The American Journal of Surgery 217 (2019) 757–763

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Postoperative development of sarcopenia is a strong predictor of a poor prognosis in patients with adenocarcinoma of the esophagogastric junction and upper gastric cancer☆

Kensuke Kudou [a, b], Hiroshi Saeki [a, *], Yuichiro Nakashima [a], Shun Sasaki [a], Tomoko Jogo [a], Kosuke Hirose [a], Qingjiang Hu [a], Yasuo Tsuda [a], Koichi Kimura [a, b], Ryota Nakanishi [a], Nobuhide Kubo [a], Koji Ando [a], Eiji Oki [a], Tetsuo Ikeda [a, b], Yoshihiko Maehara [a, c]

[a] Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Endoscopy and Endoscopic Surgery, Fukuoka Dental College, Fukuoka, Japan
[c] Department of Surgery, Kyushu Central Hospital, Fukuoka, Japan

ARTICLE INFO

Article history:
Received 4 June 2018
Accepted 6 July 2018

Keywords:
Postoperative sarcopenia
Gastric cancer
Adenocarcinoma of esophagogastric junction

ABSTRACT

Background: There were few studies assessed the postoperative sarcopenia in patients with cancers. The objective of present study was to assess whether postoperative development of sarcopenia could predict a poor prognosis in patients with adenocarcinoma of esophagogastric junction, (AEG) and upper gastric cancer (UGC).
Methods: Patients with AEG and UGC who were judged as non-sarcopenic before surgery were reassessed the presence of postoperative development of sarcopenia 6 months after surgery. Patients were divided into the development group or non-development group, and clinicopathological factors and prognosis between these two groups were analyzed.
Results: The 5-year overall survival rates were significantly poorer in the development group than non-development group (68.0% vs. 92.6%, $P = 0.0118$). Multivariate analyses showed that postoperative development of sarcopenia was an independent prognostic factor for poor overall survival ($P = 0.0237$).
Conclusions: Postoperative development of sarcopenia was associated with a poor prognosis in patients with AEG and UGC.

Introduction

In 1989, Rosenberg[1] referred to the progressive systematic skeletal muscle loss with atrophy or aging as sarcopenia. The presence of sarcopenia is approximately 20% in adults aged <70 years to >50% in those aged >70 years.[2] Sarcopenia has been suggested as a risk factor for physical disability, limitation of function, and ultimately death.[3] The number of reports on the relationship between cancer and sarcopenia is increasing.[4–11]

We previously reported that preoperative sarcopenia can predict a poor prognosis in patients of the adenocarcinoma esophagogastric junction (AEG) and upper gastric cancer (UGC).[12] Our data showed that sarcopenia was an independent poor prognostic factor for overall survival (OS) for AEG and UGC. On the other hand, few studies have assessed the clinical significance of postoperative development from non-sarcopenia to sarcopenia in patients with cancers. Previous reports have suggested that postoperative skeletal muscle loss can predict recurrence of hepatocellular carcinoma[13] as well as shorter OS in patients with renal cell carcinoma[14] and urothelial carcinoma of the bladder.[15] However, the relation between postoperative decrease in skeletal muscle mass and gastrointestinal cancers remains controversial.

Some predictive biomarkers of survival in patients with

Abbreviations and acronyms: AEG, adenocarcinoma of esophagogastric junction; UGC, upper gastric cancer; CT, computed tomography; SMI, skeletal muscle index; BMI, body mass index; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; PNI, prognostic nutritional index; PI, prognostic index; CONUT, controlling nutritional status; RFS, recurrence-free survival; OS, overall survival.

☆ This paper is not based on a previous communication to a society or meeting.

* Corresponding author. FACS, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku Fukuoka-shi, Fukuoka 812-8582, Japan.
E-mail address: h-saeki@surg2.med.kyushu-u.ac.jp (H. Saeki).

https://doi.org/10.1016/j.amjsurg.2018.07.003
0002-9610/

malignancies were recently reported. Representative predictive biomarkers include the platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), prognostic nutrition index (PNI), prognostic index (PI), and controlling nutritional status (CONUT) score.[16–18] These inflammation-based scores have exhibited prognostic significance in patients with various types of malignancies.[16,18–20] However, no studies have analyzed whether these biomarkers can predict postoperative development of sarcopenia.

