Impact of Body Weight Loss on Recurrence After Curative Gastrectomy for Gastric Cancer

HIDEMASA KUBO, SHUHEI KOMATSU, DAISUKE ICHIKAWA, TSUTOMU KAWAGUCHI, TOSHIYUKI KOSUGA, KAZUMA OKAMOTO, HIROTAKA KONISHI, ATSUSHI SHIOZAKI, HITOSHI FUJIWARA and EIGO OTSUJI

Division of Digestive Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto, Japan

Abstract. *Background: This study was designed to assess the prognostic role of body weight loss (BWL) after curative gastrectomy for gastric cancer patients. Patients and Methods: We analyzed a total of 102 consecutive patients who underwent curative gastrectomy for stage II or III gastric cancer between 2005 and 2011. Postoperative BWL during the first 6 months in patients was calculated from their hospital records. Results: Postoperative BWL was significantly higher in patients with tumours in the upper stomach, total gastrectomy, or subsequent recurrence. A postoperative BWL of 12% was the optimal cut-off value, which was strongly associated with subsequent recurrence. Patients with a postoperative BWL of 12% or higher did not have poorer overall survival but did have significantly poorer disease-free survival than patients with BWL of less than 12%. Cox proportional hazard analyses revealed that a postoperative BWL of 12% or higher was an independent prognostic factor of poor disease-free survival. Conclusion: High BWL after curative gastrectomy is related to recurrence in patients with gastric cancer.*

Gastric cancer is one of the most common causes of death from cancer worldwide (1). Because of recent advances in diagnostic techniques, less invasive treatment, and perioperative management, earlier detection of gastric cancer has been achieved and mortality and morbidity have decreased (2-6). Patients with advanced-stage disease, however, still have a poor prognostic outcome and a high incidence of recurrence. There is no doubt that tumour-related pathological factors, such as lymph node metastasis, depth of tumour invasion and lymphatic invasion, are recognized as pivotal prognostic factors. In addition, several recent studies demonstrated that such factors have a great influence on the prognosis of gastric cancer based on inflammation status (7), age and comorbidity (8), malnutrition (9), and complications (10). As a result of gastrectomy that hampers food intake, patients with gastric cancer experience loss of appetite and are predominantly at risk for body weight loss (BWL) leading to malnutrition. BWL may be caused by multiple factors. It was reported that BWL after other cancer surgery had a negative impact on the prognosis of patients (11). However, only a few studies have reported on BWL in patients with gastric cancer who underwent curative surgery (12, 13), and clinicopathological factors related to BWL and the prognostic effect of BWL in the patients have not yet been fully elucidated. To clarity this issue, as well as whether BWL should be proactively treated after surgery, this study was performed retrospectively from patients' hospital records.

Correspondence to: Shuhei Komatsu, MD, Ph.D., Division of Digestive Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachihirokoji, Kamigyo-ku, Kyoto 602-8566, Japan. Tel: +81 752515527, Fax: +81 752515522, e-mail: skomatsu@koto.kpu-m.ac.jp

Key Words: Postoperative body weight loss, recurrence, gastric cancer.

Patients and Methods

Study population and treatments. A total of 102 consecutive patients with pathological stage (pStage) II or III who underwent curative gastrectomy for gastric cancer at the Division of Digestive Surgery, Department of Surgery, Kyoto Prefectural University of Medicine, Japan, between January 2005 and December 2011, and who did not experience a recurrence for the first 6 months were retrospectively analysed from their hospital records. We excluded patients in pStage I because they rarely have recurrences, and patients in pStage IV because evaluation of the clinical and prognostic effects of postoperative BWL might be difficult after non-curative resection.

