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Laparoscopic versus open resection of gastrointestinal stromal tumors: survival outcomes from the NCDB

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Abstract

Background Studies comparing laparoscopic versus open resection of gastrointestinal stromal tumors (GIST) typically involve small comparative groups and often do not control for tumor size or stage of disease. The objective of this study was to compare adjusted survival outcomes for laparoscopic versus open GIST.

Method The National Cancer Database (NCDB) from 2010 to 2014 was evaluated for gastric and small intestinal GIST resections. After stratification by disease stage and adjustment for patient demographics, comorbidity score, tumor size, and tumor location, 90-day mortality rates were compared based on laparoscopic versus open resection. Kaplan–Meier estimates of long-term survival were also compared. A Cox proportional hazards model was used to determine hazard ratios (HR) for survival.

Results There were 5096 cases analyzed, including 2910 (57%) stage I, 954 (19%) stage II, and 1232 (24%) stage III cases. The distribution of laparoscopic versus open cases was 1291 (44%) versus 1619 (56%) for stage I, 318 (33%) versus 636 (67%) for stage II, and 286 (23%) versus 946 (77%) for stage III. There was no significant difference in adjusted 90-day mortality between laparoscopic and open resection. Kaplan–Meier estimates of long-term survival demonstrated improved overall survival curves for laparoscopic resection for stage I and stage II disease, but no significant difference for stage III disease. Factors associated with statistically significant higher adjusted overall mortality included older age (HR 1.06; $p < 0.001$), black race (HR 1.33; $p = 0.04$), higher comorbidity score (HR 1.47; $p < 0.001$), and small intestinal versus gastric tumor location (HR 1.28; $p = 0.03$). The hazards model suggested improved overall survival for females (HR 0.59; $p < 0.001$) and laparoscopic approach (HR 0.80; $p = 0.06$).

Conclusion Laparoscopic and open GIST resection have comparable 90-day mortality with possible improved long-term survival with laparoscopy for early-stage disease. These findings support the use of laparoscopy as a viable and potentially more effective approach to GIST resection.

Keywords Laparoscopic versus open surgery · GIST · Gastrointestinal stromal tumor · NCDB · Survival · Outcomes

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal malignancy of the gastrointestinal tract.

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The prevalence of GIST has been steadily increasing, with a current annual incidence of 0.78 per 100,000 people [1]. The overwhelming majority of GIST lesions are located in the stomach (55%) and small intestine (29%), whereas other locations such as colon, rectum, mesentery, and esophagus are far less common [1]. Surgical intervention is the first-line treatment for localized disease [2]. Often, these tumors are well differentiated and readily discernable from the surrounding viscera. In addition, lymph node metastasis is rare and therefore extensive lymphadenectomy is not required [3]. For these reasons, resection of GIST does not mandate anatomic resection and in most cases can be easily removed by wedge or segmental resection. The main goal of surgery

is complete removal of the mass with negative margins while avoiding violation of the tumor pseudocapsule, which when ruptured strongly predicts tumor recurrence [4].

Although there are concerns that a laparoscopic approach may lead to additional tumor manipulation and potential peritoneal contamination when compared to an open approach, multiple recent studies have shown the feasibility, safety, and oncologic non-inferiority of laparoscopy for gastric GIST resection [5–11]. Similarly, a recently published meta-analysis comparing laparoscopic versus open resection of small intestinal GIST showed no statistical difference in tumor recurrence or long-term survival, and even reported fewer postoperative complications with use of laparoscopy [12]. However, these results in favor of using a laparoscopic approach may reflect selection bias for smaller tumors that are more amenable to laparoscopic resection [8]. While some small studies performed case-matching for tumor size [7, 9, 13, 14], the current literature comparing laparoscopic versus open approaches for GIST is limited primarily to small sample sizes with minimal control for tumor size or stage of disease. The current study uses the National Cancer Database (NCDB) to compare survival after laparoscopic versus open resection of gastric and small intestinal GIST, stratified by stage of disease and controlled for patient demographics, comorbidity score, tumor location, and tumor size.

Methods

Data source

The NCDB includes Health Insurance Portability and Accountability Act (HIPAA)-compliant data prospectively collected from more than 1500 cancer programs nationwide accredited by the American College of Surgeons Commission on Cancer. As a longitudinal database, the NCDB includes long-term follow-up data that can be used for survival analysis.

Data collection

The 2010–2014 NCDB was analyzed for patients 18 years or older who underwent laparoscopic or open resection (Procedure Codes 30–80) for stage I–III GIST (Histology code 8936) located in either the stomach (Primary Site Code C160-169) or small intestine (Primary Site Code C170-C179). There was no variable for surgical approach in the database prior to 2010. Analysis was limited to tumors of the stomach and small intestine since these are the two most common sites of GIST occurrence and comprise over 96% of GIST cases in the 2010–2014 database. Patients with stage IV disease or multiple malignancies were excluded. Cases were stratified based on pathological stage of disease prior

to analysis. Converted cases were grouped with the laparoscopic cohort for an intention-to-treat analysis. Primary outcomes included 30- and 90-day mortality and long-term survival. Secondary outcomes included negative-margin rate, length of stay (LOS), and 30-day readmission rates.