In the present study, we focused on postoperative development of sarcopenia in patients with AEG and UGC and researched whether development can predict long-term outcomes. Overall, we found that postoperative development of sarcopenia could predict a poor prognosis independently in patients who underwent surgery of AEG and UGC. We propose the importance of postoperative nutritional care in patients after upper digestive surgery.

Methods

Patients

In this single-institutional retrospective analysis, we investigated patients with AEG and UGC diagnosed as adenocarcinoma pathologically, who underwent surgery from January 2005 to March 2016 in Kyushu University. Patients with other types of tumors were excluded from this analysis.

Nine patients who had undergone noncurative or palliative surgery were excluded among 157 patients. Finally, 148 patients with AEG and UGC were analyzed in this study (Fig. 1). We applied the Siewert classification regarding tumor location.[21] Siewert type I, II, and III tumors were defined as AEG and tumors in which the center was located >5 cm below the esophagogastric junction in the upper third of the stomach as UGC[12] in present study. By these criteria, 59 patients were categorized into AEG, and remaining 89 patients were categorized as UGC.

Permission to perform present retrospective study was provided by the Institutional Review Board in Kyushu University (27–192).

Criteria of sarcopenia

Computed tomography (CT) images were used for measurement of the skeletal muscle area. The skeletal muscle area was measured by manual outlining of the quadratus lumborum, psoas, transversus abdominis, erector spinae, the rectus abdominis muscle and external and internal oblique muscles of the abdomen at the level of the third lumbar vertebra.[4,12,22,23] The skeletal muscle index (SMI) was computed as follows: (cross-sectional area of the skeletal muscle at the level of the third lumbar vertebra [cm^2])/(height [m] × height [m]). Because the difference related gender in the SMI and the degree of obesity should be considered for accurate assessment, sarcopenia was evaluated based on generally accepted sex-specific and body mass index (BMI)-specific cut-off values. In men with a BMI of ≥25 kg/m^2, the threshold for sarcopenia was an SMI of 53 cm^2/m,[2] whereas in men with a BMI of <25 kg/m^2, the threshold for sarcopenia was an SMI of 43 cm^2/m.[2] In women, the threshold was an SMI of 41 cm^2/m^2 regardless of the BMI.[11,12,24] According to these criteria, 42 and 106 patients were preoperatively divided into the sarcopenia group and non-sarcopenia group, respectively (Fig. 1). In total, 106 patients in the non-sarcopenia group were reassessed after surgery. Preoperative sarcopenia was assessed using the CT images

