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Gastrointestinal

Impact of body mass index on perioperative outcomes and survival after resection for gastric cancer

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Abstract

Background

Among patients undergoing resection for gastric cancer, the impact of body mass index (BMI) on outcomes is not well understood. We sought to define the impact of non-normal BMI on short- and long-term outcomes after gastric cancer resection.

Methods

We identified 775 patients who underwent gastrectomy for adenocarcinoma between 2000 and 2012 from the multi-institutional US Gastric Cancer

Collaborative. Clinicopathologic characteristics, operative details, and oncologic outcomes were collected, and patients were stratified according to BMI.

Results

Most patients in the cohort were classified as having normal BMI (n = 338, 43.6%), followed by overweight (n = 229, 29.6%), obese (n = 153, 19.7%), and underweight (n = 55, 7.1%). After stratifying by BMI, there were no significant differences in the incidence of postoperative blood transfusions, perioperative morbidity, postoperative infectious complications, length of stay, perioperative 30-d in-hospital death, or readmission across groups (all $P > 0.05$). BMI did not impact overall or recurrence-free survival after stratifying by stage (all $P > 0.05$). However, underweight patients with low preoperative albumin levels had worse overall survival (OS) compared with that of patients of normal BMI.

Conclusions

BMI did not impact perioperative morbidity, recurrence-free, or OS in patients undergoing gastric resection for adenocarcinoma. Underweight patients with BMI <18.5 kg/m^2 and low preoperative albumin levels, however, had a significantly decreased OS after gastrectomy for cancer. These high-risk patients should have their nutritional status optimized both before and after gastrectomy in an attempt to modify this risk factor and, in turn, achieve better outcomes.

Keywords

- Gastric cancer;
- Surgery;
- Obesity;
- Underweight;
- BMI;
- Gastrectomy;
- Outcomes

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1. Introduction

Gastric cancer is the fourth most common malignancy worldwide but only the 15th most common cancer in the United States [1], [2] and [3]. Differences in the prevalence of various risk factors for the development of gastric adenocarcinoma may be partially responsible for this wide variation of incidence and include diet, tobacco, and alcohol use, as well as *Helicobacter pylori* infection. Although relatively uncommon, in 2013, over 21,000 US patients will be newly diagnosed with gastric cancer resulting in nearly 11,000 deaths [1],[2] and [3]. Surgical resection, often in combination with perioperative chemotherapy and/or radiotherapy, offers the best hope for long-term survival [4] and [5]. Although prognosis after gastric resection heavily depends on the stage of disease at presentation [6], [7] and [8], other patient level factors may impact both short- and long-term outcomes.

The impact of body mass index (BMI) on surgical outcomes has been studied in patients undergoing a variety of cancer operations of the colon [9], rectum [10], endometrium [11], pancreas [12], and liver [13] and [14]. The impact of non-normal BMI on outcomes after gastrectomy for adenocarcinoma, however, is less well defined. Although some investigators have found an association between non-normal BMI and increased perioperative complications [15], [16], [17] and [18], other investigators have reported minimal or no change in the incidence of perioperative morbidity based on BMI [19]. Furthermore, results on the impact of BMI on recurrence-free and long-term overall survival (OS) are inconsistent [16] and [20]. The reason for these disparate results is probably multifactorial. Many previous studies were small, single-center studies [16], or did not involve patients from the United States [15], [19] and [20], making it difficult to extrapolate results to a Western population with different morphometric features. In addition, most prior studies were heterogenous with regard to inclusion criteria and definition of BMI categories. For example, some studies looked exclusively at patients with abnormally high BMI and grouped underweight individuals as "normal" [16] and [21]. Categorizing low BMI patients as "normal" can be problematic, however, as low BMI has been linked to worse outcomes for other cancers [22] and [23].

Given the epidemic of obesity and the increased incidence of gastric adenocarcinoma among obese patients [24], data on the impact of BMI on gastric cancer surgery outcomes are important. Therefore, the objective of the present study was to define the impact of BMI on perioperative and long-term outcomes among patients undergoing gastric resection for adenocarcinoma using a large multi-institutional cohort of US patients.

2. Materials and methods

2.1. Patient selection

All patients undergoing gastric resection for gastric adenocarcinoma between 2000 and 2012 at one of the seven participating institutions in the US Gastric Cancer Collaborative (Johns Hopkins Hospital, Baltimore, MD; Emory University, Atlanta, GA; Stanford University, Palo Alto, CA; Washington University, St. Louis, MO; Wake Forest University, Winston-Salem, NC; University of Wisconsin, Madison, WI; The Ohio State University, Columbus, OH) were identified. Patients from the original US Gastric Cancer Collaborative cohort with metastatic stage IV disease (n = 101) were excluded from analysis. Standard demographic, clinicopathologic, tumor, and treatment-related variables were collected. Specifically, patient age, sex, presence of comorbidities, and preoperative BMI were collected. Patients were classified according to the World Health Organization BMI classification system as follows: underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30 kg/m^2) [25]. Tumor location, size, number of lesions, histologic type and grade, depth of invasion, number of lymph nodes harvested, number of metastatic lymph nodes, and the American Joint Committee on Cancer (AJCC) stage were also collected and recorded [26]. Treatment-related factors that were collected included type and extent of resection (partial *versus* total gastrectomy), operative time, estimated blood loss (EBL), and need for perioperative blood transfusion. Pathologic data included margin status, which was categorized as microscopically negative (R0) and microscopically (R1) or macroscopically (R2) positive.

