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Comparison of the influence of postoperative oral nutritional supplementation between octogenarian and non-octogenarian patients undergoing gastrectomy for cancer

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Abstract

Background Despite recent reports, the effectiveness of postoperative oral nutritional supplementation (ONS) on body weight loss and malnutrition after gastrectomy remains controversial. We aimed to elucidate the effectiveness of ONS especially in octogenarian patients undergoing oncological gastrectomy.

Methods A total of 286 consecutive patients who underwent gastrectomy for gastric cancer were eligible. Postoperative body weight loss, malnutrition, and sarcopenia were compared between patients with and without postoperative ONS among octogenarian patients aged ≥ 80 years and non-octogenarian patients aged < 80 years.

Results In this study, 36 (62.1%) octogenarian and 121 (53.1%) non-octogenarian patients continued postoperative ONS for three months. The clinicopathologic characteristics were not different between the ONS (–) and ONS (+) groups among the octogenarian and non-octogenarian patients. The changes in body weight and serum albumin levels at postoperative 1 year were different between the ONS (–) and ONS (+) groups ($P = 0.03$ and $P = 0.04$, respectively) among the octogenarian patients, but not between the two groups among the non-octogenarian patients ($P = 0.99$ and $P = 0.29$, respectively). Also, the decline in psoas muscle mass index at postoperative 6 months and 1 year was significantly lower in the ONS (+) group than in the ONS (–) group ($P < 0.01$ and $P < 0.01$, respectively). In addition, similar results were found in octogenarian patients who underwent distal gastrectomy.

Conclusions Postoperative ONS could prevent body weight loss, malnutrition, and sarcopenia especially in octogenarian patients who underwent gastrectomy for gastric cancer.

Keywords Gastric cancer, Gastrectomy, Postoperative oral nutritional supplementation

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Background

Gastric cancer is one of the most common types of cancer and the fifth leading cause of cancer-related deaths worldwide [1]. Gastrectomy with concomitant lymphadenectomy continues to be a major approach for the treatment of resectable gastric cancer [2]. However, in patients with gastric cancer, postoperative malnutrition after gastrectomy remains a major complication and is associated not only with a remarkable deterioration in quality of life but also with reduced immune function and worse long-term prognosis [3, 4]. Therefore, preventing body weight loss, malnutrition, and sarcopenia after gastrectomy is critical.

Recently, several reports have demonstrated the effectiveness of postoperative oral nutritional supplementation (ONS), defined as supplementary oral intake of dietary food for special medical purposes in addition to the normal food intake, with the aim to prevent body weight loss [5–8]. However, other studies reported that ONS did not prevent body weight loss after gastrectomy [9, 10]. Thus, the effectiveness of postoperative ONS in patients with gastric cancer remains controversial. Furthermore, despite the increasing number of octogenarian patients undergoing gastrectomy for gastric cancer, the effectiveness of ONS in this patient population remains unclear.

We aimed to determine the effectiveness of postoperative ONS especially in octogenarian patients who underwent oncological gastrectomy. In addition, we determined whether the effectiveness of ONS were different between octogenarian and non-octogenarian patients.

Methods

Patients

We retrospectively reviewed data from 403 consecutive patients who underwent surgery for gastric disease between 2017 and 2021 at University of Yamanashi Hospital. Also included were neoadjuvant chemotherapy cases and cases of non-curative resection such as R1 and R2 resections. After excluding 87 patients with non-gastric cancer and non-gastrectomy and 30 patients with incomplete data that could not be followed up 1 year due to transfer or death, 286 patients were eligible for this study. A patient flow diagram was shown in Fig. 1. This study was approved by the institutional review board and performed under the ethical standards of the Declaration of Helsinki and its later amendments.