Statistical analysis

Data management was completed using SAS 9.4. All analyses were performed using the computing and programming environment R. Continuous variables were reported as means with standard deviation (SD), and categorical variables were reported as frequencies with percentages. Univariate analysis was performed using t tests for continuous variables and Chi-square tests with Yates' correction for categorical variables. Logistic regression was used to determine adjusted odds ratios (AOR) for categorical variables and adjusted relative mean difference (ARM) for continuous variables. Key patient and tumor characteristics identified a priori as potential risk factors for mortality were used in the adjusted multivariate model and included age, gender, race, Hispanic ethnicity, Charlson/Deyo comorbidity score, tumor location, and tumor size.

Overall survival time was calculated in months from the date of diagnosis to the date of death, or if censored, the date of last contact. Survival time was considered to be right-censored if the patient was lost-to-follow-up or alive at the end of the study period. A Kaplan–Meier estimator was used to estimate overall long-term survival. The log-rank statistic was used to test for equality of survival outcomes when comparing key sub-populations based on surgical approach, either laparoscopic or open resection.

A Cox proportional hazards model was used to determine adjusted hazards ratios for survival, adjusting for the same key patient and tumor characteristics that were used in the multivariate regression model. Only cases with one reported cancer diagnosis (Sequence Number 00) were used for survival analysis to avoid confounding from patients diagnosed with or treated for other malignancies. Robust standard errors were used to guard against model misspecification. Holm's method was used to adjust p values for multiple comparisons. All p values were two-sided with an α of 0.05.

Results

There were 5096 cases analyzed, including 2910 (57%) stage I, 954 (19%) stage II, and 1232 (24%) stage III cases. The distribution of laparoscopic versus open cases was 1291 (44%) versus 1619 (56%), respectively, for stage I disease; 318 (33%) versus 636 (67%), respectively, for stage II disease; and 286 (23%) versus 946 (77%), respectively, for stage III disease.

Patient demographics and Charlson/Deyo comorbidity scores are listed in Table 1. For all stages, patients were predominately of white race and non-Hispanic ethnicity, with a relatively equal distribution between male and female genders. When compared to the open group on univariate analysis, the laparoscopic group included younger patients with stage I (63.4 vs. 64.4 years, respectively; $p = 0.0435$) and stage II disease (61.0 vs. 63.3 years, respectively; $p = 0.0152$), a lower percentage of white patients with stage II disease (68% vs. 77%, respectively; $p = 0.0040$), and a higher percentage of black patients with stage II disease (23% vs. 17%, respectively; $p = 0.0342$). There were no statistically significant differences between the laparoscopic and open surgery groups for any of the other patient demographics or comorbidity scores.

Tumor specimen details and outcomes of interest are listed in Table 2. Laparoscopic resection was associated with a greater percentage of gastric vs. small intestinal GIST for both stage I (87% vs. 75%, respectively; $p < 0.0001$) and stage III (59% vs. 51%, respectively; $p < 0.0315$) disease, but not for stage II disease (61% vs. 56%, respectively; $p = 0.1324$). Laparoscopic resection was also associated with smaller tumors for all stages of disease (stage I: 3.7 vs. 4.2 cm, respectively; $p < 0.0001$; stage II: 6.7 vs. 8.9 cm, respectively; $p < 0.0001$; stage III: 9.5 vs. 12.4 cm, respectively; $p < 0.0001$). There was no significant difference between laparoscopic and open resection for the ability to obtain negative margins for any stage (stage I: 94% vs. 94%,

respectively; $p = 0.6862$; stage II: 92% vs. 91%, respectively; $p = 0.5446$; stage III: 84% vs. 83%, respectively; $p = 0.7168$). The conversion to open surgery rate was 10.8% for stage I, 19% for stage II, and 25% for stage III, with an overall conversion rate of 14.3%. On univariate analysis, there was no difference between laparoscopic and open resection for 30-day mortality for stage I disease (0.94% vs. 1.0%, respectively; $p = 0.9108$), but laparoscopic resection was associated with decreased 90-day mortality (0.9% vs. 2.0%, respectively; $p = 0.0391$) and 30-day readmissions (2.4% vs. 4.5%, respectively; $p = 0.0033$). On univariate analysis for stage II and stage III disease, there was no difference between laparoscopic and open resection for 30-day mortality (stage II: 1.3% vs. 1.8%, respectively; $p = 0.7580$; stage III: 0.92% vs. 1.0%, respectively; $p = 0.8090$), 90-day mortality (stage II: 1.3% vs. 2.0%, respectively; $p = 0.6215$; stage III: 2.4% vs. 2.6%, respectively; $p = 0.8845$), or 30-day readmissions (stage II: 2.8% vs. 4.4%, respectively; $p = 0.3135$; stage III: 5.3% vs. 4.4%, respectively; $p = 0.6270$). Laparoscopic resection was associated with a shorter length of stay compared to open resection on univariate analysis for all stages (stage I: 4.0 vs. 7.0 days, respectively; $p < 0.0001$; stage II: 4.7 vs. 7.0 days, respectively; $p < 0.0001$; stage III: 6.3 vs. 8.3 days, respectively; $p < 0.0001$).

