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Is minimally invasive surgery for large gastric GIST actually safe? A comparative analysis of short- and long-term outcomes

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Abstract

Introduction While minimally invasive surgery (MIS) is frequently utilized to remove small gastric gastrointestinal stromal tumors (GIST), MIS surgery for tumors ≥ 5 cm is currently not endorsed by national guidelines as standard of care due to concerns of safety and inferior oncologic outcomes. Hence this study investigates the perioperative and long-term outcomes of MIS for T3 gastric GIST measuring 5–10 cm.

Methods The National Cancer Database (NCDB) 2017 was queried for gastric GIST measuring 5–10 cm or T3 category. Inclusion criteria were known: stage, size, comorbidities, grade, lymphovascular invasion, type of surgery, approach, conversion info, margin status, mitotic rate, neoadjuvant and adjuvant treatment, hospital stay, readmission, 30- and 90-day mortality, complete follow-up, type of institution, and hospital gastric surgery case volume. Binary logistic regression, linear regression models, and Kaplan–Meier survival analysis were used.

Results In 3765 patients, mean tumor size was 67.3 mm; 26.3% MIS; and 73.8% open. Median hospital stay was shorter for MIS (4.77 vs 7.04 days, $p < 0.001$). There was no significant difference in incidence of R1 margins [2.9% MIS vs. 3.1% open ($p = 0.143$)], unplanned readmission [2.9% MIS and 4.1% open (OR 0.474 $p = 0.025$)], 30-day mortality [0.5% MIS vs 1.2% open (OR 0.325, $p = 0.031$)], and 90-day mortality [0.9% MIS vs 2.1% open (OR 0.478 $p = 0.036$)]. Cox regression models for OS showed no difference in survival ($p = 0.137$, HR 0.808).

Conclusion This analysis provides substantial evidence that MIS for gastric GIST ≥ 5–10 cm may not only offer improved postoperative morbidity but also oncologic safety. Moreover, as both approaches lead to similar long-term survival, national guidelines may need to incorporate this new information.

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Andrew B. Crocker and Eduardo A. Vega have contributed equally to this study.

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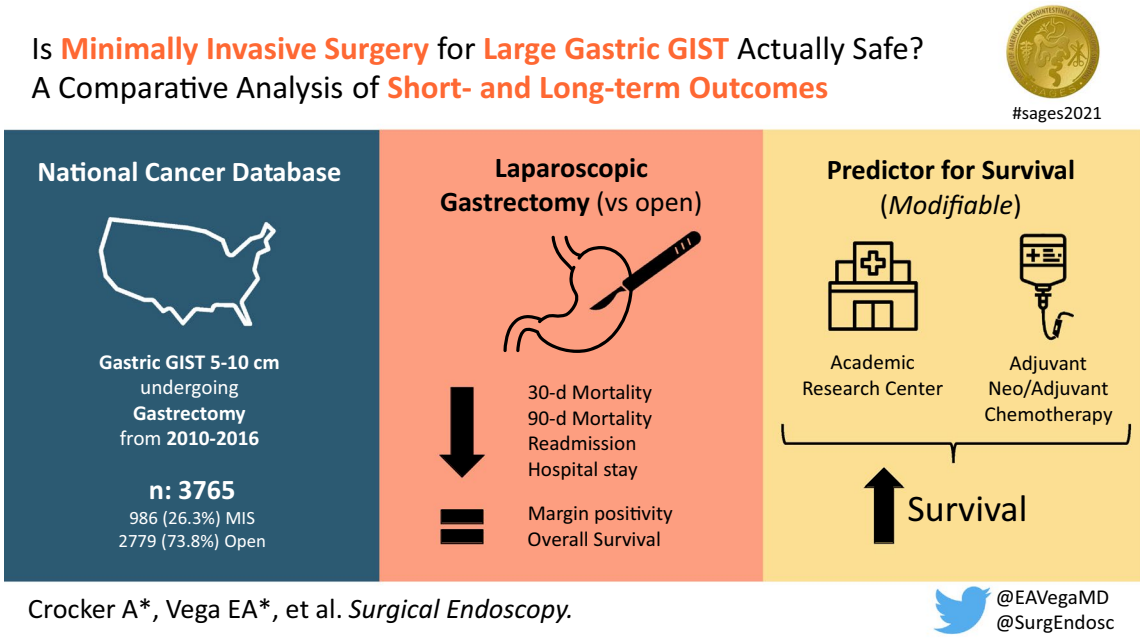
Graphical abstract



Keywords Gastric GIST · Laparoscopic · MIS · Mortality · Morbidity · Overall survival

Introduction

Surgical resection with negative margins remains the primary treatment goal in the management of gastric GIST [1–3]. For small gastric GIST, a laparoscopic approach (MIS) has been demonstrated to be associated with less postoperative morbidity and equivalent long-term survival [4–6]. Hence, currently the National Comprehensive Cancer Network® (NCCN) guidelines recommend a laparoscopic approach for GIST < 5 cm for experienced laparoscopists [3].