Treatment with postoperative ONS

All patients received ENSURE® H liquid (Abbott Medical Japan, Tokyo, Japan) or ENORAS® liquid (Otsuka Pharmaceutical Factory, Tokyo, Japan) as ONS in addition to regular meals. Administration of ONS at dosage of 300–400 kcal/day was initiated within postoperative six days and continued for at least three months. ONS (+) group

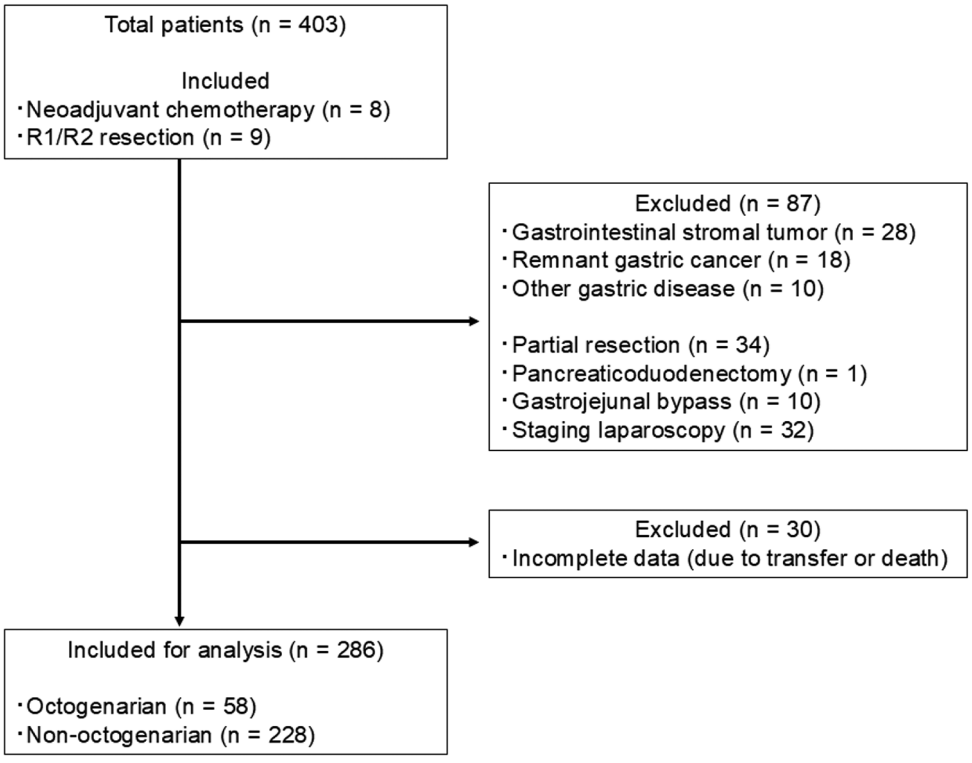

Fig. 1 Patient flow diagram of the present study

was that was able to continue with ONS, and ONS (-) group was that was not able to continue with ONS.

Measurement of psoas muscle mass index

Psoas muscle mass index (PMI) was determined by analyzing axial computed tomography images of bilateral psoas muscles obtained at the level of L3 using the SYNAPSE VINCENT® image analysis system (Fujifilm Medical, Tokyo, Japan). The following formula was used: PMI = bilateral psoas muscle area (cm^2)/body height (m^2).

Gastric cancer treatment, gastrectomy, and postoperative follow-up

The treatment strategy for gastric cancer was decided by a multidisciplinary tumor board based on the Japanese Guidelines for the Treatment of Gastric Cancer [2]. Postoperative follow-up include hematologic tests, radiologic assessment of the gastrointestinal tract, endoscopy, computed tomography, and ultrasonography. Follow-up procedures were performed every three months for at least two years and periodically thereafter, for at least five years. ONS adherence was confirmed by direct confirmation with the patients and families by a multidisciplinary team including doctors, nurses, pharmacists, and dieticians. Also, nutritional guidance was provided by nutritionists on a routine basis before surgery, before discharge, postoperative 6 months, and postoperative 1 year.

Definition

The clinical and pathological tumor stages of gastric cancer were classified based on the Union for International Cancer Control TNM staging, 8th Edition [11]. Performance status was categorized based on the American Society of Anesthesiologists-Physical Status (ASA-PS) and the Eastern Cooperative Oncology Group performance score scales (ECOG-PS) [12, 13]. The Clavien-Dindo (C-D) grading system was used to classify postoperative complications, including pneumonia, anastomotic leakage, and pancreatic fistula, within one month after surgery [14], and C-D grade ≥ II complications were considered clinically significant.

Statistical analysis

All statistical analyses were conducted with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [15]. Data were presented as medians (range) or numbers (%). Patient characteristics were statistically compared between those with and without ONS using Fisher's exact test or the Mann–Whitney U test, as appropriate. Simultaneously, interactions were also assessed, in which the effect of the ONS on body weight loss was evaluated according to the state of other causal variables. A two-sided probability level of <0.05 was considered to indicate significant difference. For P for interaction, $P<0.1$ was considered to have a clinical interaction.

