


# Laparoscopy-assisted distal gastrectomy is feasible also for elderly patients aged 80 years and over: effectiveness and long-term prognosis

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## Abstract

**Background** Elderly patients usually have concurrent ailments, and the safety and effectiveness of laparoscopy-assisted distal gastrectomy (LADG) for these patients have been controversial. This study aimed to evaluate whether laparoscopy-assisted distal gastrectomy is safe and effective for elderly patients aged 80 years and over, as well as to clarify their long-term prognosis.

**Methods** A total of 31 patients aged 80 years and over who underwent LADG in our hospital were retrospectively reviewed. Peri- and postoperative data were compared with those of 38 patients aged 65 years and younger. The median follow-up period of the elderly and younger group was 56.0 and 63.0 months, respectively, and their prognosis was examined.

**Results** There were significant differences between the two groups in preoperative respiratory and renal functions, hemoglobin, and nutritional index. Significant differences in postoperative complications were seen only in pneumonia and delirium. There were no hospital deaths, but the 3-year and 5-year overall survival rates were significantly lower in the elderly group than in the non-elderly group. However, in the elderly group, only one patient died of gastric cancer recurrence, whereas four died of cardiovascular disease and three died of pneumonia during follow-up. Therefore, the recurrence-free survival rate was not significantly different between the groups.

**Conclusions** LADG seems to be safe and effective even for elderly patients, and their prognosis was satisfactory. However, careful monitoring for cardiovascular and pulmonary disease should be observed during the follow-up period.

**Keywords** Complication · Elderly · Gastrectomy · Gastric cancer · Laparoscopic surgery

The average age of patients with gastric cancer undergoing gastrectomy has been increasing in recent years. The natural life expectancy of elderly patients is obviously shorter than that of younger patients, and elderly patients usually have various comorbidities such as cardiovascular diseases [1, 2] and decreased respiratory function, leading to limited use of the procedure. In addition, elderly patients' postoperative complications such as delirium and sarcopenia are also problems [3]. Therefore, it is controversial whether severe invasive surgery, for example, combined with resection of another organ should be performed for such elderly patients. Consequently, in such cases, some patients hesitate to have invasive treatment in spite of surgeons' recommendation.

For the reasons described above, more minimally invasive procedures should be performed in elderly patients. Laparoscopy-assisted distal gastrectomy (LADG) has been recognized as a minimally invasive treatment for early gastric cancer. Many authors have reported its safety and effectiveness compared with open distal gastrectomy [4–9]. However, few studies of LADG in elderly patients, especially those aged 80 years and over, have been reported. Therefore, it is necessary to study the safety, effectiveness, and prognosis of LADG for elderly patients.

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Thus, in this study, patients with gastric cancer aged 80 years and over who underwent LADG in our hospital were retrospectively reviewed, and peri- and postoperative data were collected, analyzed, and compared with those of young patients aged 65 years and younger who underwent LADG in the same period.

## Materials and methods

### Patient characteristics

Between 2007 and 2012, 31 patients aged 80 years and over underwent curative LADG (complete resection with no microscopic residual tumor, R0 in the Japanese Classification of Gastric Carcinoma: 3rd English edition [10]) for primary gastric cancer at Ehime University Hospital (elderly group). In the same period, 38 patients with gastric cancer aged 65 years and younger underwent the same operation (non-elderly group). Patients were completely involved in the decision-making process, and written informed consent was obtained from all patients. The present study was approved by the institutional review board of our hospital.

In both groups, LADG was performed by the same procedure, i.e., five surgical ports and CO<sub>2</sub> pneumoperitoneum set at 10 mmHg. According to the Japanese gastric cancer treatment guidelines [11], D1+ for early gastric cancer or D2 lymphadenectomy for advanced cancer was performed with a resection of more than the lower two-thirds of the stomach including the tumor. Retrieval of specimens was performed via an approximately 5-cm incision in the upper abdomen. Finally, Roux-en-Y reconstruction was performed using laparoscopic linear staplers.

