groups, namely, those who underwent minimally invasive technique for total gastrectomy and those who underwent an open operation. You also show that the minimally invasive technique was not associated with embarrassed oncologic quality parameters, namely, margin status and lymph node harvest and assessment.

I would like to voice 5 points of discussion for this study and for your presentation.

First, what were the proportion of minimally invasive groups? Were those cases performed robotically and not purely laparoscopically? Did you observe any difference between those two treatment subgroups within the minimally invasive group?

You point out that over a third of the patients in this study did not receive any form of systemic chemotherapy. Yet, less than half of these patients received neoadjuvant chemotherapy, which I guess is against most of the national trends in this country given that the majority of patients in North America present with advanced stages of gastric cancer. You do show that in your study that two-thirds of the patients captured by the NCDB did in fact have advanced stage disease based on either an advanced primary stage or nodal status.

I just was curious as to what would explain that discrepancy between the number of patients with advanced stages of gastric cancer that were apparent in the NCDB and yet didn't receive any form of chemotherapy or neoadjuvant chemotherapy.

Did you look at 90-day perioperative mortality as a marker and were they evenly distributed between minimally invasive and the open groups?

Point number 3 is that 10% of the patients in the open and the minimally invasive gastrectomy groups had a positive surgical margin. Now, radiotherapy data would be available in the NCDB. I did not see that in your presentation that you addressed patients who received external beam radiotherapy or stereotactic radiotherapy as part of their modality treatment.

Point number 4 is more what is your insight into how close of a surrogate marker for quality and for postoperative complications is length of stay, and very low, surprisingly, very low 30-day hospital readmission rate for this large series of patients. This is a total gastrectomy, an operation that is accustomed to having major and minor postoperative morbidity, but yet we observed less than 10% readmission. Do you feel that you are capturing all the potential postoperative complications that may be associated with a minimally invasive or the open approach in your study?

How would you propose that we study this issue between the impact of postoperative complications and disease-specific survival and overall survival, for patients undergoing elective operations for cancer in this country? As you know, we are going to be merging the ACS NSQIP database with the NCDB, and obviously it would be great potential to study this issue even further.

Lastly, as you pointed out, while there is no major statistical significance between overall survival for the patients receiving open total gastrectomy and minimally invasive total gastrectomy, how do you try to explain the trend if there was an increased

overall survival in the patients who underwent the minimally invasive approach with a total gastrectomy?

Again, congratulations on a very neat study and very well presented. I look forward to further discussion.

Dr Patrick Sweigert: The first question about the proportion that we perform robotically, we had roughly 1,200 MIS total patients; 207 of them were performed robotically. I think that was around 17%, a small percentage. We though with respect to this study the meat was in combining them and determining, since they have similar drawbacks, potentially, oncologically where there's no tactile feedback, both robotically and laparoscopically, that those sort of considerations we would be able to draw those conclusions preparing a lumped MIS group to open. But it's obviously a potential topic for future study looking at robot versus laparoscopic.

We did evaluate laparoscopic versus robotic in terms of survival. There was no difference noted, although we may be underpowered.

With respect to the chemotherapy question, obviously the MAGIC trial, 2006, demonstrated improved overall survival with perioperative chemotherapy compared to no chemotherapy, and obviously that was something that really struck us when we saw the number of patients that received no chemotherapy.

I think that the reasons for that may be first the limitations in the data set. There are patients in this data set that were treated at multiple institutions, so it's possible that abstracters are falsely labeling patients with no chemotherapy. So, we selected patients that had most of their treatment and definitely their surgical treatment at the institution, but there may be some that are missing.

The other part of it may be that those recommendations are obviously for all EG junction, tumors, and gastric tumors. These may represent a more morbid population because they are requiring a total gastrectomy, so potentially fewer of them are healthy enough to receive chemo.

The 90-day mortality question, there were no differences between the 2 groups that we note, MIS versus open. I think you mentioned receipt of radiation therapy among those 2 groups, and there were no differences. None of the patients who died within 90 days received chemo at all, even neoadjuvant.

I think you mentioned the positive margins and how many patients who received radiation, so actually we are limited in what we can present on the slides, but we did control for receipt of radiation in the propensity score matching. So that was accounted for in a binary fashion. But obviously there's more to be studied in that area.

Length of stay as a quality measure, I think it is an important quality measure, obviously, and has a lot of implications for patients and for costs. I do think the NCDB is very limited in what you can look at in terms of postoperative outcomes, especially compared to NSQIP that has much cleaner outcomes. So, combining them can obviously give a lot of advantages, but I do think we are capturing a real length of stay difference between the 2 groups. It's possible that with respect to the overall survival difference that that is accountable to the fact that maybe the MIS patients are getting to adjuvant therapy quicker, or maybe there could be a selection bias, that those MIS patients are treated in more robust cancer centers that have access to, in general, improved oncologic care. So that difference needs to be ferreted out a little bit, and adding NSQIP variables would be certainly helpful in doing that.