The primary outcomes of interest were perioperative 30-d morbidity, as well as long-term OS. The highest grade of complication was recorded based on the Clavien–Dindo classification system [27]. Infectious complications were categorized together and included both superficial and deep surgical site wound infections as well as deep intra-abdominal collections or sepsis. Data on postoperative outcome metrics such as total hospital length of stay (LOS), location of discharge (home *versus* non-home), and incidence of hospital readmission were also collected. Date of last follow-up, vital status, recurrence-free survival (RFS), and recurrence-related information were also collected on all patients.

2.2. Statistical analysis

Discrete variables were described as medians with interquartile range (IQR), and categorical variables were described as totals and frequencies. Univariate comparisons were assessed using the chi-squared or Wilcoxon rank-sum test as appropriate. Univariate and multivariate logistic regression models were assessed to determine the association of relevant clinicopathologic preoperative factors with perioperative morbidity. Variables of statistical significance on univariate analysis and factors of clinical significance or potential confounders were included in the multivariate model. RFS and OS time were calculated from the date of surgery. Survival adjusted for censoring was calculated using the Kaplan–Meier method and medians compared using the log-rank test. The impact of various clinicopathologic factors on OS was assessed using a Cox proportional hazards model. All analyses were carried out with STATA version 13.0 (StataCorp, College Station, TX), and a*P* value of <0.05 (two-tailed) was considered statistically significant.

3. Results

3.1. Clinicopathologic characteristics of cohort

A total of 775 patients who underwent gastric resection for adenocarcinoma were identified. Median age was 66.1 y (IQR: 56.8–71.4). The majority of patients were male (*n* = 446, 57.6%) and of white race (*n* = 488, 63.4%). Preoperative malnutrition was common among the cohort, as 28.5% of patients (*n* = 221) had a preoperative albumin <3.5 g/dL. Comorbidities were also prevalent, with hypertension (*n* = 394, 51.4%) and cardiac disease (*n* = 168, 21.9%) being the most common. Most patients in the cohort were classified as having a normal BMI (*n* = 338, 43.6%), followed by overweight (*n* = 229, 29.6%), obese (*n* = 153, 19.7%), and underweight (*n* = 55, 7.1%). Median age was similar among BMI groups (*P* = 0.06; Table 1). There were differences in race according to BMI, as there was a higher proportion of patients of black race who were underweight (*n* = 12, 22.2%) and obese (*n* = 39, 25.5%; *P* < 0.001). Hypertension, diabetes, and cardiac disease were also more common among overweight and obese patients (all *P* < 0.02). Perhaps not surprisingly, the proportion of patients with low preoperative albumin levels <3.5 g/dL was higher among underweight patients (*n* = 30, 54.6%; *P* < 0.001).

Table 1.

Clinicopathologic characteristics of patients who underwent resection for gastric adenocarcinoma.

Clinicopathologic characteristics	Normal 18.5–24.9 kg/m^2 (*n* = 338)	Underweight <18.5 kg/m^2 (*n* = 55)	Overweight 25.0–29.9 kg/m^2 (*n* = 229)	Obese ≥30 kg/m^2 (*n* = 153)	*P* value
Age, y (IQR)	65.8 (56.4–76.3)	67.7 (77.6–57.7)	67.1 (58.2–74.7)	63.7 (56.0–71.4)	0.06
Male sex	193 (57.1)	29 (52.7)	145 (63.3)	79 (51.6)	0.12
Ethnicity					<0.001
Caucasian	211 (63.0)	33 (61.1)	142 (62.3)	102 (66.7)	
Black	52 (15.5)	12 (22.2)	31 (13.6)	39 (25.5)	
Asian	43 (12.8)	9 (14.8)	32 (14.0)	1 (0.7)	
Preoperative albumin <3.5 g/dL	92 (27.2)	30 (54.6)	59 (25.8)	40 (26.1)	<0.001
Comorbidities					
Hypertension	160 (47.8)	20 (38.5)	118 (51.8)	96 (63.6)	0.003
Diabetes	49 (14.7)	5 (9.6)	48 (21.1)	45 (29.8)	<0.001
Cardiac disease	57 (17.1)	10 (19.2)	59 (25.9)	42 (27.6)	0.02