While laparoscopic surgery is recommended to surgically remove small gastric gastrointestinal stroma tumors by national and international guidelines, laparoscopy for tumors ≥ 5 cm remains an area of significant controversy [3, 7]. While smaller studies from Europe and Asia are available to address the clinical question whether MIS for smaller GIST is safe, no large studies focusing on MIS for large GIST greater than 5 cm are available today. As the incidence of this tumor type continues to rise, the oncological safety and efficacy of MIS for large gastric GIST remains an important clinical ambiguity.

Therefore, this study aims at examining the operative outcomes and mortality of MIS versus open surgical approach in the management of large gastric GIST ≥ 5–10 cm. This study assesses not only on perioperative morbidity and postoperative mortality but also oncologic outcomes. Using a dataset reflective of national practice patterns, data on the efficacy of a laparoscopic approach could not only inform treatment care discussion but also updating of national practice guidelines for GIST.

Patients and methods

Database and cohort selection

The National Cancer Database (NCDB) was queried for patients diagnosed with gastric GIST (ICD O-3 8936) with tumors measuring 5–10 cm who underwent gastric resection from January 2010 through December 2017. Surgery codes queried were 20–27/30–33 (local or partial gastrectomy), 40–42 (distal or subtotal gastrectomy), 50–52 (total gastrectomy), and 60–63/80 (extended gastrectomy).

Patient specific inclusion criteria were: T3 category, N-category, tumor size, Charlson-Deyo comorbidity score, tumor grade, surgical approach, margin status, facility type, complete follow-up, details of chemotherapy, hospital stay, 30-day readmission status, 30- and 90-day mortality and complete follow-up.

Variables

Patient age, tumor size, length of hospital stay, and survival time, and the index hospital were recorded as continuous variables. Sex, T3 category, Charlson-Deyo comorbidity score, facility type, chemotherapy type, surgical approach (open or laparoscopic), margin status, nodal status, 30-day readmission to the same facility, 30-day mortality, and 90-day mortality were recorded as categorical variables.

In the NCDB, Charlson-Deyo comorbidity scores were recorded as 0 for no comorbidity, 1 for any single comorbidity, and 2 for ≥ 2 comorbidities present. Facility types were recorded as community cancer program, comprehensive community cancer program, academic/research program (including National Cancer Institute–designated cancer centers), and integrated network cancer program. The NCDB records patient readmission to the same facility within 30 days. The data are stored as "unplanned readmission," "planned readmission" (for chemotherapy, intravenous line placement, and so on), and "unplanned and planned readmission" (patients who were admitted on different occasions for planned and unplanned indications). To analyze unplanned readmissions, all patients with an episode of an unplanned readmission were included.

Statistical analysis

Categorical variables were presented as frequencies with percentages and analyzed with $\chi 2$ tests. Continuous variables were presented as median or means with interquartile range or standard deviation where appropriate; Initially, continuous variables were analyzed with Kruskal–Wallis tests.

To correct for confounders, multivariable binary logistic regression models were constructed to adjust for the possible confounding effects of age, sex, tumor grade, tumor size, Charlson-Deyo comorbidity score, facility type, and neoadjuvant and adjuvant chemotherapy and radiotherapy. With this, the impact of laparoscopic approach on 30- and 90-day mortality, readmission and margin status were calculated separately. Similarly, linear regression models were used to correct for confounders and calculated the impact of laparoscopic approach on hospital stay.

For survival analyses, initially Kaplan Meier survival analysis were performed to compare MIS to open approaches. Later Cox multivariable regression models were used to identify the factors affecting overall survival (OS) as well as the impact of laparoscopic approach on OS. $P \leq 0.05$ were considered statistically significant; all tests were 2-sided. Analyses were performed with SPSS 22.0 (IBM Corporation, Armonk, NY).

