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ORIGINAL ARTICLE

Effects of laparoscopic-assisted gastrectomy on elderly patients with gastric cancer

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Summary

Purpose: *Although the acceptance of laparoscopy-assisted gastrectomy (LAG) for the treatment of gastric cancer (GC) has been increasing, it is still controversial that LAG is an applicable treatment method for elderly patients since elderly patients are usually complicated with other diseases. Therefore, this study aimed to investigate the prognostic differences between elderly patients and non-elderly patients after receiving LAG.*

Methods: *Patients (n = 306) who received LAG for the treatment of GC from April 2009 to December 2014 were included in the study. The patients were divided into the elderly group (≥65 years, n=120) and the non-elderly group (< 65 years, n=186). The postoperative outcomes as well as the morbidity and the survival rates were compared between the two groups.*

Results: *American Society of Anesthesiologists (ASA) score and comprehensive complication index (CCI) score in the elderly group were significantly higher than those in the non-elderly group ($p<0.05$). In terms of surgical outcomes, there was no significant difference in blood loss or postoperative hospital stay between the elderly group and the non-elderly group. As for postoperative comorbidities, there were significant differences in intraperitoneal hemorrhage and pleural effusion between the elderly group and the non-elderly group. Moreover, the median follow-up time was 38.5 months, and the overall survival of elderly patients with comorbidities was significantly lower than that of the elderly patients without comorbidities ($p<0.05$).*

Conclusions: *LAG can be performed safely and successfully in the elderly population with acceptable postoperative and long-term results.*

Key words: *laparoscope, gastrectomy, gastric cancer, elderly patients*

Introduction

Although the GC morbidity has been declined, it is still the fifth most common malignancy in the world. With the prolongation of life and the rapid improvement of medical care, there is an increasing trend in the proportion of patients diagnosed with GC in the elderly population [1]. It has been reported that the elderly patients are poor in physical quality and accompanied by advanced age-related diseases, which may result in significant increases in the incidence of postoperative comorbidities and related mortality after surgery [2]. Therefore, most of the elderly patients choose conservative treatment, instead of radical resection. With the development of science and technology, there has been a revolutionary change in the operation mode, and laparoscopic surgery has been gradually replacing

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the status of open surgery. Different from the conventional open surgery, laparoscopic-assisted total gastrectomy (LATG), a minimally invasive operation, was suggested to have the advantages of less damage to the body, less postoperative pain, fast recovery of gastrointestinal function and less impact on the body immunity [3-5]. Since Kitano et al [6] first reported laparoscopy-assisted gastrectomy (LAG), and a number of clinical studies provided further evidence for the efficacy of LAG in the treatment of early GC [7-9]. In a multi-center, randomized, controlled trial (KLASS-01) investigating the short-term efficacy of LAG for GC in Korea, the results showed that LAG was safe for patients with stage I GC, and had a lower incidence of incision comorbidities compared with conventional open distal gastrectomy [10]. Similarly, a prospective phase III clinical study (JCOG0912) in Japan has also confirmed the safety of applying LAG in patients with stage I GC [11]. Concerning the long-term follow-up results, a multicenter phase II clinical study (JCOG0703) concluded that patients with stage I GC undergoing LAG had similar long-term outcomes to those undergoing open distal gastrectomy [12].

It has been demonstrated that, since LAG is minimally invasive, it could achieve prognostic effects in elderly patients with early GC similar to those in the non-elderly patients [13]. However, there are few studies on LAG in elderly patients at present; moreover, related studies had a relatively small sample size, and failed to provide sufficient data on the postoperative long-term results of elderly patients performed with LAG.

In this study, 306 patients undergoing LAG were enrolled, including 120 patients ≥65 years, and the short-term surgical outcome and long-term survival of patients in the elderly group and non-elderly group were evaluated.

Methods

Patients

GC patients receiving LAG (n=306) in the Department of Gastrointestinal Surgery IV in Peking University Cancer Hospital from April 2009 to December 2014 were included in the study. In this study, patients with history of preoperative chemotherapy were excluded. The clinicopathological data of all patients were collected from medical records, surgical records and pathological records. Written informed consent of each patient was obtained prior to any medical intervention, and the study was approved by the Ethics Committee of Peking University Cancer Hospital & Institute (Beijing, China) (No. 2012071710). According to the age difference, all patients were divided into the elderly group (≥65 years, n=120) and the non-elderly group (age <65 years, n=186). The clinicopathological features, short-term surgical findings and overall survival (OS) rate were compared between the two groups.