Clinicopathologic characteristics	Normal 18.5–24.9 kg/m^2 (*n* = 338)	Underweight <18.5 kg/m^2 (*n* = 55)	Overweight 25.0–29.9 kg/m^2 (*n* = 229)	Obese ≥30 kg/m^2 (*n* = 153)	*P* value
Pulmonary disease	38 (11.3)	8 (15.4)	28 (12.3)	20 (13.3)	0.83
Chemotherapy					
Neoadjuvant	29 (23.4)	9 (16.4)	49 (21.4)	25 (16.3)	0.27
Adjuvant	176 (56.6)	18 (36.7)	113 (51.6)	73 (51.1)	0.07
Laparoscopic	34 (10.1)	5 (9.1)	16 (7.0)	15 (9.8)	0.64
Operation type					0.89
Total	197 (58.3)	33 (60.0)	137 (59.8)	95 (62.1)	
Partial	141 (41.7)	22 (40.0)	92 (40.2)	58 (37.9)	
Lymphadenectomy					0.06
D1	93 (27.6)	22 (40.0)	94 (41.2)	62 (40.5)	
D2	222 (65.9)	29 (52.7)	127 (55.7)	84 (54.9)	
EBL	200 (100–350)	200 (100–300)	250 (125–400)	200 (150–400)	0.21
Operative time, min	236 (185–300)	218 (161–289)	233 (179.5–298.5)	240 (187–294)	0.85
Intraoperative blood transfusion	25 (7.6)	10 (18.5)	24 (10.8)	13 (8.8)	0.16
Peritoneal drain	184 (54.4)	30 (55.6)	119 (52.2)	76 (49.7)	0.76
Resection margin					0.03
R0	331 (97.9)	51 (92.7)	225 (98.3)	152 (99.4)	
R1	7 (2.1)	4 (7.3)	4 (1.8)	1 (0.7)	
Tumor morphology					0.84
Diffuse	77 (33.5)	14 (30.4)	44 (27.9)	30 (32.6)	
Intestinal	144 (62.6)	31 (67.4)	110 (69.6)	58 (63.0)	
Mixed	9 (3.9)	1 (2.2)	4 (2.5)	4 (4.4)	

Clinicopathologic characteristics	Normal 18.5–24.9 kg/m^2 (n = 338)	Underweight <18.5 kg/m^2 (n = 55)	Overweight 25.0–29.9 kg/m^2 (n = 229)	Obese ≥30 kg/m^2 (n = 153)	P value
Tumor location					0.75
Antrum	115 (34.5)	25 (46.3)	82 (36.4)	59 (40.4)	
Body	130 (39.0)	18 (33.3)	83 (36.9)	54 (37.0)	
Gastro-esophageal junction	20 (6.0)	4 (7.4)	22 (9.8)	11 (7.5)	
Multiple lesions	16 (4.8)	2 (3.7)	11 (5.0)	6 (4.1)	0.85
Size, cm, median (IQR)	4 (2.5–6.8)	5.3 (3.6–7.5)	4.3 (2.5–6.5)	3.5 (2–5.5)	0.15
T-stage					0.09
T1	81 (24.3)	9 (16.7)	56 (24.7)	49 (32.2)	
T2	45 (13.5)	5 (9.3)	34 (15.0)	20 (13.2)	
T3	97 (29.1)	22 (40.7)	81 (35.7)	50 (32.9)	
T4	110 (33.0)	18 (33.3)	56 (24.7)	33 (21.7)	
Lymph node metastasis	196 (58.5)	38 (69.1)	147 (64.8)	83 (54.3)	0.09
Lymph nodes harvested, median (IQR)	17 (11–24.5)	16 (5–26)	17 (12–25)	17 (12–25)	0.63
AJCC stage					0.12
I	92 (27.8)	12 (21.8)	67 (29.8)	55 (36.2)	
II	94 (28.4)	10 (18.2)	53 (23.6)	35 (23.0)	
III	145 (43.8)	33 (60.0)	105 (46.7)	62 (40.8)	
Tumor grade					0.66
Moderate-to-well	119 (35.2)	15 (27.3)	74 (32.3)	53 (34.6)	
Poor-to-moderate	219 (64.8)	40 (72.7)	155 (67.7)	100 (65.4)	
Signet ring	133 (40.3)	21 (39.6)	88 (40.2)	63 (42.3)	0.9

Clinicopathologic characteristics	Normal 18.5–24.9 kg/m^2 (n = 338)	Underweight <18.5 kg/m^2 (n = 55)	Overweight 25.0–29.9 kg/m^2 (n = 229)	Obese ≥30 kg/m^2 (n = 153)	P value
					7
LVI	136 (45.0)	29 (60.4)	90 (44.6)	50 (37.3)	0.05
PNI	67 (27.5)	19 (47.5)	54 (32.5)	32 (27.8)	0.07

Table options

Before surgery, 162 patients (20.9%) received neoadjuvant chemotherapy, which did not differ across BMI groups (P = 0.27). Only 3.8% of patients (n = 24) received neoadjuvant radiotherapy, which also did not differ across BMI groups (P = 0.30). At the time of surgery, resection involved either a partial (n = 462, 59.6%) or total (n = 313, 40.4%) gastrectomy; the majority of patients underwent an associated D1 (n = 271, 35.1%) or D2 (n = 462, 59.8%) lymphadenectomy. Median EBL was 200 mL (IQR: 100–400) with only a small subset of patients requiring an intraoperative blood transfusion (n = 72, 9.3%). Operative details and metrics such as operative approach (laparoscopic *versus* open), extent of resection (partial*versus* total gastrectomy) and lymphadenectomy, operative time, EBL, need for intraoperative blood transfusion, and use of peritoneal drains did not differ among BMI groups (all P > 0.05).

