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ORIGINAL ARTICLE

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Comparison of the effects of open and laparoscopic approach on body composition in gastrectomy for gastric cancer: A propensity score-matched study

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Abstract

Aim: To compare the effects of open (OG) and laparoscopic gastrectomy (LG) on body composition and muscle strength.

Methods: This study performed a propensity score matching analysis using cases from a large-scale, multicenter, phase III randomized controlled trial concerning oral nutritional supplements after gastrectomy and analyzed both the whole and matched cohorts. Measurements of body composition and hand grip strength (HGS) were performed at baseline (preoperatively) and at 1, 2, 3, 6, and 12 months after gastrectomy.

Results: Of 835 patients, 275 and 560 underwent OG and LG, respectively. Skeletal muscle mass (SMM) and HGS loss were significantly lesser in the LG group than in the OG group. The propensity score-matched analysis, including 120 pairs of patients, confirmed that the % SMM loss values at 1, 2, 3, 6, and 12 POM were −4.5%, −4.0%, −4.7%, −4.6%, and −5.8% in the OG group and −3.0%, −1.9%, −2.4%, −2.2%, and −2.7% in the LG group, respectively. The % SMM loss was significantly lesser in the LG group than in the OG group (repeated measures ANOVA $p < 0.001$). The HGS loss was non-significantly smaller in the LG group than in the OG group.

Conclusion: Skeletal muscle mass loss was significantly lesser in the LG group than in the OG group in both cohorts, indicating that LG may be more effective than OG for maintaining muscle mass.

KEYWORDS
body composition, laparoscopic gastrectomy, open gastrectomy, propensity score matching, skeletal muscle mass

1 | INTRODUCTION

Gastric cancer is one of the most common malignant cancers and the third leading cause of death worldwide.[1] Surgical resection with lymphadenectomy is the standard treatment with open gastrectomy (OG) regarded as the gold standard for potentially curative gastric cancer. However, since Kitano et al.[2] first reported laparoscopic gastrectomy (LG) for early gastric cancer in 1994, its use has gradually increased worldwide. Following recent surgical developments, indications for LG have been extended to advanced gastric cancer[3]; nevertheless, surgeons performing LG require adequate training and experience.

Minimally invasive surgery of the stomach is increasingly being performed globally. Large randomized trials have shown the benefits of LG over conventional OG, including less intraoperative blood loss, reduced postoperative incisional pain, earlier recovery of bowel function and resumption of oral intake, less nausea and vomiting, and a shorter hospital stay while maintaining oncological safety.[4–6] However, according to published reports, body composition changes in the early postoperative period was similar between the OG and LG groups in early gastric cancer.[7,8] Moreover, it has been reported that postoperative recovery of muscle mass is accelerated in patients who underwent LG compared to those who underwent OG,[9] but there is currently no consensus on the effects of different surgical approaches on body composition.

This study assessed oral nutritional supplements (ONS) use in patients after gastrectomy through a large-scale, multicenter, phase III randomized controlled trial by recruiting more than 1000 patients from over 20 hospitals (Racol trial). The patients underwent open or laparoscopic distal, proximal, or total gastrectomy for histologically proven primary gastric cancer. This study aimed to compare the loss of body weight (BW), body composition, muscle strength, and nutritional status among patients who underwent OG and LG using propensity score matching analysis using cases enrolled in the Racol trial.

2 | METHODS

2.1 | Ethics statements

The Racol trial was organized by the Osaka University Clinical Research Group for Gastroenterological Studies and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients. This trial was registered in the UMIN Clinical Trials Registry (UMIN-CTR) (UMIN000011919). Moreover, the study protocol was approved by the institutional review board of each participating hospital before conducting the study.

2.2 | Study design and patients

The Racol trial is a large-scale, multicenter, open-label phase III randomized controlled trial, where 22 institutions in Japan participated between November 11, 2013, and July 13, 2017, enrolling 1003 patients with gastric cancer who underwent gastrectomy. Patients were assigned to the ONS and control groups. In the ONS group, enteral nutrition with Racol® NF (Otsuka Pharmaceuticals Factory) 400 mL (400 kcal) per day for 12 weeks was initiated. The primary endpoint was BW loss 1 year after gastrectomy. The details of the Racol trial have been reported.[10] The present study employed data of who underwent OG and LG (Figure 1). The key eligibility criteria for the Racol trial were ages 20–85 years, Eastern Cooperative Oncology Group performance status (PS) of 0–2, patients who underwent distal (including pylorus preservation), proximal, or total gastrectomy (DG, PG, and TG, respectively) for histologically proven primary gastric cancer with no clinical distant metastasis, and adequate organ function. Another criterion was the absence of postoperative complications affecting the beginning of the oral diet, such as anastomotic leakage or pancreatic fistula. Other postoperative complications were evaluated based on the frequency of Clavien–Dindo II or higher complications. The present study excluded cases of recurrence within the first postoperative year, which might affect postoperative nutritional status.