### Preoperative data collection

The patients' characteristics, including gender, comorbidities, and number of drugs administered, were collected. In addition, patient status, including cardiorespiratory and renal functions, evaluated by echocardiography, spirometry, and serum blood urea nitrogen and creatinine levels, was evaluated. As an objective evaluation of patient status, the prognostic nutritional index [12] ( $10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{peripheral lymph cell count (/mm}^3\text{)}$ ), the modified Glasgow prognostic score [13] (score 2, both elevated C-reactive protein ( $\geq 10$  mg/L) and hypoalbuminemia ( $< 35$  g/L); score 1, elevated C-reactive protein and no hypoalbuminemia; score 0, abnormalities in neither C-reactive protein nor serum albumin), and the American Society for Anesthesia-Physical Status were also examined. In addition, each patient's risks of postoperative complication and death were calculated with using the American College of Surgeons National Surgical Quality Improvement

Program (ACS-NSQIP) Surgical Risk Calculator [14]. Intraoperative data, such as operation time and the amount of intraoperative bleeding, and postoperative data, such as complications according to the Clavien–Dindo classification, were evaluated. Histological data, hospital stay, and survival rates were also collected as postoperative data and analyzed statistically.

### Statistical analyses

The characteristics of both groups were compared using Chi-square tests and Mann–Whitney U test. The survival rate after surgery was analyzed using Kaplan–Meier survival curves and compared with the log-rank test. All data were calculated using commercially available software, Prism 5 for Macintosh, version 5.0 f (GraphPad Software, San Diego, CA, USA), and significance was established at  $P < 0.05$ . Because the patient with gastric cancer aged over 80 years itself was rare, the sample size of the present study was small. Therefore, we used non-parametric statistical methods; however, it may not be adequate.

## Results

### Patients' characteristics

Of the 31 patients in the elderly group, 21 were males and 10 were females, with a mean age of 82.9 years (range 80–91 years). In contrast, the mean age was 55.1 years (range 37–64 years) for the 38 patients (25 males, 13 females) in the non-elderly group. In the elderly group, all patients had several comorbidities, mainly including cardiovascular and cerebrovascular diseases such as coronary artery disease, arrhythmia, and brain infarction. Therefore, they required drug therapy (average four drugs), and 12 patients (37.5%) took anticoagulant or antiplatelet drugs. Yet, 22 patients in the non-elderly group required an average of only one drug for their comorbid conditions. There were significant differences in the numbers of comorbidities and drugs, but not in gender (Table 1).

Significant differences were observed in %vital capacity, forced expiratory volume 1.0% on spirometry, and serum blood urea nitrogen, creatinine, and hemoglobin levels. In addition, there were also significant differences in the prognostic nutritional index and the American Society for Anesthesia-Physical Status. However, there were no significant differences in cardiac ejection fraction and %fractional shortening on echocardiography and the modified Glasgow prognostic score between the two groups (Table 1). Also, in the risk of a perioperative complication or death calculated by ACS-NSQIP risk calculator, statistical significant

