World J Surg (2013) 37:1072–1081
DOI 10.1007/s00268-013-1942-8

World Journal of Surgery

# Impact of Obesity on Early Surgical and Oncologic Outcomes after Total Gastrectomy with "Over-D1" Lymphadenectomy for Gastric Cancer

**Giacomo Pata · Leonardo Solaini · Stefano Roncali · Mario Pasini · Fulvio Ragni**

Published online: 14 February 2013


**Abstract**
*Introduction* The purpose of the present study was to assess the impact of body mass index (BMI) on perioperative and pathologic outcomes after total gastrectomy with "over-D1" dissection for gastric cancer.
*Methods* Data on 161 patients undergoing total gastrectomy between 2005 and 2011 were reviewed. Patients were grouped into three categories by BMI: BMI $< 25$ kg/m$^2$ (63 normal-weight patients; 39.1 %), BMI $\geq 25$–$<30$ kg/m$^2$ (73 overweight patients; 45.3 %), and BMI $\geq 30$ kg/m$^2$ (25 obese patients; 15.6 %) and matched for the analysis of perioperative and cancer-related outcomes.
*Results* Operative time was longer for obese patients. Medical (mainly pulmonary) and surgical (mainly bleeding and wound infection) complications occurred more frequently in overweight/obese subjects. However, they were mostly managed conservatively (grade I–II in the Clavien-Dindo classification). The overall postoperative mortality was 0.9 %. Multivariate analysis identified the American Society of Anesthesiologists score and splenectomy, but not obesity, as independent risk factors for postoperative complications. The median number of lymph nodes retrieved differed significantly from group to group: obese 21 (IQR 18–26), versus overweight 24, versus normal weight 28 ($p = 0.031$). No difference was found in lymph node ratio and cancer-related parameters.
*Conclusions* Obese patients with operable gastric cancer can be candidates for standard extensive surgical resection, provided that pre-existing co-morbidities and potential intraoperative and postoperative complications are considered.

## Introduction

The World Health Organization projects that by 2015 more than 1.6 billion adults will be overweight and 700 million will be obese [1]. Obesity has been shown to be a risk factor for gastrointestinal cancer, and thus the effect of obesity on surgical outcomes in a cancer population is a timely issue [2–5]. Just like other sites of malignancy, an increased risk of gastric cancer has been noted in the obese population, probably caused by higher abdominal pressure and the resulting gastroesophageal reflux [6, 7]. Obese cancer patients have often been perceived as being at high risk of surgical complications. In fact, several technical disadvantages of gastrectomy for obese patients are expected, including poorer surgical visibility, blood oozing from soft tissues, a dissection plane hindered by adipose tissue, difficulty with anastomosis, and so forth. Several studies have demonstrated increased postoperative morbidity and mortality after gastrectomy with extended (≥D2) LN dissection in obese patients [8–13]. The effect of obesity on oncologic outcomes has been examined to a more limited extent. While some data have indicated obesity as an adverse factor impairing the oncologic adequacy of D2 dissection for gastric cancer [11], other studies have not noted similar results [14]. However, obesity has been defined very broadly in these studies and most authors

G. Pata (✉) · S. Roncali · M. Pasini · F. Ragni
2nd Division of General Surgery, Department of Medical and Surgical Sciences, Brescia Civic Hospital, P. le Spedali Civili 1, 25124 Brescia, Italy
e-mail: giacomopata@alice.it

L. Solaini
2nd Division of General Surgery, Department of Medical and Surgical Sciences, University of Brescia School of Medicine, 25124 Brescia, Italy

have included small numbers of “really” obese patients. Significantly, little is known to date about early surgical outcomes of obese patients undergoing “over-D1” lymph node dissection. In the present study we aimed to assess the impact of body mass index (BMI) as a surrogate marker for obesity in a patient cohort that has undergone total gastrectomy with “over-D1” LN dissection (TG-D1+) for gastric adenocarcinoma. The objectives include analysis of perioperative and cancer-related outcomes. Our hypothesis, based on previous literature, was that obesity would have negative effects on perioperative and pathologic outcomes of patients with gastric cancer undergoing a potentially curative total gastrectomy.

## Methods

A retrospective case-matched study was performed on 191 consecutive patients who underwent total gastrectomy for gastric cancer between January 2005 and September 2011 at the 2nd Division of General Surgery, Brescia Civic Hospital, Brescia, Italy. Exclusion criteria were as follows: surgery for gastric stump carcinoma and for tumors arising at or crossing the esophagogastric junction; preoperative chemotherapy; palliative resections; LN dissections different from “over-D1”; M1 gastric cancer patients; laparoscopy-assisted gastrectomies; and the presence of another malignancy. We have 161 patients left for the analysis. Patient weight and height were retrieved from anesthesia records, as charted on the day of surgery. BMI was defined as the patient’s weight in kilograms divided by height (in meters) squared. Patients were divided into three categories based on BMI: normal-weight (BMI $< 25$ kg/m$^2$), overweight (BMI $\geq 25$–$<30$ kg/m$^2$), or obese (BMI $\geq 30$ kg/m$^2$), according to the World Health Organization definition [15]. A total of 63 (39.1 %) subjects were classified as normal-weight patients; 73 (45.3 %) were classified as overweight, and 25 (15.6 %) were classified as obese patients. These three groups were matched for the analysis of perioperative and cancer-related (oncologic) outcomes. All patients were preoperatively evaluated by esophagogastroduodenoscopy and abdominal computed tomography (CT). In patients suspected of having metastasis to distant organs, positron emission tomography (PET)/CT scan, chest CT, or magnetic resonance imaging was selectively performed. Anesthesia records were accessed to define the American Society of Anesthesiologists (ASA) score, the intraoperative estimated blood loss (EBL), and operative time. The ASA score was used to compare patient’s preoperative overall physical health [16]. Common co-morbidities included diabetes mellitus, hypertension, cerebrovascular disease, coronary artery disease, arrhythmias, pulmonary disease, and liver and renal dysfunction. The postoperative complications were categorized according to the Clavien-Dindo classification [17] (Appendix). Risk factors analyzed for postoperative complications included gender, age, ASA score, BMI, pTNM stage, long-term anti-platelet therapy, operative time, and splenectomy. Postoperative pathology reports were accessed to determine tumor location; differentiation, number, and status of resected LN, and T status. The final pathologic stage was classified according to the 7th edition of the AJCC Cancer Staging Manual [18]. As the AJCC Cancer Staging Manual recommends that a minimum of 16 lymph nodes be examined, the patients most likely to be understaged (examined lymph nodes $\leq$15) were removed from the oncologic outcomes analysis.