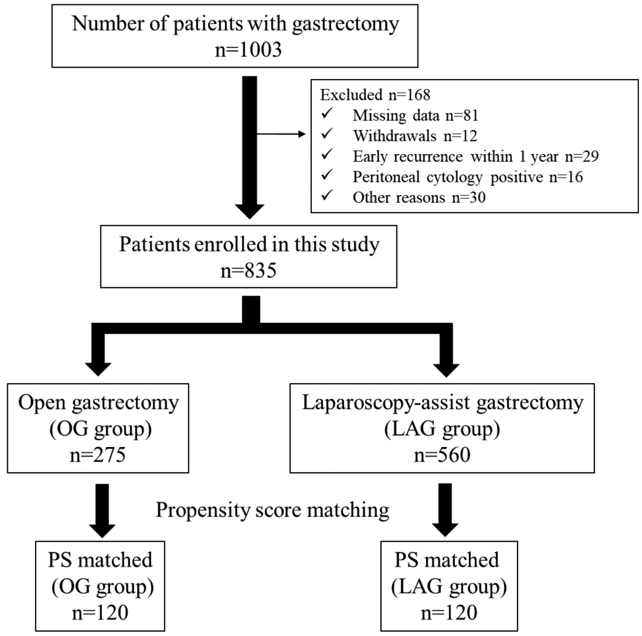


FIGURE 1 Flow diagram of this study. LG, laparoscopic gastrectomy; OG, open gastrectomy; PS propensity score.

2.3 | Surgical procedures

All patients underwent standard gastrectomy and lymph node dissection. D1 plus lymphadenectomy (D1 + dissection) was performed in patients with cT1 tumors without regional lymph node metastasis, while D2 lymphadenectomy was performed in patients with cT1 tumors with regional lymph node metastasis and cT2-4 tumors. The surgical approach (open or laparoscopic) and reconstruction method were not specified; hence the institution determined the surgical approach. A small abdominal incision (<6 cm) was made for the removal of the specimen and reconstruction for the laparoscopic surgical procedure. Meanwhile, an upper abdominal incision extending from the xiphoid to the umbilicus was made in the open surgical procedure. At least one expert gastric surgeon performed >100 gastrectomies. The operative methods were performed in accordance with the Japanese Gastric Cancer Treatment Guidelines[11] and the 14th edition of the Japanese Classification of Gastric Carcinoma.[12] The guidelines recommend laparoscopic surgery for early gastric cancer and open surgery for advanced gastric cancer; however, laparoscopic surgery is sometimes performed even for cases of advanced gastric cancer. Originally, laparoscopic surgery should have been performed under clinical trials. Postoperative management was performed according to the clinical protocol of each participating institution.

2.4 | Body composition analyses

Segmental body composition was analyzed using the HBF-214 scale (OMRON Healthcare Co., Ltd.). Measurements of BW and body composition were performed at baseline (preoperatively) and at 1, 3, 6, and 12 postoperative months (POM). BW loss was defined as follows: % BW loss = (preoperative BW − postoperative BW) × 100/preoperative BW. Skeletal muscle mass (SMM) loss was defined as follows: % SMM loss = (preoperative SMM − postoperative SMM) × 100/preoperative SMM. Body fat mass (BFM) loss was defined as follows: % BFM loss = (preoperative BFM − postoperative BFM) × 100/preoperative BFM.

2.5 | Measurement of hand grip strength

Hand grip strength (HGS) was measured using a digital hand dynamometer (T.K.K.5401, TAKEI). Patients were instructed to squeeze the dynamometer as hard as possible while sitting upright, with arms by their sides, elbows flexed at 180°, and forearms in a neutral position. The grip handle of the dynamometer was adjusted according to the patient's hand size to obtain the optimal grip position. The patient's left and right HGS values were measured, and their mean values were further analyzed. HGS measurements were performed at baseline (preoperatively) and 1, 3, 6, and 12 POM. HGS loss was defined as follows: % HGS loss = (preoperative HGS − postoperative HGS) × 100/preoperative HGS.

2.6 | Evaluation of nutritional indices

The Controlling Nutritional Status (CONUT), which evaluates the nutritional status of patients with cancer, was calculated according to three parameters (serum albumin concentration, total cholesterol concentration, and total lymphocyte count in peripheral blood) and was classified into four categories (normal, mild, moderate, and severe risk of malnutrition), as described in Appendix S1.

2.7 | Statistical analysis and propensity-matched analysis

The values are expressed as medians and ranges. The chi-square or Wilcoxon signed-rank test was used to compare continuous variables. Univariate logistic regression analysis was conducted to identify factors associated with BW loss. Variables with a $p < 0.05$ were included in the multivariate logistic regression model. Odds ratios with 95% confidence intervals were calculated, and a $p < 0.05$ was considered statistically significant. Propensity-matched analysis was conducted using a logistic regression model and the following covariates: age, PS, ONS, cT factor, cN factor, gastrectomy type, pStage, and adjuvant chemotherapy. For variables recorded repeatedly in the same patient over different time points during the study (months 1–12), the overall between-group differences were analyzed with repeated measures analysis of variance (ANOVA). This study compared both the whole cohort and the matched cohort. All calculations were performed using JMP Pro 16 software (SAS Institute Inc.).