Results of the multivariate logistic regression model are listed in Table 3. Adjusted 30-day mortality could not be performed due to model instability. There was no statistically significant difference between laparoscopic and open

Table 1 Patient demographics and comorbidity scores for laparoscopic versus open GIST resection, stratified by pathologic stage

	Stage I			Stage II			Stage III		
	Laparoscopic $N = 1291$	Open $N = 1619$	p value	Laparoscopic $N = 318$	Open $N = 636$	p value	Laparoscopic $N = 286$	Open $N = 946$	p value
Age [years, mean (SD)]	63.4 (12.7)	64.4 (13.0)	0.04	61.0 (13.2)	63.3 (13.4)	0.02	64.2 (13.6)	62.6 (14.0)	0.09
Female	685 (53)	861 (53)	0.98	163 (51)	338 (53)	0.63	133 (47)	430 (45)	0.81
Race									
White	945 (73)	1170 (72)	0.60	215 (68)	487 (77)	<0.01	215 (75)	670 (71)	0.17
Black	256 (20)	339 (21)	0.49	74 (23)	110 (17)	0.03	48 (17)	200 (21)	0.13
Asian	57 (4.4)	81 (5)	0.51	17 (5.3)	33 (5.2)	0.92	17 (5.9)	59 (6.2)	0.97
Other	14 (1.1)	18 (1.1)	0.94	7 (2.2)	4 (0.63)	0.07	5 (1.7)	10 (1.1)	0.53
Hispanic ethnicity	66 (5.1)	92 (5.7)	0.55	18 (5.7)	38 (6)	0.96	19 (6.6)	43 (4.5)	0.20
Charlson/Deyo Score									
0	901 (70)	1130 (70)	>0.99	228 (72)	462 (73)	0.82	201 (70)	692 (73)	0.38
1	302 (23)	381 (24)	0.96	70 (22)	132 (21)	0.72	59 (21)	192 (20)	0.97
2+	88 (6.8)	108 (6.7)	0.94	20 (6.3)	42 (6.6)	0.96	26 (9.1)	62 (6.6)	0.18
Mean (SD)	0.37 (0.61)	0.37 (0.61)	0.99	0.35 (0.59)	0.34 (0.60)	0.81	0.39 (0.65)	0.33 (0.59)	0.14

Results are provided as frequencies (%) unless otherwise indicated

SD standard deviation

Table 2 Tumor pathology and patient outcomes for laparoscopic versus open GIST resection, stratified by pathologic stage

	Stage I			Stage II			Stage III		
	Laparo-scopic $N = 1291$	Open $N = 1619$	p value	Laparo-scopic $N = 318$	Open $N = 636$	p value	Laparo-scopic $N = 286$	Open $N = 946$	p value
Location			<0.01			0.13			0.03
Stomach	1119 (87)	1213 (75)		194 (61)	354 (56)		168 (59)	485 (51)	
Small intestine	172 (13)	406 (25)		124 (39)	282 (44)		118 (41)	461 (49)	
Tumor size (cm)									
<= 2	258 (20)	236 (15)	<0.01	6 (1.9)	9 (1.4)	0.78	4 (1.4)	10 (0.11)	0.87
2–5	698 (54)	835 (52)	0.34	134 (42)	156 (25)	<0.01	23 (8.0)	55 (5.8)	0.22
5–10	309 (24)	504 (31)	<0.01	121 (38)	275 (43)	0.14	156 (55)	334 (35)	<0.01
> 10	10 (0.77)	33 (2.0)	0.01	56 (18)	195 (31)	<0.01	100 (35)	530 (56)	<0.01
Mean (SD)	3.7 (2.1)	4.2 (2.4)	<0.01	6.7 (4.6)	8.9 (7.9)	<0.01	9.5 (8.0)	12.4 (8.8)	<0.01
Surgical extent									
Partial/subtotal gastrectomy	1126 (87)	1313 (81)	<0.01	260 (82)	471 (74)	0.01	217 (76)	605 (64)	<0.01
Total gastrectomy	45 (3.5)	125 (7.7)	<0.01	31 (9.7)	62 (9.7)	>0.99	23 (8.0)	111 (12)	0.10
Partial/total gastrectomy with partial esophagectomy	92 (7.1)	107 (6.6)	0.63	12 (3.8)	35 (5.5)	0.31	17 (5.9)	52 (5.5)	0.89
Partial/total gastrectomy with resection of other involved organs	24 (1.9)	68 (4.2)	0.01	15 (4.7)	66 (10)	<0.01	28 (9.8)	177 (19)	<0.01
Gastrectomy not otherwise specified	4 (0.31)	6 (0.37)	0.78	0 (0)	2 (0.31)	0.80	1 (0.35)	1 (0.11)	0.95
Conversion to open	140 (10.8)	N/A	–	59 (19)	N/A	–	71 (25)	N/A	–
Margin status									
Positive	50 (3.9)	66 (4.1)	0.85	18 (5.7)	40 (6.3)	0.8107	31 (11)	105 (11)	0.9877
Positive microscopic	28 (2.2)	38 (2.3)	0.84	10 (3.1)	22 (3.5)	0.9493	16 (5.6)	70 (7.4)	0.3589
Positive macroscopic	0 (0)	2 (0.12)	0.58	1 (0.31)	1 (0.16)	0.62	2 (0.7)	7 (0.74)	0.94
Residual, not otherwise specified	22 (1.7)	26 (1.6)	0.95	7 (2.2)	17 (2.7)	0.83	13 (4.5)	28 (3.0)	0.26
Negative	1216 (94)	1518 (94)	0.69	293 (92)	577 (91)	0.54	240 (84)	783 (83)	0.72
Mortality (30 days)	9 (0.94)	13 (1.0)	0.91	3 (1.3)	9 (1.8)	0.76	2 (0.92)	8 (1.0)	0.81
Mortality (90 days)	9 (0.95)	26 (2.0)	0.04	3 (1.3)	10 (2.0)	0.62	5 (2.4)	20 (2.6)	0.88
Readmission (30 days)	31 (2.4)	73 (4.5)	<0.01	9 (2.8)	28 (4.4)	0.31	15 (5.3)	41 (4.4)	0.63
Length of stay [days, mean (SD)]	4.0 (4.4)	7.0 (6.5)	<0.01	4.7 (4.3)	7.0 (6.8)	<0.01	6.3 (5.5)	8.3 (8.0)	<0.01