Results

Patient characteristics

The study cohort was categorized into the ONS (–) and ONS (+) groups among octogenarian patients aged ≥ 80 years and non-octogenarian patients aged < 80 years (Table 1). Postoperative ONS was administrated in 36 (62.1%) and 121 (53.1%) patients in the octogenarian and non-octogenarian patient groups.

Among the octogenarian patients, age, sex, ASA-PS, ECOG-PS, preoperative nutritional status, clinical stage, pathological stage, type of gastrectomy, and postoperative complications did not differ between ONS (–) and ONS (+) groups. Although there was no significant difference, the rate of postoperative chemotherapy was higher in the ONS (+) group than in the ONS (–) group (22.2% vs. 4.5%, $P=0.13$). The results were similar among the non-octogenarian patients.

Changes in body weight

Figure 2 shows the comparison of changes in body weight between ONS (–) and ONS (+) groups. Among the octogenarian patients, the mean body weight change at postoperative 6 months was 91.1% ± 7.3% in ONS (–) group and 94.9% ± 9.3% in the ONS (+) group ($P=0.11$). In addition, the mean body weight change at postoperative 1 year was 87.9% ± 13.4% in the ONS (–) group and 94.8% ± 10.0% in the ONS (+) group, indicating that the decline in body weight at postoperative 1 year was significantly lower in the ONS (+) group than in ONS (–) group ($P=0.03$). Among non-octogenarian patients, the mean body weight change did not differ between the ONS (–) and ONS (+) groups at postoperative 6 months and 1 year ($P=0.88$ and $P=0.99$, respectively).

Changes in serum immunonutritional factors

Next, we compared the postoperative levels of serum albumin, C-reactive protein (CRP), and total lymphocyte count between ONS (–) and ONS (+) groups. As shown in Fig. 3a, among the octogenarian patients, serum albumin levels at postoperative 6 months and 1 year were significantly higher in ONS (+) group than in ONS (–) group ($P=0.04$, $P=0.04$, respectively), although preoperative albumin levels were not significantly different between the two groups. Postoperative serum CRP and total lymphocyte levels did not differ between the ONS (–) and ONS (+) groups (Supplemental Fig. 1a). Among the non-octogenarian patients, there were no significant differences in postoperative serum albumin, CRP, and total lymphocyte levels between the ONS (–) and ONS (+) groups (Fig. 3b, Supplemental Fig. 1b). Based on these