3 | RESULTS

3.1 | Characteristics of the patients

Among the 1003 patients, 123 had no BW data for reasons such as negligence in weighing patients, withdrawals, deaths, and termination of the protocol treatment at the surgeon's discretion owing to various medical or surgical events. Additionally, 29 cases of recurrence within 1 year after gastrectomy and 16 cases of cy1 were excluded. Subsequently, 835 patients were enrolled in this study (Figure 1); 275 were included in the OG group, and the remaining 560 were included in the LG group before propensity score matching. Table 1 presents the background characteristics of the patients. After propensity score matching, 120 patients each were included in the OG and LG groups (Figure 1). Table 1 shows the clinical characteristics of patients before and after propensity score matching. Thereafter, no significant differences in background characteristics were observed between the two groups.

3.2 | Surgical and pathological outcomes

The surgical and pathological outcomes in each group are summarized in Table 2. The median operative time was significantly longer in the LG group than in the OG group ($p < 0.001$). In contrast, the median amount of blood loss was significantly lower in the LG group than in the OG group ($p < 0.001$). Table 2 shows the surgical and pathological outcomes of patients before and after propensity score matching. After matching, the two groups had no significant differences in the surgical procedure, pathological T factor, pathological N factor, pathological stage, postoperative complications, or presence or absence of adjuvant chemotherapy.

TABLE 1 Characteristics of gastric cancer patients before (whole cohort) and after propensity score matching (matched cohort).

	Whole cohort			Matched cohort		
	OG, *n* = 275 (%)	LAG, *n* = 560 (%)	*p* Value	OG, *n* = 120 (%)	LAG, *n* = 120 (%)	*p* Value
Age (year)			<0.001			0.31
Median, range	69, 33–85	67, 31–85		68, 34–85	67, 35–85	
Gender			0.041			0.13
Male	191 (69.4)	349 (62.3)		85 (70.8)	74 (61.7)	
Female	84 (30.6)	211 (37.7)		35 (29.2)	46 (38.3)	
Body mass index (kg/m^2)			0.93			0.26
Median, range	22.6, 14.6–32.3	22.8, 15.2–32.8		23.2, 16.4–32.3	22.4, 16.6–31.8	
PS			0.018			0.90
0	231 (84.0)	515 (92.0)		109 (90.9)	107 (89.2)	
1	32 (11.6)	35 (6.2)		10 (8.3)	12 (10.0)	
2	4 (1.5)	5 (0.9)		1 (0.8)	1 (0.8)	
Unknown	8 (2.9)	5 (0.9)		0 (0)	0 (0)	
ONS			0.85			0.80
+	138 (50.2)	277 (49.5)		59 (49.2)	61 (50.8)	
–	137 (49.8)	283 (50.5)		61 (50.8)	59 (49.2)	
Body weight (kg)			0.50			0.34
Median, range	59.7, 34.7–92.4	59.8, 34.5–99.4		60.5, 36.7–86.6	58.8, 36.7–89.7	
Skeletal muscle mass (kg)			0.27			0.19
Median, range	18.8, 10.1–27.6	17.7, 9.1–29.9		18.9, 10.2–27.6	17.2, 9.7–26.9	
Body fat mass (kg)			0.11			0.78
Median, range	15.8, 4.4–31.5	16.1, 3.7–32.4		16.1, 6.5–26.3	15.7, 3.7–29.5	
Basal metabolic rate (kcal)			0.95			0.18
Median, range	1408, 885–1910	1400, 885–2058		1426, 932–1839	1356, 927–1835	
Hand grip strength (kg)			0.56			0.24
Median, range	28.2, 2.9–61.6	29.4, 6.7–57.2		28.3, 2.9–61.6	26.8, 9.1–50.6	
cT			<0.001			0.90
1, 2	87 (31.6)	510 (91.1)		73 (60.8)	72 (60.0)	
3, 4	188 (71.3)	50 (8.9)		47 (39.2)	48 (40.0)	
cN			<0.001			1.00
0, 1	221 (80.4)	551 (92.5)		113 (94.2)	113 (94.2)	
2, 3	54 (19.6)	9 (1.6)		7 (5.8)	7 (5.8)	
cStage			<0.001			0.81
1, 2	190 (69.1)	549 (98.0)		110 (91.7)	111 (92.5)	
3, 4	85 (30.9)	11 (2.0)		10 (8.3)	9 (7.5)	

Abbreviations: BMI, body mass index; ONS, oral nutritional supplement; PS, performance status.

3.3 | Body weight and composition changes

In the whole cohort, the % BW loss was significantly lesser in the LG group than in the OG group at 1, 2, and 3 POM ($p<0.001$, $p=0.0011$, and $p=0.0047$, respectively; Figure 2A). The % SMM loss was significantly lesser in the LG group than in the OG group at 1, 2, 3, 6, and 12 POM ($p=0.0015$, $p<0.001$, $p=0.0013$, $p=0.0031$, and $p=0.0027$, respectively; Figure 2B). The % BW and % SMM losses were significantly different between the two groups with repeated measures ANOVA ($p=0.038$ and $p<0.001$, respectively). The % BFM loss was significantly lesser in the LG group than in the OG group at 3 POM ($p=0.046$); however, there was no significance in this count from month 1 to month 12 between the two groups as evaluated by repeated measures ANOVA (Figure 2C).