Almost all patients without gastric stenosis took food until dinner the day before surgery. Curative gastrectomy with lymphadenectomy was performed based on the Japanese gastric cancer treatment guidelines (14, 15). Surgical procedures comprised distal gastrectomy, total gastrectomy, and proximal gastrectomy according to the preoperative stage and tumour location. Prophylactically, one or two drainage tubes for subsequent leakage or pancreatic fistulae were placed for radical gastrectomy. The nasogastric tube was

removed on postoperative day 1. Oral intake of rice gruel was started on postoperative day 3 or 4. At the time of discharge, almost all patients were taking regular food. Postoperative complications were assessed by Clavien-Dindo classification (16, 17).

Resected specimens were examined and evaluated by pathologists based on the 14th Japanese Classification of Gastric Carcinoma (18) and the 7th Tumour-Node-Metastasis classification (19). All patients were examined in the outpatient clinic, where abdominal ultrasound, computed tomography, and measurement of levels of carcinoembryonic antigen and carbohydrate antigen 19-9 were performed every 3 to 6 months after surgery.

Assessment of postoperative BWL. For all patients examined, body weight, height, body mass index (BMI), and BWL before and 6 months after surgery were analysed. Postoperative BWL was calculated by the following formula: BWL (%)=(preoperative BMI–postoperative BMI at 6 months)/preoperative BMI×100. The body weight of obese patients was reduced more substantially than was that of patients with normal BMI after gastrectomy (data not shown) because the total food intake of obese patients became similar to that of non-obese patients after surgery. In other words, the preoperative food intake of obese patients was relatively higher than that of non-obese patients. Therefore, to examine the clinical effect of critical BWL in patients with a preoperative BMI of 25 kg/m^2 or higher, we modified the formula as follows: BWL (%)=(25–postoperative BMI at 6 months)/preoperative BMI×100.

Statistical analysis. The Mann–Whitney *U*-test was used for unpaired continuous variables of postoperative BWL. Receiver-operating characteristic (ROC) curves and the area under the ROC curve (AUC) were used to assess the feasibility of using postoperative BWL at 6 months after gastrectomy as a predictive marker for subsequent recurrence. The Youden index was used to determine the cut-off value for postoperative BWL (20). The chi-square test or Fisher's exact probability test was used for categorical variables.

For the analysis of overall (OS) and disease-free (DFS) survival rates, survival curves were estimated using the Kaplan–Meier method, and statistical differences were examined using the log-rank test. Univariate and multivariate survival analyses were performed using the likelihood ratio test of the stratified Cox proportional hazards model. A value of $p<0.05$ was considered statistically significant. All statistical analyses were performed using JMP 10.0 software program (SAS Institute, Cary, NC, USA).

Results

Patients' characteristics. Surgical procedures comprised of distal gastrectomy in 55 patients, total gastrectomy in 44, and proximal gastrectomy in three. D2 or D2+ lymphadenectomy was performed in 74 patients and D0-1+ lymphadenectomy was performed in 28 patients, based on the Japanese guidelines (15). Disease in eight patients was staged as pT1, in 17 as pT2, in 35 as pT3, and in 42 as pT4. Of 102 patients, disease in 49 was categorized as pStage II, whereas in 53 patients it was categorized as pStage III. Eight patients had postoperative complication assessed by the Clavien-Dindo classification as grade II or higher, and 94 patients had no complications or Clavien-Dindo grade I complication.

Table I. *Association between body weight loss (BWL) and clinicopathological variables.*