Table 1 Patient characteristics

Characteristics	Age ≥ 80			Age < 80		
	ONS (-) *n* = 22 (37.9%)	ONS (+) *n* = 36 (62.1%)	*P* value	ONS (-) *n* = 107 (46.9%)	ONS (+) *n* = 121 (53.1%)	*P* value
Age (years) [a]	83 (80–91)	83 (80–92)	0.63	69 (36–79)	70 (42–79)	0.09
Sex [b]						
Male	13 (55.9)	24 (66.7)	0.59	75 (70.1)	83 (68.6)	0.89
Female	9 (40.9)	12 (33.3)		32 (29.9)	38 (31.4)	
Preoperative BMI (kg/m^2) [a]	22.5 (17.1–26.3)	21.7 (17.0-34.1)	0.89	22.6 (16.2–34.2)	22.6 (14.9–33.2)	0.26
ASA-PS [b]						
1	0 (0.0)	5 (13.9)	0.06	13 (12.1)	8 (6.6)	0.27
2	19 (86.4)	20 (55.6)		79 (73.8)	99 (81.8)	
3	3 (13.6)	11 (30.6)		15 (14.0)	14 (11.6)	
ECOG-PS [b]						
0	11 (50.0)	20 (55.6)	0.70	97 (90.7)	113 (93.4)	0.39
1	10 (45.5)	13 (36.1)		10 (9.3)	7 (5.8)	
2	1 (4.5)	3 (8.3)		0 (0.0)	1 (0.8)	
Serum albumin (g/dL) [a]	3.9 (2.9–4.4)	3.8 (2.6–4.5)	0.67	4.1 (2.5-5.0)	4.1 (2.2-5.0)	0.55
Serum CRP (mg/dL) [a]	0.17 (0.10–7.35)	0.12 (0.10–5.11)	0.45	0.10 (0.00-9.31)	0.10 (0.10–4.29)	0.75
Serum lymphocyte (/μL) [a]	1240 (760–2620)	1250 (420–3260)	0.80	1580 (380–3050)	1520 (650–5330)	0.41
Preoperative PMI [a]	4.5 (2.8–8.7)	4.6 (2.2–7.5)	0.66			
Histology [b]						
Differentiated	20 (90.9)	24 (66.7)	0.06	51 (47.7)	59 (48.8)	0.90
Undifferentiated	2 (9.1)	12 (33.3)		56 (52.3)	62 (51.2)	
Neoadjuvant chemotherapy [b]						
No	22 (100)	35 (97.2)	1.00	106 (98.1)	114 (94.2)	0.07
Yes	0 (0.0)	1 (2.8)		1 (0.9)	7 (5.8)	
Clinical T stage [b]						
T1	11 (50.0)	15 (41.7)	0.84	73 (68.2)	65 (53.7)	0.12
T2	4 (18.2)	9 (25.0)		10 (9.3)	22 (18.2)	
T3	3 (13.6)	7 (19.4)		13 (12.1)	17(14.0)	
T4	4 (18.2)	5 (13.9)		11 (10.3)	17 (14.0)	
Clinical N stage [b]						
N0	16 (72.7)	30 (83.3)	0.39	89 (83.2)	100 (82.6)	0.93
N1	4 (18.2)	2 (5.6)		8 (7.5)	7 (5.8)	
N2	2 (9.1)	3 (8.3)		8 (7.5)	11 (9.1)	
N3	0 (0.0)	1 (2.8)		2 (1.9)	3 (2.5)	
Pathological T stage [b]						
T1	14 (63.6)	17 (47.2)	0.54	71 (66.4)	68 (56.2)	0.19
T2	2 (9.1)	7 (19.4)		10 (9.3)	13 (10.7)	
T3	5 (22.7)	8 (22.2)		16 (15.0)	17 (14.0)	
T4	1 (4.5)	4 (11.1)		10 (9.3)	23 (19.0)	
Pathological N stage [b]						
N0	16 (72.7)	22 (61.1)	0.89	74 (69.2)	77 (63.6)	0.08
N1	3 (13.6)	7 (19.4)		17 (15.9)	14 (11.6)	
N2	2 (9.1)	5 (13.9)		9 (8.4)	9 (7.4)	
N3	1 (4.5)	2 (5.6)		7 (6.5)	21 (17.4)	
Type of gastrectomy						
Distal	17 (77.3)	29 (80.6)	0.24	74 (69.2)	69 (57.0)	0.10
Total	3 (13.6)	7 (19.4)		27 (25.2)	37 (30.6)	
Proximal	2 (9.1)	0 (0.0)		6 (5.6)	15 (12.4)	
Surgical approach [b]						
Open	2 (9.1)	5 (13.9)	0.70	19 (17.8)	18 (14.9)	0.59
Laparoscopic	20 (90.9)	31 (86.1)		88 (82.2)	103 (85.1)	
Field of dissection [b]						

Table 1 (continued)

Characteristics	Age ≥ 80			Age < 80		
	ONS (-) *n* = 22 (37.9%)	ONS (+) *n* = 36 (62.1%)	*P* value	ONS (-) *n* = 107 (46.9%)	ONS (+) *n* = 121 (53.1%)	*P* value
D1	2 (9.1)	4 (11.1)	1.00	13 (12.1)	18 (14.9)	0.12
D1+	11 (50.0)	18 (50.0)		58 (54.2)	49 (40.5)	
D2	9 (40.9)	14 (38.9)		36 (33.6)	54 (44.6)	
Curability						
R0	22 (100)	36 (100)	NA	105 (98.1)	115 (95.0)	0.29
R1/R2	0 (0.0)	0 (0.0)		2 (1.9)	6 (5.0)	
Operation time (min) [a]	377 (203–752)	392 (165–599)	0.71	367 (162–732)	392 (53–749)	0.57
Blood loss (mL) [a]	88 (6-500)	106 (4-851)	0.52	73 (1-1328)	69 (0-1488)	0.82
Pneumonia [b]	2 (9.1)	0 (0.0)	0.14	3 (2.8)	5 (4.1)	0.73
Anastomotic leakage [b]	1 (4.5)	0 (0.0)	0.38	1 (0.9)	2 (1.7)	1.00
Pancreatic fistula [b]	0 (0.0)	2 (5.6)	0.52	14 (13.1)	7 (5.8)	0.07
Hospital stay (day) [a]	10 (8–48)	11 (8–24)	0.25	11 (7–43)	10 (7–27)	0.10
Postoperative therapy [b]						
No	21 (95.5)	28 (77.8)	0.13	80 (74.8)	86 (71.1)	0.55
Yes	1 (4.5)	8 (22.2)		27 (25.2)	35 (28.9)	