**Table 1** Characteristics of patients in the two groups

		Elderly group	Non-elderly group	P value
Age (y) (range)		82.9 (80–91)	55.1 (37–64)	<0.01
Gender (Male:Female)		21:10	25:13	N.S.
BMI (kg/m <sup>2</sup> ) (mean ± S.D.)		23.2 ± 3.6	22.0 ± 2.9	N.S.
Number of comorbidities (mean)		2	1	<0.01
Number of drugs (mean)		4	1	<0.01
Anticoagulant or antiplatelet drugs (patients, %)		12 (38%)	4 (11%)	<0.01
Cardiac function	EF (%)	69.1 (53.1–79.2)	64.0 (42.7–74.5)	N.S.
Mean (range)	%FS	38.8 (27.5–48.0)	35.1 (21.5–43.2)	N.S.
Respiratory function	%VC (%)	94.4 (50.5–127.5)	113.6 (78.8–149.6)	<0.01
Mean (range)	FEV1.0%	72.8 (44.5–88.5)	79.4 (57.5–96.7)	<0.05
Renal function	BUN (mg/dL)	19.2 (10.0–42.0)	15.6 (10.0–47.0)	<0.01
Mean (range)	Cre (mg/dL)	0.9 (0.5–2.0)	1.0 (0.44–7.47)	<0.05
Hemoglobin (mg/dL)		12.0 (8.2–15.9)	13.2 (7.2–16.8)	<0.05
Mean (range)				
ASA-PS	1	3	20	<0.001
	2	24	16	
	3	4	2	
mGPS	0	27	36	N.S.
	1	1	2	
	2	3	0	
PNI mean (range)		45.7 (35.2–54.6)	50.4 (35.5–57.4)	<0.001
%Risk mean (range) any morbidity		21.5 (14.7–32.2)	14.1 (11.1–28.9)	<0.001
Serious morbidity		18.1 (12.0–28.6)	11.2 (8.6–24.4)	<0.001
Mortality		1.07 (0.2–3.4)	0.18 (0–1.4)	<0.001

%risk of morbidity and mortality were calculated using the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator

BMI body mass index, EF ejection fraction, %FS %functional shortening, %VC %vital capacity, FEV1.0% forced expiratory volume % in 1.0 s, BUN blood urea nitrogen, Cre creatinine, ASA-PS American Society for Anesthesia-Physical Status, mGPS modified Glasgow prognostic score, PNI prognostic nutrition score, N.S. not significant

differences were observed in both mortality and morbidity risks between the two groups (Table 1).

### Operative data

In the elderly group, D1 lymphadenectomy was performed in 24 patients and D2 lymphadenectomy was performed in seven patients. At the same time, in the non-elderly group, D1 and D2 lymphadenectomies were performed in 18 and 10 patients, respectively. There was no significant difference in the grade of lymph node dissection between the two groups, but the mean number of harvested lymph nodes was larger in the non-elderly group than in the elderly group ( $P < 0.01$ ). The mean operation time was 297.5 min in the elderly group and 324.8 min in the non-elderly group ( $P < 0.05$ ). Mean intraoperative bleeding was 102.2 mL in the elderly group and 39.0 mL in the non-elderly group, but there was no significant difference (Table 2).

Postoperative complications  $\geq$ Grade II according to the Clavien–Dindo classification occurred in 10 patients in the elderly group (Table 3). In these 10 patients, two Grade III (one anastomotic stenosis and one pancreatic fistula)

and eight Grade II complications (three severe delirium, one pneumonia, one anastomotic bleeding, one abdominal abscess, one pancreatic fistula, and one ileus) occurred. At the same time, among the 38 patients aged 65 years and younger,  $\geq$ Grade II complications occurred in six patients (15.8%), including three Grade III (two pancreatic fistula and one anastomotic bleeding) and three Grade II (two arrhythmia and one pancreatitis). There were no hospital deaths in both groups, and, in addition, there was no significant difference in the complication rate between the groups. The hospital stay after surgery was significantly longer in the elderly group than in the non-elderly group (18.1 days and 11.6 days, respectively,  $P < 0.05$ ) (Table 2).

### Prognosis

Results of histological examinations of resected specimens were similar in both groups; the pathological stages according to the Japanese Classification of Gastric Carcinoma were therefore similar (Table 2). The median follow-up periods of the elderly and younger groups were 56.0 (8–101 months) and 63.0 (4–112 months), respectively. The

**Table 2** Perioperative parameters in the two groups

		Elderly group	Younger group	<i>P</i> value
Operation time (min), mean (range)		297.5 (195–455)	324.8 (240–510)	<0.05
Intraoperative bleeding (mL), mean (range)		102.2 (5–785)	39.0 (0–200)	N.S.
Lymph node dissection (JGCA classification)	D1+ D2	24 7	18 10	N.S.
Number of harvested lymph nodes mean (range)		25.0 (8–53)	37.4 (12–79)	<0.01
Combined resection of another organ (Yes:No)		29:2	34:4	N.S.
Start of solid food oral intake (postoperative day), mean (range)		4.3 (3–7)	3.4 (3–15)	N.S.
Hospital stay after surgery (days) Mean (range)		18.1 (8–85)	11.6 (7–28)	<0.05
Histology (intestinal:diffuse)		23:8	21:17	N.S.
Depth of invasion	m sm mp ss se	13 13 2 3 0	18 14 0 3 2	N.S.
p-Stage (JGCA classification)	I II III	25 6 0	31 4 3	N.S.