Results

Patients characteristics

Patient characteristics by surgical approach are summarized in Table 1. The NCDB search identified 3765 patients meeting inclusion criteria (Fig. 1). Of those, 1878 (49.9%) were male. Mean tumor size was 67.1 mm for the entire cohort, with a mean tumor size of 65.2 mm in the MIS group, and 67.8 in the open surgical group. 986 (26.3%) underwent MIS, and 2779 (73.8%) underwent open gastrectomy. Median hospital stay was 5 days for MIS (0–60), and 7 (0–86) days for open gastrectomy groups. Patients were most likely to undergo cancer surgery at academic tertiary care centers (41.1%) or comprehensive cancer centers (35.8%). Of note 310 (31%) patients were NX in the MIS approach compared to 370 (13%) in the open approach group.

Short term and oncologic outcomes

Patient factors indicative of short-term outcomes such as hospital stay, 30-day readmissions, and oncologic outcomes, including margin status and 30- and 90-day survival, were included in the multivariable analysis. All factors are summarized in Table 2. After correcting for confounders, MIS was associated with shorter hospital stay 4.7 vs 6.3 days (beta − 0.203, $p < 0.001$). Multivariable regression models showed statistically significant benefit in 30-day mortality, 0.5% in MIS vs 1.2% in open surgery (OR 0.325, $p = 0.031$), and 90-day mortality, 0.9% in MIS vs 2.1% in an open approach (OR 0.478 $p = 0.036$). Unplanned readmission rates differed significantly with 2.9% for MIS and 4.1% for open surgery (OR 0.474 $p = 0.025$. However, no difference was seen in R1 margin rate (2.9% laparoscopic vs 3.1% open, $p = 0.143$) (Table 2).

Survival analyses

Kaplan Meier survival analysis showed similar survival between open and laparoscopic surgery groups (log-rank, $p = 0.27$). Overall survival was 119 months for open surgery group vs 121 months for the laparoscopic group. Figure 2, Supplemental Table 1.

After correcting for confounders, Cox multivariable regression models are shown in Table 3. Cox regression models for OS showed no difference in survival between laparoscopic and open approaches ($p = 0.125$, HR 0.828). Surgery at an academic ($p < 0.001$, HR 0.583) or comprehensive cancer centers ($p = 0.003$, HR 0.666) was also associated with improved survival relative to community hospitals. Notably, there was a statistically significant

Table 1 Patient demographic and characteristics

	All cohort		Laparoscopic		Open		
	n	Percent	*n*	Percent	*n*	Percent	*P* value
Number	3765	100	986	26.3	2779	73.8	
Age (year), (mean, range)	64.4	18–90	64.9	23–90	64.2	20–90	0.607
Sex, female	1878	49.9	462	46.9	1416	51	0.086
Charleson-Deyo							0.138
None	2651	70.4	669	67.8	1982	71.3	
1	833	22.1	234	23.7	599	21.6	
2	204	5.4	65	6.6	139	5	
≥3	77	2	18	1.8	59	2.1	
Type of facility							*0.004*
Community	239	6.3	41	4.2	198	7.1	
Comprehensive comm	1349	35.8	346	35.1	1003	36.1	
Academic/research	1547	41.1	425	43.1	1122	40.4	
Integrated network	479	12.7	138	14	341	12.3	
Tumor size (mm), (mean, range)	67.3	50–99	65.2	50–99	67.8	50–99	0.079
Mitotic rate							*<0.001*
<5	2997	79.6	748	75.9	1169	42.1	
≥5	768	20.4	238	24.1	1610	57.9	
N-category							
N0	1701	45.2	665	67.4	2380	85.6	*<0.001*
N1	40	1.1	11	1.1	29	1	
NX	2024	53.7	310	31.4	370	13.3	
Lymphovacular invasion	46	1.2	15	1.5	31	1.1	0.293
KIT Gene IHC							*<0.001*
Elevated	1226	32.5	492	49.9	729	26.2	
Normal	88	2.3	36	3.7	52	1.9	
Unknown	2456	65.3	458	46.5	1998	71.9	
Type of surgery							*0.010*
Partial gastrectomy	10,716	78.5	742	75.3	1867	67.2	
Proximal gastrectomy	614	4.5	106	10.8	270	9.7	
Distal gastrectomy	1224	9	120	12.2	497	17.9	
Total gastrectomy	800	5.9	18	1.8	145	5.2	
Chemotherapy							0.070
None	2334	62	616	62.5	1718	61.8	
Neoadjuvant	180	4.8	52	5.3	128	4.6	
Adjuvant	1160	30.8	297	30.1	863	31.1	
Adjuvant/neoadjuvant	91	2.4	21	2.1	70	2.5	
R1 margins	114	3.0	28	2.9	86	3.1	0.492
Lenght of stay, days (median, range)	6.43	0–86	4.77	0–60	7.04	0–86	*<0.001*
30-day readmission	144	3.8	29	2.9	115	4.1	*0.001*
30-day mortality	38	1	5	0.5	33	1.2	*0.020*
90-day mortality	70	1.9	8	0.9	62	2.1	*0.045*

