ORIGINAL ARTICLE

Influence of Overweight on Patients With Gastric Cancer After Undergoing Curative Gastrectomy

An Analysis of 689 Consecutive Cases Managed by a Single Center

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Hypothesis: Overweight (body mass index [calculated as weight in kilograms divided by height in meters squared], ≥25.0) has an effect on surgical results, postoperative complications, and long-term survival in patients with gastric cancer who underwent curative gastrectomy.

Design: Retrospective study from January 1, 1992, through December 31, 2002.

Setting: Wakayama Medical University Hospital.

Patients: This study included 689 patients who underwent curative gastrectomy (R0). Patients who underwent laparoscopic gastrectomy, gastrectomy with pancreaticoduodenectomy, gastrectomy with another organ resection (liver, colon, or ovary), or gastrectomy with thoracotomy were not included.

Main Outcome Measures: Duration of operation, amount of blood loss, incidence of postoperative complications, and survival analysis.

Results: The mean (SD) duration of the operation was longer in the overweight group (315 [75] minutes) than in the normal-weight group (277 [85] minutes) ($P<.001$). The mean (SD) intraoperative blood loss was larger in the overweight group (882 [764] mL) than in the normal-weight group (536 [410] mL) ($P<.001$). The rates of postoperative complications (anastomotic leakage, pancreatic fistula, and intra-abdominal abscess) were significantly higher in the overweight group ($P<.05$). Multivariate logistic regression analysis identified that postoperative complications were significantly associated with being overweight ($P=.01$) and with undergoing pancreatectomy ($P=.03$). Disease-specific and overall survival did not show any significant difference between the 2 groups.

Conclusions: Being overweight is not a poor risk factor for survival in patients with gastric cancer, although it is independently predictive of postoperative complications.

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In a Japanese randomized controlled trial, Japan Clinical Oncology Group Study 9501 (JCOG9501), there was no difference in the incidence of major postoperative complications between the standard D2 dissection and D2 with extended para-aortic dissection (D3) in patients with gastric cancer (hereinafter referred to as gastric cancer patients) undergoing gastrectomy.[1] However, 2 large European randomized controlled trials that compared D1 and D2 dissections reported an increase in surgical morbidity and mortality in the D2 dissection group.[2,3] These studies failed to show a survival benefit in the D2 dissection group. Japanese patients are generally slender, with a lower body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) than white patients. These differences in patient physique may partly explain the high mortality and morbidity. In fact, the JCOG9501 data showed that overweight patients with a BMI greater than 25.0 are at increased risk for the postoperative complications of abdominal abscess and pancreatic fistula after gastrectomy with D2 dissection.[4]

See Invited Critique at end of article

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The following are critiques of the JCOG9501 trial. First, there was an extremely low number of patients with concomitant disease because the eligibility criteria for this trial were severe. Therefore, the JCOG9501 trial results do not reflect the risk of the postoperative complications of overweight patients with serious concomitant disease. Second, this trial did not include D1 dissection. Japan, compared with Western countries, has a higher number of patients with early gastric cancer. Approximately half of the gastric cancer patients have mucosal or submucosal gastric cancer at the time of diagnosis.[5] According to the Japanese Research Society for Gastric Cancer Rules, the extent of lymphadenectomy should be a modified D1 for mucosal gastric cancer.[6] In Western countries, a traditional D1 dissection is performed on 95% of gastric cancer patients, regardless of the tumor stage.[7] Therefore, we considered it essential to clarify the effects of overweight on postoperative complications in consecutive gastric cancer patients.

The survival of gastric cancer patients is related to various factors, such as the histological aggressiveness of the tumor, patient age, and the preoperative medical and nutritional conditions of the patient.[8] The relationship between being overweight and the overall prognosis in gastric cancer patients is an important issue to resolve, and this relationship remains controversial.[9-12]

For these reasons, our study was conducted to investigate the effects of overweight on the duration of operation, amount of blood loss, incidence of postoperative complications, and survival rate in gastric cancer patients who underwent curative gastrectomy.

METHODS

PATIENTS

From January 1, 1992, through December 31, 2002, a total of 1058 patients underwent surgery for gastric cancer at Wakayama Medical University Hospital. This study included 689 patients who underwent curative gastrectomy (International Union Against Cancer R0 resection), which is defined as an absence of residual tumor microscopically.[13] Mean (SD) patient age was 63.6 (12.3) (range, 24-95) years. There were 497 men and 192 women. These 689 patients were followed up for at least 5 years or until death. Patients with cancer in another organ or patients who underwent laparoscopic gastrectomy, gastrectomy with pancreaticoduodenectomy, gastrectomy with an additional organ resection (liver, colon, or ovary), or gastrectomy with thoracotomy were excluded. None of the patients received preoperative neoadjuvant chemotherapy. Patient height and body weight were measured preoperatively, and the BMI standard calculation was as recommended by the National Institutes of Health Consensus Development Conference in 1985 as an accurate index for the prediction of medically significant obesity.[14] Patients with a BMI of 25.0 or greater were classified as overweight by World Health Organization criteria.[15] According to National Institutes of Health criteria, a BMI of 25.0 to 29.9 is classified as overweight, and a BMI of 30.0 or greater is classified as obesity.[16] In this study, patients were assigned to the following 2 groups according to their BMI: BMI of less than 25.0 (BMI $<$25.0 group) and BMI of 25.0 or greater (BMI $\geq$25.0 group).