On pathology, a microscopically negative margin (R0) was achieved in the overwhelming majority of patients (n = 759, 97.9%). Of note, underweight patients did have a slightly higher incidence of R1 resections (7.3%) compared with those patients of normal (2.1%) or high (1.3%) BMI (P = 0.03). Median tumor size was 4 cm (IQR: 2.5–6.5) with most patients having solitary tumors (n = 719, 95.4%). About one-third of patients had a diffuse-type tumor (n = 165, 31.4%), whereas the remaining tumors were either intestinal (n = 343, 65.2%) or mixed (n = 18, 3.4%) type. Most tumors were locally advanced and penetrated the subserosal (T3 tumors: n = 250, 32.6%) or serosal layer (T4 tumors: n = 217, 28.3%). Lymph node metastasis was common (n = 464, 60.3%). Based on the AJCC staging system, patients with stage III disease were most common (n = 345, 45.2%) and approximately one-quarter of patients had stage I (n = 226, 29.6%) or stage II (n = 192, 25.2%) disease. Of note, tumor morphology, tumor size, and number of lesions did not differ across BMI categories (all P > 0.05). Extent of disease, including depth of invasion, lymph node involvement, and distant spread, were also similar across BMI groups (all P > 0.05; Table 1). Underweight patients had no difference in tumor t-stage (P = 0.09), lymph node involvement (P = 0.09), lymphovascular invasion (LVI) (P = 0.05), or perineural invasion (PNI; P = 0.07). Over one-half of patients received some form of adjuvant chemotherapy (*n* = 380, 52.6%), which did not differ across BMI groups (*P* = 0.07). Similarly, the proportion of patients receiving adjuvant radiotherapy (*n* = 247, 34.8%) did not differ across BMI groups (*P* = 0.22).

3.2. Short- and long-term outcomes

A total of 325 patients (42.0%) experienced a perioperative complication (Table 2). Most complications were minor and classified as Clavien–Dindo grade I (*n* = 42, 12.7%) or grade II (*n* = 152, 45.8%); a subset of patients had major complications (grade III: *n* = 62, 18.7%; grade IV: *n* = 48, 14.5%). Median LOS was 8 d (IQR: 7–12) with most patients being discharged to home (*n* = 700, 90.3%). Nearly one-quarter of patients (*n* = 171, 22.2%) were readmitted to the hospital after discharge.

Table 2.

Incidence of perioperative morbidity and overall mortality.

Perioperative morbidity and overall mortality	Total (*N* = 775)	Normal (*n* = 338)	Under (*n* = 55)	Overweight (*n* = 229)	Obese (*n* = 153)	*P*value
Postoperative blood transfusion	109 (14.1)	54 (16.0)	8 (14.5)	28 (12.2)	19 (12.4)	0.16
Complications	325 (42.0)	142 (42.0)	27 (49.1)	90 (39.5)	66 (43.1)	0.61
Infectious complications	193 (28.8)	87 (29.0)	15 (30.0)	53 (26.4)	38 (31.9)	0.76
Clavien–Dindo stage of worst complication						0.93
I	42 (12.7)	18 (12.4)	3 (10.7)	12 (13.2)	9 (13.2)	
II	152 (45.8)	65 (44.8)	16 (57.1)	39 (42.9)	32 (47.1)	
III	62 (18.7)	27 (18.6)	4 (14.3)	18 (19.8)	13 (19.1)	
IV	48 (14.5)	21 (14.5)	3 (10.7)	14 (15.4)	10 (14.7)	
In-hospital death	26 (3.4)	14 (5.7)	2 (5.0)	7 (4.2)	3 (2.6)	0.93
LOS, d	8 (7, 12)	8 (7, 11)	9 (7, 14)	8 (7, 13)	8 (7, 11)	0.29
Non-home discharge	75 (9.7)	30 (8.9)	7 (12.7)	25 (11.0)	13 (8.5)	0.84
Readmission	171 (22.2)	71 (21.1)	16 (29.1)	48 (21.1)	36 (23.7)	0.55

Perioperative morbidity and overall mortality	Total (*N* = 775)	Normal (*n* = 338)	Under (*n* = 55)	Overweight (*n* = 229)	Obese (*n* = 153)	*P*value
Recurrence	212 (29.0)	85 (26.9)	21 (44.7)	63 (28.8)	43 (29.1)	0.10
Death	352 (45.4)	152 (45.0)	37 (67.3)	93 (40.6)	70 (45.8)	0.005