In the matched cohort, The % BW loss was significantly lesser in the LG group than in the OG group at 1 POM ($p=0.0044$; Figure 3A). The median % SMM loss values at 1, 2, 3, 6, and 12 POM were −4.5%, −4.0%, −4.7%, −4.6%, and −5.8% in the OG

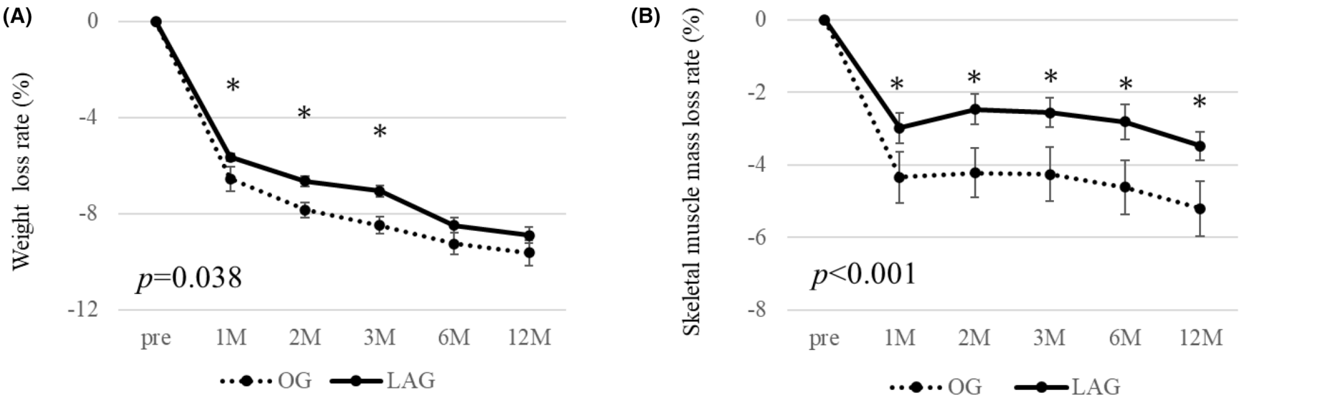
TABLE 2 Surgical and pathological outcomes.

	Whole cohort			Matched cohort		
	OG, *n* = 275 (%)	LAG, *n* = 560 (%)	*p* Value	OG, *n* = 120 (%)	LAG, *n* = 120 (%)	*p* Value
Surgical procedure			<0.001			0.96
TG	111 (40.4)	117 (20.9)		43 (35.8)	43 (35.8)	
DG	152 (55.3)	403 (72.0)		70 (58.3)	69 (57.5)	
PG	12 (4.3)	40 (7.1)		7 (5.8)	8 (6.7)	
Lymph node dissection			<0.001			0.87
D1+	27 (9.8)	405 (72.3)		24 (20.0)	25 (20.8)	
D2	248 (90.2)	155 (27.7)		96 (80.0)	95 (79.2)	
Operation time (min)			<0.001			<0.001
Median, range	246, 99–579	288, 120–595		238.5, 113–579	305, 140–471	
Blood loss (g)			<0.001			<0.001
Median, range	300, 10–2120	45, 0–760		300, 10–2120	50, 0–700	
pT			<0.001			0.23
0	1 (0.3)	0 (0)		0 (0)	0 (0)	
1	69 (25.1)	421 (75.2)		50 (41.7)	51 (42.5)	
2	53 (19.3)	58 (10.4)		27 (22.5)	20 (16.7)	
3	105 (38.2)	51 (9.1)		31 (25.8)	27 (22.5)	
4	47 (17.1)	30 (5.3)		12 (10.0)	22 (18.3)	
pN			<0.001			0.58
0	133 (48.4)	469 (83.8)		73 (60.8)	76 (63.3)	
1	55 (20.0)	53 (9.5)		17 (14.2)	22 (18.3)	
2	42 (15.3)	26 (4.6)		21 (17.5)	16 (13.4)	
3	45 (16.3)	12 (2.1)		9 (7.5)	6 (5.0)	
pStage			<0.001			0.76
1	95 (34.6)	454 (81.1)		62 (51.7)	65 (54.2)	
2	93 (33.8)	70 (12.5)		34 (28.3)	29 (24.2)	
3	87 (31.6)	36 (6.4)		24 (20.0)	26 (21.6)	
Overall complications (≧CD Grade II)	21 (7.6)	23 (4.1)	0.037	10 (8.3)	7 (5.8)	0.45
Intra-abdominal abscess	8 (2.9)	6 (1.1)	0.061	5 (4.2)	3 (2.5)	0.47
Postoperative bleeding	0 (0)	5 (0.9)	0.045	0 (0)	1 (0.8)	0.24
Ileus	3 (1.1)	1 (0.2)	0.084	0 (0)	0 (0)	1.00
Wound infection	6 (2.2)	6 (1.1)	0.22	2 (1.7)	2 (1.7)	1.00
Anastomotic stricture	2 (0.7)	2 (0.4)	0.48	1 (0.8)	0 (0)	0.24
Pneumonia	6 (2.2)	3 (0.5)	0.038	2 (1.7)	0 (0)	0.095
Adjuvant chemotherapy			<0.001			0.58
+	130 (47.3)	71 (12.7)		42 (35.0)	38 (31.7)	
–	145 (52.7)	489 (87.3)		78 (65.0)	82 (68.3)	

Abbreviations: CD, Clavien–Dindo; DG, distal gastrectomy; PG, proximal gastrectomy; TG, total gastrectomy.