Results are provided as frequencies (%) unless otherwise indicated

SD standard deviation

Table 3 Multivariate logistic regression model for laparoscopic versus open GIST resection, stratified by pathologic stage

	Stage I		Stage II		Stage III	
	AOR/ARM (95% CI)	p value	AOR/ARM (95% CI)	p value	AOR/ARM (95% CI)	p value
Mortality (30 days)	0.59 (0.26, 1.31)	0.38	0.82 (0.20, 3.30)	>0.99	0.82 (0.31, 2.15)	>0.99
Negative margins	0.94 (0.66, 1.34)	0.27	0.92 (0.52, 1.64)	0.73	1.12 (0.74, 1.69)	>0.99
Readmission (30 days)	0.65 (0.41, 1.03)	0.20	0.58 (0.26, 1.29)	0.55	1.18 (0.61, 2.27)	>0.99
Length of stay (days)	0.64 (0.59, 0.70)	<0.01	0.71 (0.62, 0.81)	<0.01	0.76 (0.67, 0.87)	<0.01

AOR adjusted odds ratio, *ARM* adjusted relative mean, *CI* confidence interval

resection for adjusted 90-day mortality for any stage (stage I: AOR 0.59; $p = 0.38$; stage II: AOR 0.82; $p = 0.99$; stage III: AOR 0.82; $p = 0.99$), for the ability to obtain negative margins for any stage (stage I: AOR 0.94; $p = 0.27$; stage II: AOR 0.92; $p = 0.73$; stage III: AOR 1.12; $p = 0.99$), or for 30-day readmissions for any stage (stage I: AOR 0.65; $p = 0.20$; stage II: 0.58; $p = 0.55$; stage III: AOR 1.18; $p = 0.99$). Adjusted relative mean difference in LOS for laparoscopic resection was shorter than for open resection for all stages (stage I: ARM 0.64; $p < 0.0001$; stage II: 0.71; $p < 0.0001$; stage III 0.76; $p < 0.0001$). Unadjusted Kaplan–Meier survival curves are illustrated in Figs. 1, 2, and 3, with significantly increased overall long-term survival for laparoscopic compared to open resection for stage I ($p = 0.032$) and stage II ($p = 0.017$) disease, but no significant difference in survival for stage III disease ($p = 0.736$).

Table 4 lists the stratified Cox proportional hazards ratios (HR) for survival after laparoscopic versus open resection, adjusted for the same key patient and tumor characteristics that were used for adjustment in the multivariate logistic regression model. Factors associated with increased risk of mortality included older age (HR 1.06 per year; $p < 0.0001$), black versus white race (HR 1.33; $p = 0.04$), small intestinal versus gastric GIST (HR 1.28; $p = 0.03$), and higher Charlson/Deyo comorbidity score (HR 1.47 per unit; $p < 0.0001$). Female versus male gender was associated with a decreased risk of mortality (HR 0.59; $p < 0.0001$). Laparoscopic surgery was associated with a 20% reduction in the adjusted hazard of mortality, but this finding was not statistically significant at the 5% significance level.