Table options

Overall operative morbidity was similar after gastrectomy in obese patients (43.1%) compared with overweight (39.5%), normal weight (42.0%), or underweight (49.1%) patients (*P* = 0.61). Specifically, the incidence of surgical site wound infections was comparable in obese (11.6%) and overweight (12.0%) patients compared with that in normal weight (9.0%) and underweight patients (6.3%; *P* = 0.52). Similarly, there were no differences in the rate of other postoperative complications—either minor or major (all*P* > 0.05). On univariate analyses, there was no difference in the incidence of postoperative blood transfusions, LOS, or readmission across the different BMI groups (all *P* > 0.05). In contrast, older patients (age ≥65 y: odds ratio [OR] 1.37, 95% confidence interval [CI] 1.02–1.82; *P* = 0.03), those with low preoperative albumin levels (OR 1.44, 95% CI 1.05–1.97;*P* = 0.02), and patients with more advanced tumors (T4 tumors: OR 1.56, 95% CI 1.05–2.31 and stage III: OR 1.52, 95% CI 1.08–2.14; both *P* < 0.05) were at higher risk for a perioperative complication (Table 3). After adjusted analyses, only age ≥65 y (OR 1.56, 95% CI 1.11–2.19; *P* = 0.01) remained independently associated with a higher risk of experiencing a perioperative complication. The overall incidence of perioperative 30-d in-hospital death was 3.4% (*n* = 26); BMI was not associated with perioperative mortality (obese, 2.6% *versus* overweight, 2.6% *versus* normal weight, 4.1% *versus* underweight, 3.6%; *P* = 0.84).

Table 3.

Univariate/multivariate analysis of risk factors associated with perioperative morbidity.

	Univariate analysis			Multivariate analysis		
Risk factors	OR	95% CI	*P* value	OR	95% CI	*P* value
Age, y						
<65	Ref			Ref		
≥65	1.37	1.02–1.82	0.03	1.74	1.17–2.58	0.006
BMI						
Normal	Ref					
Underweight	1.33	0.75–2.37	0.33	1.18	0.55–2.51	0.67
Overweight	0.90	0.64–1.27	0.55	0.93	0.60–1.45	0.76

	Univariate analysis			Multivariate analysis		
Risk factors	OR	95% CI	*P* value	OR	95% CI	*P* value
Obese	1.05	0.71–1.54	0.82	1.07	0.65–1.76	0.79
Low albumin (<3.5 g/dL)	1.44	1.05–1.97	0.02	1.25	0.82–1.91	0.30
Comorbidities						
Hypertension	1.26	0.94–1.68	0.12	1.28	0.86–1.91	0.23
Diabetes	0.90	0.62–1.30	0.58	0.74	0.45–1.24	0.25
Cardiac disease	1.11	0.79–1.57	0.55	0.98	0.61–1.57	0.93
Pulmonary disease	1.33	0.86–2.05	0.20	1.18	0.68–2.02	0.56
Op time >300 min	0.99	0.74–1.33	0.96	1.04	0.72–1.50	0.72
Tumor size (cm)	1.01	0.97–1.06	0.54			
Tumor type						
Diffuse	Ref					
Intestinal	0.89	0.61–1.30	0.56			
Mixed	1.26	0.48–3.34	0.64			
T-Stage						
I	Ref			Ref		
II	1.02	0.63–1.67	0.93	0.88	0.40–1.91	0.74
III	1.15	0.79–1.69	0.47	1.24	0.46–3.35	0.67
IV	1.56	1.05–2.31	0.03	1.26	0.43–3.64	0.67
Stage						
I	Ref			Ref		
II	0.98	0.66–1.46	0.93	0.99	0.38–2.55	0.98
III	1.52	1.08–2.14	0.02	1.19	0.36–3.95	0.78
Grade						
Well-to-moderate	Ref					
Moderate-to-poor	1.10	0.82–1.50	0.52			
LN positive	1.27	0.95–1.71	0.10			
LVI	1.48	1.09–2.01	0.01	1.07	0.69–1.65	0.78
PNI	1.41	0.99–2.03	0.06			
Signet ring cell	1.03	0.77–1.39	0.82			

Table options

Median OS among the entire cohort was 35.9 mo; 1-, 3-, and 5-y OS was 75.6%, 49.7%, and 39.2%, respectively. Median RFS was 25.8 mo and 1-, 3-, and 5-year RFS was 83.5%, 36.7%, and 16.7%, respectively. Although RFS did not differ among patients with normal and non-normal BMI (log-rank:

all *P* > 0.05; Fig. 1), underweight patients had a shorter median OS (18.9 mo) *versus* normal (36.2 mo), overweight (53.8 mo), and obese (44.9 mo) patients (*P* = 0.003). Patients who were underweight also had a worse 5-y survival (13.4%)*versus* patients who were normal (36.0%), overweight (47.3%), or obese (42.7%;*P* < 0.001). Interestingly, underweight patients with a low preoperative albumin level (<3.5 g/dL) had a shorter median OS (13.5 mo) *versus* underweight patients with normal preoperative albumin level (25.9 mo; *P* = 0.03).