Preoperative routine examinations

Preoperative routine examinations included laboratory tests (such as routine blood test, routine urine test, biochemical tests of liver and renal function, electrolyte test, tumor markers, blood grouping, hepatitis, syphilis and HIV), imaging examination (such as total abdominal CT plain scan + enhancement, upper gastrointestinal radiography, etc.), endoscopy, cardiovascular and pulmonary function tests (such as electrocardiogram, pulmonary function and cardiac color Doppler ultrasound). The following situation should be identified: surgical contraindications, tumor size, tumor location, perigastric vessels, lymph nodes and adjacent organs.

Operative techniques

Laparoscopic resections with regional lymph nodes dissection were performed in accordance with the Japanese Gastric Cancer Treatment Guidelines [14]. The patients were placed supine with legs apart and were tilted 20-30° head-up. The operator stood on the right side of the patients, the assistant stood opposite to the operator and the cameraman stood between the patients' legs. A 10-mm camera port was introduced 2 cm below the umbilicus the by Veress needle technique or the open technique. The carbon dioxide pressure was up to 10 mmHg and then another four ports were introduced: a 10-mm trocar was inserted in the left anterior axillary line, 2-3cm below the costal margin as major operation port. Later, a 5 mm trocar was inserted contralaterally as main assistant port. Two 5-mm trocars were inserted in the right and left midclavicular line at the umbilicus level as accessory port. A Nathanson liver retractor was placed for liver traction. After the laparoscopic procedure, a 6-cm laparotomy incision was made in the midline of upper abdomen. Billroth type I, Billroth type II or Roux-en-Y gastrojejunostomy was performed in distal gastrectomy while Roux-en-Y esophagojejunostomy was used in total gastrectomy. Esophagogastrostomy was performed for patients who received proximal gastrectomy. All the reconstruction procedures above were performed with extracorporeal approaches using circular staplers or linear staplers.

Evaluation on safety and effectiveness of surgery

For safety evaluation, the operation time, blood loss and American Society of Anesthesiologists (ASA) [15] physical status classification of enrolled patients were measured. For effectiveness evaluation, landing time, feeding time and intubation time and comprehensive complication index (CCI) score were involved.

ASA physical status classification: (1) ASA I, normal and healthy; ASA II, mild systemic disease; ASA III, severe systemic disease, limited daily activities, but not yet incapacitated for work; ASA IV, severe systemic disease, incapacitated for work, and faced with a constant threat to life; and ASA V, not expected to survive for 24 h, surgery or not.

The Clavien-Dindo classification was used to classify the postoperative complications into grades I-V [16]: grade I: there was no need for drugs, endoscopy, surgery and other treatment of complications, but it included general symptomatic treatment drugs such as antipyretic, antiemetic, analgesic, electrolytes, including local infection of incision, physiotherapy and other treatment; grade II: incision infection needed antibiotic treatment, blood transfusion and so on total parenteral nutrition and drugs; grade III: further treatment such as surgery, endoscopy and interventional radiotherapy is needed, in which level IIIa does not need general anesthesia, and level IIIb needs general anesthesia; grade IV: serious life-threatening complications, including central nervous system complications and ICU monitoring treatment, in which grade IVa is single organ dysfunction, and grade IVb is multiple organ dysfunction; grade V: death. The CCI was obtained by on-line computation through the website (www.mdcalc.com).

