Table 5 Data on patients who survived more than 5 years after surgery

Patient No.	1	2	3	4	5
Gender, age	M, 54	M, 58	F, 72	F, 74	M, 65
Survival time (months)	136	107	100	72	71
Radical operation	R0	R0	R0	R0	R0
Degree of liver metastases	H1	H1	H2	H1	H1
Number of liver tumor	1	1	3	1	1
Size of liver tumor (cm)	2.5	2.5	2.3	1.5	0.8
Hepatic operation	Right lobectomy	Partial resection	MCT	Left lobectomy	MCT
HAI	CDDP+5FU+MMC	MMC+5FU	MMC+CDDP+5FU	No treatment	CDDP+5FU
Histology	PAP	PAP	PAP	TB1	TB2
Lymphatic invasion	ly1	ly2	ly1	ly2	ly1
Venous invasion	v1	v3	v2	v3	v2
Tumor depth of inversion	T2	T2	T2	T3	T3
Lymph node metastases	n0	n1	n1	n2	n2
CEA (ng/ml)	0.5	2.1	144.9	0.5	10.3
CA19-9 (ng/ml)	7.0	Unknown	18.0	2.0	1.0

survival according to a multivariate analysis. It has also been reported that the number of metastatic tumors is a significant prognostic factor [3, 5, 13] and that the favorable survival outcome for patients with solitary metastases has been no worse than that for a solitary metastases of colorectal cancer [20–22]. In addition, it has been reported that extended lymph node metastases lead to difficulty in radical operations and that the proportion of liver metastases increases with an increased degree of lymph node metastases [19, 23]. Therefore, we strongly indicate that a solitary liver metastatic tumor and no-distant lymph node metastases (≤N1) are good candidates for surgical resection.

Our study demonstrated that in patients with H1 and 2 synchronous metastases without peritoneal dissemination who received the surgical treatment for the metastatic tumors, the cumulative 1- and 5-year survival rates were 80.0% and 60.0%, and this survival period of a surgical treatment for liver metastases is dramatically elongated in comparison to those that have been previously reported [3–5, 7, 13, 14, 24]. In addition, the radical operation including the surgical treatment for liver metastases is a significantly independent prognostic factor of survival according to our univariate and multivariate analyses. Furthermore, it has recently been reported that there were no significant differences in the effect of hepatectomy between synchronous and metachronous metastases [5]. Therefore, synchronous liver metastases from gastric cancer are not necessarily a contraindication for attempts at curative resective therapy of both the primary site and the metastatic site.

Whether the surgical margin is a prognostic factor of survival in gastric cancer patients with metastatic liver tumors remains controversial [5, 6, 13, 19]. On the other hand, in patients with liver metastases from colorectal cancer, a wedge resection with a tumor-free margin of less than 5 to 10 mm is justified because the occurrence of satellite nodules around the main metastatic lesion is reportedly rare [22] and a non-anatomically limited liver resection has become a standard surgical procedure [20, 21]. In the present study, two patients treated for H1 and 2 metastases with only MCT, of which the surgical margin may be less than that of a hepatic resection, [18] survived more than 5 years. In addition, other authors have reported that MCT is equally effective as a hepatic resection in the treatment of two to nine hepatic metastatic tumors from colorectal carcinoma [17, 18]. Therefore, we recognized that a limited resection including MCT may be enough in the treatment of liver metastases from gastric cancer, although the positive surgical margins should be avoided.

Conclusion

Our findings indicate that a radical operation including the surgical treatment for metastatic liver tumors should be performed to improve the prognosis in gastric cancer patients with synchronous H1 and 2 metastases if there is no peritoneal dissemination. A minimum surgical margin is sufficient for a resection of liver metastases, and furthermore, a solitary liver metastatic tumor and no-distant lymph node metastases are the preferable prognostic factors for survival.

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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 ≥ 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)

Risk Factors	Univariate Analysis		Multivariate Analysis	
	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)

Risk Factors	D1 Subgroup (n=177)		D2 Subgroup (n=405)				D3 Subgroup (n=107)			
	Univariate Analysis		Univariate Analysis		Multivariate Analysis		Univariate Analysis		Multivariate Analysis	
	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

Stage[a]	Survival Rate, % of Patients						
	1 Year		3 Years		5 Years		
	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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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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Evaluation of Double Tract Reconstruction After Total Gastrectomy in Patients with Gastric Cancer: Prospective Randomized Controlled Trial

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Abstract

Background The double tract (DT) method was compared with the Roux-en-Y (R-Y) method to identify the optimal reconstruction procedure after total gastrectomy for patients with gastric cancer. The DT reconstruction is as simple as the R-Y, and it can be safely performed even after total gastrectomy. However, these have been no studies evaluating the usefulness of DT reconstruction in comparison to R-Y reconstruction.