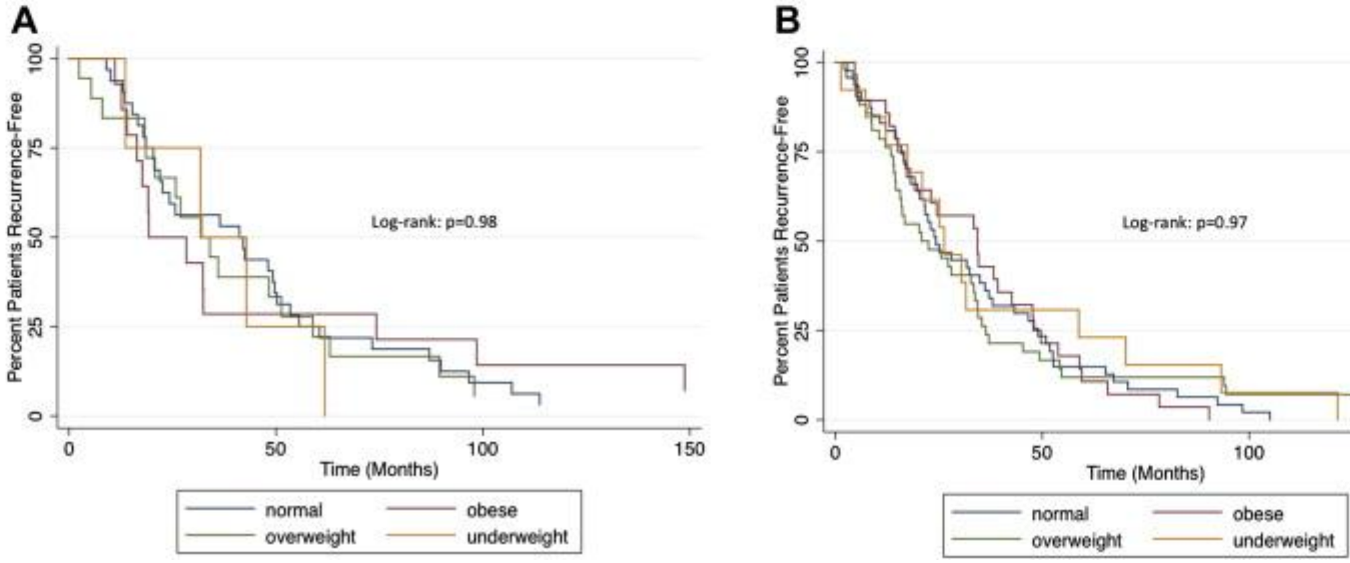

Fig. 1.

RFS, stratified by BMI among patients with (A) stage I and stage II disease, and (B) stage III disease. (Color version of the figure is available online.)

Figure options

Adjusting for disease stage, underweight patients had a shorter OS compared with patients who were normal, overweight, or obese (Fig. 2). On univariate analysis, other factors associated with shorter median OS included low preoperative albumin levels (<3.5 g/dL: 20.9 mo *versus* ≥3.5 g/dL: 45.57 mo; *P* < 0.001), large tumor size (>5.0 cm: 26.0 mo *versus*≤5.0 cm: 46.2 mo; *P* ≤ 0.001), as well as LVI (LVI: 20.2 mo *versus* no LVI: 67.9 mo;*P* < 0.001) and PNI (PNI: 17.0 mo *versus* no PNI: 48.0 mo; *P* < 0.001). Furthermore, patients with increasing T-stage, lymph node involvement, and advanced AJCC stage tumors had worse OS (all *P* < 0.001). After adjusting for all competing risk factors in the multivariate Cox proportional hazards model, advanced T-stage and LVI remained associated with significantly decreased OS (both *P* < 0.05); however, BMI and preoperative albumin levels were not (Table 4; both *P* > 0.05). Interestingly, receipt of chemotherapy also had a protective survival effect (hazard ratio 0.62, 95% CI 0.46–0.84; *P* = 0.002).