JGCA Japanese Gastric Cancer Association

**Table 3** Postoperative complications according to the Clavien–Dindo classification

		Elderly group	Non-elderly group	<i>P</i> value
Number of complications		11 (31.3%)	7 (15.8%)	N.S.
Grade (Clavien–Dindo classification)				
I	SSI (superficial, deep)	0 (0, 0)	1 (1, 0)	N.S.
II	Pneumonia	3 (1 duplicated)	0	<0.05
	Ileus	1	0	N.S.
	Delirium	3 (1 duplicated)	0	<0.05
	Pancreatic fistula	1	1	N.S.
	Arrhythmia	0	2	N.S.
	Anastomotic bleeding	1	0	N.S.
IIIa	Anastomotic bleeding	0	1	N.S.
	Anastomotic stenosis	1	0	N.S.
	Pancreatic fistula	1	2	N.S.
IIIb, IV		0	0	N.S.

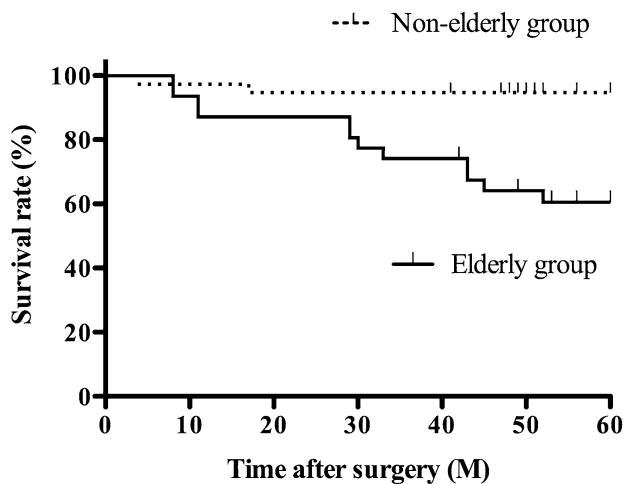
SSI surgical site infection, N.S. not significant; pancreatic fistula overlaps organ space SSI

3-year overall survival rate (OS) was 74.2% in the elderly group and 94.7% in the non-elderly group ( $P < 0.05$ ), and the five-year OS was also lower in the elderly group (60.5%) than in the non-elderly group (94.7%;  $P < 0.05$ ) (Fig. 1). The causes of death in the elderly group were as follows: cardiovascular disease four; pneumonia three; suffocation due to miss-swallowing three; acute peritonitis due to ileus one; another cancer one; and recurrence of gastric cancer one. Finally, no significant difference was observed in five-year recurrence-free survival (RFS) between the two groups (96.8% in the elderly group and 94.7% in the non-elderly group) (Fig. 2).

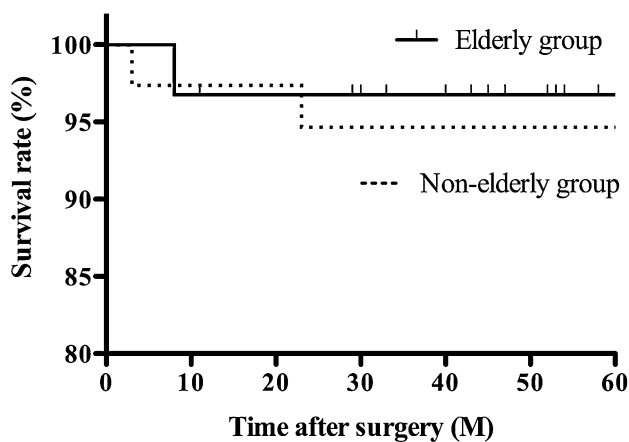
## Discussion

According to the Japanese gastric cancer treatment guidelines, surgery seems to be one of the most reliable treatments for early gastric cancer [11]. Gastrectomy with lymphadenectomy is expected to extend patients' life expectancies, and it may consequently contribute more to younger than to older patients, because natural life expectancies are shorter in elderly patients than younger patients.