### Operative procedure

Total gastrectomy always included a formal “over-D1” lymphadenectomy (LN stations 1–8a of the Japanese classification), also called D1.5 or D1+ lymphadenectomy. Briefly, lymphadenectomy comprised en bloc removal of all lymphatic tissue in the left and right paracardial regions, in suprapyloric and infrapyloric sites, along the lesser and greater curvatures, along the left gastric artery, and along the common hepatic artery. Dissection of the splenic artery and the celiac trunk, as well as the hepatoduodenal ligament, was performed only in patients who had enlarged nodes at this area on preoperative or intraoperative staging. In cases of invasion of neighboring structures by the tumor, combined resection was employed, with removal on demand of adjacent organs or part of organs. The spleen was removed only if the tumor was close to or directly invading either the tail of the pancreas or the splenic hilum, and/or suspected LN involvement was evident. Advanced sealing devices were never used. Intestinal continuity was restored by means of mechanical standard Roux-en-Y esophagojejunostomy performed with a 25 mm circular stapling device in all patients. A naso-jejunal tube was inserted intraoperatively and was removed by the third postoperative day (POD 3) in most patients. One or more abdominal drains were routinely placed before abdominal fascia closure. All patients received prophylactic antibiotics (ceftriaxone 2–3 g/day) starting half an hour before the laparotomy and continuing for a mean of 72 h. Subcutaneous thromboembolic prophylaxis with low molecular weight heparin (LMWH) 3,000–6,000 IU/day was administrated to all patients. For patients on long-term aspirin therapy, LMWH replaced antiplatelet therapy for 1 week before operation. Before recommencing oral nutrition, the integrity of the esophagoenteral anastomosis was controlled with water-soluble contrast swallow X-ray 5–6 days after operation.

### Evaluation of surgical outcomes

We considered as primary outcome measures the perioperative clinical course, the rates and severity of postoperative complications, and the length of hospital stay. Mortality was defined as lethal outcome during the operation or within the first 30 postoperative days. Postoperative complications, calculated for the same period, were classified as surgical or medical complications. Major bleeding was arbitrarily defined as any bleeding causing hemoglobin reduction $\geq$3 g/dl or requiring transfusion of $\geq$2 red blood cell units. The cancer-related parameters were considered secondary outcome measures. These outcomes were studied to assess whether the BMI of the patient was a determinant of safety and oncologic adequacy for total gastrectomy. In addition, preoperative variables in terms of the patients' baseline characteristics, co-morbidity, and perioperative course were analyzed to determine whether they had predictive values as risk factors for postoperative complications.

### Statistical analysis

One-way analysis of variance (ANOVA) was used to compare continuous variables with normal distribution (presented as mean and 95 % confidence interval [95 % CI] of the mean). The Mann–Whitney *U* test and Kruskal–Wallis one-way analysis of variance (ANOVA) were used to compare continuous variables not normally distributed (presented as median and interquartile range [IQR]). Normality of the distribution of variables was determined with the D'Agostino-Pearson test. The Chi square test or Fisher's exact test, when appropriate, was used to compare categorical variables. Patients with grade II or greater complications based on the Clavien-Dindo classification [17] (Appendix) were defined as having postoperative morbidity. Correlation analysis between BMI and morbidity grade, operative time, intraoperative EBL, postoperative hospital stay, numbers of retrieved lymph nodes (LN), numbers of metastatic LN, and the ratio of number of metastatic LN to total LN resected (lymph-node ratio) was performed with Spearman's rank test. Univariate logistic regression analysis was carried out to identify the risk factors for postoperative morbidity. The identified variables were subsequently entered into a multivariate logistic regression analysis in stepwise manner. Odds ratios (OR) and 95 % CI were calculated when indicated. For each analysis, the following potential predictive variables for postoperative complication were taken into account: age, gender, BMI, ASA score, splenectomy, operative time, long-term antiplatelet therapy, and TNM stage. A $p$ value $< 0.05$ was considered statistically significant. All tests were two-sided. Statistical analysis was performed with statistical software for biomedical research (McCalc Software for Windows, version 10.2.0.0, Mariakerke, Belgium).