Methods A group of 44 patients with gastric cancer were intraoperatively randomized for R-Y ($n = 23$) or DT reconstruction ($n = 21$) after total gastrectomy (TG). Body weight, food intake, nutritional conditions, and quality of life (QOL) were determined at 3 and 12 months after the operation. This study is registered with ClinicalTrials.gov, no. NCT00746161.

Results Food intake significantly decreased soon after the operation. No differences were observed between the DT and R-Y groups. The body weight decreased throughout the ensuing period ($P < 0.05$) and thereafter gradually recovered. However, no differences were observed between the two groups. Among the nutritional laboratory parameters, serum prealbumin, retinol-binding protein, total cholesterol, and triglyceride were decreased soon after the operation. The changes of those parameters were not substantially different between the two groups. The postoperative QOL was evaluated, and no differences were observed between those groups.

Conclusions There were no particular advantages in the DT method after TG in comparison to the simple R-Y method in terms of body weight, QOL, and nutritional conditions, suggesting that the DT method might not be recommended after TG for patients with gastric cancer.

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Introduction

Since Schlatter succeeded in performing a total gastrectomy (TG) [1], many types of reconstruction after TG have been proposed. However, no optimal reconstruction method has yet become universally accepted. The Roux-en-Y anastomosis (R-Y), first applied by Orr after TG [2], is still utilized as the preferred reconstruction in Japan, as well as in many Western countries, because it is simple to perform and decreases esophageal reflux [3]. However, this procedure is not satisfactory in terms of postoperative dietary intake, nutritional status, and the quality of life of patients [3, 4].

A great deal of research is still being done to validate the potential advantages of various procedures [4]. Most of these efforts to improve the postoperative status have focused on two basic concepts. One is creating a reservoir to substitute for the stomach, and the other is preservation of the duodenal passage. A jejunal pouch is often used to replace the gastric reservoir. A number of prospective clinical studies, including randomized controlled trials have been conducted to explore the benefit of a jejunal pouch [3, 5–9], and most of those studies have shown potential advantages of this gastric substitute reconstruction [4, 10]. Most recently, a randomized trial with a large number of patients showed long-term benefits of pouch reconstruction in terms of the quality of life, especially

after more than 2 years postoperatively [11]. However, the surgical procedure for constructing a jejunal pouch is complicated and has not led to a consensus in terms of the length or location of the pouch.

On the other hand, there have been no prospective clinical trials specifically addressing the question of whether duodenal passage is important for the reconstruction after TG, although there have been several clinical studies that examined whether duodenal passage shows any benefits for the jejunal pouch reconstruction [3, 7, 12–14]. Judging generally from those results, no real advantage to duodenal passage after TG has been demonstrated [10]. A recent report showed that duodenal passage preservation helps moderate the postprandial cholecystokinin elevation, probably reflecting a decreased need for arresting the abnormally high output of other gastrointestinal hormones in patients with the aboral pouch reconstruction [15]. Therefore, it is possible that the duodenal passage may contribute to satiation in patients with TG to some extent via an almost physiologic level of the release of gastrointestinal hormone.

In 1965, Kajitani and Sato reported that use of double tract (DT) reconstruction. With this procedure, an esophagojejunostomy is performed as with the R-Y technique, and duodenojejunostomy is added about 20 cm distal from the esophagojejunostomy [16]. In Japan, this simple method, which simply adds duodenojejunostomy to R-Y, has been employed in some institutions [5]. The benefits of this method are (1) a simple procedure; (2) preservation of the duodenal passage; (3) no duodenal stump, resulting in no risk of postoperative stump rupture [5]. This DT method has been modified by performing a duodenojejunostomy about 35 to 40 cm distal from the esophagojejunostomy. This reconstruction has been employed at our hospital in patients with gastric cancer who can be expected to have long-time survival. However, there have so far been no studies that have compared the usefulness of the DT reconstruction versus the R-Y reconstruction.