CONCOMITANT DISEASE

Patients with clinically diagnosed hypertension and patients with cardiovascular disease, such as angina pectoris, or old myocardial infarction were defined as having cardiovascular disease. Patients with abnormal pulmonary function on spirograms (vital capacity ratio, $<$0.7; or the ratio of forced expiratory volume in 1 second to forced vital capacity, $<$0.6) were defined as having comorbidity with pulmonary disease.[17] Patients with an estimated creatinine clearance rate lower than 60 mL/min or a rising serum creatinine level ($>$2 mg/dL [to convert to micromoles per liter, multiply by 88.4]) were defined as having renal dysfunction.[18] Patients with liver cirrhosis (defined using the Child-Pugh classification), patients receiving treatment for liver disease, and patients with a serum aspartate aminotransferase level of greater than 2 times the upper limit of normal serum levels were defined as having liver dysfunction.[19] Diabetes mellitus was noted if the patient had a fasting blood glucose concentration of more than 126 mg/dL (to convert to millimoles per liter, multiply by 0.0555) or was receiving antidiabetic therapy. Otherwise, the results of a 75-g oral glucose tolerance test were used to diagnose diabetes mellitus.[20,21] Anemia was defined as a total hemoglobin level of less than 11 g/dL (to convert to grams per liter, multiply by 10).[22]

SURGICAL TREATMENT

Standard radical open gastrectomy was performed in all 689 patients. Distal gastrectomy was performed in 398 patients; total gastrectomy, in 258 patients; and proximal gastrectomy, in 33 patients. The extent of lymph node dissection was adjusted for the location of the primary tumor according to the general rules of the Japanese Research Society for Gastric Cancer.[6] In Japan, systemic D2 lymph node dissection is standard. In fact, D2 and D3 lymph node dissections were performed in almost three-quarters of our cases (74.3%). Tumor invasion (T) and lymph node classifications (N) followed the International Union Against Cancer criteria.[13]

POSTOPERATIVE COMPLICATIONS

To evaluate their anastomotic condition, most patients underwent an upper gastrointestinal tract water-soluble contrast study after postoperative day 5 or 7. Leakage at the anastomosis site was defined as leakage of contrast medium. Pancreatic fistula, according to the criteria of the International Study Group of Pancreatic Surgeons, was defined as any measurable drainage from an intraoperatively placed drain on or after postoperative day 3, with an amylase content greater than 3 times the upper limit of normal serum amylase level ($>$300 IU/L [to convert to microkatals per liter, multiply by 0.0167]).[23] The International Study Group of Pancreatic Surgeons has proposed a consensus definition and clinical grading for postoperative pancreatic fistula, which was defined as follows: grade A, called "transient fistula," has no clinical impact; grade B required a change in management or adjustment in the clinical pathway; and grade C required a major change in clinical management or deviation from the normal clinical pathway.[23,24] In this study, grades B and C were regarded as clinically significant pancreatic fistula. Intra-abdominal abscess was defined as intra-abdominal fluid collection with positive culture results identified by ultrasonography or computed tomography and associated with persistent fever and elevations of white blood cell and serum C-reactive protein levels. Diagnosis of postoperative pneumonia was obtained via computed tomography and hematological tests. Surgical mortality included in-hospital deaths within 30 days after surgery.

STATISTICAL ANALYSIS

We used commercially available software (StatView 5.0; Abacus Concepts, Inc, Berkeley, California) for all statistical analy-

Table 1. Clinicopathological Characteristics of the Patients[a]

	BMI ≥25.0 (n=116)	BMI <25.0 (n=573)	*P* Value
Age, mean (SD), y	63 (12)	64 (12)	.38
Sex, male/female	92/24	405/168	.07
Type of gastrectomy, DG/TG/PG	53/54/9	345/204/24	.01
Splenectomy, yes/no	48/68	156/417	.004
Pancreatectomy, yes/no	7/109	19/554	.18
Lymph node dissection, D1/D2/D3	26/69/21	151/336/86	.55
No. of resected lymph nodes, mean (SD)			
D1 dissection	22 (12)	20 (14)	.59
D2 dissection	31 (15)	30 (16)	.74
D3 dissection	41 (25)	44 (25)	.63
Type of skin incision, midline/transverse	97/19	548/25	<.001
Tumor infiltration, T1/T2/T3[b]	60/35/21	317/156/100	.76
Lymph node status, N0/N1/N2/N3[b]	76/30/6/4	379/144/36/14	.90
Tumor size, mean (SD), mm	42 (34)	37 (28)	.10
Macroscopic type, localized/infiltrative	76/40	390/183	.59
Histological type, differentiated/undifferentiated	66/50	306/267	.54
Adjuvant chemotherapy, yes/no	32/84	132/441	.34

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DG, distal gastrectomy; NS, not significant; PG, proximal gastrectomy; TG, total gastrectomy.
[a] Unless otherwise indicated, data are expressed as numbers of patients.
[b] Indicates International Union Against Cancer TNM classification.

ses. Quantitative results are expressed as mean (SD). Statistical comparison between the BMI ≥25.0 and BMI <25.0 groups was performed with χ^2 statistics or the Fisher test. Univariate and multivariate logistic regression analyses were performed to identify risk factors influencing postoperative complications (anastomotic leakage, pancreatic fistula, and intra-abdominal abscess). Risk factors with a univariate $P<.05$ were included in the multivariate analysis. Survival curves were computed using the Kaplan-Meier method and compared by means of the log-rank test. $P<.05$ was considered significant.