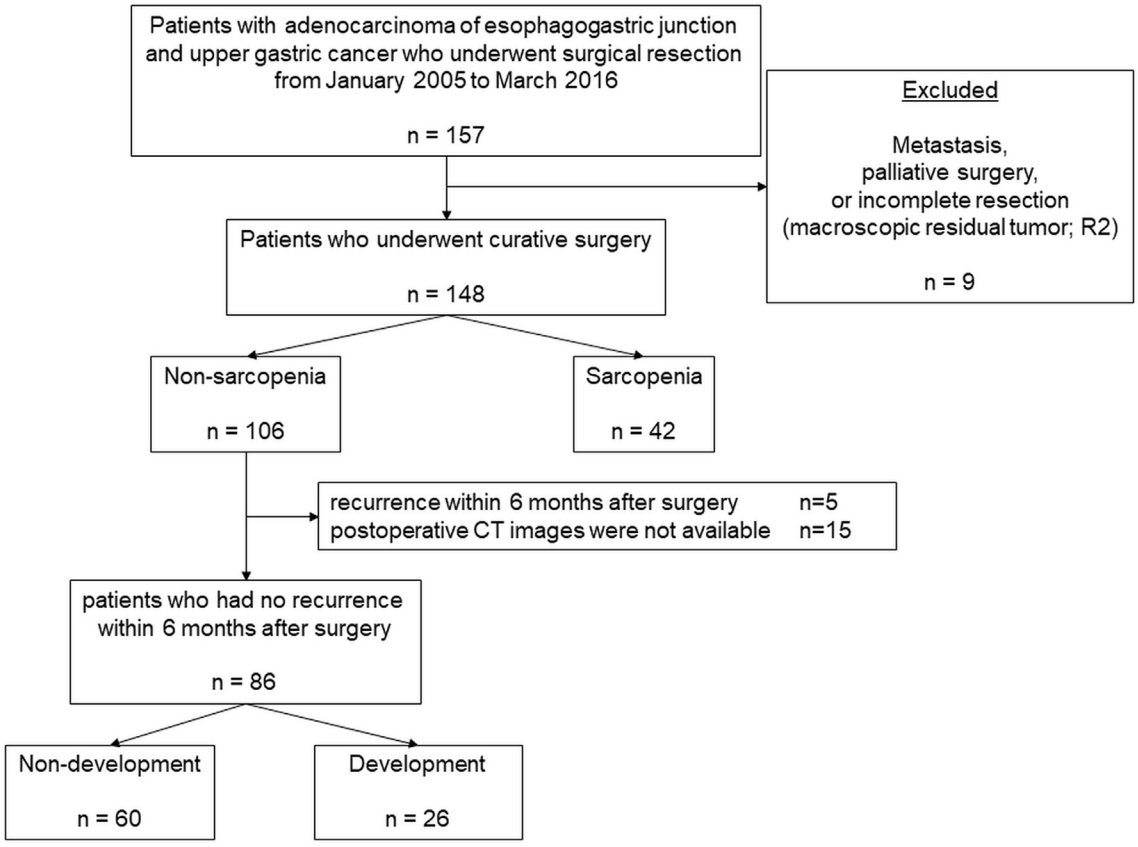

Fig. 1. Flow chart depicting the patient selection process.

obtained before surgery, and postoperative sarcopenia was assessed using the CT images obtained approximately 6 months (range, 5–7 months) after surgery. Fifteen patients whose postoperative CT images were unavailable within this period and five patients who developed recurrence within 6 months were excluded. As a result, 86 patients were eligible for assessment regarding whether postoperative development of sarcopenia had occurred 6 months after surgery (Fig. 1).

Prognostic biomarkers

The PLR, NLR, PNI, PI, and CONUT score were calculated. The blood data were inspected preoperatively. The PNI was computed as follows: 10 × serum albumin (g/dl) + 0.005 × total lymphocyte count (per mm^3).[16] Calculation of the PI was based on the white blood cell count and C-reactive protein level. The upper limits of the normal ranges for the C-reactive protein level (1.0 mg/dl) and white

Table 1
Clinicopathological features between development and non-development group.

Factor		Development of sarcopenia		*P* value
		No	Yes	
		(n = 60)	(n = 26)	
Sex	Male	47 (78.3)	19 (73.1)	0.5904
	Female	13 (21.7)	7 (26.9)	
Age		62.9 (35–91)	61.7 (43–82)	0.6772
Tumor location	AEG	18 (30.0)	16 (61.5)	0.0084
	UGC	42 (70.0)	10 (38.5)	
pStage	I	30 (50.0)	11 (42.3)	0.6393
	II-IV	30 (50.0)	15 (57.7)	
pT	T1	26 (43.3)	10 (38.5)	0.9250
	T2-T4	34 (56.7)	16 (61.5)	
pN	N0	38 (63.3)	12 (46.2)	0.1591
	N1-N3	22 (36.7)	14 (53.8)	
Serum albumin (g/dl)		4.1 (3.1–5.0)	4.2 (3.3–5.0)	0.1691
CRP (mg/dL)	<0.3	51 (85.0)	23 (88.5)	1.0000
	≥0.3	9 (15.0)	3 (11.5)	
Surgical procedure	Total gastrectomy	58 (96.7)	25 (96.2)	1.0000
	Proximal gastrectomy	2 (3.3)	1 (3.8)	
All postoperative complications	No	46 (76.7)	12 (46.2)	0.0111
	Yes	14 (23.3)	14 (53.8)	
Severe complications (CD grade ≥ IIIa)	No	56 (93.3)	21 (80.8)	0.1218
	Yes	4 (6.7)	5 (19.2)	
Neoadjuvant chemotherapy	No	55 (91.7)	26 (100.0)	0.3166
	Yes	5 (8.3)	0 (0.0)	
Adjuvant chemotherapy	No	41 (68.3)	13 (50.0)	0.1453
	Yes	19 (31.7)	13 (50.0)	
PNI	≥45	48 (80.0)	24 (92.3)	0.2112
	<45	12 (20.0)	2 (7.7)	
NLR	<2.58	39 (65.0)	19 (73.1)	0.6173
	≥2.58	21 (35.0)	7 (26.9)	
PLR	<150	40 (66.7)	14 (53.8)	0.3324
	≥150	20 (33.3)	12 (46.2)	
PI	0	56 (93.3)	23 (88.5)	0.4274
	1	4 (6.7)	3 (11.5)	
CONUT score	<2	44 (73.3)	18 (69.2)	0.7947
	≥2	16 (26.7)	8 (30.8)	
Recurrence	No	56 (93.3)	17 (65.4)	0.0020
	Yes	4 (6.7)	9 (34.6)	