Discussion

In this study, we used a large national database to analyze 5096 cases of gastric and small intestinal GIST and compare survival outcomes for patients undergoing laparoscopic versus open resection for localized disease. This was an
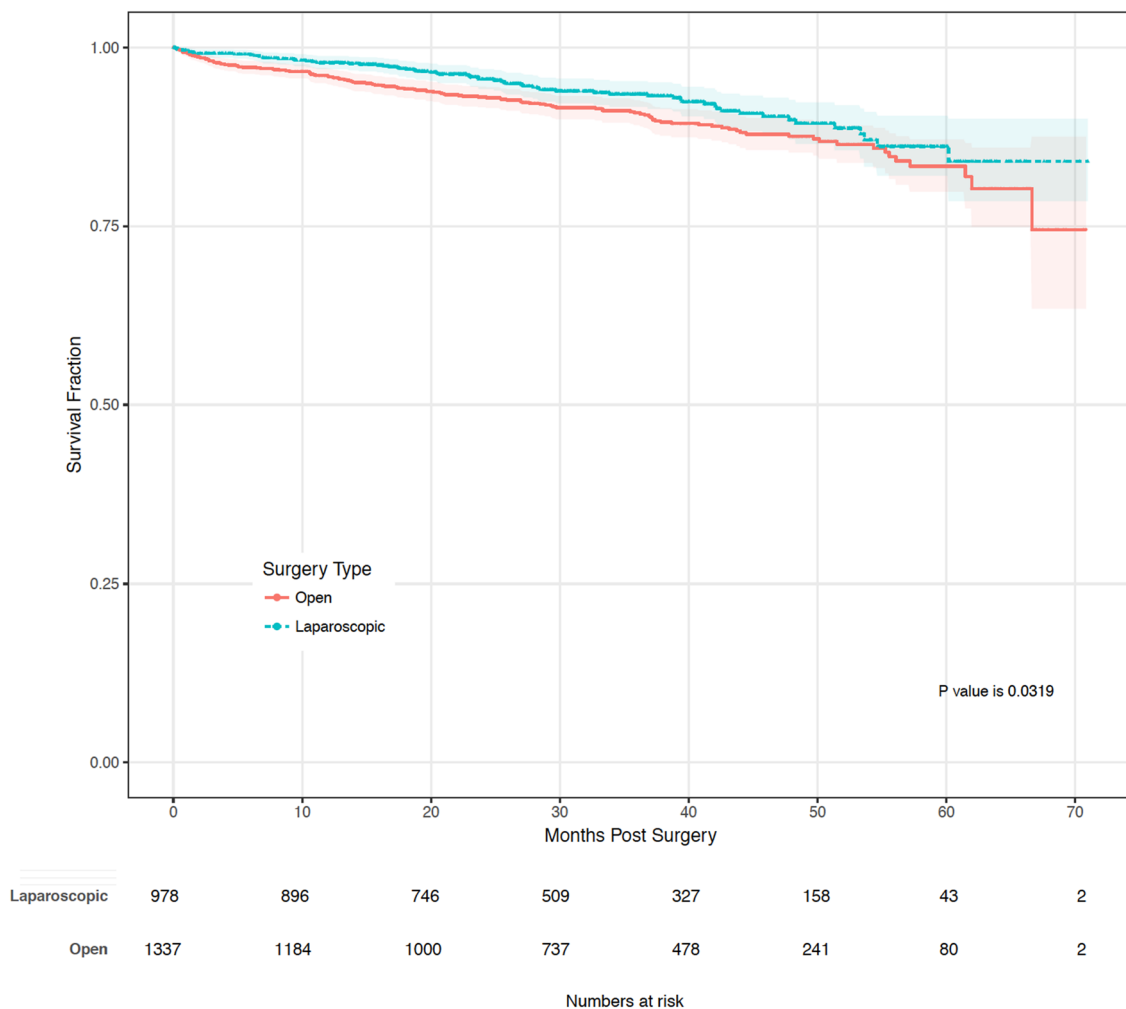