RESULTS

CLINICOPATHOLOGICAL CHARACTERISTICS OF THE PATIENTS

One hundred sixteen patients were classified as overweight (BMI, ≥25.0), and 573 patients were classified as normal weight (BMI, <25.0). Patient characteristics, disease, and surgical treatments were stratified according to the BMI group. There were no differences between the 2 groups in age, sex distribution, distribution of tumor stage and lymph node status, tumor size, and histological and macroscopic types of tumor. The frequency of total gastrectomy was higher in the BMI ≥25.0 group (46.6%) than in the BMI <25.0 group (35.6%) ($P=.01$) (**Table 1**). The frequency of splenectomy was higher in the BMI ≥25.0 group (41.4%) than in the BMI <25 group (27.2%) ($P=.004$), although there were no significant differences in the frequency of pancreatectomy (Table 1). There were no obvious differences in the extent of lymph node dissection between the 2 groups. The mean numbers of resected lymph nodes for D1, D2, or D3 dissections did not significantly differ between the 2 groups. Regarding the type of skin incision, the frequency of transverse incision was higher in the BMI ≥25.0 group (16.4% vs 4.4%; $P<.001$) (Table 1). In addition, there were no differences between the groups in the frequency of patients treated with adjuvant chemotherapy.

Table 2. Concomitant Disease

	No. (%) of Patients		
	BMI ≥25.0[a] (n=116)	BMI <25.0[b] (n=573)	*P* Value
Cardiovascular	16 (13.8)	70 (12.2)	.64
Pulmonary	7 (6.0)	25 (4.4)	.47
Renal	4 (3.4)	13 (2.3)	.51
Liver	9 (7.8)	39 (6.8)	.69
Diabetes mellitus	17 (14.7)	41 (7.2)	.02
Anemia	1 (0.9)	16 (2.8)	.33

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NS, not significant.
[a] Ranges from 25.0 to 32.0.
[b] Ranges from 12.5 to less than 25.0.

PREOPERATIVE CONCOMITANT DISEASE

The BMI ≥25.0 group showed a higher rate of comorbidity with diabetes mellitus compared with the BMI <25.0 group ($P=.02$) (**Table 2**). The prevalence of additional concomitant diseases did not significantly differ between the 2 groups.

SURGICAL RESULTS

The mean duration of operation was longer in the BMI ≥25.0 group (315 [75] minutes) than in the BMI <25.0 group (277 [85] minutes) ($P<.001$) (**Table 3**). The mean blood loss was larger in the BMI ≥25.0 group (882 [764] mL) than in the BMI <25.0 group (536 [410] mL) ($P<.001$), and significantly more

Table 3. Surgical Results of Patients After Distal Gastrectomy or Total Gastrectomy

	All Patients (N=689)			DG Subgroup (n=398)			TG Subgroup (n=258)		
	BMI ≥25.0 (n=116)	BMI <25.0 (n=573)	*P* Value	BMI ≥25.0 (n=53)	BMI <25.0 (n=345)	*P* Value	BMI ≥25.0 (n=54)	BMI <25.0 (n=204)	*P* Value
Duration of operation, mean (SD), min	315 (75)	277 (85)	<.001	281 (72)	254 (76)	.01	350 (66)	322 (85)	.03
Blood loss, mean (SD), mL	882 (764)	536 (410)	<.001	699 (898)	429 (272)	<.001	1118 (592)	714 (524)	<.001
Blood transfusion, No. of patients yes/no[a]	30/86	84/489	.006	8/45	32/313	.22	22/32	49/155	.02

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); DG, distal gastrectomy; NS, not significant; TG, total gastrectomy.
[a] Autologous transfusions were not included.

Table 4. Postoperative Complications

	No. (%) of Patients		
	BMI ≥25.0 (n=116)	BMI <25.0 (n=573)	*P* Value
Surgical complications			
Anastomotic leakage	5 (4.3)	3 (0.5)	.005
Pancreatic fistula (grades B and C)[a]	13 (11.2)	14 (2.4)	<.001
Intra-abdominal abscess	6 (5.2)	10 (1.7)	.04
Wound infection	7 (6.0)	14 (2.4)	.07
Nonsurgical complications			
Pneumonia	6 (5.2)	14 (2.4)	.13
Deterioration of liver function	1 (0.9)	12 (2.1)	.71
Mortality	0	1 (0.2)	>.99

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Pancreatic fistula was classified into 3 categories by an international study group of pancreatic surgeons, as described in the "Postoperative Complications" subsection of the "Methods" section.

patients in the BMI≥25.0 group required blood transfusion (*P*=.006) (Table 3). Furthermore, we compared the duration of operation, blood loss, and the numbers of patients requiring blood transfusion according to type of gastrectomy. Differences between the 2 groups are listed in Table 3.