AEG: adenocarcinoma of esophagogastric junction, UGC: upper gastric cancer, CRP: C-reactive protein, CD: Clavien-Dindo classification, PNI: prognostic nutritional index, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, PI: prognostic index, CONUT: controlling nutritional status.
Data are presented as n (%) with the exception of age and serum albumin, which are presented as mean (range).

blood cell count (11,000/mm^3) were used as cut-off points.[16] The PI was 0 if both values were lower than the cut-off points, and the PI was 1 if one of the two markers was elevated. The CONUT score was computed based on the serum albumin level, total cholesterol level and peripheral lymphocyte count, as previously described.[17] The optimal cut-off values of the PLR, NLR, and PNI were determined to be 150, 2.58, and 45, respectively, as previously described.[16,18]

Statistical analysis

The unpaired *t*-test or Fisher's exact test were used for assessment of differences in characteristics between the two groups. Survival curves were visualized by the Kaplan-Meier method, and the log-rank test was used for analyses. Univariate and multivariate analyses were performed with a Cox proportional hazard model to detect the independent prognostic factors. All *P* values were two-sided, and a *P* value of <0.05 was determined to be statistically significant. JMP PRO 11 software was used for all analyses in present study.

Results

Clinicopathological features according to postoperative development of sarcopenia

In total, 26 (30%) of the 86 patients in the non-sarcopenia group had converted to sarcopenia by 6 months after surgery (Fig. 1). These patients were assigned to the development group, and their clinicopathological features were compared with those of patients in the non-development group (Table 1).

With respect to tumor location, the proportion of patients with AEG was higher in the development group than non-development group ($P = 0.0084$). The incidence of all postoperative complications was also higher in the development group than non-development group ($P = 0.0111$), while the incidence of severe complications (Clavien-Dindo[25,26] grade ≥ IIIa) was not associated with the development of sarcopenia ($P = 0.1218$) (Table 1). There were no differences in any other clinicopathological or perioperative features between the two groups (Table 1).

Prognostic biomarkers and postoperative development of sarcopenia

The PNI, NLR, PLR, PI, and CONUT were calculated, and the patients were divided into two groups based on the cut-off values of these biomarkers. We examined the relationship between the values of these biomarkers and development of sarcopenia. There were no significant correlations between any of these biomarkers and development of sarcopenia (Table 1).

Postoperative development of sarcopenia and recurrence of AEG and UGC

We compared the recurrence rate between the development and non-development groups to validate whether postoperative development of sarcopenia can predict recurrence of AEG and UGC. The recurrence rate was higher in the development group than non-development group significantly ($P = 0.0020$) (Table 1).

Long-term outcomes according to postoperative development of sarcopenia

The prognosis was compared between patients in the development group and non-development group. Among all patients, the 3-year and 5-year RFS and OS rates were significantly lower in the development group than non-development group (3-year RFS: 62.7% vs. 93.1%, 5-year RFS: 62.7% vs. 93.1%, $P = 0.0004$; 3-year OS: 82.0% vs. 92.6%, 5-year OS: 68.0% vs. 92.6%, $P = 0.0118$) (Fig. 2).