Comprehensive Comm. comprehensive community hospital; *IHC* immunohistochemistry

P Value less than 0.05

survival benefit for patients who received adjuvant chemotherapy ($p = 0.032$, HR 0.964). Conversely, there was no significant benefit for those patients who underwent neoadjuvant chemotherapy for their disease burden ($p = 0.147$, HR 1.212). When comparing patients who received both adjuvant and neoadjuvant chemotherapy there was a statistically significant benefit ($p = 0.002$, HR 0.924) when this group was compared to patients who did not undergo chemotherapy.

Fig. 1 Consort diagram

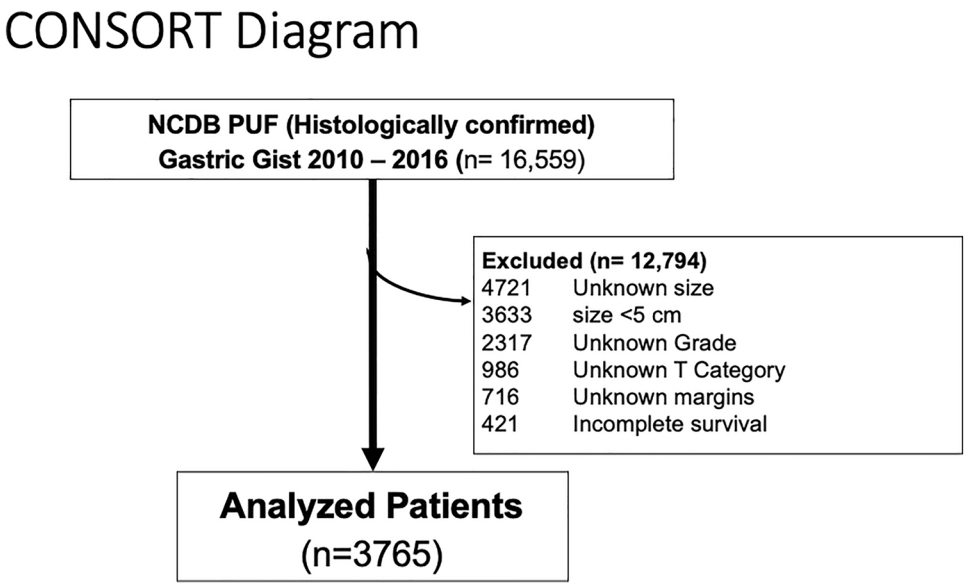


Table 2 Impact of surgical approach after correcting for confounders

	95% C I			*P* value
	OR	Lower	Upper	
Open	1.000			Reference
Margin status	1.132	0.825	1.553	0.441
30-day mortality	0.325	0.116	0.905	0.031
90-day mortality	0.478	0.224	0.956	0.034
30-day readmission	0.474	0.246	0.912	0.025
	Beta	Constant		*p* value
Hospital stay[a]	− 0.203	4.333		< 0.001

The beta coefficient is the degree of change in the outcome variable for every 1 unit of change in the predictor variable. If the beta coefficient is negative, the interpretation is that for every 1-unit increase in the predictor variable, the outcome variable will decrease by the beta coefficient value

OR odd ratio; *CI* confident interval

[a]This means after correcting for confounders using linear regression models, there was a 20.3% decrease in hospital stay in laparoscopic surgery group)

P Value less than 0.05

Discussion

This study demonstrated that a MIS vs. open approach is safe and leads to non-inferior outcomes in the management of large 5–10 cm gastric GIST. MIS was associated with improved postoperative morbidity, lower readmission rates and a shorter length of stay. Moreover, MIS vs. open surgery demonstrated a significant benefit in 30- and 90-day mortality. There was no significant difference in overall survival between open and MIS surgical approaches. Collectively, these findings suggest that a laparoscopic approach for large 5–10 cm gastric GISTs is a safe and viable option for experienced surgeons.