POSTOPERATIVE COMPLICATIONS

Details of the major postoperative complications are listed in **Table 4**. Regarding surgical complications, more patients in the BMI≥25.0 group showed anastomotic leakage (4.3% in the BMI≥25.0 group vs 0.5% in the BMI<25.0 group; *P*=.005) (Table 4). The rate of pancreatic fistula was significantly higher in the BMI≥25.0 group (11.2%) than in the BMI<25 group (2.4%) (*P*=.001) (Table 4). The rate of intra-abdominal abscess was significantly higher in the BMI≥25.0 group (5.2%) than in the BMI<25.0 group (1.7%) (*P*=.04) (Table 4). There was no difference in the rates of wound infection between the 2 groups. In addition, there was no difference in the rate of nonsurgical postoperative complications, such as postoperative pneumonia and deterioration of liver function, between the 2 groups. One patient in the BMI<25.0 group died in the hospital.

RISK FACTORS OF POSTOPERATIVE COMPLICATIONS

Univariate and multivariate analysis were performed to identify risk factors for postoperative complications (anastomotic leakage, pancreatic fistula, and intra-abdominal abscess). **Table 5** shows the results of 16 variables univariately examined as potential risk factors for the 44 patients with postoperative complications vs the 645 patients without postoperative complications. Eleven of 16 factors differed significantly between these groups (*P*<.05) (Table 5). The multivariate logistic regression analysis identified that postoperative complications were significantly associated with being overweight (BMI≥25.0 group) and undergoing pancreatectomy, with odds ratios of 2.69 (95% confidence interval, 1.26-5.54) and 3.29 (95% confidence interval, 1.14-9.55), respectively (Table 5). Furthermore, we studied risk factors for postoperative complications according to the extent of lymph node dissection. In the D1 and D2 subgroups, only a BMI of 25.0 or greater was independently predictive of developing postoperative complications (odds ratios of 12.50 in the D1 subgroup and 2.93 in the D2 subgroup) (**Table 6**). However, univariate and multivariate logistic regression analysis could not identify a BMI of 25.0 or greater as a risk factor for postoperative complications in the D3 subgroup.

SURVIVAL RATES

In disease-specific survival and overall, there were no significant differences between the BMI≥25.0 and BMI<25.0 groups in patients overall (both *P*=.11). When patients were stratified by stage, there still were no significant differences between the 2 groups (*P*>.05 for all comparisons of disease-specific and overall survival) (**Table 7**).

COMMENT

The duration of operation for overweight patients was longer than that for normal-weight patients, and the amount of intraoperative blood loss for overweight patients was larger than that for normal-weight patients. This is in accordance with other reports.[9,11] However, Gretschel et al[25] found no significant correlation between BMI and blood loss or duration of operation. Imai et al[26] have shown that dura-

Table 5. Univariate and Multivariate Analyses of Risk Factors Influencing Postoperative Complications (Anastomotic Leakage, Pancreatic Fistula, and Intra-abdominal Abscess)

	Univariate Analysis		Multivariate Analysis	
Risk Factors	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age (≥65 or <65 y)	0.99 (0.53-1.84)	.98	. . .	. . .
Sex (male or female)	2.48 (1.03-5.96)	.04	1.56 (0.61-3.95)	.35
BMI (≥25.0 or <25.0)	4.03 (2.12-7.66)	<.001	2.64 (1.26-5.54)	.01
Type of gastrectomy (DG or TG/PG)	5.72 (2.70-12.12)	<.001	1.31 (0.36-4.70)	.68
Splenectomy (yes or no)	7.06 (3.55-14.07)	<.001	2.66 (0.80-8.89)	.11
Pancreatectomy (yes or no)	9.79 (4.07-23.58)	<.001	3.29 (1.14-9.55)	.03
Lymph node dissection (D3 or D1/D2)	4.57 (2.39-8.71)	<.001	1.96 (0.88-4.36)	.10
No. of resected lymph nodes (≥30 or <30)	1.60 (0.86-2.98)	.14	. . .	. . .
Type of skin incision (midline or transverse)	3.11 (1.30-7.45)	.01	1.33 (0.49-3.64)	.58
Tumor infiltration (T3 or T1/T2)[a]	2.16 (1.09-4.27)	.03	0.66 (0.28-1.56)	.34
Lymph node status (N0 or N1-N3)[a]	1.54 (0.83-2.88)	.17	. . .	. . .
Diabetes mellitus (yes or no)	0.25 (0.03-1.82)	.17	. . .	. . .
Other concomitant disease (yes or no)	1.25 (0.67-2.34)	.48	. . .	. . .
Duration of operation (≥300 or <300 min)	4.61 (2.32-9.15)	<.001	1.37 (0.59-3.16)	.46
Blood loss (≥600 or <600, mL)	4.72 (2.41-9.24)	<.001	2.06 (0.92-4.64)	.08
Blood transfusion (yes or no)	2.34 (1.18-4.64)	.02	0.89 (0.40-1.98)	.77

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; DG, distal gastrectomy; OR, odds ratio; PG, proximal gastrectomy; TG, total gastrectomy; ellipses, not calculated because univariate $P > .05$.
[a] Indicates International Union Against Cancer TNM classification.