In Japan, it was reported that the average life expectancy at 80 years was 8.39 years in men and 11.36 years in women in 2011. Endo et al. reviewed patients with



**Fig. 1** Overall survival after surgery. Five- and three-year overall survival rates were significantly lower in the elderly group



**Fig. 2** Recurrence-free survival after surgery. No significant difference was observed in recurrence-free survival between the two groups

gastric cancer aged over 85 years and compared the survival between the operation group and the best supportive care group [1]. In their report, OS was longer in the operation group than in the best supportive care group. Therefore, age itself should not be a reason to exclude patients from surgery. Also in the present study, since only one patient died of gastric cancer recurrence in the elderly group, there was no significant difference in 5-year RFS between the two groups. Thus, surgery itself extends life expectancy even for patients aged 80 years and over.

However, elderly patients usually have concurrent ailments (e.g., diabetes, chronic obstructive pulmonary disease, heart disease, arthritis, hypertension) that could affect prognosis and survival. Indeed, it has been reported

that age above 65 years is one of the independent risk factors for postoperative complications after LADG [15].

From these reasons, risk-adjustment methodologies predicting postoperative mortality and morbidity have been required. Therefore, ACS-NSQIP was surveyed and ACS-NSQIP risk calculator has been created [14, 16]. But this survey was the cohort study and the data were derived from approximately 10% of hospitals in the United States of America. Therefore, there may be any variations. Indeed, even if the calculated risk percentage is very low, perioperative complication may occur, whereas perioperative complication may not occur, even if the calculated risk percentage is very high. Also in our study, mortality and morbidity risk percent calculated with this calculator were statistically significantly higher in the elderly group than in the younger group; however, there was no significant difference in the complication rate between the groups and no hospital deaths were observed in the two groups.

Nevertheless, it is a fact that OS was significantly lower in the elderly group than in the younger group, resulting from the fact that elderly patients died of causes other than gastric cancer during follow-up. In the present study, the main causes of death in their follow-up period were cardiovascular and pulmonary diseases, such as myocardial infarction and pneumonia. The risk of these diseases becomes higher with age; hence, Endo et al. also reported that there were no significant differences between the surgery and best supportive care groups, especially in patients aged 90 years and over [1]. However, of the patients in the present study, two patients aged 90 years and over have continued to be doing well. In addition, they showed no significantly different physical parameters before operation compared with those of the elderly group patients who died (data not shown).

It is also important to prevent perioperative complications. Jiang et al. reported that the higher the grade of complications according to the Clavien–Dindo classification was, the lower the OS after R0 resection of gastric cancer was [17]. Therefore, preventing perioperative complications may also extend the OS of elderly patients, and this provides further support to the view that surgery should be performed even for elderly patients. With regard to complications after LADG, many authors have reported that the complication rate of LADG was equal to or less than that of open distal gastrectomy (ODG) [4–7]. Lee et al. [5] reported a rate of 25.3%, and Kitano et al. [4] reported 12.7%. In the present study, the complication rate in the elderly group was 31.3%, which, though higher than that in the younger group, was not significantly different. Indeed, there were no hospital deaths related to complications in the present study.