This study was a prospective randomized controlled trial to compare the DT reconstruction with the R-Y reconstruction after a total gastrectomy in patients with gastric carcinoma. We aimed to investigate whether the DT method was more useful than the R-Y technique in terms of maintaining body weight, quality of life, and improving nutritional conditions.

Patients and methods

This randomized controlled trial was approved by the Ethical Committee on Clinical Investigation of Wakayama Medical University Hospital (WMUH). Patients were recruited into the study before surgery on the basis of whether total gastrectomy was anticipated and appropriate informed consent was obtained. Between April 2002 and December 2006 at WMUH, 44 patients who underwent a total gastrectomy with a curative resection at WMUH were enrolled in this study. The eligibility criteria included histologically proven adenocarcinoma without esophageal invasion, tumor status cT1–2, age 80 years or younger, no distant metastasis. The exclusion criteria included carcinoma in the remnant stomach; stage IV; possibility of requiring postoperative chemotherapy; history of laparotomy; history of serious heart disease, liver cirrhosis, or chronic liver disease with an indocyanine green excretion test at 15 min of 15% or more; failure to obtain informed consent.

Description of the operations

Before the reconstruction, patients were randomly assigned to undergo R-Y or DT reconstruction during the operation by the use of a computer-generated random number pattern. Splenectomy was assumed to be an assignment modulator.

The surgical procedures are shown in Fig. 1. After a total gastrectomy with lymphadenectomy, the jejunum was divided approximately 20 cm distal to the Treitz ligament. The distal jejunal limb was brought through the transverse mesocolon by the retrocolic route. For the R-Y group, the end-to-side esophagojejunostomy was mechanically performed with a circular stapler, and the stump was closed with a linear stapler. Next, the end of the Y limb was anastomosed manually to the side of the Roux limb, 40 cm

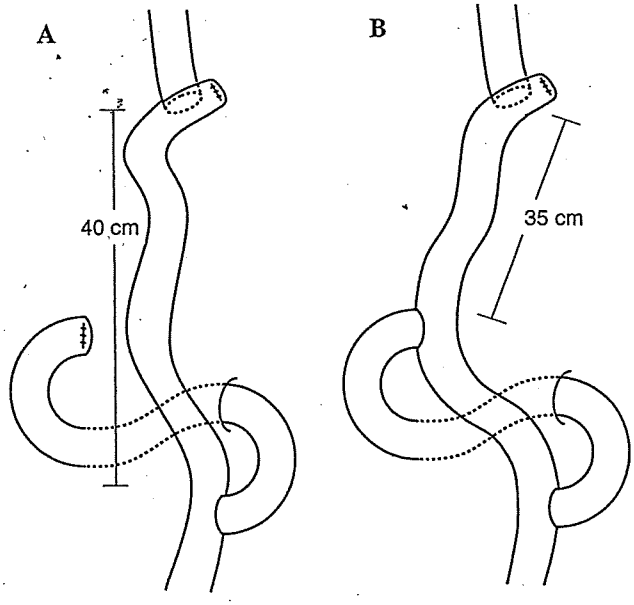

Fig. 1 Reconstruction methods after total gastrectomy, a Roux-en-Y reconstruction (R-Y). b Double-tract reconstruction (DT)

distal to the esophagojejunal anastomosis. For the DT group, prior to the esophagojejunostomy, the side-to-end jejunoduodenostomy was performed with a circular stapler, 35 cm distal to the esophagojejunal anastomosis. The end of the Y limb was anastomosed manually to the side of the Roux limb, approximately 15 cm distal to the jejunoduodenal anastomosis.

Data collection

Data were collected prospectively for all patients and included their history, clinicopathologic examinations, postoperative clinical information, and complications. Clinicopathologic data were evaluated on the basis of the General Rules for Gastric Cancer Study in Surgery and Pathology in Japan [17].

The patients were followed up according to the following protocol: Measurements of physical parameters and laboratory examinations were performed before the operation and at 3, 6, and 12 months after the surgery. A survey concerning the patients' food intake and another addressing their quality of life (QOL) were conducted using questionnaires; and endoscopic examinations were performed at 3 and 12 months after the operation.