Variable	n=102	BWL (%) (mean±SD)	*p*-Value*
Gender			
Male	61	11.8±7.99	
Female	41	12.4±6.68	0.334
Age (years)			
≤70	67	10.2±7.24	
>70	35	10.5±7.29	0.435
Tumor location			
U	29	12.8±8.75	
ML	73	9.31±6.31	**0.014**
Gastrectomy			
Distal/proximal	58	8.09±5.74	
Total	44	13.2±7.96	**<0.001**
Lymph node dissection			
<D2	29	8.61±6.10	
≥D2	73	11.0±7.54	0.073
Preoperative serum albumin (g/dl)			
≤4.0	34	10.8±7.00	
>4.0	68	10.1±7.37	0.321
Preoperative serum CRP (mg/dl			
<0.3	86	11.2±10.3	
≥0.3	16	12.2±6.86	0.320
Complication			
No	94	10.0±7.26	
Yes	8	14.1±5.81	0.062
Duration of ACT			
None	31	9.72±11.1	
0-3 Months	4	11.3±11.0	0.318
3-6 Months	8	14.6±6.36	0.090
≥6 Months	59	11.9±6.51	0.081
pT category			
pT1-2	25	9.79±6.69	
pT3-4	77	10.5±7.37	0.339
pN category			
pN–	14	10.8±8.30	
pN+	88	10.2±7.10	0.396
Recurrence			
Negative	63	7.04±7.08	
Positive	39	12.4±9.01	**0.010**

U, Upper stomach; ML, middle and lower stomach; CRP, C-reactive protein; ACT: adjuvant chemotherapy. Significant *p*-values (<0.05) are shown in bold; *Mann-Whitney *U*-test.

There were 25 patients whose preoperative BMI was 25 kg/m^2 or higher, and their BWLRs were calculated by the modified formula.

A total of 71 patients (70%) received adjuvant chemotherapy, but 31 patients (30%) did not. The duration of adjuvant chemotherapy was as follows: 0-3 months for four patients, 3-6 months for eight and 6 months or more for 59 patients. As adjuvant chemotherapy, the following drugs were administered: S-1 alone to 55 patients, tegafur-uracil to three patients, tegafur-uracil after S-1 to two patients, 5-

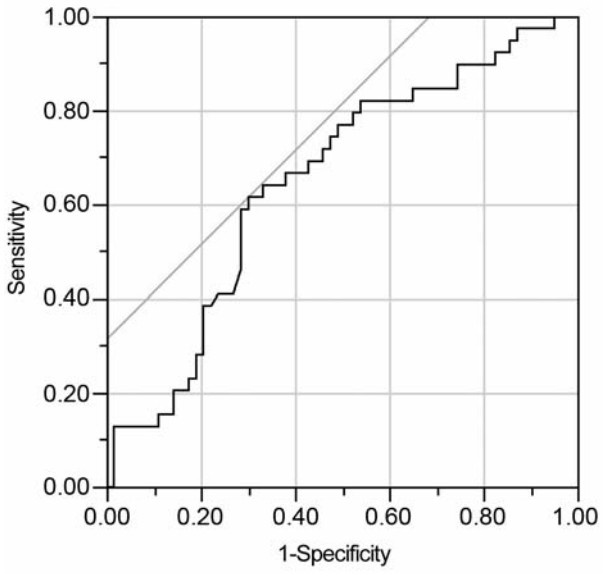

Figure 1. *Curve for tumor recurrence and body weight loss at 6 months after surgery for patients with stage II and III gastric cancer. The area under the curve was 0.634, with a sensitivity of 59.0%, a specificity of 69.8%, and an accuracy of 65.7%.*

fluorouracil after S-1 to one patient, 5-fluorouracil and cisplatin to one patient, S-1 and paclitaxel to two patients, or S-1 and cisplatin to seven patients. None of the patients received adjuvant radiotherapy or chemoradiotherapy. The mean follow-up period was 44.4 months.

Clinicopathological characteristics and postoperative BWL after curative gastrectomy in patients with pStage II or III gastric cancer. We analyzed the clinicopathological characteristics of patients and compared their postoperative BWL (Table I). Patients with tumours in the upper stomach (p=0.014), total gastrectomy (p<0.001), or subsequent recurrences (p=0.010) had a significantly higher BWL, whereas the staging factors, such as depth of invasion and lymph node metastasis, were not associated with BWLR. A higher BWL also tended to be observed after D2 or D2+ lymphadenectomy (p=0.073) and be related to the duration of adjuvant chemotherapy (3-6 months, p=0.090; 6 months or more, p=0.081) and severe complications after surgery (p=0.062).