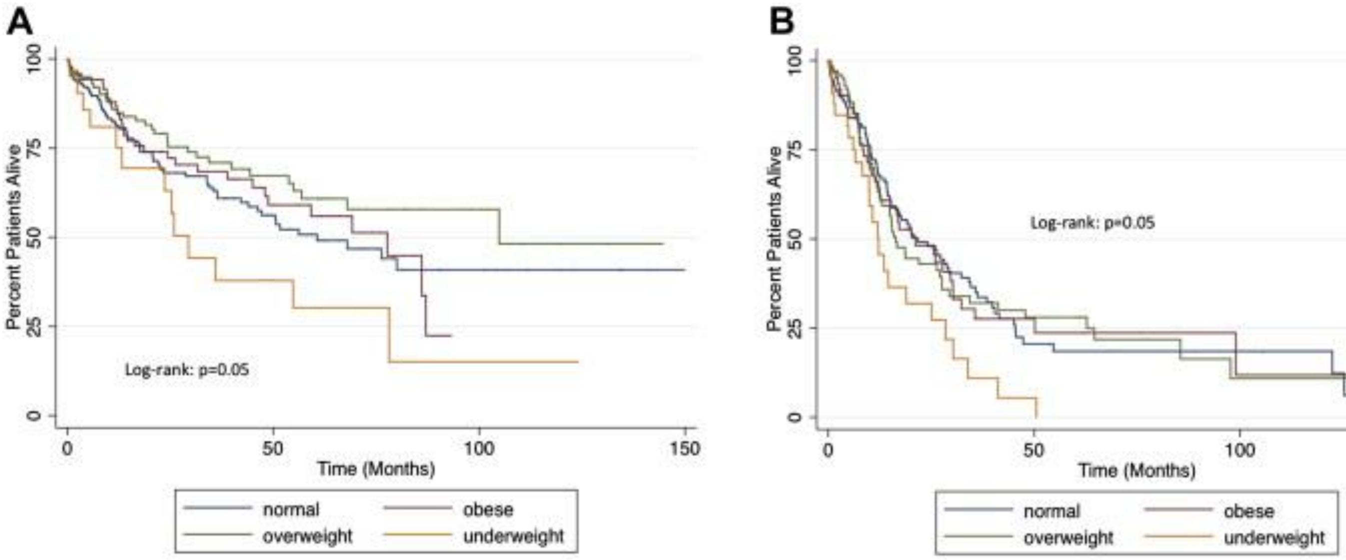

Fig. 2.

OS, stratified by BMI in patients with (A) stage I and II disease, and (B) stage III disease. (Color version of the figure is available online.)

Figure options

Table 4.

Hazard regression analysis of factors associated with OS.

Variables	Median survival (mo)	*P* value	Multivariate survival analysis Hazard ratio	95% CI	*P* value
Age, y		0.06			
<65	41.47		Ref	—	
≥65	31.60		1.85	1.38–2.47	<0.001
Race		<0.001			
Other	56.87		Ref	—	
Black	47.33		2.30	0.84–6.33	0.11
Caucasian	27.60		3.38	1.64–6.97	0.001
BMI		0.003			
Normal	36.23		Ref	—	
Underweight	18.93		1.50	0.93–2.41	0.10
Overweight	53.77		0.91	0.66–1.27	0.58
Obese	44.97		1.13	0.79–1.61	0.51
Preoperative albumin, g/dL		<0.001			
≥3.5	45.57		Ref	—	
<3.5	20.9		1.28	0.95–1.72	0.10

Variables	Median survival (mo)	*P* value	Multivariate survival analysis		
			Hazard ratio	95% CI	*P* value
Chemotherapy		0.05			
None	35.97		Ref	—	
Adjuvant/neoadjuvant	35.77		0.62	0.46–0.84	0.002
Tumor grade		0.13			
Well-to-moderate	40.43				
Poor-to-moderate	31.60				
Tumor size, cm		<0.001			
<5.0	46.23		Ref	—	
≥5.0	25.97		1.09	0.83–1.43	0.54
Tumor morphology		0.07			
Intestinal type	38.83		Ref	—	
Diffuse	29.67		1.12	0.80–1.58	0.50
Mixed	122.40		0.44	0.12–1.55	0.20
Resection margin		<0.001			
R0	36.40		Ref	–	
R1	14.30		1.52	0.67–3.45	0.32
AJCC stage		<0.001			
I	104.83		Ref	—	
II	53.77		1.00	0.47–2.10	0.99
III	18.70		1.90	0.76–4.73	0.17
T-Stage					
I	Not reached	<0.001	Ref	—	
II	42.17		2.20	1.16–4.16	0.02
III	29.27		2.01	0.91–4.45	0.08
IV	19.53		2.33	1.03–5.29	0.04
Lymph node (LN) status		<0.001			
No LN metastasis	76.27		Ref	—	
LN metastasis	26.33		0.88	0.55–1.40	0.58
LVI		<0.001			
No LVI	67.93		Ref		
LVI	20.17		1.43	1.06–1.94	0.02
PNI		<0.001			

Variables	Median survival (mo)	*P* value	Multivariate survival analysis		
			Hazard ratio	95% CI	*P* value
No PNI	47.97		Ref		
PNI	16.97		1.29	0.94–1.76	0.12
Signet ring		0.08			
Absent	39.83		Ref	—	
Present	30.23		0.91	0.68–1.22	0.53

Table options

4. Discussion

The prevalence of obesity has been increasing in both the United States and worldwide. In fact, nearly one in three Americans are currently estimated to be obese and this is expected to increase in the coming years [28]. Obesity has been associated with the development of several medical conditions including hypertension, heart disease, and cancer [29]. Furthermore, obese individuals have reduced overall life expectancy compared with that of patients who have a normal BMI [29]. Although the impact of obesity after surgical resection for several cancers has been previously investigated, the impact of BMI on short- and long-term outcomes after gastric cancer resection remains ill-defined. In particular, the impact of underweight BMI on outcomes after gastrectomy for adenocarcinoma is not well studied. In our multi-institutional study of gastric cancer patients undergoing surgical resection across the United States, we noted minimal impact of a non-normal BMI on the relative risk of experiencing perioperative complications. In fact, both patients who were underweight or overweight had a comparable risk of morbidity compared with that of normal weight patients. Similarly, in our multivariable Cox regression model, BMI did not have an impact on RFS or OS after stratifying by disease stage.