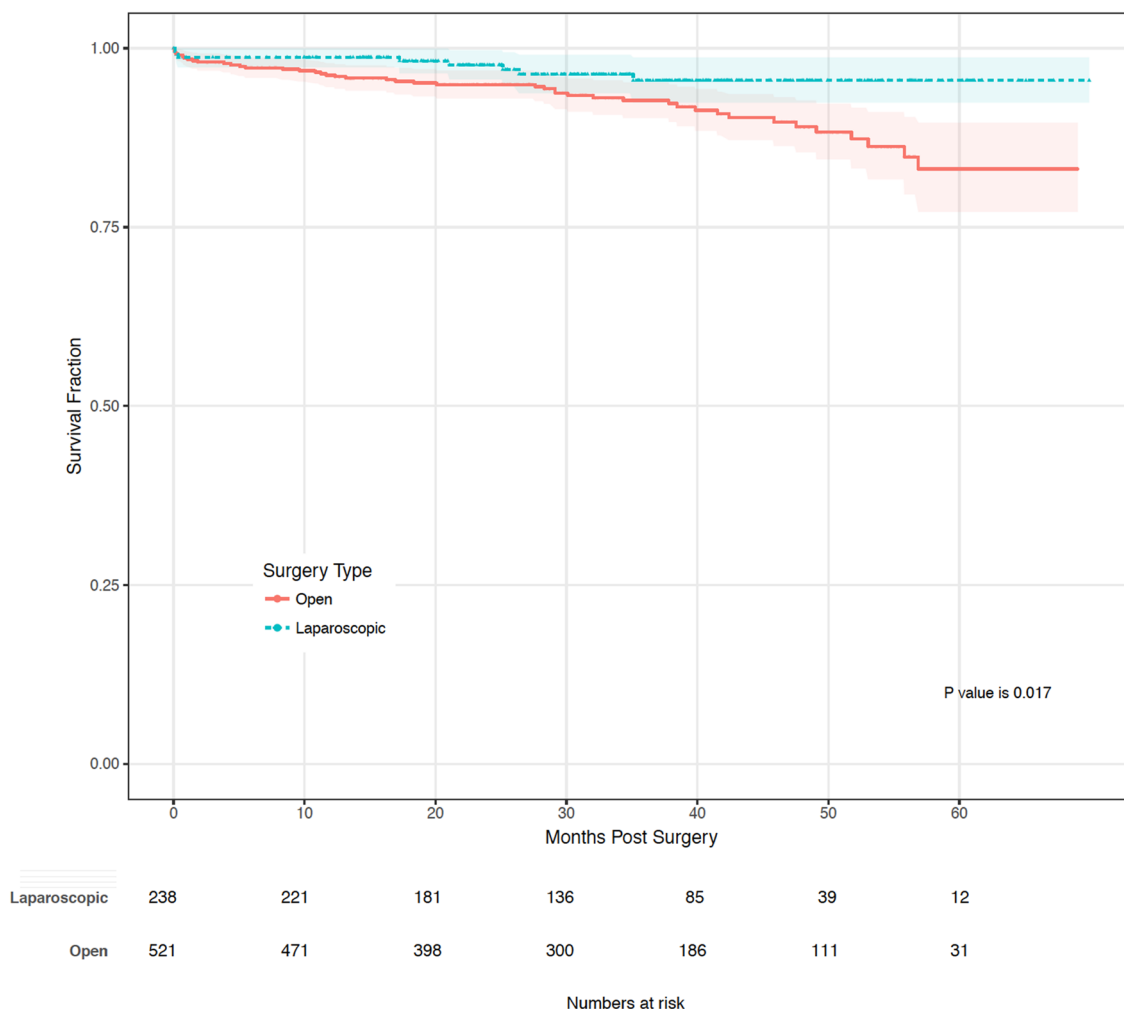**Fig. 1** Long-term overall survival Stage I

Fig. 2 Long-term overall survival Stage II

intention-to-treat analysis in which converted cases were analyzed as part of the laparoscopic group. Overall, open surgery was performed more commonly than laparoscopic surgery, and the percentage of cases that were performed open was greater for advanced stage of disease. Similarly, the rate of laparoscopic conversion to open surgery increased with advancing stage of disease, with an overall conversion rate of 14.3%. There was no significant difference between laparoscopic and open resection for 30-day mortality on univariate analysis. There was also no significant difference between laparoscopic and open approach for adjusted 90-day mortality, negative-margin rate, or 30-day readmission rates. Laparoscopy was associated with decreased adjusted LOS compared to an open approach for all stages. Kaplan–Meier long-term survival curves favored laparoscopy compared to open resection for both stage I and II GIST, but demonstrated no significant difference for stage III disease. A Cox proportional hazards model showed that older age, male gender, black race, higher Charlson/Deyo comorbidity score, and

small intestinal location were associated with worse adjusted overall survival after GIST resection, whereas use of laparoscopy was possibly associated with improved survival.