Table 6. Univariate and Multivariate Analysis of Risk Factors Influencing Postoperative Complications (D1, D2, or D3 Subgroup)

	D1 Subgroup (n=177)		D2 Subgroup (n=405)				D3 Subgroup (n=107)			
	Univariate Analysis		Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
Risk Factors	OR	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age (≥65 or <65 y)	1.08	.95	0.89 (0.38-2.105)	.799	. . .	. . .	2.34 (0.84-6.53)	.10	. . .	. . .
Sex (male or female)	NE	.98	1.66 (0.55-5.01)	.37	. . .	. . .	2.47 (0.53-11.63)	.25	. . .	. . .
BMI (≥25.0 or <25.0)	12.50	.04	4.58 (1.89-11.08)	<.001	2.93 (1.07-8.02)	.04	2.47 (0.80-7.61)	.12	. . .	. . .
Type of gastrectomy (DG or TG/PG)	0.95	.97	4.63 (1.77-12.10)	.002	0.43 (0.04-5.07)	.50	9.54 (1.21-75.10)	.03	7.49 (0.92-60.92)	.66
Splenectomy (yes or no)	NE	.98	6.88 (2.62-18.05)	<.001	8.86 (0.76-103.89)	.08	2.95 (0.79-10.34)	.11	. . .	. . .
Pancreatectomy (yes or no)	NE	NE	8.48 (2.03-35.41)	.003	3.33 (0.63-17.63)	.16	3.95 (1.21-12.86)	.03	2.56 (0.77-8.57)	.13
No. of resected lymph nodes (≥30 or <30)	NE	.98	2.22 (0.91-5.41)	.08	. . .	. . .	0.53 (0.19-1.49)	.23	. . .	. . .
Type of skin incision (midline or transverse)	NE	.98	3.65 (1.14-11.70)	.03	1.17 (0.27-5.09)	.84	2.34 (0.54-10.09)	.25	. . .	. . .
Tumor infiltration (T3 or T1/T2)[a]	NE	.9821	0.98 (0.28-3.44)	.98	. . .	. . .	1.61 (0.58-4.44)	.36	. . .	. . .
Lymph node status (N0 or N1-N3)[a]	NE	.98	0.53 (0.19-1.46)	.22	. . .	. . .	1.78 (0.54-5.88)	.34	. . .	. . .
Diabetes (yes or no)	NE	.97	0.47 (0.06-3.63)	.47	. . .	. . .	NE	.98	. . .	. . .
Other concomitant disease (yes or no)	NE	.97	1.14 (0.47-2.78)	.78	. . .	. . .	1.83 (0.63-5.27)	.27	. . .	. . .
Duration of operation (≥300 or <300 min)	2.31	.50	2.18 (0.92-5.18)	.08	. . .	. . .	NE	.97	. . .	. . .
Blood loss (≥600 or <600 mL)	6.92	.12	3.74 (1.539.16)	.004	2.04 (0.75-5.51)	.16	2.61 (0.80-8.56)	.12	. . .	. . .
Blood transfusion (yes or no)	3.28	.34	1.83 (0.65-5.19)	.25	. . .	. . .	1.63 (0.57-4.68)	.36	. . .	. . .

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; DG, distal gastrectomy; NE, not able to estimate; OR, odds ratio; PG, proximal gastrectomy; TG, total gastrectomy; ellipses, not calculated because univariate $P > .05$.
[a] Indicates International Union Against Cancer TNM classification.

tion of operation was the only significant risk factor for postoperative complications after gastrectomy. According to Hawn et al,[27] a higher BMI was associated with duration of operation in general surgery, but it was not associated with postoperative complications. In this study, the duration of operation and the amount of intraoperative blood loss were not directly identified as risk factors for postoperative complications, although being overweight was directly recognized as a potential risk factor. Our results are in accord with the results of clinical trial JCOG9501, that being overweight increased the risk of postoperative complications in patients undergoing a D2 but not a D3 dis-

Table 7. Disease-Specific and Overall Survival Rates According to Cancer Stage

	Survival Rate, % of Patients						
	1 Year		3 Years		5 Years		
Stage[a]	BMI ≥25.0	BMI <25.0	BMI ≥25.0	BMI <25.0	BMI ≥25.0	BMI <25.0	*P* Value[b]
			Disease-Specific Survival				
All	93.7	95.0	82.8	87.6	77.1	84.4	.11
IA	100.0	98.9	98.0	96.9	95.4	96.4	.99
IB	100.0	98.1	95.0	89.5	89.1	88.3	.79
II	88.9	94.2	57.1	81.8	44.4	73.4	.052
IIIA	83.9	83.0	62.9	66.0	52.4	58.9	.93
IIIB and IV	50.0	74.9	37.5	54.1	37.5	41.2	.24
			Overall Survival				
All	88.7	93.0	76.8	83.1	68.3	77.0	.11
IA	94.4	97.0	86.8	92.7	84.5	89.3	.48
IB	95.5	97.1	90.7	85.6	79.3	81.1	.80
II	83.3	91.9	53.6	77.7	41.7	64.1	.08
IIIA	85.7	79.4	58.4	59.6	39.0	53.2	.66
IIIB and IV	50.0	72.8	37.5	49.5	37.5	37.7	.34

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Indicates International Union Against Cancer TNM classification.
[b] Survival curves were computed using Kaplan-Meier methods and compared using log-rank tests.

section.[4] In our study, the incidence of postoperative complications in normal-weight patients was 3.6% in the D2 dissection subgroup. However, this incidence has increased to 14.0% in normal-weight patients undergoing a D3 dissection (data not shown). Therefore, we believe that being overweight does not independently predict the development of postoperative complications in the D3 subgroup. For D2 dissection, other researchers also evaluated the relationship between overweight patients and the rate of postoperative complications.[9,11] However, few such reports on the effects of overweight on postoperative complications in patients after D1 gastrectomy have been published. In our D1 dissection subgroup, only being overweight was identified as an adverse predictor of postoperative complications after gastrectomy. Therefore, surgical care is needed when performing gastrectomy with not only D2 but also D1dissection in overweight patients.