The food intake was evaluated as the percent change in comparison to the preoperative food intake at each time point. The gain or loss of body weight was calculated as the percentage of the body weight ratio (% BW) by the formula for body weight at each time point/preoperative weight. As a nutritional parameter, the prognostic nutritional index (PNI) [18] was used. It is calculated by the formula for percentage of $10 \times (\text{Alb}) + 0.005 \times (\text{Lymph})$, where Alb is the serum albumin level (g/dl), and Lymph is the total lymphocyte count (mm^3). Postoperative QOL was evaluated using an original questionnaire as the QOL score. This questionnaire contained 13 questions concerning symptoms of reflux, dumping syndrome, and other upper abdominal complaints after eating (Table 1). Each question was worth up to 4 points as the QOL score, and full marks was a score of 52 points.

Study endpoints

The primary endpoint was the percent body weight ratio at 12 months after the operation. Secondary endpoints were PNI and QOL score at 3 and 12 months after the operation.

Statistical analyses

The study design to predict the number of patients necessary for statistical validity (two-sided) was based on the premise of improving the percent body weight ratio from 70% to 90%, with the α set at 0.05 and the β set at 0.2, yielding a power of 80%. This indicated that 62 patients were required in each arm of this study, for a total study population of 124 patients. The statistical evaluation was carried out by use of the two-tailed χ^2 test, Fisher's exact test, and Student's t-test. Results were reported as the mean ± SD. Significance was defined as $P < 0.05$. An interim analysis using the Bonferroni's method was planned to be calculated with 40 patients (20 patients per arm). However, it has taken almost 4 years to enroll 40 patients; moreover, at this interim analysis, the percent body weight ratio was similar for the DT and R-Y groups. In addition, recently, adjuvant chemotherapy after a curative operation has become the standard treatment [19, 20]; and the patients with stage II or III gastric carcinoma have been administered anticancer drugs postoperatively. Postoperative chemotherapy was included in the exclusion criteria in the present study because it was considered to influence both the postoperative nutritional state and QOL. As a result, this study was terminated.

This study is registered with ClinicalTrials.gov, no. NCT00746161.

Table 1 Questionnaire about postoperative symptoms

1. Do you suffer from vomiting?
2. Do you feel satiety?
3. Can you eat enough?
4. Do you have heartburn?
5. Do you have regurgitation?
6. Do you belch excessively?
7. Do you feel much gas in the abdomen?
8. Do you suffer from much flatus?
9. Do you have diarrhea?
10. Are you constipated?
11. Do you have abdominal discomfort immediately after eating?
12. Do you have abdominal discomfort about 2 hours after eating?
13. Are you satisfied with your condition now?

Each question was worth up to four points. For questions 1, 2, and 4–12, a score of 4 was assigned if the answer was "no," 3 for "rarely," 2 for "sometimes," and 1 for very often. For questions 3 and 13, the scores were assigned as 4 for "excellent," 3 for "good," 2 for "fair," and 1 for "poor"

Results

The 44 patients who underwent total gastrectomy for gastric carcinoma underwent randomization: 23 underwent R-Y and 21 underwent DT. One patient in the R-Y group died of a myocardial infarction.

There was no significant difference between those two groups in terms of the clinicopathologic features, except age (Table 2). There was no significant difference in the surgical background or postoperative complications (Table 3).

Table 2 Clinicopathologic features of the patients

Feature	R-Y group ($n = 23$)	DT group ($n = 21$)	Statistical significance (P)
Age	65.4 ± 8.3	58.2 ± 10.7	0.0162
Sex (M/F)	18/5	14/7	NS
Tumor diameter (mm)	53.1 ± 37.2	31.8 ± 17.2	NS
Tumor depth (pT1/pT2/pT3)	10/10/3	9/8/4	NS
Lymph node metastases (negative/positive)	16/7	16/5	NS
Stage[a] (IA/IB/II/IIIA/IIIB)	9/6/6/2/0	9/5/5/0/2	NS

[a] Evaluated on the basis of the General Rules for Gastric Cancer Study in Surgery and Pathology in Japan [17]

Table 3 Surgical background and postoperative complications

Parameter	R-Y group ($n = 23$)	DT group ($n = 21$)	Statistical significance
Operation time (minutes)	260 ± 69	254 ± 43	NS
Blood loss (ml)	513 ± 447	538 ± 456	NS
Lymph node dissection (D1/D2)	5/18	8/13	NS
Splenectomy (yes/no)	14/9	12/9	NS
Curability (R0)	23	21	NS

Food intake and body weight

The food intake significantly decreased soon after the operation. It was only 64.5% in the R-Y group and 67.5% in the DT group at 3 months. It thereafter gradually recovered during the course of the postoperative period. No differences were observed between two groups (Fig. 2). Body weight was also significantly decreased throughout the following period ($P < 0.05$), and it also gradually recovered. However, the percent BW was only 70.0% in the R-Y group and 77.8% in the DT group 1 year after the operation. No differences were observed between the two groups (Fig. 3).