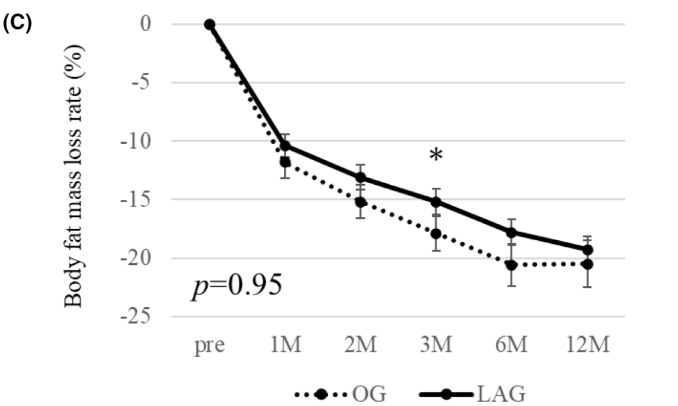
group and −3.0%, −1.9%, −2.4%, −2.2%, and −2.7% in the LG group, respectively. The % SMM loss was significantly lesser in the LG group than in the OG group, not only at 1, 2, 3, 6, and 12 POM ($p = 0.0097$, $p = 0.012$, $p = 0.011$, $p = 0.0068$, and $p = 0.0047$, respectively) but also with repeated measures ANOVA ($p < 0.001$; Figure 3B). The % BFM loss was not significantly different between the two groups (Figure 3C).

In the whole cohort, the % SMM loss was similar between the open distal gastrectomy (ODG) and the laparoscopy-assisted distal gastrectomy (LADG) groups in stage I gastric cancer. In contrast, in cStage II or III gastric cancer, the % SMM loss tended to be lower in the LADG group than in the ODG group until 12 POM; the % SMM loss at 1 and 6 POM was −5.4% and −3.8% in the ODG group and −1.9% and −2.0% in the LADG group, demonstrating significant



	OG	LAG	*P* value
1M	-6.6 %	-5.6 %	<0.001
2M	-7.8 %	-6.7 %	0.0011
3M	-8.5 %	-7.1 %	0.0047
6M	-9.3 %	-8.5 %	0.080
12M	-9.6 %	-8.9 %	0.62

	OG	LAG	*P* value
1M	-4.3 %	-3.0 %	0.0015
2M	-4.2 %	-2.5 %	<0.001
3M	-4.3 %	-2.6 %	0.0013
6M	-4.6 %	-2.8 %	0.0031
12M	-5.2 %	-3.5 %	0.0027



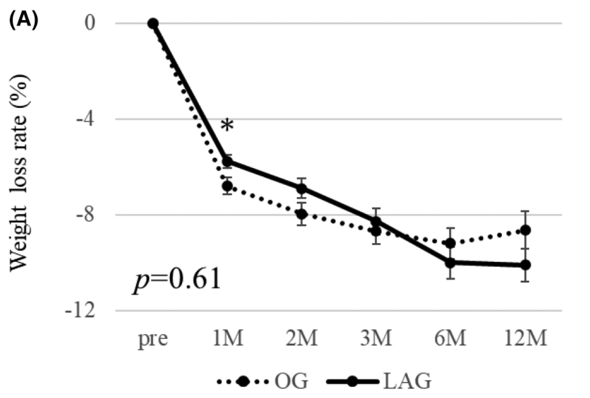
	OG	LAG	*P* value
1M	-11.8 %	-10.4 %	0.10
2M	-15.2 %	-13.1 %	0.12
3M	-17.9 %	-15.2 %	0.046
6M	-20.6 %	-17.8 %	0.12
12M	-20.5 %	-19.3 %	0.43

FIGURE 2 Comparison of body composition changes (A) weight, (B) skeletal muscle mass, and (C) body fat mass after gastrectomy between the OD group and LG group in whole cohort. Asterisks indicate a significant difference between the two groups ($p < 0.05$). p value was calculated by repeated measures ANOVA. LG, laparoscopic gastrectomy; M, month; OG, open gastrectomy.

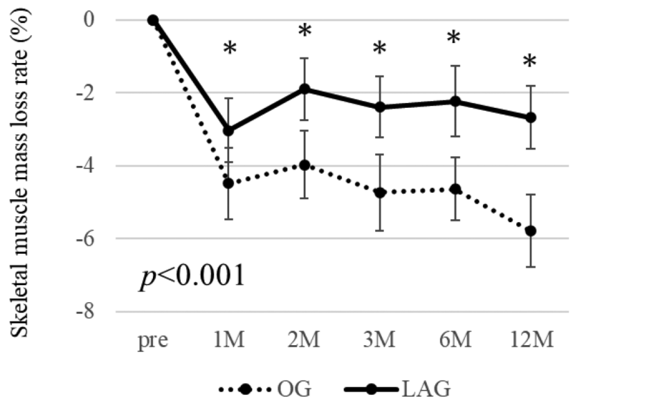
differences ($p = 0.015$ and $p = 0.034$, respectively; Appendix S2). In TG, a significant difference in SMM loss between the open total gastrectomy (OTG) and laparoscopy-assisted total gastrectomy (LATG) groups was observed at 3 and 6 POM ($p = 0.027$ and $p = 0.023$, respectively) in cStage I gastric cancer. Meanwhile, the % SMM loss was similar between the OTG and LATG groups in stage II or III gastric cancer (Appendix S3).