An important finding of this study is the equivalence between MIS and open approach in achieving negative margins. Positive margins occurred in 2.9% and 3.1% ($p = 0.143$) of cases in the MIS vs. open arms, respectively. It has been previously shown in a small retrospective study of GIST with a mean tumor size of 4.4 cm, that all GIST were removed with R0 margins [8]. Similarly, a meta-analysis of 11 nonrandomized studies with a cohort of 765 patients found that MIS for GIST was associated with no statistically significant difference in margin positivity (Odds Ratio [OR], 0.501; 95% CI 0.157–1.603; $P = 0.244$) [9]. Since prior data have shown that achieving negative margins may be the most important prognostic factor for long-term survival [10], our results validate an important

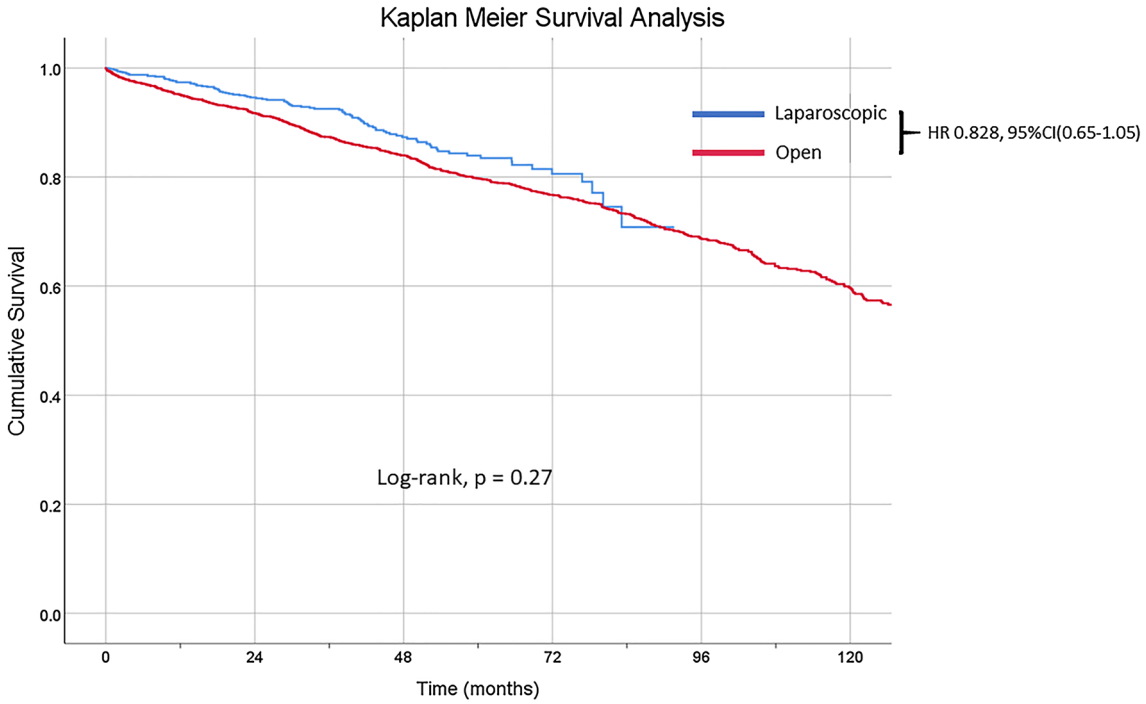


Fig. 2 Kaplan–Meier survival curve by surgical approach

parameter of oncologic safety for MIS for large gastric GIST.

In the postoperative setting, our data suggest that MIS for large gastric GIST was associated with a significantly reduced hospital stay and lower readmission rates relative to open surgery. Specifically, the MIS cohort demonstrated a significantly lower hospital stay than the open group, with a median length of stay of 4 days for laparoscopic surgery versus 6 days for open surgery. In addition, the MIS cohort was associated with a significantly lower unplanned readmission rate, as compared to open surgery. In contrast, a Taiwanese case series of 39 patients with gastric GIST greater than 5 cm found no significant difference in hospital stay between MIS and open surgery which may be due to cultural differences in practice patterns [11]. Another retrospective study of 82 patients with large gastric GIST ≥ 5 cm found no difference in perioperative outcomes relative to open surgery, but a shorter postoperative length of hospital stay [12]. The significant reduction in length of stay for MIS surgery in this study when compared to prior literature may be the result of a larger patient cohort and cultural biases of post-operative patient management. Moreover, while reduced postoperative morbidity and length of stay has been reported as a common benefit of MIS relative to open surgery, the data presented here are unique in that despite larger incisions required to extract the larger GIST, MIS still reduced postoperative morbidity.