On the other hand, cachectic patients are often in a nutritionally poor or insufficient condition, and a poor preoperative nutritional condition is an important factor relating to morbidity and mortality.[10] In our series, 35 patients were classified as cachectic patients (BMI, <17.5), and 538 patients were classified as normal-weight patients (BMI, ≥17.5 to <25.0). However, there was no difference between the 2 groups in the rates of postoperative complications (data not shown).

In gastrectomy[28] and in colorectal surgery,[29] diabetes mellitus has been reported to be one of the major risk factors contributing to the development of organ/space surgical site infection. The critical role played by polymorphonuclear neutrophils in the host defense mechanism against infection has encouraged the study of various aspects of neutrophil function in diabetic patients.[30,31] Overweight patients are at increased risk for the development of diabetes mellitus.[32] In fact, in our study, the incidence of diabetes was significantly higher in overweight compared with normal-weight patients. However, diabetes did not correlate with the development of postoperative complications. This is probably because the blood glucose level was well controlled during the perioperative period in our series. Indeed, poor control of blood glucose level impairs polymorphonuclear neutrophil functions including phagocytosis and bacterial-killing activities.[28] However, further detailed studies of this issue may be necessary.

Other researchers reported a significant reduction in the total number of nodes removed after D2 dissection in overweight compared with normal-weight patients.[4,9] However, we found no correlation between BMI and the number of resected lymph nodes. Anatomical dissections by Wagner et al[33] demonstrated that a mean of 27 lymph nodes could be recovered during a D2 dissection. The German Gastric Cancer Study set the criteria for a D2 lymphadenectomy as more than 25 lymph nodes removed.[34] We showed a mean lymph node count of 30 in patients who underwent a D2 lymphadenectomy, having performed meticulous lymphadenectomy to eradicate local disease in both overweight and normal-weight gastric cancer patients. According to our disease-specific survival analysis, there was no apparent relationship between overweight and prognosis in gastric cancer patients. Dhar et al[9] reported that overweight patients more frequently underwent an apparently unsuccessful lymphadenectomy compared with patients with low BMI and had a higher ratio of diseased to removed lymph nodes. In this study, the possibility exists that extending survival in overweight patients correlates with radical lymphadenectomy because it has been recommended to excise regional lymph nodes to achieve excellent survival in gastric cancer patients.[35]

The presence of comorbid disease associated with being overweight, such as cardiovascular diseases, liver dysfunction, pulmonary diseases, and diabetes, may negatively affect the prognosis of postoperative patients.[36] Furthermore, obesity and overweight are risk factors for several human ma-

lignant neoplasms, including endometrial, renal, esophageal, breast, and colon cancers.[37] However, in this study, there were no significant differences between overweight and normal-weight patients in overall survival. Possible reasons for this discrepancy may be that the proportion of overweight patients in this study was low (16.8%) and that there were few obese patients (BMI, ≥30.0 [1.2%]). Another possible reason is that the rates of all comorbidities were not significantly different between overweight and normal-weight patients.

In conclusion, being overweight increased the risk of postoperative complications in gastric cancer patients undergoing gastrectomy. However, being overweight did not predict poor survival. Greater care is needed when performing gastrectomy with radical lymph node dissection for gastric cancer in overweight patients.