Cut-off value of BWL associated with subsequent recurrence. To find a cut-off point of BWL that could predict a subsequent recurrence in patients, we used the AUC with the Youden index (Figure 1). The value of the AUC was 0.634 and the optimal cut-off point of BWL was observed at 12% with a sensitivity of 59.0%, a specificity of 69.8%, and an accuracy of 65.7%.

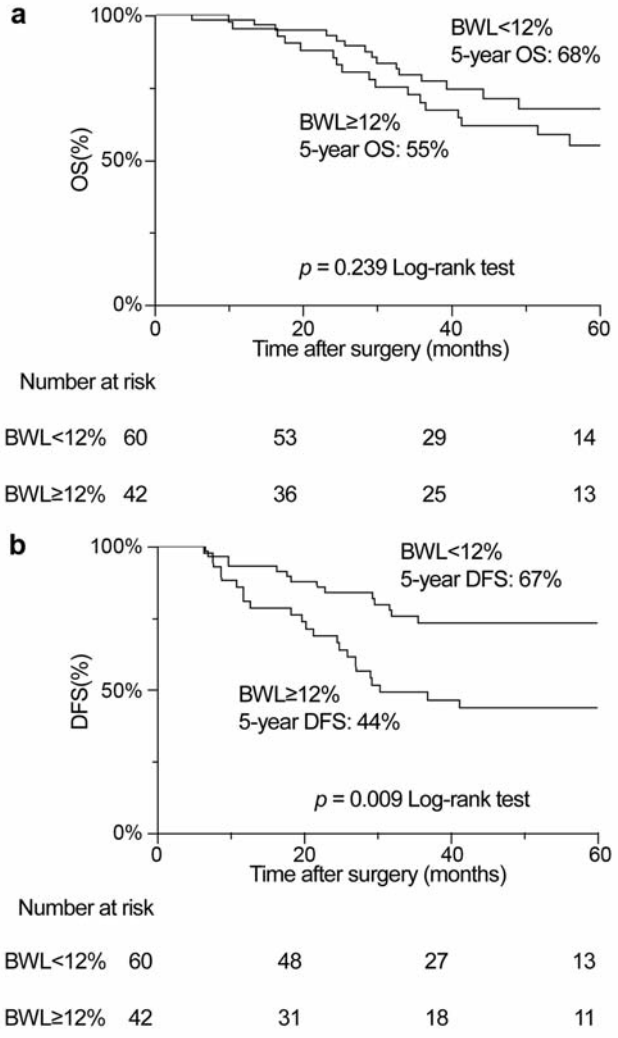

Figure 2. *Comparisons of Kaplan–Meier curves of five-year overall survival (OS) (a) and disease-free survival (DFS) (b) between patients based on body weight loss (BWL) during the first 6 months after surgery. The log-rank test was used for statistical analysis. All 102 patients analysed in this study were divided into two groups by BWL: BWL≥12% (n=42) and BWL<12% (n=60).*

Comparison of clinicopathological factors between patients with and without 12% BWL. We next compared the clinicopathological features between patients with a BWL of 12% or more and those without (Table II). Long duration of adjuvant chemotherapy and subsequent recurrence were significantly associated with BWL of 12% or higher (p=0.001 and p=0.004, respectively).

Survival outcomes. The OS and DFS curves are represented in Figure 2. There was no difference in OS between patients with a postoperative BWL of 12% or higher and those with a BWL of less than 12% (Figure 2a), whereas those with a

postoperative BWL of 12% or higher had a significantly poor DFS (p=0.009). The 5-year DFS rates of patients with a BWL of 12% or higher and less than 12% was 44% and 67%, respectively (Figure 2b).