Post-operative mortality and overall survival is a critical measure in an MIS approach to large gastric GIST. The findings of this study demonstrated that an MIS approach was statistically superior for 30- and 90-day mortality. Additionally, multivariable Cox regression models for OS showed no difference in survival between MIS and open approaches. One meta-analysis of a laparoscopic approach for large gastric GIST greater than 5 cm found that laparoscopic surgery was associated with a superior 5 year disease-free and overall survival [13]. However, data from a retrospective analysis of 153 patients found that for large gastric GIST greater than 5 cm there was no significant difference in long-term disease-free survival between an MIS and open approach [14]. Similarly, a meta-analysis of 7 Asian and European studies showed no difference in overall survival between the two approaches [15]. Because GIST commonly has long survival intervals necessitating long follow-ups, confirming non-inferiority not only post-operatively but also long-term, validates the oncologic safety of a MISapproach.

The role of systemic therapy in the management of GIST is an important consideration when caring for patients with large GIST. While in the adjuvant setting, treatment is generally directed to reduce the risk of recurrence or metastasis for tumors with high-risk traits such as large tumor size, high mitotic rate, or complex anatomic location, in the neoadjuvant setting treatment goals are reduction in GIST size to facilitate organ preservation [16, 17]. In this study, large gastric GIST patients

Table 3 Cox regression model of factors affecting survival corrected for confounders

Factor	HR	95.0% CI		*P* value
		Lower	Upper	
Age, year, (mean, range)	1.069	1.057	1.082	< 0.001
Sex, female	1.313	1.136	1.517	< 0.001
Charleson-Deyo				
None				Reference
1	1.578	1.214	2.053	*0.001*
2	1.710	1.164	2.513	*0.006*
≥ 3	2.346	1.35	4.077	*0.002*
Type of facility				
Community	1.000			Reference
Comprehensive comm	0.666	0.510	0.870	*0.003*
Academic/research	0.583	0.445	0.764	*< 0.001*
Integrated network	0.647	0.477	0.879	*0.005*
Tumor Size (mm), (mean, range)	1.013	1.005	1.021	*0.002*
Mitotic rate				
< 5	1.000			Reference
≥ 5	1.524	1.262	1.839	*< 0.001*
N-category				
N0	1.000			Reference
N1	1.544	1.138	2.097	*0.005*
NX	0.554	0.281	1.093	0.088
Lymphovacular invasion, yes	2.608	1.360	5.003	*0.004*
KIT gene IHC				
Normal				Reference
Elevated	1.337	1.133	1.578	*0.001*
Unknown	0.586	0.298	1.152	0.121
Type of surgery				
Partial gastrectomy	1.000			Reference
Proximal gastrectomy	0.867	0.712	1.057	0.157
Distal gastrectomy	0.836	0.631	1.108	0.213
Total gastrectomy	1.673	1.217	2.299	*0.002*
Chemotherapy				
None				Reference
Neoadjuvant	1.212	0.935	1.57	0.147
Adjuvant	0.964	0.943	0.991	0.032
Adjuvant/neoadjuvant	0.924	0.904	0.958	*0.002*
R1 Margins	1.643	1.307	2.065	*< 0.001*
Hospital length of stay, days (median, range)	1.028	1.021	1.035	*< 0.001*
Surgical approach				
Open	1.000			Reference
Laparoscopic	0.828	0.650	1.054	0.125

Comprehensive Comm. comprehensive community hospital; *IHC* immunohistochemistry; *HR* hazard ratio; *CI* confident interval

P Value less than 0.05

who received both neoadjuvant and adjuvant chemotherapy had a statistically significant survival benefit. When examined individually, only adjuvant therapy was associated with a significant survival benefit when compared to patients who received no chemotherapy, with neoadjuvant chemotherapy offering no statistically significant survival benefit. These findings of adjuvant therapy have been well supported in the literature. The ACOSOG Z9001 trial comprised of 713 patients with GIST greater than 3 cm showed that adjuvant Imatinib therapy was associated with

improved recurrence free survival (RFS) relative to surgery alone (98% versus 83% at one year; hazard ratio [HR] 0.35; $P < 0.0001$) [18]. Similarly, in the EORTC 62,024 study of 908 high-risk GIST patients who received adjuvant chemotherapy vs surgery alone, the adjuvant group had a significantly improved RFS of 69% compared to 63% at 5 years ($P < 0.001$) [19]. The findings of this study confirm on a population level, that adjuvant therapy plays an important role in reducing disease recurrence in high-risk tumors.