The current study confirms previous findings supporting non-inferior overall survival for laparoscopic compared to open resection of gastric and small intestinal GIST. Koh et al. [15] performed a meta-analysis comparing a total of 143 laparoscopic versus 192 open resections for gastric GIST and found no difference in overall survival (OR 0.53, 95% CI 0.18–1.69; $p = 0.285$). In a meta-analysis examining operative approach for small intestinal GIST, Chen et al. [12] compared a total of 67 laparoscopic versus 113 open resections and found that there was no significant difference in mortality rate (RR 1.70, 95% CI 0.84–16.04; $p = 0.64$). Neither of these studies controlled for the effect of tumor size, which can lead to selection bias since laparoscopic resections have been associated with smaller tumor size compared to open surgery in the current study, as well as in the existing literature [7, 8, 16, 17]. However, in a meta-analysis
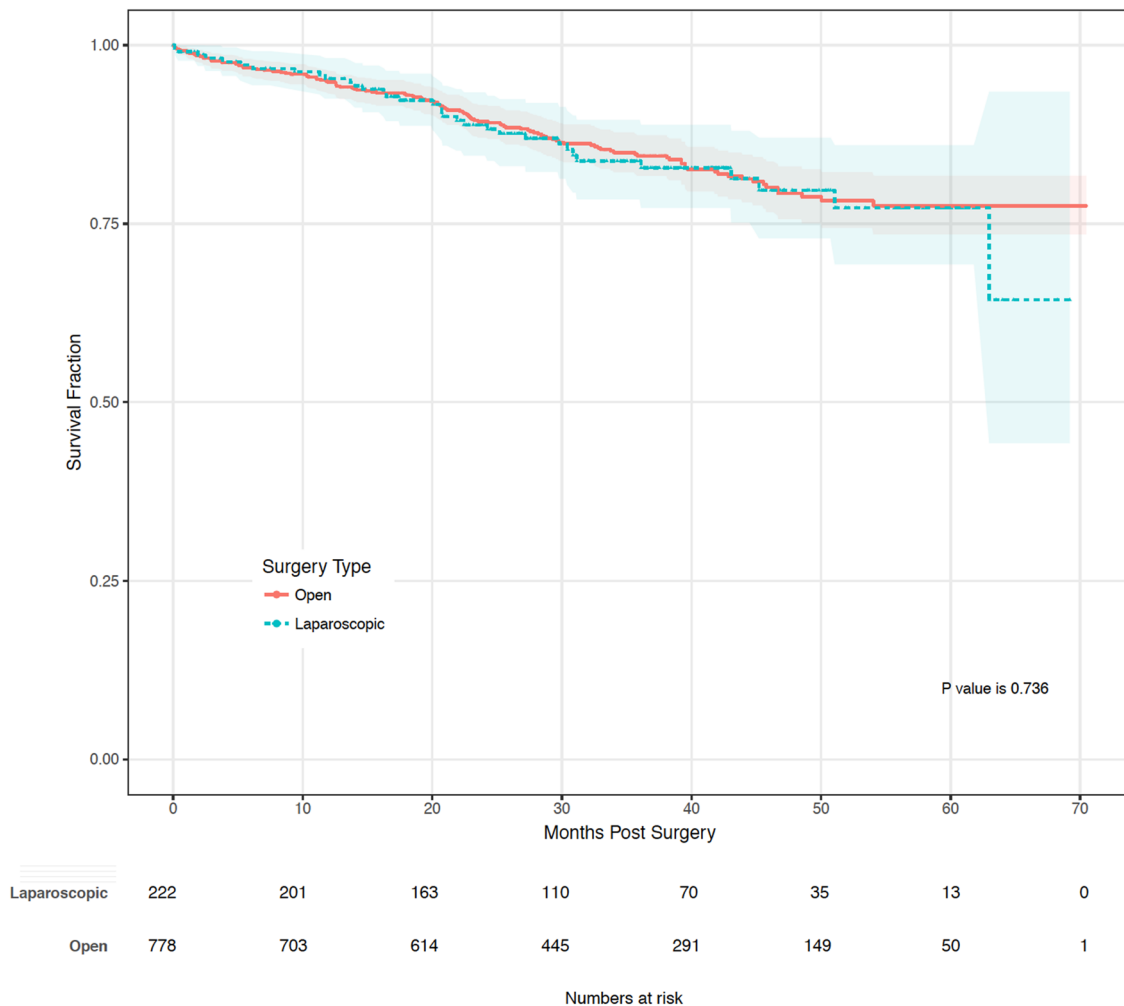
Fig. 3 Long-term overall survival Stage III

of five recently published studies, Cui et al. [5] compared a total of 100 laparoscopic versus 109 open resections for gastric GIST and found no difference in disease-free survival (HR 0.64, 95% CI 0.35–1.19, $p = 0.157$) even when the mean tumor size for both groups was statistically similar. These results are concordant with the current study, which demonstrated no difference between laparoscopic and open approach for 90-day mortality after adjustment for tumor size and other patient and tumor characteristics. Furthermore, the current study demonstrated no difference between laparoscopic and open resection in the ability to obtain negative margins (i.e., an R0 resection), which is consistent with other published findings [18, 19].

In the current study, laparoscopy was associated with improved unadjusted, long-term overall survival compared to open resection for stage I and stage II disease based on Kaplan–Meier curves. In addition, a Cox proportional hazards model demonstrated an HR of 0.80 (95% CI 0.63–1.01; $p = 0.06$), suggesting a potentially beneficial effect of

laparoscopy for adjusted overall survival. Although this finding did not meet the $p < 0.05$ threshold for significance, other studies have reported improved survival outcomes with laparoscopic versus open resection for GIST. Piessen et al. [8] compared a total of 224 laparoscopic versus 224 open propensity-score-matched gastric GIST resections from 61 European centers between 2001 and 2013 and found that laparoscopic resection was associated with improved 5-year disease-free survival (91.7% vs. 85.2%, respectively; $p = 0.011$; HR 0.521, CI 0.275–0.988, $p = 0.046$), and 5-year overall survival (94.8% vs. 88.3%; $p = 0.014$). Lian et al. [6] recently performed a meta-analysis of 7 studies and compared 203 laparoscopic versus 214 open gastric GIST resections of tumors ≥ 5 cm and also found that a laparoscopic approach was associated with improved disease-free survival (HR 0.40, 95% CI 0.17–0.91; $p = 0.03$) and overall survival (HR 0.11, 95% CI 0.03–0.43, $p = 0.002$).