Comparison of DFS in patients with gastric cancer after curative gastrectomy. Univariate and multivariate analysis using the Cox proportional hazard model demonstrated that a BWL of 12% or higher was an independent prognostic factor of poor DFS (hazard ratio=2.69 (95% confidence interval=1.42-5.21; p=0.002) (Table III).

Discussion

The aim of the study was to assess the prognostic effect of BWL after gastrectomy in patients with gastric cancer. Recent studies in some malignant diseases identified that BWL after esophagectomy (11), after allogenic hematopoietic stem cell transplantation (21) or during radiotherapy (22) were reported to have a negative impact on prognosis. In gastric cancer, however, there exist only a few reports on poor outcomes associated with BWL. Yu *et al*. reported that BWL between 6 and 12 months after surgery was an independent poor prognostic factor (12). In addition, Lee *et al*. revealed that a BWL of more than 30% at 6 months after surgery was significantly associated with an early recurrence (13). In this study, we recorded a potential risk of subsequent recurrences associated with BWL even in the first 6 months after surgery. Moreover, we verified that the BWL cut-off value of 12%, which is lower than that in a previous report (13), was crucial for predicting patients with subsequent recurrence. Our results imply that nutritional insufficiency at an early stage after surgery and higher BWL could affect recurrence in patients after curative surgery for gastric cancer. We, therefore, should reconsider how patients with BWL should be treated after gastrectomy.

The immune system is highly dependent upon the adequate availability of nutrients, such as amino acids (23), specific vitamins, minerals and trace elements (24, 25). BWL may be closely linked to the deficiency of these nutrients. In this study, we hypothesized that poor outcomes after curative gastrectomy might be due to an impaired immune response as a consequence of BWL in patients with gastric cancer. To verify this hypothesis, we investigated which clinico-pathological factors are related to BWL, and whether BWL is indeed associated with poor outcomes in patients. Consequently, we clearly demonstrated that BWL during the first 6 months after surgery is significantly associated with clinical factors, such as tumour in the upper stomach, total gastrectomy, and subsequent recurrence. In addition, we suggest that a postoperative BWL of 12% or higher is an independent risk factor for subsequent recurrence in patients with stage II or III gastric cancer.

Table II. *Risk factors associated with recurrence in 102 patients after curative gastrectomy.*

Variable (n=102)	BWL		*p*-Value*
	<12% n=60 (%)	≥12% n=42 (%)	
Gender			
Male	40 (67%)	21 (50%)	
Female	20 (33%)	21 (50%)	0.091
Age (years)			
≤70	35 (58%)	32 (76%)	
>70	25 (42%)	10 (24%)	0.058
Tumor location			
U	15 (25%)	14 (33%)	
ML	45 (75%)	28 (67%)	0.360
Gastrectomy			
Distal/proximal	38 (63%)	20 (48%)	
Total	22 (37%)	22 (52%)	0.115
Lymph node dissection			
<D2	18 (30%)	10 (24%)	
≥D2	42 (70%)	32 (76%)	0.488
Preoperative serum albumin (g/dl)			
≤4.0	20 (33%)	14 (33%)	
>4.0	40 (67%)	28 (67%)	1.000
Preoperative serum CRP (mg/dl)			
<0.3	50 (83%)	36 (86%)	
≥0.3	10 (17%)	6 (14%)	0.744
Complication			
No	57 (95%)	37 (88%)	
Yes	3 (5%)	5 (12%)	0.206
Duration of ACT			
None	27 (45%)	4 (10%)	
0-3 Months	5 (8%)	3 (7%)	
3-6 Months	1 (2%)	3 (7%)	
≥6 Months	27 (45%)	32 (76%)	**0.001**
pT category			
pT1-T2	14 (23%)	11 (26%)	
pT3-T4	46 (77%)	31 (74%)	0.742
pN category			
pN-	6 (10%)	8 (19%)	
pN+	54 (90%)	34 (81%)	0.195
Recurrence			
Negative	44 (73%)	19 (45%)	
Positive	16 (27%)	23 (55%)	**0.004**

BWL: Body weight loss at 6 months after surgery; U, upper stomach; ML, middle and lower stomach; CRP, C-reactive protein; ACT: adjuvant chemotherapy. Significant p-values (<0.05) are shown in bold; *Chi square test or Fisher's test.