This study has important limitations. First, while the NCDB accurately reflects US hospital-based practice patterns, it is a retrospective data set and hence subject to confounding inherent to any retrospective data (i.e., unmeasured biases). Moreover, our cohort contained significantly more open than MIS surgical cases. While this was controlled for as described in the method section of the manuscript confounding cannot be entirely excluded. To further control for selection bias and disproportionate cohorts propensity score matching was performed. Propensity score matching (algorithm 1:1, caliper 0.1, data not shown) led to the same results. Second, NCDB does not provide genotyping data, which have been shown to impact on outcomes. However, while high-risk mutation clearly plays a role in oncologic outcomes, it is unlikely that it would have impacted on choice of surgical approach. Additionally, the significant proportion of "unknown" c-kit status in our cohort may reflect secular trends in diagnosis (more frequent use of DOG-1 testing) and histopathological analysis without immunohistology. Finally, due to limitations of the data set, we were unable to include some operative factors in our analysis, most notably cases converted from laparoscopic to open, and cases involving adjacent organ resection. Because direct extension of GIST into neighboring organs necessitating multivisceral resection is rare and from our personal experience conversion is infrequent as well, it is unlikely that the conclusions of the study would have been significantly influenced by these factors. Despite the limitations mentioned above, this study remains the largest assessment of gastric GIST ≥ 5 cm management to date, and one of the few conducted on an American cohort.

Conclusion

Based on the data reported, a MIS approach for large gastric GIST 5–10 cm is not only associated with improved postoperative morbidity relative to open surgery, but is ontologically safe (i.e., margin status). Moreover, as our data suggest that MIS vs. open surgery provides statistically noninferiority long-term survival, this information may inform an ongoing discussion regarding national guidelines in the management of this increasingly common cancer type.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s00464-022-09066-4.

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Declarations

Conflict of interest Claudius Conrad is a consultant for Fuji, Integra, Immunitas, Stryker, and Olympus. Omid Salehi, Eduardo A. Vega, Onur C. Kutlu, Andrew B. Crocker, Sebastian Mellado, Mu Li, and Olga Kozyreva have no conflicts of interest to disclose.

References

1. Demetri GD, Benjamin RS, Blanke CD, Blay J-Y, Casali P, Choi H, Corless CL, Debiec-Rychter M, DeMatteo RP, Ettinger DS (2007) NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)—update of the NCCN clinical practice guidelines. Journal of the National Comprehensive Cancer Network 5:S-1-S-29
2. Group ESESNW (2014) Gastrointestinal stromal tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 25 Suppl 3**:**iii21–26
3. Demetri GD, Benjamin RS, Blanke CD, Blay JY, Casali P, Choi H, Corless CL, Debiec-Rychter M, DeMatteo RP, Ettinger DS, Fisher GA, Fletcher CD, Gronchi A, Hohenberger P, Hughes M, Joensuu H, Judson I, Le Cesne A, Maki RG, Morse M, Pappo AS, Pisters PW, Raut CP, Reichardt P, Tyler DS, Van den Abbeele AD, von Mehren M, Wayne JD, Zalcberg J, Force NT (2007) NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)--update of the NCCN clinical practice guidelines. J Natl Compr Canc Netw 5 Suppl 2**:**S1–29; quiz S30
4. Sasaki A, Koeda K, Obuchi T, Nakajima J, Nishizuka S, Terashima M, Wakabayashi G (2010) Tailored laparoscopic resection for suspected gastric gastrointestinal stromal tumors. Surgery 147:516–520
5. Ye X, Kang WM, Yu JC, Ma ZQ, Xue ZG (2017) Comparison of short- and long-term outcomes of laparoscopic vs open resection for gastric gastrointestinal stromal tumors. World J Gastroenterol 23:4595–4603
6. Xu C, Chen T, Hu Y, Balde AI, Liu H, Yu J, Zhen L, Li G (2017) Retrospective study of laparoscopic versus open gastric resection for gastric gastrointestinal stromal tumors based on the propensity score matching method. Surg Endosc 31:374–381
7. Casali PG, Abecassis N, Aro HT, Bauer S, Biagini R, Bielack S, Bonvalot S, Boukovinas I, Bovee J, Brodowicz T, Broto JM, Buonadonna A, De Alava E, Dei Tos AP, Del Muro XG, Dileo P, Eriksson M, Fedenko A, Ferraresi V, Ferrari A, Ferrari S, Frezza AM, Gasperoni S, Gelderblom H, Gil T, Grignani G, Gronchi A, Haas RL, Hassan B, Hohenberger P, Issels R, Joensuu H, Jones RL, Judson I, Jutte P, Kaal S, Kasper B, Kopeckova K, Krakorova DA, Le Cesne A, Lugowska I, Merimsky O, Montemurro M, Pantaleo MA, Piana R, Picci P, Piperno-Neumann S, Pousa AL, Reichardt P, Robinson MH, Rutkowski P, Safwat AA, Schoffski P, Sleijfer S, Stacchiotti S, Sundby Hall K, Unk M, Van Coevorden F, van der Graaf WTA, Whelan J, Wardelmann E, Zaikova O, Blay JY, Committee EG, Euracan (2018) Gastrointestinal stromal