I do think that most of it is going to be that piece of time to adjuvant chemo. It's possible that there are some differences in wound complication rates and sepsis, potentially, or mostly wound complications, I suspect. But it is interesting that even without the tactile feedback that you can still get adequate margins and you can still get adequate node sampling. I think that's reassuring.

Dr Vic Velanovich (Tampa, FL): Nicely presented study. I am going to apologize to you in advance because I am going to make a comment and ask you a question for which I know you do not have an answer. But at least to think about and maybe for future direction.

We spend a lot of time with the cancer trying to assess how long people live and not necessarily how well they live. The real advantage of most minimally invasive approaches is that it improves quality of life or gets them back faster to a quality of life that is more acceptable than what some open approaches can do. In the cancer world, the measure is quality adjusted life years.

So, the question that I had is, what type of quality of life data do you have demonstrating that a laparoscopic total gastrectomy is superior to an open approach, and how does that affect really overall a patient's improvement in quality of life as you are dealing with their post-cancer care?

Dr Patrick Sweigert: Thank you for that question. I think most of what's out there on this topic and larger series is Eastern data, and not in total gastrectomy necessarily but in partial gastrectomies and distal gastrectomies, there's a lot of evidence that MIS approaches are superior in terms of length of stay, faster recovery, reduced narcotics, those sorts of things. But long-term data is really limited. I didn't see anywhere in any of those quality adjusted life years, but that's obviously very important. I know the NSQIP group is interested in patient-reported outcomes and using those also while assessing these different treatment types. So it's definitely, obviously, a future direction.

Dr Carmen Mueller (Montreal, QC): Thank you very much. I really enjoyed your presentation. My question is coming as an MIS-trained surgeon who also does a lot of gastric cancer.

We go back and forth on cancer a lot in all kind of domains whether the MIS approach is really better or not. I understand why you picked a matched cohort in order to do your analysis. But I am actually more interested in your unmatched cohort, because this is a retrospective study. Some surgeon decided that they could do the case laparoscopically, so they did. But what about all the patients where that was not the case? I think we have to remember that, and this is going to be editorializing a little bit and my own opinion, but just to save one day on the hospital stay we must not compromise that patient's cancer surgery, and we have to really remember that when we are looking at all of these data.

When you looked at your unmatched cohort, were those patients different in terms of tumor size, tumor stage?

Dr Patrick Sweigert: They were slightly different. They had larger tumors, slightly higher T stage, slightly higher N stage. They were slightly more comorbid. They were more commonly treated at community centers. But I think your point is well taken that there's a certain selection bias, and the fact that a surgeon decided to do the procedure laparoscopic or robotic. So, we attempted to control for that using case volume at the institution, but that's obviously not a great surrogate. It would be interesting if we had more surgeon-level data or even things like time from certification or certain robotic measures. So those sorts of things I think would be interesting to control for. For example, how many gastrectomies you need to do, the sort of volume questions.

Dr Carmen Mueller (Montreal, QC): If we have to do a laparotomy to get the tumor out, we do it open. That's as scientific as it gets. I don't know if you had accessibility to the extraction site size.

Dr Patrick Sweigert: That's actually a limitation. We do not have access to data regarding the extraction site incision. It is certainly possible that some of these MIS cases were more hybrid approaches with large extraction sites. We propensity score matched on tumor size and there were no differences between matched cohorts but this is a limitation.

Dr Margo Shoup (Danbury, CT): To take Dr Mueller's comments one step further, also for comorbidities. Your paper is great. I think it shows if you can do this laparoscopically safely without a compromise operation, then you are not going to harm them oncologically. That's the way I look at it. But if it's somebody that has a tumor that's going to require more extensive site dissection that you think you should be doing a laparotomy, you shouldn't feel like you are forced to do it minimally invasively.

The same thing goes with comorbidity. I personally am much faster open than I am laparoscopically, so if I have somebody that has significant comorbidities and we want in and out of anesthesia as fast as possible, that would be one reason to do it open as well. I think it's a good statement to start, but it's not going to be written in stone, that this is the way it should go.

Dr Patrick Sweigert: I completely agree. We wanted to emphasize especially in the paper that we are not trying to make the argument that MIS is superior; we are just trying to make a non-inferiority type of comment that the MIS approaches are safe and oncologically efficacious. Surgeons should not put an oncologically effective operation at risk by doing a procedure MIS that should have been done open.