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REFERENCES

1. Sano T, Sasako M, Yamamoto S, et al; Japan Clinical Oncology Group. Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy: Japan Clinical Oncology Group Study 9501. *J Clin Oncol*. 2004;22(14):2767-2773.
2. Bonenkamp JJ, Songun I, Hermans J, et al. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet*. 1995;345(8952):745-748.
3. Cuschieri A, Fayers P, Fielding J, et al; Surgical Cooperative Group. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. *Lancet*. 1996; 347(9007):995-999.
4. Tsujinaka T, Sasako M, Yamamoto S, et al; Gastric Cancer Surgery Study Group of Japan Clinical Oncology Group. Influence of overweight on surgical complications for gastric cancer: results from a randomized control trial comparing D2 and extended para-aortic D3 lymphadenectomy (JCOG9501). *Ann Surg Oncol*. 2007;14(2):355-361.
5. Alberts SR, Cervantes A, van de Velde CJ. Gastric cancer: epidemiology, pathology and treatment. *Ann Oncol*. 2003;14(suppl 2):ii31-ii36.
6. Japanese Research Society for Gastric Cancer. *Japanese Classification of Gastric Carcinoma*. 13th ed. Tokyo, Japan: Kanehara & Co Ltd; 1999.
7. Maruyama K, Okabayashi K, Kinoshita T. Progress in gastric cancer surgery in Japan and its limits of radicality. *World J Surg*. 1987;11(4):418-425.
8. de Manzoni G, Verlato G, Guglielmi A, Laterza E, Genna M, Cordiano C. Prognostic significance of lymph node dissection in gastric cancer. *Br J Surg*. 1996; 83(11):1604-1607.
9. Dhar DK, Kubota H, Tachibana M, et al. Body mass index determines the success of lymph node dissection and predicts the outcome of gastric carcinoma patients. *Oncology*. 2000;59(1):18-23.
10. Moriwaki Y, Kunisaki C, Kobayashi S, Harada H, Imai S, Kasaoka C. Does body mass index (BMI) influence morbidity and long-term survival in gastric cancer patients after gastrectomy? *Hepatogastroenterology*. 2003;50(49): 284-288.
11. Inagawa S, Adachi S, Oda T, Kawamoto T, Koike N, Fukao K. Effect of fat volume on postoperative complications and survival rate after D2 dissection for gastric cancer. *Gastric Cancer*. 2000;3(3):141-144.
12. Barry JD, Blackshaw GR, Edwards P, et al. Western body mass indices need not compromise outcomes after modified D2 gastrectomy for carcinoma. *Gastric Cancer*. 2003;6(2):80-85.
13. Sobin LH, Wittekind CH. *International Union Against Cancer (UICC): TNM Classification of Malignant Tumors*. 5th ed. New York, NY: John Wiley & Sons Inc; 1997.
14. Health implications of obesity: National Institutes of Health Consensus Development Conference statement. *Ann Intern Med*. 1985;103(6, pt 2):1073-1077.
15. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation on Obesity*. Geneva, Switzerland: World Health Organization; 1998.
16. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report.* Pi-Sunyer FX, Becker DM, Bouchard C, et al, eds. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute; 1998.
17. American Thoracic Society. Standardization of spirometry: 1994 update. *Am J Respir Crit Care Med*. 1995;152(3):1107-1136.
18. Anavekar NS, McMurray JJ, Velazquez EJ, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med*. 2004; 351(13):1285-1295.
19. Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD. *J Hepatol*. 2005;42(1)(suppl):S100-S107.
20. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 1997;20(7):1183-1197.
21. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications, part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998;15(7):539-553.
22. Rodgers GM. *NCCN Practice Guidelines in Oncology: Cancer and Treatment-Related Anemia*. Fort Washington, PA: National Comprehensive Cancer Network; 2007.
23. Kawai M, Tani M, Terasawa H, et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. *Ann Surg*. 2006;244 (1):1-7.
24. Bassi C, Dervenis C, Butturini G, et al; International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery*. 2005;138(1):8-13.
25. Gretschel S, Christoph F, Bembenek A, Estevez-Schwarz L, Schneider U, Schlag PM. Body mass index does not affect systematic D2 lymph node dissection and postoperative morbidity in gastric cancer patients. *Ann Surg Oncol*. 2003;10 (4):363-368.
26. Imai E, Ueda M, Kanao K, Miyaki K, Kubota T, Kitajima M. Surgical site infection surveillance after open gastrectomy and risk factors for surgical site infection. *J Infect Chemother*. 2005;11(3):141-145.
27. Hawn MT, Bian J, Leeth RR, et al. Impact of obesity on resource utilization for general surgical procedures. *Ann Surg*. 2005;241(5):821-826.
28. Yamashita S, Yamaguchi H, Sakaguchi M, Satsumae T, Yamamoto S, Shinya F. Longer-term diabetic patients have a more frequent incidence of nosocomial infections after elective gastrectomy. *Anesth Analg*. 2000;91(5):1176-1181.
29. Tang R, Chen HH, Wang YL, et al. Risk factors for surgical site infection after elective resection of the colon and rectum: a single-center prospective study of 2809 consecutive patients. *Ann Surg*. 2001;234(2):181-189.
30. Pozzilli P, Leslie RD. Infections and diabetes: mechanisms and prospects for prevention. *Diabet Med*. 1994;11(10):935-941.
31. Lin X, Candlish JK, Thai AC. Superoxide production by neutrophils from diabet-

ics and normal subjects in response to glucose and galactose. *Exp Mol Pathol*. 1993;58(3):229-236.
32. Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med*. 1998;338(1):1-7.
33. Wagner PK, Ramaswamy A, Rüschoff J, Schmitz-Moormann P, Rothmund M. Lymph node counts in the upper abdomen: anatomical basis for lymphadenectomy in gastric cancer. *Br J Surg*. 1991;78(7):825-827.
34. Siewert JR, Böttcher K, Stein HJ, Roder JD. Relevant prognostic factors in gastric cancer: ten-year results of the German Gastric Cancer Study. *Ann Surg*. 1998; 228(4):449-461.
35. Shiu MH, Moore E, Sanders M, et al. Influence of the extent of resection on survival after curative treatment of gastric carcinoma: a retrospective multivariate analysis. *Arch Surg*. 1987;122(11):1347-1351.
36. Pi-Sunyer FX. Medical hazards of obesity. *Ann Intern Med*. 1993;119(7 Pt 2): 655-660.
37. Bianchini F, Kaaks R, Vainio H. Overweight, obesity, and cancer risk. *Lancet Oncol*. 2002;3(9):565-574.