Serum nutritional parameters

Among the nutritional laboratory parameters, serum prealbumin, retinol-binding protein, total cholesterol, and triglycerides were decreased soon after the operation. The levels were gradually restored during the course of the postoperative period. The changes in those parameters were similar in the two groups. The serum level of other nutritional parameters—total protein, albumin, calcium, iron, transferrin—were not different between the R-Y and DT groups throughout the following period (Table 4). Immunoglobulin fractions were also examined, but no difference was recognized between the two groups. The PNI, which was calculated from the absolute lymphocyte count and serum albumin, was not significantly different either.

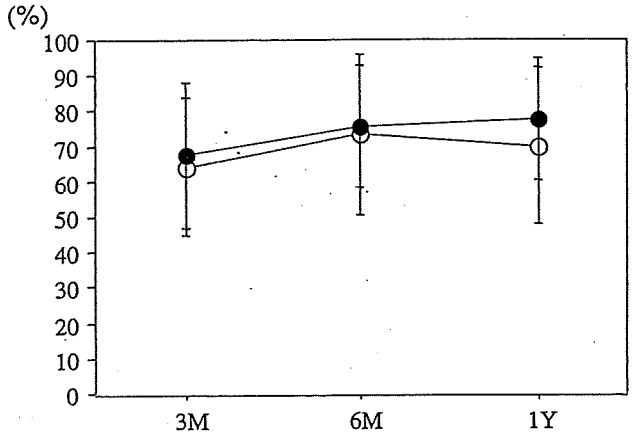

Fig. 2 Change in food intake. The food intake was evaluated as the percent change compared to the preoperative food intake at each time point. Values are expressed as the mean ± SD. R-Y group, *open circles*; DT group, *closed circles*

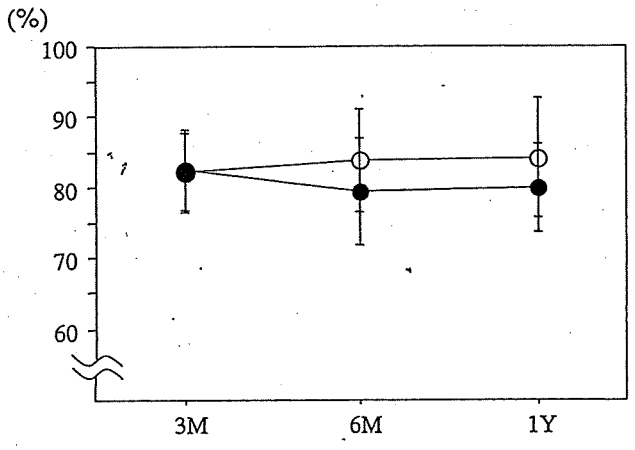

Fig. 3 Gain or loss of body weight was calculated as the percentage of the body weight ratio (%BW) compared to the preoperative body weight at each time point. Values are expressed as the mean ± SD. R-Y group, *open circles*; DT group, *closed circles*

Postoperative symptoms and QOL

The postoperative QOL was evaluated using an original questionnaire. The completed questionnaire was collected