Meanwhile, Massarweh et al. reported that the most frequent complication as well as the main cause of death

in elderly patients after abdominal surgery was pneumonia [18]. Also in the present study, pneumonia was the most frequent postoperative complication in the elderly group. Thus, the prevention of pneumonia may lead to the reduction of mortality and morbidity after LADG in elderly patients. One of the advantages of laparoscopic surgery compared with open surgery is the prevention of decreased respiratory function after surgery [19]. Memon et al. [6] reported a meta-analysis of distal gastrectomy, and they noted fewer pulmonary complications after laparoscopic gastrectomy than after open gastrectomy. They reported that the lower pulmonary complication rate was related to the shorter abdominal incision of LADG than that of ODG. It is a fact that a shorter abdominal incision leads to less pain, and less pain leads to early ambulation. In addition, it is also well known that early ambulation prevents pneumonia resulting from atelectasis. Zeng et al. [9] reported a meta-analysis of LADG versus ODG, and they noted that analgesic agent use was less after LADG than after ODG, and Kawamura et al. reported that Wong-Baker FACES pain rating scale scores were lower on postoperative days 3, 4, and 5 in the LADG group than in the ODG group [20]. Indeed, Kitano et al. reported a randomized, controlled trial that compared LADG with ODG and found that visual analog scale scores while coughing and walking after surgery were lower in the LADG group [7]. In addition, they also reported that forced vital capacity was lower after ODG than after LADG on the third day after surgery. Kawamura et al. also reported that the LADG group reached an SaO<sub>2</sub> of over 95% on room air faster than the ODG group [19]. Given the reasons described above, LADG rather than ODG should be performed for elderly gastric cancer patients to prolong OS after surgery.

Delirium is also one of the frequent complications after surgery in elderly patients. Avidan et al. reported that 10–70% of elderly patients over 60 years of age developed delirium after major surgery [21]. Early ambulation may also prevent postoperative delirium, because Schweickert et al. reported that physical and occupational therapy for patients in an intensive care unit shortened the duration of intensive care unit-associated delirium [22]. In the present study, severe delirium occurred in three of 10 patients who had complications greater than Grade II of the Clavien–Dindo classification in the elderly group. Since postoperative pain is one cause of delirium, less pain after surgery may be advantageous for preventing postoperative delirium [21]. Therefore, it is important to reduce pain after surgery, especially for elderly patients. From this perspective, LADG is the better procedure for elderly gastric cancer patients.

Based on the reasons described above, LADG is a feasible treatment for elderly gastric cancer patients. However, surgery should be performed more carefully and more

quickly than usual in elderly patients. In the present study, operation time was significantly shorter in the elderly group than in the non-elderly group, even though there was no significant difference in the grade of lymph node dissection between the groups. We think that this was related to the surgeon's natural, unconscious extra careful attitude during the operation. Although extra care was taken during the operation, blood loss during the operation tended to be greater in the elderly group than in the non-elderly group, probably due to the fact that about 40% of elderly group patients had taken anticoagulants or antiplatelet drugs. In fact, almost all types of bleeding during the operation in this group were oozing. However, no significant difference was observed in this parameter between the two groups, also likely due to the extra care during the operation.

In conclusion, surgery should not be ruled out simply on the basis of the patient's age; especially, LADG seems to be a safe and feasible treatment even for elderly patients aged 80 years and over. However, it is clear that sufficient attention should be paid to prevent complications not only in the perioperative period, but also during follow-up. In addition, it is also clear that the decision whether the surgery is performed or not should be made by the patients; therefore, surgeons are obligated to provide these patients with correct information using various methods like ACS-NSQIP risk calculator.

Consequently, if these precautionary measures are fully implemented, LADG may be the first choice for elderly patients with gastric cancer. To the best of our knowledge, this is the first report on the safety and effectiveness of LADG for elderly patients, especially those aged 80 years and over. Minimally invasive laparoscopic surgery such as LADG appears to be an option for cancer treatment in an aging society.

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#### Compliance with ethical standards

**Disclosures** Motohira Yoshida, Shigehiro Koga, Kei Ishimaru, Yuji Yamamoto, Yusuke Matsuno, Satoshi Akita, Jun Kuwabara, Kazufumi Tanigawa, and Yuji Watanabe have no conflicts of interest or financial ties to disclose.

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