3.4 | Hand grip strength changes

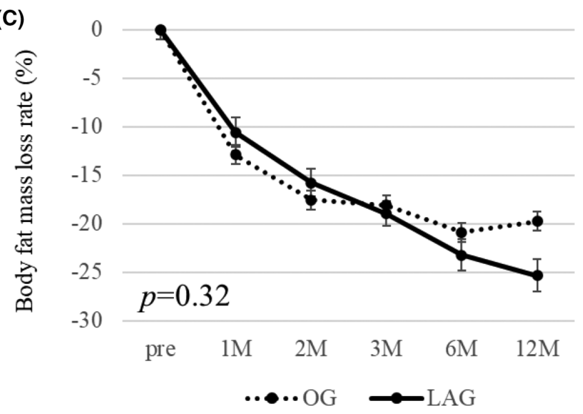
Overall, the median % HGS loss values at 2, 3, 6, and 12 POM were −%, −6.0%, −6.1%, −4.6%, and −4.1% in the OG group and −4.3%, −2.8%, −1.7%, and −2.1% in the LG group, respectively. The % HGS loss was significantly lesser in the LG group than in the OG group at 2, 3, 6, and 12 POM ($p = 0.025$, $p < 0.001$, $p = 0.0016$, and $p = 0.0071$,



	OG	LAG	*P* value
1M	-6.8 %	-5.8 %	0.0044
2M	-8.0 %	-6.9 %	0.14
3M	-8.7 %	-8.3 %	0.53
6M	-9.2 %	-10.0 %	0.69
12M	-8.6 %	-10.1 %	0.27



	OG	LAG	*P* value
1M	-4.5 %	-3.0 %	0.0097
2M	-4.0 %	-1.9 %	0.012
3M	-4.7 %	-2.4 %	0.011
6M	-4.6 %	-2.2 %	0.0068
12M	-5.8 %	-2.7 %	0.0047



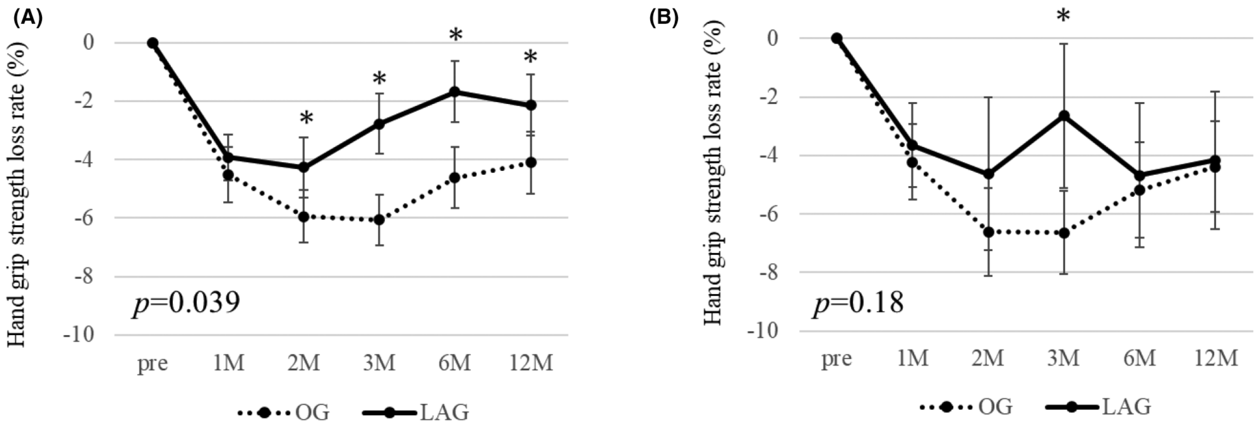
	OG	LAG	*P* value
1M	-12.9 %	-10.6 %	0.21
2M	-17.6 %	-15.8 %	0.80
3M	-18.1 %	-19.0 %	0.74
6M	-20.9 %	-23.2 %	0.17
12M	-19.8 %	-25.3 %	0.14

FIGURE 3 Comparison of body composition changes (A) weight, (B) skeletal muscle mass, and (C) body fat mass after gastrectomy between the OG group and LG group in matched cohort. Asterisks indicate a significant difference between the two groups ($p<0.05$). *p* value was calculated by repeated measures ANOVA. LG, laparoscopic gastrectomy; M, month; OG, open gastrectomy.

respectively). The % HGS loss was significantly different between the two groups with repeated measures ANOVA ($p=0.039$; Figure 4A). In the matched cohort, there was no significance from months 1 to 12 between the two groups as evaluated by repeated measures ANOVA; however, the LG group tended to experience lesser HGS loss than the OG group for approximately 3 months after gastrectomy (Figure 4B).