Factors associated with poor prognosis of AEG and UGC

To detect predictive factors for recurrence of AEG and UGC, we compared representative clinicopathological features, perioperative features, and prognostic biomarkers between patients with recurrence and those without recurrence. With respect to perioperative features, the proportion of patients with an intraoperative blood loss volume of ≥500 ml and the incidence of postoperative complications were significantly higher in the patients with recurrence ($P = 0.0470$ and $P = 0.0239$, respectively). No prognostic biomarkers were associated with recurrence of AEG or UGC. (Supplementary Table 1).

We also calculated the postoperative change in the SMI using the formula [(preoperative SMI − postoperative SMI)/preoperative SMI] × 100 and regarded this value as the rate of decrease in the SMI. The mean rate of decrease in the SMI was significantly higher in the patients with recurrence than those with non-recurrence

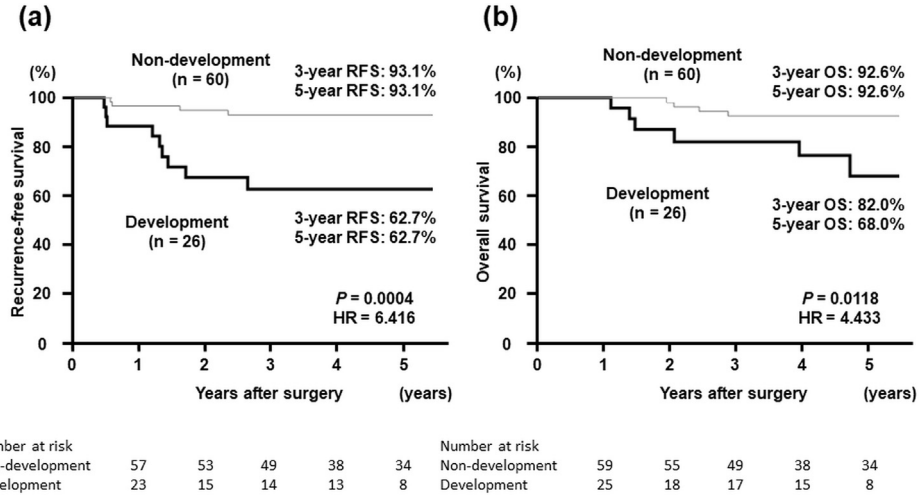

Fig. 2. Postoperative survival of patients in the development group and non-development group: (a) recurrence-free survival and (b) overall survival of all study patients. The 3-year and 5-year recurrence-free and overall survival rates were significantly lower in the development group than non-development group ($P = 0.0004$ and $P = 0.0118$, respectively).

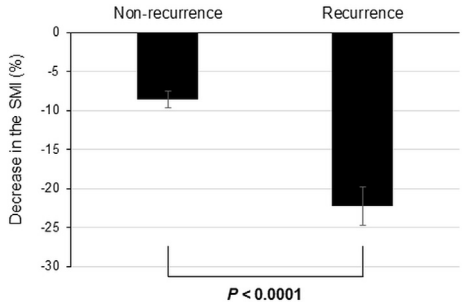

Fig. 3. Rate of decrease in the skeletal muscle index (SMI) between patients with recurrence and those with non-recurrence. The rate of decrease in the SMI was calculated as the percentage of change in the SMI as follows: [(preoperative SMI − postoperative SMI)/preoperative SMI] × 100. Data are represented as mean ± standard deviation.

(22.3% vs. 8.4%, $P < 0.0001$) (Fig. 3 and Supplementary Table 1).