Data expressed as number (%) or median (range). ONS: oral nutritional supplementation. BMI: body mass index. ASA-PS: American Society of Anesthesiologists-physical status. ECOG-PS: Eastern Cooperative Oncology Group Performance Status. CRP: C-reactive protein. PMI: Psoas muscle mass index. NA: not applicable

[a] Mann-Whitney U test. [b] Fisher's exact test

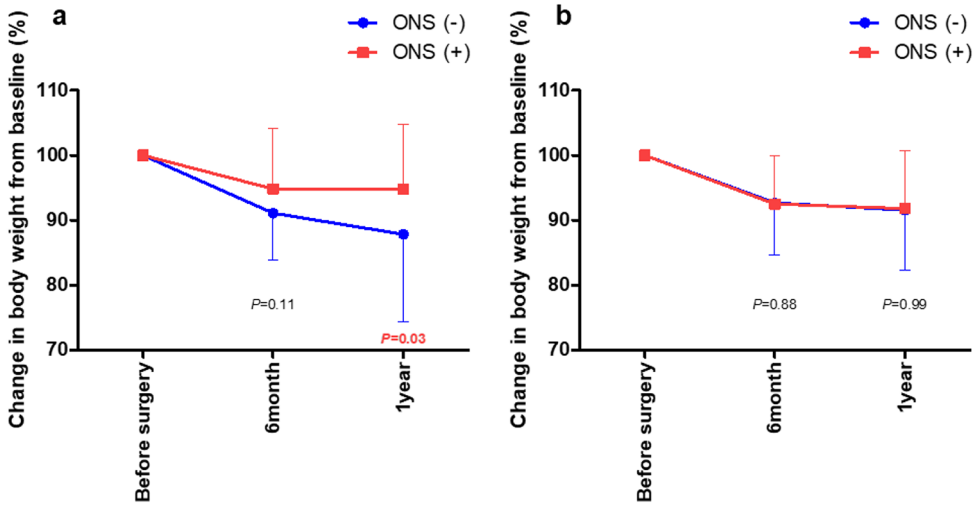

Fig. 2 Changes in body weight from baseline in patients with ONS (-) and ONS (+). (**a**) age ≥ 80 (**b**) age < 80. ONS: oral nutritional supplementation

findings, we focused on the octogenarian patients for further analyses in this study.

Postoperative sarcopenia in octogenarian patients

In addition, we compared postoperative PMI between the ONS (–) and ONS (+) groups among the octogenarian patients. As shown in Fig. 4, the decline in PMI was significantly lower in the ONS (+) group than in ONS (–) group both at postoperative 6 months and 1 year ($P<0.01$ and $P<0.01$, respectively).

Impact of ONS depending on the type of gastrectomy

Next, we investigated the impact of ONS in octogenarian patients categorized according to the type of gastrectomy. The number of octogenarian patients who underwent total or proximal gastrectomy was very low for consideration (data not shown). Among the patients who underwent distal gastrectomy, body weight tended to be better preserved in the ONS (+) group than in ONS (–) group, without significant difference (Fig. 5). Meanwhile, serum albumin level at postoperative 6 months was significantly higher in the ONS (+) group than in ONS (–) group ($P=0.03$) (Fig. 5). Also, the decline in PMI was significantly lower in the ONS (+) group than in the ONS (–) group at postoperative 6 months and 1 year ($P<0.01$ and $P<0.01$, respectively) (Fig. 5).