Table 4 Change in serum nutritional parameters after total gastrectomy

Parameter	R-Y group			DT group		
	3 Months	6 Months	1 Year	3 Months	6 Months	1 Year
TP (g/dl)	6.7 ± 0.4	6.8 ± 0.4	6.9 ± 0.4	6.9 ± 0.4	6.9 ± 0.5	6.9 ± 0.3
Alb (g/dl)	4.0 ± 0.3	4.0 ± 0.3	4.1 ± 0.3	4.1 ± 0.3	4.1 ± 0.3	4.2 ± 0.3
Prealb (mg/dl)	20.9 ± 4.5	21.9 ± 5.4	22.3 ± 4.4	20.0 ± 4.7	21.7 ± 5.6	21.1 ± 6.1
RBP (mg/dl)	3.1 ± 0.9	3.3 ± 1.0	3.4 ± 0.9	2.7 ± 0.7	2.8 ± 0.9	3.0 ± 0.6
TC (mg/dl)	158 ± 44	173 ± 33	171 ± 23	162 ± 24	168 ± 36	175 ± 32
TG (mg/dl)	82 ± 32	96 ± 32	82 ± 32	82 ± 40	89 ± 42	73 ± 19
Ca (mg/dl)	9.2 ± 0.8	9.1 ± 0.6	9.1 ± 0.5	9.1 ± 0.4	8.9 ± 0.4	9.0 ± 0.4
Fe (μg/dl)	94 ± 31	95 ± 34	116 ± 39	95 ± 36	100 ± 40	106 ± 40
Tf (mg/dl)	248 ± 57	259 ± 69	271 ± 47	250 ± 45	271 ± 58	276 ± 48

TP Total protein, *Alb* albumin, *Prealb* prealbumin, *RBP* retinol-binding protein, *TC* total cholesterol, *TG* triglyceride, *Ca* calcium, *Fe* iron, *Tf* transferrin

from 41 of 44 patients (93.2%). The QOL score was 36.6 ± 5.3 at 3 months and 41.0 ± 5.6 at 1 year in the R-Y group and 37.8 ± 6.3 at 3 months and 38.2 ± 4.9 at 1 year in the DT group. There were no significant differences between the groups. In addition, the incidence of symptoms related to dumping syndrome or reflux was similar in the two groups (data not shown).

Endoscopic examinations

Endoscopic examinations were performed at 3 and 12 months after the operation. There were no specific findings, such as reflux esophagitis, at any time in either group (data not shown).

Discussion

Gastric cancer remains the second leading cause of cancer death worldwide, with more than 600,000 deaths per year [21]; it is the most common malignancy in Japan, Asia, South America, and eastern Europe [22]. The main goal of radical surgery in patients with gastric carcinoma has been complete cure. The treatment results have markedly improved, with the most recent data from Japan showing a 3-year overall survival of patients with stage II or III to be 80.1% in the S-1 adjuvant group and 70.1% in the surgery-only group [20]. Therefore, the reconstruction method after total gastrectomy is important in terms of a promising QOL. A jejunal pouch has a potential advantage as a gastric substitute reconstruction [4, 10]. However, the incidence of overweight and obese patients has been increasing in the general population and in these patients a jejunal pouch may not be safely constructed owing to excessive fat tissue in the mesentery. In addition, being overweight increases the risk of surgical complications, blood loss, and operating time in patients with gastric carcinoma undergoing gastrectomy with D2 lymph node dissection [23, 24]. The simpler the reconstruction method is, the better it is in terms of postoperative QOL. Postoperative complications may increase when the surgical procedure is complicated; and once patients suffer some complications, it compromises the quality of postoperative life.

The DT reconstruction is as simple as the R-Y reconstruction, and it can be safely performed even after a total gastrectomy with extended lymphadenectomy. When the prospective randomized controlled trial in this report was constructed, it was expected that the DT might have some potential advantages over R-Y because it preserves the duodenal passage and maintains the continuity of the jejunum and the mesenterium at the anal side of the esophagojejunostomy. This is different from a jejunal interposition, a thus results in serial intestinal peristaltic movement. Moreover, DT has two routes, which are possibly expected to play a role as a reservoir. However, contrary to expectations, there were no substantial differences in terms of the body weight, QOL, or nutritional conditions between the DT and R-Y methods in the present study. Although these results were derived from data at the interim analysis, it has taken 4 years to enroll 40 patients. In addition, adjuvant chemotherapy after gastrectomy for patients with gastric carcinoma has recently been shown to have a significant survival benefit [19, 20]. Moreover, since then, adjuvant chemotherapy, which was included in our exclusion criteria, has become the standard treatment after gastrectomy for stage II/III disease. As a result of such preliminary findings, this study was terminated.