To identify prognostic factors for OS, we carried out univariate and multivariate analyses with a Cox proportional hazard model. The univariate analyses showed that the T-stage (T1–3 vs. T4) ($P < 0.0001$), N-stage (N0–1 vs. N2–3) ($P < 0.0001$), postoperative complications ($P = 0.0120$), and postoperative development of sarcopenia ($P = 0.0207$) were correlated with poor OS in patients with AEG and UGC. We included these four factors in the multivariate analyses and found that the T-stage, N-stage, and development of sarcopenia were independent predictive factors for OS in patients with AEG and UGC ($P = 0.0356$, $P = 0.0018$, and $P = 0.0273$, respectively) (Table 2). Additionally, the N-stage and development of sarcopenia could predict poor RFS in patients with AEG and UGC ($P = 0.0156$ and $P = 0.0101$, respectively) (Supplementary Table 2).

Discussion

In this study, the recurrence rate in patients with postoperative development of sarcopenia was higher than that in patients who did not undergo development. Both the univariate and multivariate analyses indicated that postoperative development of sarcopenia could predict a poor prognosis for OS independently. Several studies showing postoperative skeletal muscle loss in patients with other malignancies have been reported to date. Kobayashi et al.[13] reported that postoperative decrease of skeletal muscle could predict recurrence of hepatocellular carcinoma after hepatectomy. Fukushima et al.[14] reported that postoperative decrease in the SMI after cytoreductive nephrectomy was correlated with shorter OS in patients with renal cell carcinoma. Miyake et al.[15] reported that postoperative psoas muscle loss was associated with shorter OS in patients with urothelial carcinoma of the bladder. These studies as well as the present study suggest that postoperative skeletal muscle loss can be a novel prognostic factor for OS or RFS. Both Kobayashi et al.[13] and Fukushima et al.[14] evaluated the SMI 5–6 months after surgery, similar to our study. Miyake et al.[15] evaluated postoperative changes in skeletal muscle mass from 6 to 24 months after surgery. A 6-month postoperative follow-up seems to be reasonable for reassessment of the SMI because follow-up CT is generally recommended 6 months after surgery for patients with gastric cancer of any stage according to the Japanese gastric cancer treatment guidelines.[27]

The proportion of patients with AEG and the incidence of postoperative complications were higher in the development group than non-development group ($P = 0.0084$ and 0.0111, respectively). Surgical stress is often more severe in patients with AEG than UGC. Additionally, postoperative complications can delay recovery of the patient's physical status. Therefore, these factors can affect the progression of postoperative sarcopenia. However, our multivariate analysis showed that development of sarcopenia could predict poor prognosis, whereas tumor location and postoperative complications were not significant. We also evaluated prognostic biomarkers. Previous studies showed that these biomarkers were predictors of poor prognosis in patients with gastric

Table 2
Univariate and multivariate analyses for overall survival.

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Male (vs female)	3.050 (0.572–56.25)	0.2211	–	
Age < 65 y (vs ≥ 65 y)	1.613 (0.448–7.487)	0.4761	–	
AEG (vs UGC)	1.587 (0.441–5.709)	0.4671	–	
T-Stage (T4 vs T1-3)	13.19 (3.743–51.88)	<0.0001	4.971 (1.111–27.18)	0.0356
N-Stage (N2-3 vs N0-1)	19.89 (4.924–132.6)	<0.0001	12.83 (2.466–100.1)	0.0018
IBL ≥ 500 ml (vs < 500 ml)	2.288 (0.635–8.241)	0.1975	–	
Postoperative complication	5.137 (1.427–23.85)	0.0120	0.603 (0.098–3.956)	0.5848
PNI < 45 (vs ≥ 45)	0.489 (0.027–2.606)	0.4561	–	
NLR ≥ 2.58 (vs < 2.58)	0.255 (0.014–1.361)	0.1225	–	
PLR ≥ 150 (vs < 150)	0.416 (0.063–1.663)	0.2305	–	
PI = 1 (vs PI = 0)	4.359 (0.656–17.48)	0.1114	–	
CONUT score ≥ 2 (vs < 2)	0.281 (0.015–1.497)	0.1558	–	
Development of sarcopenia	4.433 (1.263–17.37)	0.0207	4.801 (1.192–22.18)	0.0273

HR: hazard ratio, CI: confidence interval, AEG: adenocarcinoma of esophagogastric junction, UGC: upper gastric cancer, IBL: intraoperative blood loss, PNI: prognostic nutritional index, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, PI: prognostic index, CONUT: controlling nutritional status.

cancer.[18–20] Analysis of the relationships between these biomarkers and postoperative development of sarcopenia showed no correlation. Univariate and multivariate analyses for OS revealed that these biomarkers were not associated with long-term outcomes of AEG and UGC in our study (Table 2). We targeted patients who were judged as non-sarcopenic before surgery and excluded patients with preoperative sarcopenia. This might have resulted in selection of patients whose general conditions were relatively good, and this bias might have masked the significance of these biomarkers.