Table 1. Clinical demographics of patients in non-elderly and elderly group

	Non-elderly (n=186)	*Elderly (n=120)*	*p*
Age median (range)	42 (24-64)	73 (65-87)	
Sex, n (%)			0.648
Male	57 (30.6)	41 (34.2)	
Female	129 (69.4)	79 (65.8)	
BMI (kg/m^2)			0.801
Median (range)	22.3 (14.8-32.4)	26.2 (15.4-39.3)	
ASA, n (%)			0.452
I	13 (6.9)	12 (10.0)	
II	140 (7.5)	91 (7.6)	
III	33 (1.8)	17 (1.4)	
Tumor size (mm)			0.774
Median (range)	7.8 (0.1-15.3)	7.5 (0.7-14.3)	
Tumor location, n (%)			0.183
Upper 1/3	45 (24.2)	37 (30.8)	
Middle 1/3	48 (25.8)	20(16.7)	
Lower 1/3	93 (50)	63(52.5)	
Surgical approach, n (%)			
Proximal	26 (14.0)	18 (15)	
Distal	101 (54.3)	67 (55.8)	
Total	59 (31.7)	35 (29.2)	
pT stage, n(%)			0.242
T1	37 (19.9)	22 (18.3)	
T2	31 (16.7)	17 (14.2)	
T3	87 (46.7)	60 (50)	
T4	31 (16.7)	21 (17.5)	
pN stage, n(%)			0.168
N0	64 (34.4)	52 (43.3)	
N1	49 (26.3)	23 (19.2)	
N2	30 (16.1)	23 (19.2)	
N3	43 (23.1)	22 (18.3)	
pTNM, n (%)			0.669
I	51 (27.4)	32 (26.7)	
II	55 (29.6)	42 (35)	
III	80 (43.0)	46 (38.3)	
Histological differentiation, n (%)			0.684
Well differentiated	6 (3.2)	5 (4.2)	
Moderately differentiated	90 (48.4)	65(54.2)	
Poorly differentiated	82 (44.1)	46(38.3)	
Signet ring-cell type	8 (4.3)	4(3.3)	

Non-elderly group: <65 years old; Elderly group: ≥65 years old

Disease-free survival and long-term survival

The OS was calculated from the first day after surgery until death from any cause or the final follow-up date. The patients were followed up, for the first time, two weeks after discharge. Subsequently, follow-up was conducted every 3 months in the first 2 years, every 6 months for 2-5 years, and every year thereafter. The thresholds of cross-sectional imaging and endoscopy were very low for patients, and symptoms of suspected recurrence failed to be found by inquiring medical history or carrying out clinical examinations during follow-up. All the patients were followed up for 5 years after surgery.

Statistics

All the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Student's t-test was used to compare the continuous variables, and x^2 test or Fisher's exact test were used for categorical variables as appropriate. Survival curves were constructed using Kaplan-Meier method and differences between the groups were analyzed with log-rank test. All the reported p values were two-sided. A p value <0.05 was considered statistically significant.

Results

Patient characteristics

All the patients (n=306) were divided into the elderly group (n=120) and the non-elderly group (n=86), and the clinical features of the two groups were analyzed. The average age of elderly patients and non-elderly patients was 73 and 42 years, respectively. Compared with non-elderly patients, elderly patients were more likely to develop comorbidities (p<0.05). There were no significant differences in BMI, gender, tumor size, tumor location, tissue type and postoperative pathological TNM stage between the two groups (Table 1).

Operation and postoperative results

In Table 2, the details of postoperative comorbidities are listed. The incidence of comorbidities in the elderly group was significantly higher than that in the non-elderly group, and the reason may be that elderly patients had higher incidence of pulmonary infection than the non-elderly patients (p<0.05). The most common comorbidity was pleural effusion (n=23, 19.2%) in the elderly group and gastric spasm (n=27, 14.5%) in the non-elderly group, respectively. Intraabdominal hemorrhage (elderly group: 6/120, 5%; non-elderly group: 2/186, 1%, p<0.05) and pleural effusion (elderly group: 23/120, 19.2%; non-elderly group: 12/186, 6.5%, p<0.05) were obviously more common in the elderly group when compared with the non-elderly group. In addition, the number of postoperative comorbidities was compared between the two groups, and the results showed that the presence of complication in the non-elderly group (17.19%) was higher than that in the elderly group. Although the elderly group had higher incidence of postopera-

Table 2. Operative variables and complications

	Non-elderly (n=186) *n (%)*	*Elderly (n=120)* *n (%)*	*p*
Comorbidities			0.05*
0	107 (87.5)	49 (40.8)	
1	52 (27.6)	42 (35.0)	
2	21 (11.3)	19 (15.8)	
3	3 (1.6)	9 (7.5)	
4	2 (1.1)	1 (0.8)	
5	1 (0.5)	0 (0.0)	
Postoperative complications			0.078
Gastroparesis	27 (14.5)	11 (9.2)	0.167
Anastomotic bleeding	3 (1.6)	3 (2.5)	0.586
Duodenal stump leak	2 (1.1)	3 (2.5)	0.339
Anastomotic leak	4 (2.2)	3 (2.5)	0.842
Abdominal bleeding	2 (1.1)	6 (5.0)	0.036*
Lymphatic leak	7 (3.8)	2 (1.7)	0.291
Pleural effusion	12 (6.5)	23 (19.2)	0.001**
Duct infection	1 (0.5)	3 (2.5)	0.141
Others	15 (8.1)	5 (4.2)	0.179