## Results

Characteristics of patients in terms of demographics, preoperative co-morbidities, and preoperative laboratory values are shown in Table 1. Overall, the median age of the study population was 71 years (IQR 62–77 years), the male/female ratio was 93/68, and the mean BMI was 25.7 kg/m$^2$ (95 % CI 25.2–26.3 kg/m$^2$). In particular, the mean BMI of normal-weight patients was 22.6 kg/m$^2$ (95 % CI 22.2–23.1 kg/m$^2$); the mean BMI of overweight patients was 26.3 kg/m$^2$ (95 % CI 26–26.6 kg/m$^2$), and the mean BMI of obese patients was 31.9 kg/m$^2$ (95 % CI 31.4–32.4 kg/m$^2$). The BMI difference between normal-weight patients, overweight patients, and obese patients was statistically significant ($p < 0.001$). There were no significant differences in age, gender, preoperative hemoglobin, and antiplatelet therapy assumption among the three study groups. Overall the co-morbidity rate was similar in the three study groups, although patients in the overweight and obesity groups showed more severe dysfunctions. Furthermore, diabetes mellitus and arterial hypertension were significantly more frequent among overweight and obese subjects than in those of normal weight. This reflects the significant differences in ASA class ($p = 0.025$) between the three groups, with 60.3 and 68 % of overweight and obese patients, respectively, in class III–IV versus 38.1 % in the normal weight group. There were no differences between the three study groups in terms of tumor location, Lauren histological classification, and TNM stage (Table 1). As for surgical outcomes (Table 2), extended resections were performed in 38 cases, including two patients with resection of the colon, one with bilateral annessiectomy, one with distal pancreatectomy, and 36 with splenectomy (no significant inter-group differences).

### Perioperative morbidity and mortality

Operative time (OT) was longer for obese patients (median 180 min; IQR 149–190 min) compared with both the overweight patients (median 160 min; IQR 140–180 min) and the normal-weight patients (median 142 min; IQR 120–160 min); $p = 0.0005$. Obese patients were more likely to have a greater operative EBL (median 300 ml) compared with both the overweight patients (median 100 ml) and the normal-weight patients (median 0 ml); $p < 0.0001$. Similar results were obtained when BMI was modeled as a continuous variable rather than categorical variables: rho ($\rho$) for OT = 0.36, 95 % CI 0.22–0.5; $p < 0.0001$; $\rho$ for EBL = 0.42; 95 % CI 0.29–0.54;

**Table 1** Baseline characteristics of the patients who underwent TG-D1+

| | Normal weight (BMI < 25 kg/m$^2$) ($n$ = 63) | Overweight (BMI 25 to <30 kg/m$^2$) ($n$ = 73) | Obese (BMI ≥ 30 kg/m$^2$) ($n$ = 25) | $p$ value |
|---|---|---|---|---|
| Body mass index (BMI), kg/m$^2$: mean; 95 % CI | 22.6; 22.2–23.1 | 26.3; 26–26.6 | 31.9; 31.4–32.4 | <0.001 |
| Age, years; median; IQR; range[a] | 70; 63–78;41–88 | 67; 61–75; 33–84 | 70; 62–79; 51–90 | 0.301 |
| Male/female ratio | 33/30 | 44/29 | 16/9 | 0.513 |
| Preoperative co–morbidities[b] | 61 (96.8 %) | 73 (100 %) | 25 (100 %) | 0.207 |
| Coronary artery disease | 13 (20.6 %) | 15 (20.5 %) | 4 (16 %) | |
| Arrhythmia | 8 (12.7 %) | 10 (13.7 %) | 3 (12 %) | |
| Cerebrovascular disease | 7 (11.1 %) | 7 (9.6 %) | 2 (8 %) | |
| Diabetes mellitus | 3 (4.8 %) | 14 (19.2 %) | 5 (20 %)* | |
| Hypertension | 25 (39.7 %) | 41 (56.2 %) | 17 (68 %)** | |
| Pulmonary dysfunction | 10 (15.9 %) | 13 (17.8 %) | 5 (20 %) | |
| Liver dysfunction | 6 (9.5 %) | 7 (9.6 %) | 4 (16 %) | |
| Renal dysfunction | 7 (11.1 %) | 8 (11 %) | 3 (12 %) | |
| Antiplatelet therapy | 13 (20.6 %) | 12 (16.4 %) | 6 (24 %) | 0.873 |
| Preoperative hemoglobin, g/dl: mean; 95 % CI | 12.7; 12.5–12.9 | 12.5; 12.1–12.9 | 12.4; 12.1–12.7 | 0.371 |
| ASA grade | | | | 0.025 |
| I | 2 (3.2 %) | 0 | 0 | |
| II | 37 (58.7 %) | 29 (39.7 %) | 8 (32 %) | |
| III | 24 (38.1 %) | 38 (52.1 %) | 15 (60 %) | |
| IV | 0 | 6 (8.2 %) | 2 (8 %) | |
| Tumor site | | | | 0.115 |
| Proximal third | 4 (6.3 %) | 14 (19.2 %) | 3 (12 %) | |
| Middle third | 43 (68.3 %) | 35 (47.9 %) | 14 (56 %) | |
| Lower third | 16 (25.4 %) | 24 (32.9 %) | 8 (32 %) | |
| Lauren classification | | | | 0.363 |
| Intestinal | 41 (65.1 %) | 52 (71.2 %) | 14 (56 %) | |
| Diffuse | 22 (34.9 %) | 21(28.8 %) | 11 (44 %) | |
| TNM stage[c] | | | | 0.951[d] |
| IA | 12 (20.3 %) | 10 (14.9 %) | 4 (17.4 %) | |
| IB | 7 (11.9 %) | 7 (10.5 %) | 2 (8.7 %) | |
| IIA | 5 (8.5 %) | 7 (10.5 %) | 3 (13 %) | |
| IIB | 6 (10.2 %) | 7 (10.5 %) | 2 (8.7 %) | |
| IIIA | 9 (15.2 %) | 16 (23.9 %) | 5 (21.8 %) | |
| IIIB | 11 (18.7 %) | 12 (17.9 %) | 4 (17.4 %) | |
| IIIC | 9 (15.2 %) | 8 (11.8 %) | 3 (13 %) | |