There are a few limitations in present study. First, this was a single-institutional retrospective study. However, the prospective studies are thought to be impractical or difficult to evaluate the clinical significance of sarcopenia. Also, few studies focusing on patients with gastrointestinal tumors has investigated the clinical importance of postoperative sarcopenia. Therefore, accumulation of the findings obtained from retrospective studies of patients with other malignancies from various institutes would be meaningful. The data from the present study offer beneficent information regarding the clinical value of postoperative decrease in the skeletal muscle mass. Second, some criteria for sarcopenia are available. We applied internationally accepted criteria; however, the criteria for sarcopenia were not integrated in many studies on sarcopenia.[4–12,23] Whether the criteria used in the present study might help to precisely reflect the clinical impact of sarcopenia requires further study.

Our study has shown that postoperative loss of skeletal muscle can predict a poor prognosis in patients with AEG and UGC, but one question remains unanswered: Is depletion of skeletal muscle mass an effect or cause of tumor progression? Indeed, cancer cells generally grow rapidly and require high levels of nutrition. This may cause nutrition disorders and resultant skeletal muscle loss. However, recent studies have shown that some myokines, which are secreted by muscle cells, can regulate the growth of cancer cells. Aoi et al.[28] reported that a novel myokine, secreted protein acidic and rich in cysteine (SPARC), suppresses growth of colon tumor via exercise by increasing apoptosis. Hojman et al.[29] reported that exercise-induced muscle-derived cytokines inhibit growth of mammary cancer cells. These results suggest that nutritional support and increased muscle mass may contribute to prevention of tumorigenesis by secreting myokines. The relationship between sarcopenia and myokines in patients with malignancies requires further investigation.

The clinical significance of postoperative sarcopenia remains controversial. Since postoperative therapeutic strategy should be determined according to the pathological diagnosis within 2 months after surgery, postoperative sarcopenia at 6 months after surgery does not affect adjuvant treatment plan. We should pay attention to avoid decrease of patients' skeletal muscle mass within postoperative 6 months. Intensive dietary counselling, oral nutritional supplementation and promotion of exercise during postoperative period might be beneficial.

Conclusions

Postoperative development of sarcopenia could predict a poor prognosis in patients who underwent surgical treatment for AEG and UGC. Our results suggest that strict attention may be needed for patients who exhibit a progressive decrease in the volume of skeletal muscle after surgery for AEG and UGC.

Disclosure of potential conflicts of interest

The authors declare that they have no conflict of interest.

Acknowledgment

We thank Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amjsurg.2018.07.003.