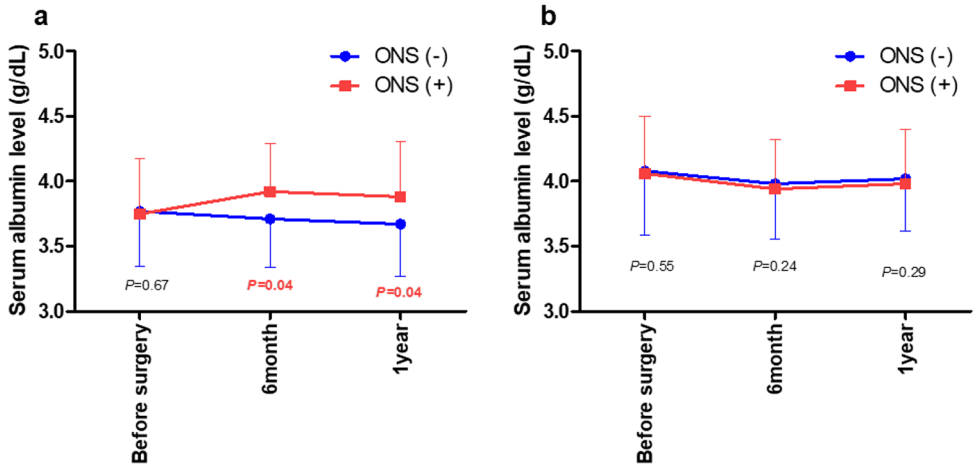

Fig. 3 Serum albumin level in patients with ONS (-) and ONS (+). (**a**) age ≥ 80 (**b**) age < 80. ONS: oral nutritional supplementation

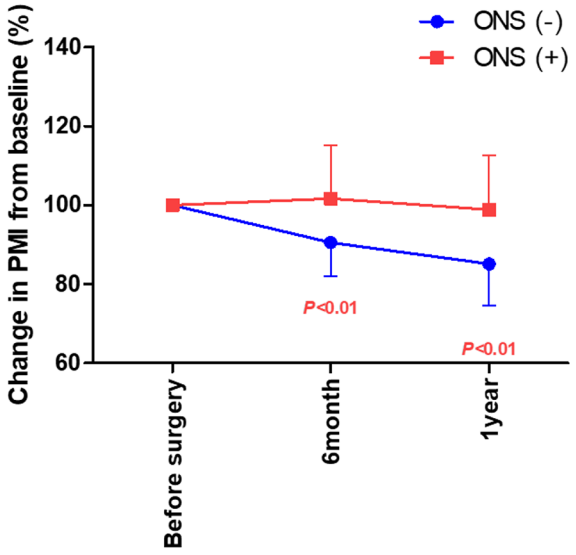

Fig. 4 Changes in PMI from baseline among the octogenarian patients. ONS: oral nutritional supplementation. PMI: psoas muscle mass index

Interaction analyses for the influence of ONS on body weight loss

Finally, we performed interaction analyses for the effect of ONS on body weight loss more than 10% at postoperative 1 year. Interaction analysis revealed that the effect of ONS on body weight loss differed depending on age (P for interaction = 0.08), as well as preoperative albumin level (Fig. 6).

Discussion

In this study, our analyses to compare the effectiveness of ONS between octogenarian and non-octogenarian patients who underwent gastrectomy revealed that ONS prevented body weight loss in octogenarian, but not in non-octogenarian, patients. Also, the decline in postoperative serum albumin levels and PMI was significantly lower in the ONS (+) group than in the ONS (–) group among octogenarian patients. To the best of our knowledge, this is the first study to demonstrate the