95 % CI: 95 % confidence interval of the mean

*Difference was statistically significant: $p = 0.031$; **difference was statistically significant: $p = 0.032$

[a] IQR (interquartile range) represents the numerical difference between the 25th and 75th percentiles

[b] At least one co-morbidity

[c] Patients with ≤15 lymph nodes examined were removed from group analysis

[d] Stage I–II versus III

$p < 0.0001$. Postoperative complications are listed in Table 2. Medical complications occurred in the overweight and obesity groups two to three times more frequently, respectively, than in the control group ($p = 0.031$). Pulmonary dysfunction was the most frequent complaint observed in the former groups, and surgical complications, including postoperative bleeding, had a higher incidence in overweight and obese subjects than among normal-weight patients ($p = 0.034$) (Table 2). Major bleeding was the most common surgical complication, and its incidence was higher in the overweight and obese groups (30.1 and 52 %, respectively) than in the normal-weight group (23.8 %);

**Table 2** Surgical outcomes, postoperative complications and cancer-related parameters after TG-D1+

| | Normal weight (BMI < 25 kg/m²) ($n$ = 63) | Overweight (BMI 25 to < 30 kg/m²) ($n$ = 73) | Obese (BMI ≥ 30 kg/m²) ($n$ = 25) | $p$ value |
|---|---|---|---|---|
| Operative time, min: median; IQR[a] | 142; 120–160 | 160; 140–180 | 180; 149–190 | 0.0005 |
| Intraoperative estimated blood loss, ml; median; IQR[a] | 0; 0–200 | 100; 0–300 | 300; 200–525 | <0.0001 |
| Number of lymph nodes harvested: median; IQR[a] | 28; 24–38 | 24; 19–28 | 21; 18–26 | 0.031 |
| Metastatic lymph nodes: median; IQR[a] | 3; 0–9 | 3; 0–7 | 2; 0–5 | 0.567 |
| Lymph node ratio[d]: median; IQR[a] | 0.1; 0–0.4 | 0.12; 0–0.3 | 0.1; 0–0.21 | 0.646 |
| Splenectomy | 14 (22.2 %) | 15 (20.5 %) | 7 (28 %) | 0.742 |
| Diet start, days: median; IQR[a] | 6; 5–7 | 6; 5–6.5 | 6; 5–7 | 0.820 |
| Medical complications, patients (%)[b] | 6 (9.5 %) | 16 (21.9 %) | 8 (32 %) | 0.031 |
| Cardiac | 2 (3.2 %) | 3 (4.1 %) | 1 (4 %) | |
| Pulmonary* | 3 (4.8 %) | 9 (12.3 %) | 6 (24 %) | |
| Liver dysfunction | 0 | 1 (1.4 %) | 0 | |
| Renal dysfunction | 3 (4.8 %) | 3 (4.1 %) | 1 (4 %) | |
| Deep venous thrombosis | 2 (3.2 %) | 1 (1.4 %) | 0 | |
| Surgical complications, patients (%)[b] | 18 (28.6 %) | 35 (47.9 %) | 13 (52 %) | 0.034 |
| Anastomotic leakage/reoperated patients | 2 (3.2 %)/1 (1.6 %) | 1 (1.4 %)/1 (1.4 %) | 0 | |
| Duodenal stump leakage/reoperated patients | 4 (6.4 %)/3 (4.8 %) | 4 (5.5 %)/3 (4.1 %) | 2 (8 %)/1 (4 %) | |
| Intestinal ischemia/reoperated patients | 2 (3.2 %)/2 (3.2 %) | 1 (1.4 %)/1 (1.4 %) | 0 | |
| Intestinal obstruction/reoperated patients | 2 (3.2 %)/1 (1.6 %) | 0 | 1 (4 %)/0 | |
| Acute pancreatitis/reoperated patients | 2 (3.2 %)/1 (1.6 %) | 0 | 1 (4 %)/0 | |
| Pancreatic fistula/reoperated patients | 1 (1.6 %)/1 (1.6 %) | 1 (1.4 %)/0 | 1 (4 %)/0 | |
| Wound infection** | 0 | 2 (2.7 %) | 3 (12 %) | |
| Abdominal infection | 0 | 1 (1.4 %) | 0 | |
| Major bleeding[c], ***/transfused patients/reoperated patients | 15 (23.8 %)/12 (19 %)/0 | 22 (30.1 %)/13 (17.8 %)/1 (1.4 %) | 13 (52 %)/5 (20 %)/1 (4 %) | |
| Postoperative hemoglobin reduction, g/dl: median; IQR[a] | 2.2; 1.4–2.9 | 2.4; 1.7–2.4 | 2.3; 1.3–2.8 | 0.332 |
| Hospital stay, days: median; IQR[a] | 10; 9–12 | 11; 9–14 | 11; 9–13 | 0.112 |
| Mortality | 0 | 1 (1.4 %) | 0 | 0.545 |

*Difference was statistically significant: $p = 0.033$; **difference was statistically significant: $p = 0.013$; ***difference was statistically significant: $p = 0.035$

[a] IQR (interquartile range) represents the numerical difference between the 25th and 75th percentiles

[b] More than one complication may be reported in the same patient

[c] Any bleeding causing hemoglobin reduction ≥3 g/dl or requiring transfusion of ≥2 red blood cell units

[d] The ratio of number of metastatic lymph nodes (LN) to total LN resected per patient