References

1. Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr*. 1997;127:990S–991S.
2. Von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. *J Cachex Sarcopenia Muscle*. 2010;1:129–133.
3. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: european consensus on definition and diagnosis: report of the european working group on sarcopenia in older people. *Age Ageing*. 2010;39:412–423.
4. Harimoto N, Shirabe K, Yamashita YI, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. *Br J Surg*. 2013;100:1523–1530.
5. Fujiwara N, Nakagawa H, Kudo Y, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. *J Hepatol*. 2015;63:131–140.
6. Go SI, Park MJ, Song HN, et al. Sarcopenia and inflammation are independent predictors of survival in male patients newly diagnosed with small cell lung cancer. *Support Care Canc*. 2016;24:2075–2084.
7. Miyamoto Y, Baba Y, Sakamoto Y, et al. Sarcopenia is a negative prognostic factor after curative resection of colorectal cancer. *Ann Surg Oncol*. 2015;22:2663–2668.
8. Choi Y, Oh DY, Kim TY, et al. Skeletal muscle depletion predicts the prognosis of patients with advanced pancreatic cancer undergoing palliative chemotherapy, independent of body mass index. *PLoS One*. 2015;10. e0139749.
9. Dodson S, Baracos VE, Jatoi A, et al. Muscle wasting in cancer cachexia: clinical implications, diagnosis, and emerging treatment strategies. *Annu Rev Med*. 2011;62:265–279.
10. Tamandl D, Paireder M, Asari R, et al. Markers of sarcopenia quantified by computed tomography predict adverse long-term outcome in patients with resected oesophageal or gastro-oesophageal junction cancer. *Eur Radiol*. 2016;26:1359–1367.
11. Tegels JJ, van Vugt JL, Reisinger KW, et al. Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes. *J Surg Oncol*. 2015;112:403–407.
12. Kudou K, Saeki H, Nakashima Y, et al. Prognostic significance of sarcopenia in patients with esophagogastric junction cancer or upper gastric cancer. *Ann Surg Oncol*. 2017;24(7):1804–1810.
13. Kobayashi A, Kaido T, Hamaguchi Y, et al. Impact of postoperative changes in sarcopenic factors on outcomes after hepatectomy for hepatocellular carcinoma. *J Hepatobiliary Pancreat Sci*. 2016;23(1):57–64.
14. Fukushima H, Nakanishi Y, Kataoka M, et al. Postoperative changes in skeletal muscle mass predict survival of patients with metastatic renal cell carcinoma undergoing cytoreductive nephrectomy. *Clin Genitourin Canc*. 2017;15(2):e229–e238.
15. Miyake M, Morizawa Y, Hori S, et al. Clinical impact of postoperative loss in psoas major muscle and nutrition index after radical cystectomy for patients with urothelial carcinoma of the bladder. *BMC Canc*. 2017;17(1):237.
16. Kinoshita A, Onoda H, Imai N, et al. Comparison of the prognostic value of inflammation-based prognostic scores in patients with hepatocellular carcinoma. *Br J Canc*. 2012;107(6):988–993.
17. Ignacio de Ulibarri J, Gonzalez-Madrono A, et al. CONUT: a tool for controlling nutritional status. First validation in a hospital population. *Nutr Hosp*. 2005;20:38–45.
18. Yamanaka T, Matsumoto S, Teramukai S, et al. The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in advanced gastric cancer. *Oncology*. 2007;73(3-4):215–220.
19. Pan QX, Su ZJ, Zhang JH, et al. A comparison of the prognostic value of preoperative inflammation-based scores and TNM stage in patients with gastric cancer. *OncoTargets Ther*. 2015;8:1375–1385.
20. Kuroda D, Sawayama H, Kurashige J, et al. Controlling Nutritional Status (CONUT) score is a prognostic marker for gastric cancer patients after curative resection. *Gastric Cancer*. 2017. https://doi.org/10.1007/s10120-017-0744-3 [Epub].
21. Siewert JR, Stein HJ. Carcinoma of the cardia: carcinoma of the gastroesophageal junction—classification, pathology and extent of resection. *Dis Esophagus*. 1996;9:173–182.
22. Yoshizumi T, Shirabe K, Nakagawara H, et al. Skeletal muscle area correlates with body surface area in healthy adults. *Hepatol Res*. 2014;44:313–318.
23. Matsubara Y, Matsumoto T, Aoyagi Y, et al. Sarcopenia is a prognostic factor for overall survival in patients with critical limb ischemia. *J Vasc Surg*. 2015;61:

945–950.
24. Martin L, Birdsell L, Macdonald N, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol*. 2013;31:1539–1547.
25. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.
26. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250:187–196.
27. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;20(1):1–19.
28. Aoi W, Naito Y, Takagi T, et al. A novel myokine, secreted protein acidic and rich in cysteine (SPARC), suppresses colon tumorigenesis via regular exercise. *Gut*. 2013;62(6):882–889.
29. Hojman P, Dethlefsen C, Brandt C, et al. Exercise-induced muscle-derived cytokines inhibit mammary cancer cell growth. *Am J Physiol Endocrinol Metab*. 2011;301(3):E504–E510.