An additional benefit of laparoscopy is that, based on the findings from the current study, laparoscopic resection is

Table 4 Cox proportional hazards model for overall survival after GIST resection with stratification by pathologic stage

	Hazard ratio (95% CI)	*p* value
Age	1.06 (1.04, 1.07)	< 0.01
Gender		< 0.01
Male	1	< 0.01
Female	0.59 (0.48, 0.73)	< 0.01
Race		< 0.01
White	1	< 0.01
Black	1.33 (1.02, 1.73)	0.04
Asian	0.54 (0.28, 1.03)	0.06
Other	0.81 (0.19, 3.33)	0.77
Ethnicity		< 0.01
Non-Hispanic	1	< 0.01
Hispanic	0.95 (0.53, 1.69)	0.86
Tumor location		< 0.01
Stomach	1	< 0.01
Small intestine	1.28 (1.02, 1.62)	0.03
Charlson/Deyo Score	1.47 (1.27, 1.70)	< 0.01
Tumor size	1.00 (0.99, 1.01)	0.84
Surgical approach		< 0.01
Open	1	< 0.01
Laparoscopic	0.80 (0.63, 1.01)	0.06

CI confidence interval

associated with a 24–36% decrease in LOS even after adjustment for patient and tumor characteristics. Multiple other studies have likewise reported decreased LOS associated with laparoscopic resection [5, 8, 12, 13, 15, 19]. Additionally, other reported advantages of laparoscopic GIST resection include decreased operative time, decreased blood loss, and decreased overall complications [7, 10, 12]. Readmission rates for laparoscopic versus open GIST resection are rarely reported in the literature. The current study found no significant difference for adjusted 30-day readmission between laparoscopic and open resection.

Another important finding from this study is that 90% of the tumors excised laparoscopically in the stage III group were ≥ 5 cm in size, with a mean size of 9.5 cm, whereas current international guidelines discourage the use of laparoscopy for tumors > 5 cm [20, 21]. Although the patients that underwent open resection for stage III tumors had a larger mean tumor size (12.4 cm), logistic regression controlling for tumor size revealed no difference in the 90-day mortality rate. This finding is similar to a number of other emerging reports that survival after laparoscopic resection is non-inferior to open resection even for large GIST > 5 cm [5–8, 13, 14, 19]. Furthermore, 40% of the laparoscopic stage III cases were performed for small intestinal GIST, suggesting that laparoscopic resection is a feasible option even for locally advanced, small intestinal GIST.

The current study also found that small intestinal GIST was associated with worse overall survival when compared with gastric GIST (HR 1.28, 95% CI 1.02–1.62, *p* = 0.03), a finding which has previously been described [22]. Emergent surgery is performed 3–4 times as frequently for small intestinal compared to gastric GIST, presumably due to symptoms of intestinal obstruction mandating urgent surgery [23, 24]. This may partially explain the worse hazard ratio observed for small intestinal GIST in this study, as emergency surgery for other types of cancer has been associated with more aggressive tumor biology, increased complications, shorter disease-free survival, and higher overall mortality [25]. Moreover, a clinicopathologic analysis of a large series of small intestinal GIST tumors showed more aggressive behavior and higher propensity for metastasis in jejunal and ileal GIST when compared with gastric GIST, a finding which could further account for this difference [22]. However, a worse prognosis for small intestinal lesions has not been universally reported. A study by Tabrizian et al. [24] showed that, despite a higher incidence of emergency surgery in patients with small intestinal GIST, no difference was noted in either recurrence rate or overall survival when compared with gastric lesions. Further investigation into the tumor biology and clinical characteristics of small intestinal GIST is needed to clarify the long-term prognosis and to aid in risk stratification of patients for laparoscopic versus open resection.

There are several limitations to this study. As a retrospective analysis, this study is subject to possible selection bias, inaccurate data input, coding errors, and missing data. In particular, the NCDB has a number of missing variables that are important to the characterization and prognosis of GIST including mitotic index, presence of platelet-derived growth factor receptor alpha (PDGFRA) mutation, histology, and cellularity of tumors [26]. The inability to adjust for these variables may confound the results of this study. Other specific data such as body mass index, surgeon laparoscopic experience, precise tumor location, and presence of pseudo-capsule rupture are also influential parameters that are not available variables in the NCDB and thus are not accounted for in our adjusted analysis. Additionally, disease-free survival and causes of mortality are not reported in the NCDB. Despite these limitations, this study involved a robust sample size from a longitudinal national database to compare survival outcomes after laparoscopic versus open resection of gastric and small intestinal GIST while controlling for tumor size and stage of disease.

Conclusion

To our knowledge, this is the largest study to date comparing survival between laparoscopic and open resection for gastric and small intestinal GIST. Results from this study

demonstrate that laparoscopic resection for both gastric and small intestinal GIST is a viable technique that is non-inferior to open resection for oncologic outcomes. There is no significant difference between laparoscopic and open resection for short-term survival or negative-margin rate, and there may possibly be improved long-term survival with the use of laparoscopy for early-stage disease. Laparoscopy is also associated with a reduction in LOS. Further research is needed to risk stratify patients for laparoscopic versus open surgery, particularly for small intestinal GIST and for patients with advanced disease.

Compliance with ethical standards

Disclosures Dr. Smith is an educational consultant for Stryker, not relevant to this work. Drs. Inaba, Dosch, Koh, Sujatha-Bhaskar, and Nguyen, and Ms. Pejcinovska have no conflicts of interest or financial ties to disclose.

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