tumours: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 29:iv68-iv78
8. Novitsky YW, Kercher KW, Sing RF, Heniford BT (2006) Long-term outcomes of laparoscopic resection of gastric gastrointestinal stromal tumors. Ann Surg 243:738
9. Koh Y-X, Chok A-Y, Zheng H-L, Tan C-S, Chow PK, Wong W-K, Goh BK (2013) A systematic review and meta-analysis comparing laparoscopic versus open gastric resections for gastrointestinal stromal tumors of the stomach. Ann Surg Oncol 20:3549–3560
10. Di Vita M, Zanghì A, Cavallaro A, Cardì F, Uhlig M, Ursi P, Lo Menzo E, Panebianco V, Cappellani A (2019) Gastric GIST and prognostic models. Which is the best to predict survival after surgery. Ann Ital Chir 90:31–40
11. Hsiao C-Y, Yang C-Y, Lai I-R, Chen C-N, Lin M-T (2015) Laparoscopic resection for large gastric gastrointestinal stromal tumor (GIST): intermediate follow-up results. Surg Endosc 29:868–873
12. Khoo CY, Goh BKP, Eng AKH, Chan WH, Teo MCC, Chung AYF, Ong HS, Wong WK (2017) Laparoscopic wedge resection for suspected large (>/=5 cm) gastric gastrointestinal stromal tumors. Surg Endosc 31:2271–2279
13. Lian X, Feng F, Guo M, Cai L, Liu Z, Liu S, Xiao S, Zheng G, Xu G, Zhang H (2017) Meta-analysis comparing laparoscopic versus open resection for gastric gastrointestinal stromal tumors larger than 5 cm. BMC Cancer 17:760
14. Lin J, Huang C, Zheng C, Li P, Xie J, Wang J, Lu J (2014) Laparoscopic versus open gastric resection for larger than 5 cm primary gastric gastrointestinal stromal tumors (GIST): a size-matched comparison. Surg Endosc 28:2577–2583
15. Yu M, Wang DC, Wei J, Lei YH, Fu ZJ, Yang YH (2021) Meta-analysis on the efficacy and safety of laparoscopic surgery for large gastric gastrointestinal stromal tumors. Am Surg 87:450–457
16. Sanchez-Hidalgo JM, Duran-Martinez M, Molero-Payan R, Rufian-Pena S, Arjona-Sanchez A, Casado-Adam A, Cosano-Alvarez A, Briceno-Delgado J (2018) Gastrointestinal stromal tumors: a multidisciplinary challenge. World J Gastroenterol 24:1925–1941
17. Dematteo RP, Gold JS, Saran L, Gonen M, Liau KH, Maki RG, Singer S, Besmer P, Brennan MF, Antonescu CR (2008) Tumor mitotic rate, size, and location independently predict recurrence after resection of primary gastrointestinal stromal tumor (GIST). Cancer 112:608–615
18. Dematteo RP, Ballman KV, Antonescu CR, Maki RG, Pisters PW, Demetri GD, Blackstein ME, Blanke CD, von Mehren M, Brennan MF, Patel S, McCarter MD, Polikoff JA, Tan BR, Owzar K, American College of Surgeons Oncology Group Intergroup Adjuvant GST (2009) Adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. Lancet 373:1097–1104
19. Casali PG, Le Cesne A, Poveda Velasco A, Kotasek D, Rutkowski P, Hohenberger P, Fumagalli E, Judson IR, Italiano A, Gelderblom H, Adenis A, Hartmann JT, Duffaud F, Goldstein D, Broto JM, Gronchi A, Dei Tos AP, Marreaud S, van der Graaf WT, Zalcberg JR, Litiere S, Blay JY (2015) Time to definitive failure to the first tyrosine kinase inhibitor in localized GI stromal tumors treated with imatinib as an adjuvant: a European Organisation for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group Intergroup Randomized Trial in Collaboration With the Australasian Gastro-Intestinal trials group, UNICANCER, French Sarcoma Group, Italian Sarcoma Group, and Spanish Group for Research on Sarcomas. J Clin Oncol 33:4276–4283