INVITED CRITIQUE

The World Health Organization projects that by 2015 more than 1.6 billion adults will be overweight and 700 million will be obese.[1] In addition, obesity has been demonstrated to be a risk factor for several abdominal malignant neoplasms.[2-4] Therefore, the effect of obesity on surgical outcomes in a cancer population is a timely issue.[2,5]

The article by Ojima et al addresses the issue of obesity and its effects on short-term surgical outcomes and 5-year survival for gastric cancer patients. Despite the fact that only 8 patients in this study were obese (BMI >30.0), the authors demonstrated that overweight patients (BMI ≥25.0) with gastric cancer present a technical challenge to the surgeon. In the hands of a group experienced in gastric surgery, there was an increased need for total gastrectomy and splenectomy in overweight patients. In addition, overweight patients (BMI >25) undergoing D2 lymphadenectomy were noted by others[6,7] to have prolonged operative times and increased blood loss. The increased technical difficulty is likely to have contributed to the increased incidence of postoperative surgical complications such as anastamotic leakage, pancreatic fistula, and intra-abdominal abscess seen in the overweight patients who underwent a D2 resection. These data are consistent with those of a previously published randomized study of morbidity comparing D2 and D3 lymphadenectomy from the Japan Clinical Oncology Group.[8]

Patients are generally older and more overweight and present with more comorbidities in Western series of gastric cancer.[9] As a result, the morbidity and mortality for radical gastrectomy have been reported to be higher in Western series.[10] Despite the demonstration of a survival benefit for more complete lymph node dissections in patients with gastric cancer,[11,12] D2 lymph node dissection is not widely used in the United States. The explanation for this decreased rate of D2 resections in Western populations has, in the past, been attributed to inadequate training in proper surgical technique.[13,14] Although this may be 1 explanation, Ojima et al raise the question as to whether it is prudent to recommend D2 lymphadenectomy for all patients. Perhaps, as suggested by Lamb et al,[15] it may be more prudent in the Western population to individualize patient care by balancing radicality with safety. By taking into account a patient's risk factors, such as age, location and stage of tumor, obesity, and overall health, perhaps surgeons should customize a sound surgical plan that optimizes the extent of lymphadenectomy while minimizing morbidity.

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1. World Health Organization. Obesity and overweight. http://www.who.int/mediacentre/factsheets/fs311/en/index.html. Accessed May 8, 2008.
2. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospective studied cohort of US adults. *N Engl J Med*. 2003;348(17):1625-1638.
3. Nock NL, Thompson CL, Tucker TC, Berger NA, Li L. Associations between obesity and changes in adult BMI over time and colon cancer risk. *Obesity (Silver Spring)*. 2008;16(5):1099-1104.
4. Giovannucci E, Michaud D. The role of obesity and related metabolic disturbances in cancers of the colon, prostate, and pancreas. *Gastroenterology*. 2007;132(6):2208-2225.
5. Tamakoshi K, Wakai K, Kojima M, et al; JACC Study Group. A prospective study of body size and colon cancer mortality in Japan: the JACC Study. *Int J Obes Relat Metab Disord*. 2004;28(4):551-558.
6. Kodera Y, Ito S, Yamamura Y, et al. Obesity and outcome of distal gastrectomy with D2 lymphadenectomy for carcinoma. *Hepatogastroenterology*. 2004; 51(58):1225-1228.
7. Dhar DK, Kubota H, Tachibana M, et al. Body mass index determines the success of lymph node dissection and predicts the outcome of gastric carcinoma patients. *Oncology*. 2000;59(1):18-23.
8. Tsujinaka T, Sasako M, Yamamoto S, et al; Gastric Cancer Surgery Study Group of Japan Clinical Oncology Group. Influence of overweight on surgical complications for gastric cancer: results from a randomized control trial comparing D2 and extended para-aortic D3 lymphadenectomy (JCOG9501). *Ann Surg Oncol*. 2007;14(2):355-361.
9. Griffin SM. Gastric cancer in the East: same disease, different patient. *Br J Surg*. 2005;92(9):1055-1056.
10. Bonenkamp JJ, Songun I, Hermans J, et al. Randomized comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet*. 1995;345(8952):745-748.
11. Volpe CM, Driscoll DL, Douglass HO Jr. Outcome of patients with proximal gastric cancer depends on extent of resection and number of resected lymph nodes. *Ann Surg Oncol*. 2000;7(2):139-144.
12. Volpe CM, Driscoll DL, Miloro SM, Douglass HO Jr. Survival benefit of extended D2 resection for proximal gastric cancer. *J Surg Oncol*. 1997;64 (3):231-236.
13. Sue-Ling HM, Johnston D. D1 versus D2 dissection for gastric cancer [letter]. *Lancet*. 1995;345(8963):1515-1516.
14. Bonenkamp JJ, Songun I, Hermans J, et al; Dutch Gastric Cancer Group. D1 versus D2 dissection for gastric cancer [reply]. *Lancet*. 1995;345(8963): 1517-1518.
15. Lamb P, Sivashanmugam T, White M, Irving M, Wayman J, Raimes S. Gastric cancer surgery: a balance of risk and radicality. *Ann R Coll Surg Engl*. 2008;90(3):235-242.