There are two major reasons why the DT method might not show any significant advantages over R-Y. First, the benefit of duodenal passage would be recognized only when the emptying time is slow, similar to that in normal persons. So far, there has only been one prospective study that

supported the benefit of duodenal passage preservation [12], but it investigated duodenal passage-preserving procedures with a pouch. It may be crucial for solid meals to enter the duodenum gradually from a pouch. Duodenal passage preservation with the aboral pouch helps moderate the postprandial cholecystokinin elevation and results in a less steep postprandial plasma somatostatin curve, but the insulin level increases to an abnormally high level, which is similar to that with R-Y [15]. It is possible that the aboral pouch does not help food flow into a duodenum slowly, and therefore it shows a diabetoid blood glucose profile and an abnormal high level of serum insulin immediately after eating. The benefit of duodenal passage might become significant by adding a jejunum pouch to the oral side of the duodenum, which thus would make food enter the duodenum slowly. In this context, the results in the present study are understandable. Second, the two passage routes in DT did not work as a reservoir at all. In the present study, all patients underwent upper gastrointestinal radiography after the operation, and most of them showed equal passage through the duodenum and the jejunum. Fujiwara et al. reported that the scintigraphic assessment of the DT shows the emptying time in this equal passage type to be shorter than that in other types—the jejunal passage-dominant type or the duodenal passage-dominant type—and that this equal passage type is preferable after TG [25]. When a jejunal pouch is constructed at the oral side, as Fujiwara et al. described, the double passages might be beneficial, otherwise it would be useless because food passes through the duodenum too fast. Of course, the possibility cannot be ruled out that the DT with a jejunal pouch may show some potential advantages over R-Y with a pouch and jejunal interposition with a pouch. It is therefore still worth conducting a prospective clinical trial comparing these reconstructions.

Conclusions

There were no substantial advantages of the DT reconstruction method after TG when compared to the simple R-Y method in terms of body weight, QOL, and nutritional conditions. These results suggest that DT without a jejunal pouch might be not recommended after TG for patients with gastric carcinoma.

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ORIGINAL ARTICLE

Association of Allogeneic Blood Transfusions and Long-Term Survival of Patients with Gastric Cancer after Curative Gastrectomy

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Abstract
Introduction The relationship between perioperative allogeneic blood transfusions and poor prognosis in patients with gastric cancer remains controversial. The aim of this study is to examine the effect of perioperative blood transfusions on long-term survival of patients undergoing curative gastric resection for gastric cancer.
Methods Eight hundred fifty-six consecutive patients with gastric cancer who underwent curative gastrectomy (R0) from January 1, 1991 through December 31, 2002 were enrolled in this retrospective study.
Results A multivariate overall survival analysis using Cox proportional hazard regression model revealed macroscopically infiltrative tumor, tumor infiltration of serosa, lymph node metastasis, blood transfusions (hazard ratio, 2.69), pulmonary disease, and liver dysfunction as prognostic factors for long-term survival. Blood transfusion was an independent prognostic factor at all stages of disease. Disease-specific and overall survival showed significant differences between the transfused and nontransfused groups (log-rank, $P<0.0001$). Based on multivariate logistic regression analysis, the need for blood transfusion was significantly associated with advanced age (≥65 years), long duration of operation (≥300 min), massive blood loss (≥1,000 ml), and anemia (Hb<10 g/dl).
Conclusions Allogeneic blood transfusion is an independent prognostic factor for long-term survival in gastric cancer patients.

Keywords Blood transfusion · Gastric cancer

Introduction

It is generally supported that allogeneic blood transfusions have various adverse outcomes after cancer surgery. In particular, blood transfusions have been associated with decreased survival of patients with hepatocellular carcinoma, lung cancer, breast cancer, head and neck cancer, colorectal cancer, and prostate cancer.[1–6] The most frequently suggested explanation for this association centers on non-specific immunosuppression arising from increased activities of regulatory T lymphocytes, decreased natural killer cell activity, stimulated anti-idiotype antibody production, and impaired lymphocyte blastogenesis.[7]

Gastric cancer remains the second leading cause of death worldwide, and it is the most common malignancy in Japan, Asia, South America, and Eastern Europe.[8] In Japan and Asia, most surgeons consider D2 gastrectomy to be the standard and optimal surgical procedure for patients with advanced gastric cancer.[9] Blood transfusions are often needed when performing gastrectomy with radical lymph nodes dissection for gastric cancer; however, the relationship between perioperative blood transfusions and poor prognosis in patients with gastric cancer remains controversial. Although many studies do not support this relationship,[10–14] some studies have affirmed that it exists.[15–19]

The aim of this study was to examine the effect of perioperative allogeneic blood transfusions on long-term

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survival in patients undergoing curative gastric resection for gastric cancer.