$p = 0.035$. However, bleeding did not require more blood transfusions or surgical revision in the inter-group analysis ($p$ = n.s.) (Table 2). Similarly, wound infection was less frequently recorded among normal-weight patients than in the control groups ($p = 0.013$). Table 3 shows the postoperative complications recorded in the three study groups. Complications (Clavien classification) correlated closely with both the BMI and ASA grade: $\rho$ for BMI = 0.29; 95 % CI 0.14–0.43; $p = 0.0003$; $\rho$ for ASA = 0.45; 95 % CI 0.32–0.57; $p < 0.0001$. Although complications were more frequently observed in overweight and obese subjects, they were managed conservatively in most cases and did not require significant extension of hospital stay (grade I–II complications). Hence no significant difference was found when patients with no complication or grade I complications were compared with patients with grade II or greater complications in inter-group analysis (normal-weight versus overweight versus obese patients) ($p = 0.648$) (Table 3). In fact obese patients had similar median length of stay (11 days, IQR 9–13 days) to overweight (11 days, IQR 9–14 days) and normal-weight (10 days, IQR 9–12 days) patients; $p = 0.112$. Hospital stay was closely related to postoperative complications (Clavien classification) ($\rho = 0.50$; 95 % CI 0.38–0.61; $p < 0.0001$) but not to BMI ($\rho = 0.056$; 95 % CI −0.1 to 0.21; $p = 0.49$). The postoperative 30-day death rate was 0.9 % (one patient in the overweight group). The death occurred on POD 3 as a result of septic shock following anastomotic leakage.

### Impact of BMI on oncologic outcomes

The median number of lymph nodes retrieved was 25 (IQR 19–36) per patient. There was a significant difference in the median number of LN harvested when stratified by BMI: obese, 21 (IQR 18–26) versus overweight, 24 (IQR 19–28) versus normal weight, 28 (IQR 24–38); $p = 0.031$ (Table 2). Overall, 12/161 (7.5 %) patients had ≤15 LN harvested. According to BMI class, the proportion was: normal weight, 4/63 (6.4 %); versus overweight, 6/73 (8.2 %); versus obese, 2/25 (8 %); $p = 0.91$. Some 70.2 % of patients enrolled in the study had LN metastases (N+). Specifically, the percentage of patients with N + was similar in each BMI category (obese, 64 % versus overweight, 72.6 % versus normal weight, 70 %; $p = 0.713$) (Table 1). BMI was not associated with a higher incidence of LN with metastatic involvement, as the median number of metastatic LN was 2–3 per patient for each BMI category ($p = 0.567$) (Table 2). The ratio of the number of metastatic LN to total LN resected per patient (lymph node ratio) was also comparable ($p = 0.646$) (Table 2). Similar results were obtained when BMI was modeled as a continuous variable rather than as a categorical variable: $\rho$ for number of LN retrieved = 0.2; 95 % CI 0.1–0.3; $p = 0.003$; $\rho$ for number of metastatic LN = −0.007; 95 % CI −0.16–0.15; $p = 0.93$; $\rho$ for LN ratio = −0.003, 95 % CI −0.16–0.15; $p = 0.97$.

### Predictors of postoperative complications

Patients with grade II or greater complications were considered positive for postoperative morbidity. At univariate analysis, the patient's age, BMI, ASA score, antiplatelet therapy assumption, and splenectomy were found to be predictive of postoperative complications. Conversely gender, operative time, and TNM stage were not significantly correlated to postoperative 30-day morbidity or mortality (Table 4). At multivariate analysis, only ASA score and splenectomy were confirmed as independent risk factors for postoperative complications (Table 4). In particular, ASA score was closely associated to both medical ($\rho = 0.34$; 95 % CI 0.2–0.47; $p < 0.0001$) and surgical postoperative complications ($\rho = 0.42$; 95 % CI 0.28–0.54; $p < 0.0001$). No significant difference was found between the respective areas under the curve (AUC) with receiver operating characteristic (ROC) curve analysis (difference between AUC = −0.022; $p = 0.765$).

## Discussion

Several large randomized controlled trials in Europe have reported increased postoperative morbidity after gastrectomy with ≥D2 LN dissection when compared with less extended lymphadenectomy [19–24]. The greater number of obese patients in European countries than in Asian countries may have an impact on this unfavorable outcome. BMI is a widely accepted indicator of obesity. Higher BMI is related to prolonged operating time, increased intraoperative bleeding, and a decreased number of dissected LN. It is also associated with postoperative morbidity, postoperative hospital death, and poor long-

**Table 3** Postoperative complications according to the Clavien-Dindo classification [17] after TG-D1+

| Clavien-Dindo classification | Normal weight (BMI < 25 kg/m$^2$) ($n = 63$) | Overweight (BMI 25 to < 30 kg/m$^2$) ($n = 73$) | Obese (BMI ≥ 30 kg/m$^2$) ($n = 25$) | $p$ value[a] |
|---|---|---|---|---|
| No complications | 39 (61.9 %) | 29 (39.8 %) | 6 (24 %) | 0.648 |
| Grade I | 6 (9.5 %) | 12 (16.4 %) | 7 (28 %) | |
| Grade II | 11 (17.5 %) | 15 (20.5 %) | 9 (36 %) | |
| Grade IIIa | 3 (4.8 %) | 5 (6.8 %) | 2 (8 %) | |
| Grade IIIb | 4 (6.3 %) | 8 (11 %) | 1 (4 %) | |
| Grade IVa | 0 | 3 (4.1 %) | 0 | |
| Grade IVb | 0 | 0 | 0 | |
| Grade V | 0 | 1 (1.4 %) | 0 | |