3.5 | Effects of the surgical approach on nutritional status

In the matched cohort, the incidence of patients with a CONUT score of ≥3 at 2, 3, and 12 POM were 24.4%, 21.9%, and 21.8% in the OG group and 14.0%, 11.8%, and 10.5% in the LG group, respectively. The CONUT score tended to be lower in the LG group

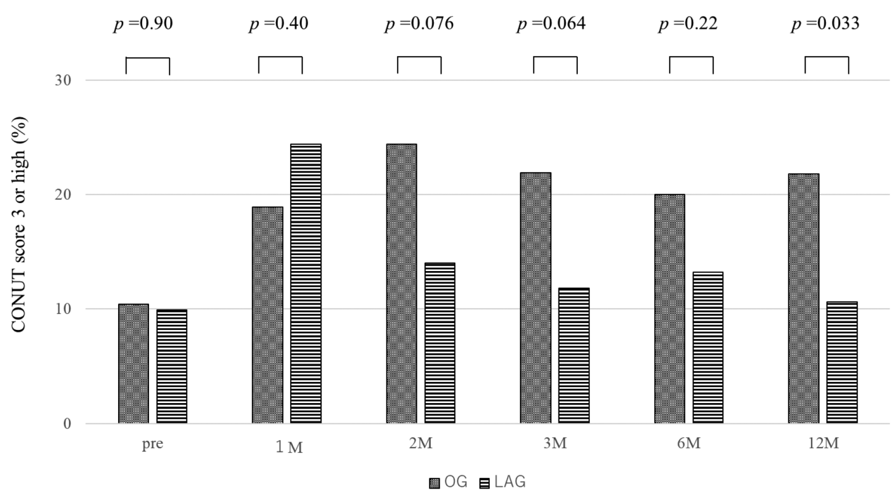


	OG	LAG	*P* value
1M	-4.5 %	-3.9 %	0.27
2M	-6.0 %	-4.3 %	0.025
3M	-6.1 %	-2.8 %	<0.001
6M	-4.6 %	-1.7 %	0.0016
12M	-4.1 %	-2.1 %	0.0071

	OG	LAG	*P* value
1M	-4.2 %	-3.7 %	0.37
2M	-6.6 %	-4.6 %	0.10
3M	-6.6 %	-2.6 %	0.024
6M	-5.2 %	-4.7 %	0.83
12M	-4.4 %	-4.2 %	0.44

FIGURE 4 Comparison of hand grip strength changes (A) whole cohort, (B) matched cohort after gastrectomy between the OG group and LG group. Asterisks indicate a significant difference between the two groups ($p < 0.05$). *p* value was calculated by repeated measures ANOVA. LG, laparoscopic gastrectomy; M, month; OG, open gastrectomy.

FIGURE 5 Comparison of percentage of the CONUT score 3 or higher between the OG and LG groups in matched cohort. LG, laparoscopic gastrectomy; M, month; OG, open gastrectomy.



than in the OG group at 2, 3, and 12 POM ($p=0.076$, $p=0.064$, and $p=0.033$, respectively; Figure 5).

4 | DISCUSSION

This study is the first report concerning changes in BW, SMM, BFM, and HGS, while also evaluating the nutritional status of patients after OG or LG at multiple institutions. The % BW loss in the LG group was comparable to that in the OG group in the matched cohort. However, our study revealed that the % SMM loss was remarkably lesser in the LG group than in the OG group. Furthermore, although the difference was not significant, the % HGS loss tended to be lower in the LG group than in the OG group.

Several studies have compared changes in body composition relatively early after surgery between the LG and OG groups.[7–9] Abdiev et al. reported that after gastrectomy, all patients showed a continuous reduction of fat mass during the first 6 months of follow-up, regardless of the type of gastric resection or the operative approach. Meanwhile, the decrease in muscle mass at 1 month postoperatively was suppressed in the LADG group compared with the ODG group.[9] We observed that the % SMM loss was similar between the ODG and LADG groups in stage I gastric cancer. Aoyama et al.[8] reported analogous results for approximately 3 POM. In contrast, in cStage

II or III gastric cancer, the % SMM loss tended to be lower in the LADG group than in the ODG group until 12 POM. In the TG group, there were no significant differences in the % SMM loss between the LATG and OTG subgroups at 1 and 2 POM in cStage I gastric cancer. Aoyama et al.[7] also reported no significant difference in the % SMM loss between the two groups until 3 months after TG; nevertheless, a significant difference was observed in the present study at 3 and 6 POM. The % SMM loss was similar between the OTG and LATG subgroups in stage II or III gastric cancer.

The physical activity of the patient and nutritional status could additionally influence SMM after surgery. First, postoperative pain plays a crucial role as a smaller wound in the laparoscopic approach may decrease stress due to wound pain. Takiguchi et al. previously compared the impact of LADG and ODG on early postoperative pain and physical activity by using the visual analog scale and Active Tracer, a device that measures spontaneous body movements. They reported that compared to ODG, LADG reduced postoperative pain and was more beneficial for early recovery of physical activity.[13] Corresponding to previous reports,[14–16] LG correlated with lesser pain and greater physical activity level than OG.[17,18] Additionally, previous studies demonstrated a lower magnitude of postoperative pain and significantly lower levels of acute inflammatory parameters, such as white blood cell count and C-reactive protein (CRP) levels in the LADG than in the ODG group on postoperative days 1, 3, and 7.[13,18] We found that the median CRP level at 2 and 3 POM was 0.08 and 0.10 in the OG group and 0.05 and 0.04 in the LG group, respectively, there were significant differences ($p=0.048$ and $p=0.0038$; Appendix S4). Thus, minimally invasive surgery may not only affect perioperative inflammation but also impact recovery during the early postoperative period. Moreover, minimally invasive surgery causes less surgical pain and physical stress than open surgery, which may result in faster recovery and less muscle weakness and loss of SMM.