Materials and Methods

Patients

From January 1, 1991, through December 31, 2002, a total of 1,122 patients underwent surgery for gastric cancer at Wakayama Medical University Hospital. Of these patients, 856 underwent curative gastrectomy (International Union Against Cancer [UICC] R0 resection), which is defined as an absence of microscopic residual tumor.[20] Patients with cancer in another organ or patients who underwent gastrectomy with pancreaticoduodenectomy, gastrectomy with additional hepatic resection, or gastrectomy with thoracotomy were excluded. None of the patients received preoperative neoadjuvant chemotherapy. The 856 patients were followed for at least 5 years or until death. The lost cases were treated as censored data for the analysis of survival rates. The median follow-up interval for patients from the date of surgery was 78 months. Follow-up data were obtained from the hospital database, which includes the patients' background, surgical data, tumor characteristics, and survival time. Perioperative periods were defined as 1 week before and after the operation. Tumor invasion (T) and lymph node status (N) were classified by International Union Against Cancer (UICC) criteria.[20]

Concomitant Disease

Patients with clinically diagnosed hypertension and patients with cardiovascular disease, such as angina pectoris or previous myocardial infarction, were defined as having cardiovascular disease. Patients with abnormal pulmonary function on spirograms (vital capacity ration <0.7 or forced expiratory volume in one second/forced vital capacity <0.6) were defined as having pulmonary disease as a comorbidity.[21] Patients with an estimated creatinine clearance lower than 60 ml/min or a rising serum creatinine (>2 mg/dl) were defined as having renal dysfunction.[22] Patients with liver cirrhosis (per the Child–Pugh classification), patients receiving treatment for liver disease, and patients with a serum aspartate aminotransferase (AST) greater than twice the normal upper limit of serum AST were defined as having liver dysfunction.[23] Diabetes mellitus was noted if the patient had a fasting blood glucose concentration >126 mg/dl or was receiving antidiabetic therapy. Otherwise, the results of a 75-g oral glucose tolerance test were used to diagnose diabetes mellitus.[24] Anemia was defined as preoperative total hemoglobin <10 g/dl.[25]

Surgical Treatment

Standard radical gastrectomy (distal gastrectomy, total gastrectomy, or proximal gastrectomy) was performed in all 856 patients. The extent of lymph node dissection was adjusted for the location of primary tumor according to the Japanese Research Society for Gastric Cancer rules.[26] Laparoscopy-assisted gastrectomy was used to treat early gastric cancers.

Blood Transfusions

The general indication for blood transfusions was intraoperative blood loss of >1,000 ml or a hemoglobin concentration of <8 g/dl, although transfusions were done depending on the discretion of the anesthetist and the surgical team responsible for the care of the patient in the perioperative period. In the period of this research, packed red blood cells were separated from whole blood and stored in citrate–phosphate–dextrose–adenine anticoagulant solution without leukodepletion.

Statistical Analysis

StatView 5.0 software (Abacus Concepts, Inc., Berkeley, CA, USA) was used for all statistical analyses. Quantitative results are expressed as the mean±standard deviation (SD). Statistical comparisons between the transfused and non-transfused groups were performed with χ^2 statistics. Survival curves were computed using the Kaplan–Meier method and compared by means of the log-rank test; $P<0.05$ was considered significant. Univariate and multivariate Cox proportional hazards model was used to evaluate factors that independently affected postoperative survival. Prognostic factors with a univariate $P<0.1$ were included in the multivariate analysis. Prognostic factors with a multivariate $P<0.05$ were defined as independent prognostic factors. Univariate and multivariate logistic regression analyses were performed to identify risk factors influencing blood transfusion requirements on perioperative periods. Risk factors with a univariate $P<0.1$ were included in the multivariate analysis. Risk factors with a multivariate $P<0.05$ were defined as independent risk factors.

Results

Patient Characteristics

Patient characteristics are detailed in Table 1. Among the 856 patients, 154 (18.0%) underwent perioperative allogeneic blood transfusions; the remaining 702 received no transfusions. In transfused patients, 50 patients received 400 ml of