[a] Patients with no complications or grade I complications were compared with patients having grade II or greater complications in inter-group analysis (normal-weight versus overweight versus obese patients: $p$ = not significant)

**Table 4** Univariate and multivariate logistic regression analyses of potential risk factors for complications (classified according to the Clavien-Dindo classification [17]) after TG-D1+

| Independent variables | Univariate analysis[a] | | Multivariate analysis | |
|---|---|---|---|---|
| | OR (95 % CI) | *p* value | OR (95 % CI) | *p* value |
| Age | 1.05 (1.01–1.08) | 0.01 | – | – |
| ASA score | 4.16 (2.23–7.75) | <0.0001 | 4.32 (2.26–8.28) | <0.0001 |
| Splenectomy | 4.65 (2.1–10.27) | 0.0001 | 5.14 (2.15–12.27) | 0.0002 |
| BMI | 1.13 (1.02–1.24) | 0.016 | – | – |
| Antiplatelet therapy | 2.74 (1.23–6.1) | 0.014 | – | – |
| Operative time | 1 (0.99–1.01) | 0.36 | – | – |
| Gender | 0.93 (0.49–1.78) | 0.82 | – | – |
| TNM stage | 1.07 (0.9–1.26) | 0.45 | – | – |

Patients with grade II or greater complications based on the Clavien-Dindo classification were considered positive for postoperative morbidity

OR (95 % CI): odds ratio and 95 % confidence interval

[a] Of all the variables tested in univariate analysis, only those with $p$ values $\leq 0.05$ were entered into multivariate analyses in a stepwise manner until all variables remaining in the model were significant

term survival after D2 dissection for gastric cancer [8, 11–13, 25]. Therefore the effects of splenectomy or pancreatectomy during D2 dissection in obese patients must be carefully considered [21–24]. It is worth noting that, to date, there are poor data on the effect of BMI on early surgical outcomes and LN retrieval after open TG-D1+. To avoid subjectivity and imprecision in complication reporting, we adopted the Clavien-Dindo classification [17]. It has been increasingly used in the surgical literature and in studies addressing the role of obesity in gastric cancer surgery [26]. First of all, our study revealed a significant difference in the way of presenting symptoms and ASA grade across the BMI spectrum. In fact, obesity turned out to be linked to a greater risk of other co-morbidities, mainly diabetes mellitus and arterial hypertension, both of which significantly affect the ASA grading. We observed greater operative blood loss, higher incidence of pulmonary dysfunction and wound infection in high BMI classes, most notably in the morbidly obese group. However, the majority of such perioperative complications were minor and required either no therapy at all or a simple routine intervention (grade I–II complications). Thus we did not observe a significant increase in complication rate and severity, duration of in-hospital stay, or operative mortality across the BMI spectrum. This is in contrast with reports after D2 dissection, which however dealt with different classification scales [9, 12, 26–28]. Results from our logistic regression analysis are relevant. On univariate analysis, BMI along with the patient's age, ASA score, antiplatelet therapy assumption, and splenectomy turned out to be predictive of postoperative complications, whereas on multivariate analysis BMI lost statistical significance and only ASA score and splenectomy were confirmed as independent risk factors. Data from other institutions also showed that BMI was not an independent predictor of postoperative complications, but rather a confounding factor when associated with higher ASA score [25, 28]. As expected, the operative time increased with increasing weight and was especially evident in patients with morbid obesity. Similar conclusions have been drawn after D2 LN dissection [9, 12, 25–29]. It is clear that morbid obesity may increase the technical challenge of total gastrectomy even when coupled with "over-D1" lymphadenectomy. We did not find any association between BMI (or morbid obesity) and any of the cancer-related parameters despite a detailed analysis of factors, including tumor site, TNM stage, Lauren classification, lymph node status, and lymph node ratio. This observation seems to be in contrast to increasing epidemiologic evidence of a link between gastric cancer and obesity. Nevertheless, findings similar to those from our study have been reported [29]. Few researchers have assessed whether LN harvest is compromised by obesity. In the present study the increased individual BMI significantly correlated with the decreased number of retrieved LN, indicating that excessive intra-abdominal visceral fat precludes the complete dissection of LN. Furthermore, during the handling of a specimen the isolation of LN from the retrieved soft tissue with abundant fat might be more difficult than retrieval in non-obese patients. Data in the literature are contradictory. Some authors have reported a lower LN yield in obese patients after D2 dissection [11, 25, 29, 30], whereas other studies have failed to corroborate these findings [14, 31]. Our median number of LN retrieved (25) was in line with reports in literature of open TG-D1+, which range from 15 to 30 LN harvested [32, 33]. Also, in our series, 12/161 patients (7.5 %) had ≤15 LN harvested, and this figure is consistent with large published series [19, 23, 34, 35]. Patients with BMI ≥ 25 kg/m$^2$ were more likely to be under-staged, although not statistically. It is of note that the difference in the prevalence and degree of "overweight" patients between Far East and Western countries makes data from Asian institutions hard to compare with studies like this one or others from European or US hospitals. In addition, most Asian patients classified as obese should be classified as overweight for comparison with Western studies [25, 27, 29, 30]. In fact, in Europe and the USA obesity is defined as BMI > 30 kg/m$^2$, which accounts for 20–25 % of these populations [36, 37]. This percentage is significantly higher than the 15 and 1.0 % prevalence of patients having BMI ≥ 25 and BMI > 30 kg/m$^2$, respectively, as reported in a large randomized Japanese study [9]. Significantly, about 45 % of patients enrolled in the present study were overweight, and 15 % were obese. In addition, the mean BMI of our study population was almost 27 kg/m$^2$, which is far higher than values reported in Korean or Japanese studies (range 22–23.5 kg/m$^2$) [25, 26, 30, 31, 38, 39]. This result agrees with the difference in BMI found in a comparative study between Japanese and US patients undergoing surgery for gastric carcinoma [40]. It is noteworthy that the overall incidence of esophagojejunal anastomosis leakage was 1.9 % in the present study, comparable with the lower anastomotic leak rate cited by centers with adequate case loads, which ranges between 1.3 and 15.9 % [41–44]. Meanwhile, the relatively high incidence of duodenal stump dehiscence (6.2 %) needs to be stressed. This finding should be considered as a consequence of a not routinely hand-sewn duodenal stump until 2010. After an internal audit of our achievements to date, we decided to carry out hand sewing of the duodenal stump on a routine basis. Since that decision was taken, no similar complications have been reported.