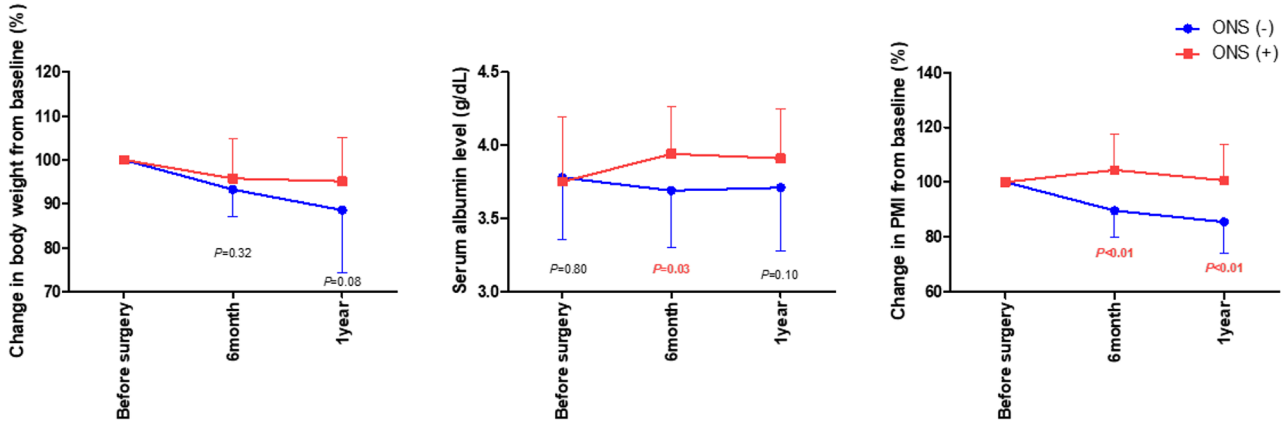

Fig. 5 Changes in body weight, serum albumin level, and PMI among the octogenarian patients who underwent distal gastrectomy. ONS: oral nutritional supplementation. PMI: psoas muscle mass index

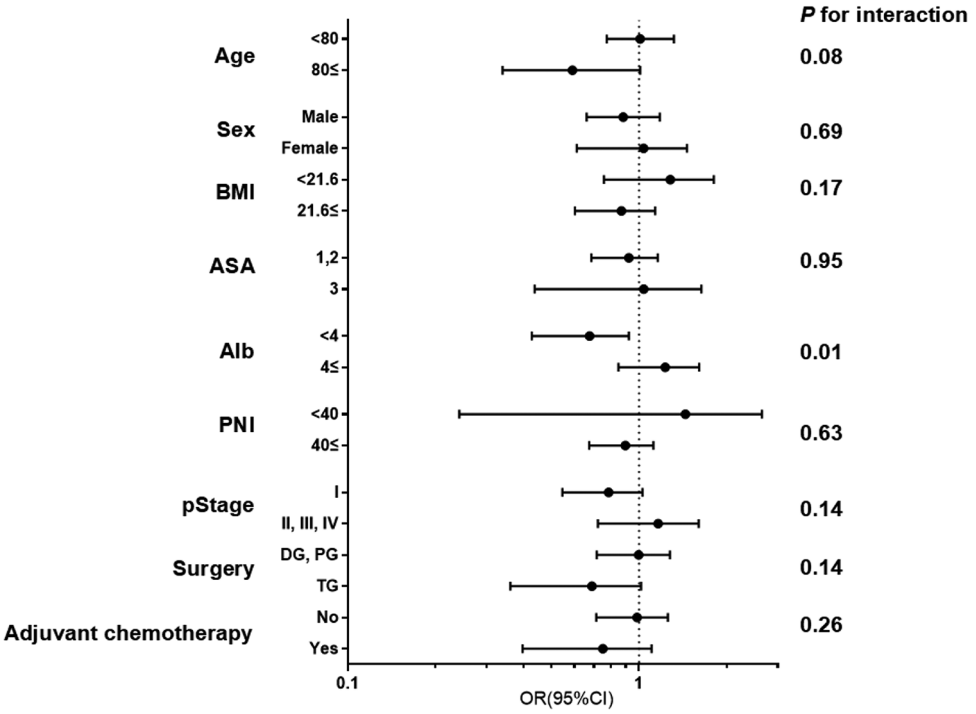

Fig. 6 Interactions analysis for the influence of ONS on body weight loss of more than 10% at postoperative 1 year. BMI: body mass index. ASA: American Society of Anesthesiologists-physical status. Alb: albumin. PNI: Prognostic Nutritional Index. pStage: pathological stage. VATS: video assisted thoracic surgery. OR: odds ratio. CI: confidence interval

effectiveness of ONS after oncological gastrectomy especially in octogenarian patients.

Body weight loss after gastrectomy, with a reported incidence of 10–15%, is associated with malnutrition, an inevitable, and serious issue that correlates with decline in postoperative quality of life, decreased immune functions, discontinuation of S-1 adjuvant chemotherapy, and poor prognosis in patients with gastric cancer [16–19]. Also, sarcopenia is associated with postoperative infection and delayed recovery [20]. Thus, the prevention of body weight loss and sarcopenia after gastrectomy is a critical issue that should be addressed.