Second, the SMM showed a sharp decline in the early postoperative period due to muscle catabolism and lack of food intake.[19] In the LG group, earlier recovery of gastrointestinal function may enable prompt resumption of oral intake[20]; however, LG is less effective than OG regarding appetite loss, as well as pain and physical activity level.[17,18] Furthermore, our study examined the postoperative nutritional status using the CONUT score, demonstrating that the LG group reported better nutritional status in the early postoperative period than the OG group.

Body fat mass continuously decreased postoperatively due to depletion of glycogen storages resulting from reduced oral intake and impaired carbohydrate digestion after gastrectomy.[9] Moreover, in the whole cohort, a greater proportion of patients in the OG group had advanced cancer as well as recurrent cancer compared with the LG group. Cancer cells require large amounts of glucose, which may cause abnormalities in enzymes involved in glucose metabolism,[21] resulting in the breakdown of fat cells and subsequent BFM loss in the OG group compared to the LG group. In the matched cohort, the % BFM loss was similar in both groups.

Miyazaki et al.[10] reported that a daily ONS ≥200 kcal/day for 3 months after gastrectomy may have potential advantages in preventing % BW loss beyond the duration of oral administration. Kimura et al.[22] showed that daily ONS (300 kcal/day) for 6–8 weeks reduced % BW loss not only at 6–8 weeks postoperatively but also at 1 year in patients who underwent TG. Additionally, patients who receive ONS may exhibit improved completion rates for adjuvant chemotherapy (S-1).[23] However, there have been no reports on whether nutritional intervention can prevent SMM loss after gastrectomy. Thus, our future studies will focus on investigating the effects of nutritional interventions on SMM.

Minimally invasive surgery, represented by laparoscopic surgery, is widely accepted as curative treatment for gastric cancer. A robotic surgical system, meanwhile, has several technical advantages compared with laparoscopic instruments. Postoperative complications following robotic gastrectomy are fewer or comparable to those following laparoscopic gastrectomy, and postoperative recovery is reportedly faster following robotic gastrectomy.[24,25] However, there are no reports of randomized controlled trials comparing the long-term oncological outcomes of robotic versus laparoscopic gastrectomy. Meanwhile, long-term results of distal gastrectomy for cStage II/III advanced gastric cancer reported non-inferiority of LADG over ODG.[26] These results may lead to the recommendation of LADG for locally advanced gastric cancer. We have reported that LADG is associated with less postoperative SMM loss than ODG in cStage II/III advanced gastric cancer, which may help support the recommendation for LADG over ODG for locally advanced gastric cancer.

This study has some limitations. First, as it was designed as a non-randomized study, unmeasured confounding factors may have affected the results. Presently, laparoscopic surgery is the standard for early gastric cancer in Japan, while some institutions perform minimally invasive surgery, including laparoscopic and robotic surgery for advanced gastric cancer.[27,28] Therefore, since it is difficult to set up a randomized controlled trial, we performed a propensity score matching analysis and adjusted the background factors to create a comparison similar to a randomized controlled trial. Second, because the Racol trial was limited to cases in which Racol® NF could be taken 1 week after gastrectomy, only cases without major complications, including anastomotic leakage and pancreatic fistula, were enrolled. Third, body composition was analyzed using a bioelectrical impedance analyzer, which could not directly measure SMM. However, a positive correlation between muscle mass, as measured using a bioelectrical impedance analyzer and muscle strength was also observed. Fourth, the study did not specify the method of reconstruction that might affect the postoperative nutritional status.

Conclusively, SMM loss was significantly lesser in the LG group than in the OG group in both cohorts. Furthermore, although there was no significant difference, the % HGS loss tended to be lower in the LG group than in the OG group in the matched cohort. These results indicate that LG may be more useful than OG for maintaining muscle mass.

AUTHOR CONTRIBUTIONS

Tomohira Takeoka and Kazuyoshi Yamamoto designed the study and drafted paper. Yuichiro Doki and Hidetoshi Eguchi chaired the study group. Yasuhiro Miyazaki wrote the protocol. Kazuyoshi Yamamoto and Yasuhiro Miyazaki were responsible for data management. All authors except Hidetoshi Eguchi recruited patients into the study. All authors revised the paper and approved the final version.

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CONFLICT OF INTEREST STATEMENT

Yukinori Kurokawa is an Associate Editor of the *Annals of Gastroenterological Surgery*. Yuichiro Doki is an Editorial Board Member of the *Annals of Gastroenterological Surgery*. The other authors declare no conflict of interests for this article.

ETHICS STATEMENT

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Human Ethics Review Committee of Osaka International Cancer Institute and it conforms to the provisions of the Declaration of Helsinki (Approval no. 1611259187).

Informed consent: All informed consent was obtained from the participates.

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CONSENT FOR PUBLICATION

All the authors consented to publication.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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