In summary, our analysis indicates that obesity per se is not associated with an increased perioperative morbidity or mortality after TG-D1+, although obese patients had longer operative time, higher risk of perioperative blood loss, and a higher incidence of wound infection. In contrast, ASA grade was closely associated with postoperative complications. In particular, the presence of a medical comorbidity, as reflected by ASA class, increased the risk of both surgical and medical complications. This finding must be carefully considered when dealing with obese patients, who usually have a high ASA score: >60 % of our overweight and obese patients were in class III–IV compared with <40 % in the normal-weight group. In the present study, obesity affected operative oncologic outcomes. In particular, the number of lymph nodes retrieved was lower in obese subjects, although lymph node status and lymph node ratio were comparable in obese and non-obese patients.

We are aware that the surgeon factor might be a bias for this study. However, most of the procedures were performed by the chief surgeon (R.F.), and the rest were performed by only the most experienced members of the surgical team (all of them consultant surgeons). Also, the composition of the surgical team remained the same throughout the entire study period. In addition, the short study period was chosen to avoid all possible biases linked to the rotation of the team members and it covers the phase of professional "maturity" of the whole surgical team, corresponding to the "plateau" of the learning curve. We therefore believe that the impact of this variable on the outcomes, if present, is minimal.

In conclusion, this study showed that in experienced units and in the absence of severe ASA score, obese patients should not be denied TG-D1+ based on BMI only. That said, a word of caution is needed about the greater risk of perioperative blood loss, which could lead to potentially serious complications.

## Appendix

See Table 5

**Table 5** Clavien-Dindo classification [17] of postoperative complications adopted in the present study

| Grades | Definition |
|---|---|
| I | Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions |
| | Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, and electrolytes and physiotherapy |
| | This grade also includes wound infections opened at the bedside |
| II | Requiring pharmacological treatment with drugs other than such allowed for grade I complications |
| | Blood transfusions and total parenteral nutrition are also included |
| III | Requiring surgical, endoscopic or radiological intervention: |
| IIIa | Intervention not under general anesthesia |
| IIIb | Intervention under general anesthesia |
| IV | Life-threatening complications (including central nervous system complications)[a] requiring IC/ICU management: |
| IVa | Single-organ dysfunction (including dialysis) |
| IVb | Multiorgan dysfunction |
| V | Death of the patient |