Patients with gastric cancer are predominantly at-risk for malnutrition due to loss of appetite, which is a sequelae of gastrectomy that hampers food intake. Malnutrition is a sub-acute or chronic state in which a combination of varying degrees of undernutrition and inflammation leads to a change in body composition and diminished function (26). As shown in a previous study related to BWL (27),

Table III. *Univariate and multivariate cox proportional hazards analysis of clinicopathological factors associated with disease-free survival (DFS).*

			Univariate			Multivaliate		
Factor	n	5-Year DFS (%)	HR	95% CI	*p*-Value	HR	95% CI	*p*-Value
Gender								
Male	61	58.9	1					
Female	41	54.3	1.237	0.678-2.323	0.513		-	
Age (years)								
≤70	67	56.6	1					
>70	35	59.9	0.937	0.457-1.810	0.851		-	
Tumor location								
U	29	39.8	1					
ML	73	64.3	0.555	0.294-1.08	0.083		-	
Gastrectomy								
Distal/proximal	58	61.9	1					
Total	44	52.3	1.241	0.657-2.334	0.502		-	
Lymph node dissection								
<D2	28	68.5	1					
≥D2	74	53.4	1.656	0.799-3.871	0.183		-	
Albumin (g/dl)								
≤4.0	34	48.5	1					
>4.0	68	61.1	0.855	0.447-1.718	0.648		-	
CRP (mg/dl)								
<0.3	86	57.3	1					
≥0.3	16	56.9	0.995	0.375-2.212	0.991		-	
Complication								
No	94	57.2	1					
Yes	8	62.5	1.031	0.249-2.858	0.96		-	
Duration of ACT								
None	31	58.6	1					
0-3 Months	8	60.0	1.110	0.247-3.658				
3-6 Months	4	50.0	1.347	0.207-5.125				
≥6 Months	59	57.5	1.058	0.518-2.329	0.986		-	
pT category								
pT1-2	25	86.3	1			1		
pT3-4	77	49.1	4.373	1.577-18.14	**0.003**	5.226	1.870-21.77	**0.001**
pN category								
pN–	14	45.0	1					
pN+	88	59.2	0.558	0.269-1.304	0.166		-	
BWL								
<12%	60	67.2	1			1		
≥12%	42	43.7	2.299	1.222-4.434	**0.010**	2.689	1.423-5.207	**0.002**

HR, Hazard ratio; CI, confidence interval; U, upper stomach; ML, middle and lower stomach; CRP, C-reactive protein; BWL, body weight loss at 6 months after surgery. Significant *p*-values (<0.05) are shown in bold.

we found that patients with tumours in the upper stomach or after total gastrectomy had a significantly higher BWL as a result of functional impairment after gastrectomy, regardless of the staging factors, such as the depth of invasion and lymph node metastasis. In addition, as an inflammatory effect leading to malnutrition, D2 or D2+ lymphadenectomy and severe complications after surgery tended to lead to a higher BWL. Therefore, these risk factors could be important in predicting severe postoperative BWL and making a decision about meticulous nutritional support.

How BWL affects tumour recurrence remains unclear. BWL in patients with cancer is not caused only by diminished nutrient intake and increased nutrient loss but also by tumour-induced dysregulation of metabolism (28, 29). Recently, a high BWL after gastrectomy was reported to be an important factor preventing patients from continuing with S-1 adjuvant chemotherapy (30). Therefore, our first hypothesis was that this poor compliance might be a risk factor for subsequent recurrence. However, in the present study, we did not find such a correlation. On the contrary, long duration of adjuvant chemotherapy was an

independent risk factor for patients with BWL of 12% or higher. A similar result was also reported by Yamaoka *et al*. who found that adjuvant chemotherapy after total gastrectomy was a risk factor for skeletal muscle loss (31). The correlation of BWL and skeletal muscle loss is still unclear, as is whether perioperative nutritional intervention with sufficient caloric intake can prevent subsequent recurrence after curative gastrectomy for patients with gastric cancer. To elucidate these issues, further studies are warranted.