Several previous studies had noted that obese patients tended to be at higher risk for perioperative morbidity after major abdominal cancer surgery [15] and [30]. In a query of the National Surgical Quality Improvement Program (NSQIP) database, Mullen *et al.* [30]reported that obese patients undergoing abdominal cancer operations were at higher risk for postoperative wound complications. In contrast, an association between BMI and the risk of perioperative complications—minor or major—was not noted in the present study. Specifically, obese patients undergoing gastric resection were at a similar risk of developing infectious postoperative complications as normal and underweight patients. One possible explanation for the disparate findings of the present study and the report by Mullen *et al.* was that our study included only gastric cancer patients undergoing gastrectomy, whereas the previous study by Mullen *et al.* included a wide array of cancer operations of the esophagus, stomach, liver, pancreas, colon, and rectum [30]. Compared with the study by Mullen *et al.*, our data suggest that among a more homogenous cohort of surgical patients undergoing gastrectomy only, the incidence of perioperative complications was not appreciably affected by BMI. Although non-normal BMI did not impact the risk of perioperative complications, patient age ≥65 y was independently associated with a higher risk of perioperative complications.

Non-normal BMI has also been previously hypothesized to impact RFS in patients with gastric cancer [31]. Dhar *et al.* [31] reported that patients with high BMI were at an increased risk for inadequate nodal sampling during gastric cancer resection, which in turn led to a higher risk of local recurrence. In contrast, investigators from the Memorial Sloan-Kettering Cancer Center noted that high BMI was not a risk factor for either RFS or OS [16]. In the present multicenter study, we similarly noted that high BMI did not have an impact on RFS, even after stratifying by stage of disease. Furthermore, in contrast to the report by Dhar *et al.*[31], BMI did not impact adequacy of lymph node sampling as patients across all BMI categories had an equivalent number of lymph nodes sampled at the time of surgery. In fact, all measured operative metrics such as operative time, blood loss, and need for blood transfusion were equivalent among the different BMI groups.

There has also been interest in understanding the potential impact of BMI on OS after oncologic surgery. In the study by Mullen *et al.* [30] using NSQIP data, the authors noted that underweight patients undergoing a range of abdominal cancer operations were at higher risk of immediate perioperative death compared with patients of normal BMI. In the present study, when operative procedures were restricted to gastrectomy only, BMI was not associated with perioperative mortality (obese, 2.6% *versus* overweight, 2.6% *versus*normal weight, 4.1% *versus* underweight, 3.6%; $P = 0.84$). Unlike the Mullen *et al.* study, which was restricted to examining only 30-d perioperative mortality found in the NSQIP database, the present study was able to investigate long-term outcomes. In looking at long-term survival, although underweight patients were noted to have a significantly shorter median and 5-y OS compared with patients of normal BMI (Fig. 2), this association disappeared in our multivariable model after adjusting for competing risk factors. Interestingly, underweight patients with a low preoperative albumin did seem to do particularly poorly. These data suggest that rather than baseline weight, overall nutritional status and weight loss may play a more important role. Research in cancer cachexia has identified an association with endogenous transmitters and inflammatory markers that contribute to a negative nitrogen balance, fatigue, and worse outcomes [32] and [33]. Perhaps not surprisingly, on adjusted analysis in our Cox proportional hazards model, BMI did not remain associated with long-term survival. Rather, in a competing risk model, other tumor-specific biological factors such as advanced T-stage and the presence of LVI and PNI dictated long-term survival outcome.

The present study had several limitations. As with all retrospective analysis, selection bias was a possibility. For example, operative strategy—including whether an operation was even offered or not—could have been based, in part, on BMI. Given that only patients who actually underwent surgery were included in the analytic cohort, the possibility that BMI itself may have been used to select patients for surgery could lead to a selection bias. It seems highly unlikely, however, that BMI was used as a surgical selection criterion in the overwhelming majority of patients with gastric cancer. Another limitation involves sample size. Although probably the largest, multi-institutional series of surgical gastric cancer patients in the United States, only 7.1% of our cohort was classified as being underweight according to BMI—making some subset analyses underpowered. Finally, although the multi-institutional nature of the cohort lends greatly to the generalizability of the present study, it did preclude standardized treatment patterns and protocols. This lack of treatment standardization should, however, have minimal impact on the main hypothesis being tested.

5. Conclusions

In conclusion, BMI did not impact perioperative morbidity among patients undergoing gastric resection for adenocarcinoma. Although tumor-specific biological factors such as tumor stage were the main drivers of long-term outcome on adjusted analyses, BMI (i.e., <18.5 kg/m^2) did not independently impact survival. Among underweight patients, however, there was a suggestion that long-term outcome was particularly poor among those patients with a low preoperative albumin. As such, these high-risk patients should have their nutritional status optimized both before and after gastrectomy in an attempt to modify this risk factor and, in turn, achieve better outcomes.

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Disclosure

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