IC: intermediate care; ICU: intensive care unit

[a] Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks

## References


1. World Health Organization (2012) Obesity and overweight. http://www.who.int/mediacentre/factsheets/fs311/en/index.html. Accessed 1 April 2012
2. Calle EE, Rodriguez C, Walker-Thurmond K et al (2003) Overweight, obesity, and mortality from cancer in a prospective studied cohort of US adults. N Engl J Med 348:1625–1638
3. Nock NL, Thompson CL, Tucker TC et al (2008) Associations between obesity and changes in adult BMI over time and colon cancer risk. Obesity (Silver Spring) 16:1099–1104
4. Giovannucci E, Michaud D (2007) The role of obesity and related metabolic disturbances in cancers of the colon, prostate, and pancreas. Gastroenterology 132:2208–2225
5. Kojima M, Wakai K, Tamakoshi K, JACC Study Group et al (2004) A prospective study of body size and colon cancer mortality in Japan: the JACC study. Int J Obes Relat Metab Disord 28:551–558
6. Lindblad M, Rodríguez LA, Lagergren J (2005) Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric noncardia adenocarcinoma among men and women in a nested case control study. Cancer Causes Control 16:285–294
7. Lagergren J, Bergström R, Nyrén O (1999) Association between body mass and adenocarcinoma of the esophagus and gastric cardia. Ann Intern Med 130:883–890
8. Kodera Y, Sasako M, Yamamoto S et al (2005) Identification of risk factors for the development of complications following extended and superextended lymphadenectomies for gastric cancer. Br J Surg 92:1103–1109
9. Tsujinaka T, Sasako M, Yamamoto S et al (2007) Influence of overweight on surgical complications for gastric cancer: results from a randomized control trial comparing D2 and extended paraaortic D3 lymphadenectomy (JCOG9501). Ann Surg Oncol 14:355–361
10. Moriwaki Y, Kunisaki C, Kobayashi S et al (2003) Does body mass index (BMI) influence morbidity and long-term survival in gastric cancer patients after gastrectomy? Hepatogastroenterology 50:284–288
11. Dhar DK, Kubota H, Tachibana M et al (2000) Body mass index determines the success of lymph node dissection and predicts the outcome of gastric carcinoma patients. Oncology 59:18–23
12. Kodera Y, Ito S, Yamamura Y et al (2004) Obesity and outcome of distal gastrectomy with D2 lymphadenectomy for carcinoma. Hepatogastroenterology 51:1225–1228
13. Inagawa S, Adachi S, Oda T et al (2000) Effect of fat volume on postoperative complications and survival rate after D2 dissection for gastric cancer. Gastric Cancer 3:141–144
14. Gretschel S, Christoph F, Bembenek A et al (2003) Body mass index does not affect systematic D2 lymph node dissection and postoperative morbidity in gastric cancer patients. Ann Surg Oncol 10:363–368
15. http://www.who.int/mediacentre/factsheets/fs311/en/index.html. Accessed 1 April 2012
16. http://www.asahq.org/clinical/physicalstatus.htm. Accessed 1 April 2012
17. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
18. Washington K (2010) 7th Edition of the AJCC cancer staging manual: stomach. Ann Surg Oncol 17:3077–3079
19. Cuschieri A, Weeden S, Fielding J et al (1999) Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical co-operative group. Br J Cancer 79:1522–1530
20. Cuschieri A, Fayers P, Fielding J et al (1996) Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomized controlled surgical trial. The surgical cooperative group. Lancet 347:995–999
21. Hartgrink HH, van de Velde CJ, Putter H et al (2004) Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. J Clin Oncol 22:2069–2077
22. Bonenkamp JJ, Songun I, Hermans J et al (1995) Randomized comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet 345:745–748
23. Edwards P, Blackshaw PG, Barry J (2003) Randomized comparison of D1 versus modified D2 gastrectomy for gastric cancer. Br J Surg 90(Suppl 1):1888–1892
24. Jansen EPM, Boot H, Verheij M et al (2005) Optimal locoregional treatment in gastric cancer. J Clin Oncol 23:4509–4517
25. Lee JH, Paik YH, Lee JS et al (2007) Abdominal shape of gastric cancer patients influences short-term surgical outcomes. Ann Surg Oncol 14:1288–1294
26. Sugisawa N, Tokunaga M, Tanizawa Y et al (2012) Intraabdominal infectious complications following gastrectomy in patients with excessive visceral fat. Gastric Cancer 15:206–212
27. Nobuoka D, Gotohda N, Kato Y et al (2011) Influence of excess body weight on the surgical outcomes of total gastrectomy. Surg Today 41:928–934
28. Ojima T, Iwahashi M, Nakamori M et al (2009) Influence of overweight on patients with gastric cancer after undergoing curative gastrectomy: an analysis of 689 consecutive cases managed by a single center. Arch Surg 144:351–358
29. Oh SJ, Hyung WJ, Li C et al (2009) Effect of being overweight on postoperative morbidity and long-term surgical outcomes in proximal gastric carcinoma. J Gastroenterol Hepatol 24:475–479
30. Tokunaga M, Hiki N, Fukunaga T et al (2009) Effect of individual fat areas on early surgical outcomes after open gastrectomy for gastric cancer. Br J Surg 96:496–500
31. Tanaka K, Miyashiro I, Yano M et al (2009) Accumulation of excess visceral fat is a risk factor for pancreatic fistula formation after total gastrectomy. Ann Surg Oncol 16:1520–1525
32. Mariette C, Castel B, Toursel H et al (2002) Surgical management and long-term survival after adenocarcinoma of the cardia. Br J Surg 89:1156–1163
33. Ichikura T, Chochi K, Sugasawa H et al (2005) Modified radical lymphadenectomy (D1.5) for T2–3 gastric cancer. Langenbecks Arch Surg 390:397–402
34. Mullaney PJ, Wadley MS, Hyde C et al (2002) Appraisal of compliance with the UICC/AJCC staging system in the staging of gastric cancer. Union international Contra la Cancrum/American joint committee on cancer. Br J Surg 89:1405–1408
35. Wang J, Dang P, Raut CP et al (2012) Comparison of a lymph node ratio-based staging system with the 7th AJCC system for gastric cancer: analysis of 18,043 patients from the SEER database. Ann Surg 255:478–485
36. Seidell JC, Flegal KM (1997) Assessing obesity: classification and epidemiology. Br Med Bull 53:238–252
37. Kuczmarski RJ, Flegal KM, Campbell SM et al (1994) Increasing prevalence of overweight among US adults. The national health and nutrition examination surveys, 1960 to 1991. J Am Med Assoc 272:205–211
38. Jee SH, Sull JW, Park J et al (2006) Body-mass index and mortality in Korean men and women. N Engl J Med 355:779–787
39. Nobuoka D, Gotohda N, Konishi M et al (2008) Prevention of postoperative pancreatic fistula after total gastrectomy. World J Surg 32:2261. doi:10.1007/s00268-008-9683-9s
40. Noguchi Y, Yoshikawa T, Tsuburaya A et al (2000) Is gastric carcinoma different between Japan and the United States? Cancer 89:2237–2246

41. Gockel I, Pietzka S, Gönner U et al (2005) Subtotal or total gastrectomy for gastric cancer: impact of the surgical procedure on morbidity and prognosis—analysis of a 10-year experience. Langenbecks Arch Surg 390:148–155
42. Otsuji E, Fujiyama J, Takagi T et al (2005) Results of total gastrectomy with extended lymphadenectomy for gastric cancer in elderly patients. J Surg Oncol 91:232–236
43. Degiuli M, Sasako M, Ponzetto A et al (1997) Extended lymph node dissection for gastric cancer: results of a prospective, multicentre analysis of morbidity and mortality in 118 consecutive cases. Eur J Surg Oncol 23:310–314
44. Oh SJ, Choi WB, Song J, Yonsei Gastric Cancer Clinic et al (2009) Complications requiring reoperation after gastrectomy for gastric cancer: 17 years experience in a single institute. J Gastrointest Surg 13:239–245