Our study has limitations because it is retrospective in its design and based on a single Institution. Therefore, a prospective study with a large number of patients is needed to validate issues associated with BWL. In conclusion, our study clearly demonstrates that a high BWL after curative gastrectomy contributes to subsequent recurrence in patients with gastric cancer.

Conflicts of Interest

The Authors declare no conflicts of interest.

References

1 Jemal A, Bray F, Center MM, Ferlay J, Ward E and Forman D: Global cancer statistics. CA Cancer J Clin *61*: 69-90, 2011.

2 Bertuccio P, Chatenoud L, Levi F, Praud D, Ferlay J, Negri E, Malvezzi M and La Vecchia C: Recent patterns in gastric cancer: a global overview. Int J Cancer *125*: 666-673, 2009.

3 Tsujimoto H, Sugasawa H, Ono S, Ichikura T, Yamamoto J and Hase, K: Has the accuracy of preoperative diagnosis improved in cases of early-stage gastric cancer?. World J Surg *34*: 1840-1846, 2010.

4 Kim YW, Yoon HM, Yun YH, Nam BH, Eom BW, Baik YH, Lee SE, Lee Y, Kim YA, Park JY and Ryu KW: Long-term outcomes of laparoscopy-assisted distal gastrectomy for early gastric cancer: result of a randomized controlled trial (COACT 0301). Surg Endosc *27*: 4267-4276, 2013.

5 Yu Z, Zhuang CL, Ye XZ, Zhang CJ, Dong QT and Chen BC: Fast-track surgery in gastrectomy for gastric cancer: a systematic review and meta-analysis. Langenbecks Arch Surg *399*: 85-92, 2014.

6 Kunisaki C, Ishino J, Nakajima S, Motohashi H, Akiyama H, Nomura M, Matsuda G, Otsuka Y, Ono HA and Shimada H: Outcomes of mass screening for gastric carcinoma. Ann Surg Oncol *13*: 221-228, 2006.

7 Kubota T, Hiki N, Nunobe S, Kumagai K, Aikou S, Watanabe R, Sano T and Yamaguchi T: Significance of the inflammation-based Glasgow prognostic score for short-and long-term outcomes after curative resection of gastric cancer. J Gastroint Surg *16*: 2037-2044, 2012.

8 Ariake K, Ueno T, Takahashi M, Goto S, Sato S, Akada M and Naito H: E-PASS comprehensive risk score is a good predictor of postsurgical mortality from comorbid disease in elderly gastric cancer patients. J Surg Oncol *109*: 586-592, 2014.

9 Gibbs J, Cull W, Henderson W, Daley J, Hur K and Khuri SF: Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. Arch Surg *134*: 36-42, 1999.

10 Kubota T, Hiki N, Sano T, Nomura S, Nunobe S, Kumagai K, Aikou S, Watanabe R, Kosuga T and Yamaguchi T: Prognostic significance of complications after curative surgery for gastric cancer. Ann Surg Oncol *21*: 891-898, 2014.

11 D'Journo XB, Ouattara M, Loundou A, Trousse D, Dahan L, Nathalie T, Doddoli C, Seitz JF and Thomas PA: Prognostic impact of weight loss in 1-year survivors after transthoracic esophagectomy for cancer. Dis Esophagus *25*: 527-534, 2012.

12 Yu W, Seo BY and Chung HY: Postoperative body-weight loss and survival after curative resection for gastric cancer. Br J Surg *89*: 467-470, 2002.