Although postoperative ONS has been reported to prevent body weight loss and sarcopenia, whether nutritional support with ONS can be universally effective remains unclear [5–10]. In this study, we clearly demonstrated that postoperative ONS might be more effective in octogenarian patients than in non-octogenarian patients, in whom postoperative ONS might be unnecessary. Previous studies suggested that the effectiveness of the administration of at least 200 kcal/day of ONS within the first three months after gastrectomy [5, 21, 22]. Non-octogenarian patients might obtain enough calories from regular diet and voluntarily take other nutritional supplements whereas octogenarian patients are not expected to voluntarily take nutritional supplements and might be in calorie deficit. In addition, the better effectiveness of ONS in the octogenarian patients compared to the non-octogenarian patients observed in the present study suggests that the administration of sufficient calories with ONS might be more useful in octogenarian patients with lower basal metabolic rate compared to non-octogenarian patients. Furthermore, although few studies have demonstrated the effectiveness of ONS after distal gastrectomy, our analyses reveal its effectiveness specifically in octogenarian patients undergoing distal gastrectomy [6]. Therefore, postoperative administration of ONS is strongly recommended especially in octogenarian patients undergoing distal gastrectomy.

Almost all studies evaluating the effectiveness of ONS in patients undergoing gastrectomy refer to the importance of ONS adherence [21, 22]. In this study, the rate of ONS continuation was 54.9%, which is almost consistent with previous reports [21, 22]. Notably, in the present study, the reasons for failure to continue ONS did not include severe adverse events but were related to patient preference or poor adherence. Multidisciplinary nutrition support teams have shown potential benefits in managing patients receiving parenteral nutrition, however evidence remains limited [23]. However, nutritional education may improve adherence to postoperative ONS [24]. Therefore, aggressive intervention through nutritional guidance and short-term follow-up is important especially in octogenarian patients to prevent ONS discontinuation.

In this study, we focused on octogenarians. While some octogenarians are active and healthy, others experience

health problems associated with aging, such as decreased mobility, chronic diseases (arthritis, cardiovascular disease, etc.), and loss of strength and endurance. Our analyses of patients ages 75–80 years did not reveal that ONS was effective (data not shown), suggesting the age of 80 years was the optimal cutoff value. However, this result does not suggest that ONS is not useful for non-octogenarian patients. While non-octogenarian patients voluntarily obtain nutrition, including ONS, we believe that more aggressive nutritional support is needed for the octogenarians. In other words, we believe that ONS is necessary for both octogenarians and non-octogenarians, but that the octogenarian patients need more aggressive administration of ONS.

We also conducted analyses to evaluate the association of postoperative ONS with long-term outcomes, which did not reveal significant differences between the octogenarian patients with and without postoperative ONS due to the short follow-up period (data not shown). In addition, the current cohort did not have data on quality of life, so further studies are warranted.

This study has several limitations. First, this was a retrospective, observational study at a single institution. Second, this study included only a Japanese population and the sample size was small, and the results need to be verified in a more representative global population. Third, data were not available on the precise total caloric intake after surgery. The type and quantity of other nutrients ingested by the patients were not recorded. Moreover, the exact amount of ONS ingested and the length of time of ONS were not known in patients who received postoperative ONS. In addition, there were no data on quality of life. Therefore, further prospective, multicenter, large-scale studies focusing on octogenarian patients are required to confirm the present findings.

Conclusions

In conclusion, the present study suggested that postoperative ONS might prevent body weight loss, malnutrition and sarcopenia in octogenarian patients undergoing gastrectomy for gastric cancer and that it might be more effective in octogenarian patients.

Abbreviations

ONS	oral nutritional supplementation
PMI	Psoas muscle mass index
ASA-PS	American Society of Anesthesiologists-Physical Status
ECOG-PS	Eastern Cooperative Oncology Group performance score scales
C-D	Clavien-Dindo

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03549-5.

Supplementary Material 1

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Author contributions

Study concept and design: MS and ID. Performance of operation: MS, KY, AH, SK, and ID. Draft the manuscript: MS and ID. Acquisition of data: MS, HY, and NT. Analysis and interpretation of data: MS, SR, TK, IW, SK, FS, NY, AH, KH, and ID. All authors have revised and approved the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Yamanashi University and performed in accordance with the ethical standards of the Declaration of Helsinki and its later amendments.

Consent for publication

All study participants provided informed written consent prior to their study enrollment.

Competing interests

The authors declare no competing interests.

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