13 Lee SE, Lee JH, Ryu KW, Nam B, Kim CG, Park SR, Kook MC and Kim YW: Changing pattern of postoperative body weight and its association with recurrence and survival after curative resection for gastric cancer. Hepatogastroenterology *59*: 430-435, 2011.

14 Nakajima T: Gastric cancer treatment guidelines in Japan. Gastric cancer *5*: 1-5, 2002.

15 Japanese Gastric Cancer Association: Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric cancer *14*: 113-123, 2011.

16 Dindo D, Demartines N and Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg *240*: 205-213, 2004.

17 Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL and Makuuchi M: The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg *250*: 187-196, 2009.

18 Japanese Gastric Cancer Association: Japanese Classification of Gastric Carcinoma: 3rd English edition. Gastric cancer *14*: 101-112, 2011.

19 Sobin LH, Gospodarowicz MK and Wittekind C, editors: TNM classification of malignant tumours. 7th ed. John Wiley & Sons, 2010.

20 Akobeng AK: Understanding diagnostic tests 3: receiver operating characteristic curves. Acta Paediatr *96*: 644-647, 2007.

21 Fuji S, Mori T, Khattry N, Cheng J, Do YR, Yakushijin K, Kohashi S, Fukuda T and Kim SW: Severe weight loss in 3 months after allogeneic hematopoietic SCT was associated with an increased risk of subsequent non-relapse mortality. Bone marrow transplant *50*: 100-105, 2015.

22 Langius JAE, Bakker S, Rietveld DHF, Kruizenga HM, Langendijk JA, Weijs PJM and Leemans CR: Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy. Br J Cancer *109*: 1093-1099, 2013.

23 Li P, Yin YL, Li D, Kim SW and Wu G: Amino acids and immune function. Br J Nutr *98*: 237-252, 2007.

24 Wintergerst ES, Maggini S and Hornig DH: Contribution of selected vitamins and trace elements to immune function. Ann Nutr Metab *51*: 301-323, 2007.

25 Mora JR, Iwata M and von Andrian UH: Vitamin effects on the immune system: vitamins A and D take centre stage. Nat Rev Immunol *8*: 685-698, 2008.

26 Soeters PB, Reijven PL, van Bokhorst-de van der Schueren MA, Schols JM, Halfens RJ, Meijers JM and van Gemert WG: A rational approach to nutritional assessment. Clin Nutr *27*: 706-716, 2008.

27 Noguchi Y, Tsuburaya A, Makino T, Fukuzawa K, Nomura K, Yoshikawa T and Xu HM: Metabolic alterations in totally gastrectomised patients–caloric intake and energy consumption. Asian J Surg *15*: 97-102, 1992.
28 Rutegård M, Hughes R, Lagergren P and Blazeby JM: Determinants of global quality of life before and after major cancer surgery: an exploratory study. Qual Life Res *18*: 1131-1136, 2009.
29 Langenhoff BS, Krabbe PFM, Wobbes T and Ruers TJM: Quality of life as an outcome measure in surgical oncology. Br J Surg *88*: 643-652, 2001.
30 Aoyama T, Yoshikawa T, Shirai J, Hayashi T, Yamada T, Tsuchida K, Hasegawa S, Cho H, Yukawa N, Oshima T, Rino Y, Masuda M and Tsuburaya A: Body weight loss after surgery is an independent risk factor for continuation of S-1 adjuvant chemotherapy for gastric cancer. Ann Surg Oncol *20*: 2000-2006, 2013.
31 Yamaoka Y, Fujitani K, Tsujinaka T, Yamamoto K, Hirao M and Sekimoto M: Skeletal muscle loss after total gastrectomy, exacerbated by adjuvant chemotherapy. Gastric Cancer *18*: 382-389, 2014.

Received October 22, 2015
Revised December 12, 2015
Accepted December 18, 2015