Non-elderly group: <65 years; Elderly group: ≥65 years, *p=0.036, **p=0.01

tive comorbidities when compared with the non-elderly group, there was no statistical difference.

Postoperative recovery status in the elderly group and the non-elderly group

During operation, the operation time and the blood loss were compared between the elderly group and the non-elderly group (Table 2). The elderly group had lower average operation time (251.3±58.78 min *vs.* 259.9±55.4 min) and blood loss (98.1±94.2 mL *vs.* 103.4±82.2 mL) than the non-elderly group. There was no significant difference in the number of lymph node dissection during the operation between the elderly group and the non-elderly group (28.6 ± 11.1 *vs.* 29.9 ± 12.2), showing similar situation. Besides, there was no significant difference in the number of patients with need of conversion to an open approach between the elderly group (n=19, 15.8%) and the non-elderly group (n=22, 11.8%). Moreover, there were no significant differences between the elderly group and the non-elderly group regarding the operation time, the rate of conversion to laparotomy, the postoperative exhaust time, the feeding time (the time of first intake of fluid food after surgery) and the hospital stay (all p>0.05) (Table 3).

There were only slight differences in Clavien-Dindo classification and CCI score between elderly patients and non-elderly patients (Table 4), and the mean values of Clavien-Dindo classification and CCI score were a little higher in the elderly group when compared with the non-elderly patients, which may be resulted from the sample size, but it may also be that the safety and effectiveness of LAG for elderly patients were also worthy of affirmation.

Table 3. Overall patient outcomes from laparoscopy assisted gastrectomy

Outcomes	*Non-elderly (n=186)*	*Elderly (n=120)*	*p value*
Operative time (min)	259.9±55.4	251.3±58.7	0.152
Blood loss (mL)	103.4±82.2	98.1±94.2	0.236
Number of retrieved lymphnodes	29.9±12.2	28.6±11.1	0.744
Time to initiate oral intake(d)	23.9±73.7	11.8±6.2	0.668
Time to first ambulation(d)	1.5±1.4	1.7±1.9	0.258
Time to first flatus(d)	4.5±1.8	4.4±1.9	0.325
Postoperative hospital stay(d)	17±15.4	15±8.2	0.441
Conversion to open surgery			0.625
Yes	22	19	
No	164	101	

Non-elderly group: <65 years; Elderly group: ≥65 years

Table 4. Postoperative complications by the Clavien-Dindo classification

Complications	*Non-elderly (n=186)* *n (%)*	*Elderly (n=120)* *n (%)*	*p value*
Minor complications			0.132
Grade I	8 (4.3)	6 (5.0)	
Grade II	5 (2.7)	5 (4.2)	
Major complications			
Grade III-a	1 (0.6)	3 (2.5)	
Grade III-b	0 (0.0)	2 (1.7)	
Grade IV-a	0 (0.00)	0 (0.0)	
Grade IV-b	0 (0.00)	0 (0.0)	
Grade V	0 (0.00)	0 (0.0)	
CCI			0.115
0-20	12 (6.5)	9 (7.5)	
20-30	2 (1.1)	5 (4.2)	
30-40	0 (0.0)	2 (1.7)	
40	0 (0.0)	0 (0.0)	

Non-elderly group: <65 years; Elderly group: ≥65 years

Survival status in the elderly group and the non-elderly group

The median follow-up time was 38.5 months (ranging from 2 to 98). A total of 87 patients died during the study period. There was no significant difference in 5-year overall survival between the elderly group and the non-elderly group (p=0.142) (Figure 1A-B). For patients without comorbidity, there was no significant difference in the overall survival between the two groups (p=0.832) (Figure 1C), while in patients with comorbidities, the overall survival of elderly patients was significantly lower than that of non-elderly patients (p=0.032) (Figure 1D). In addition, for patients without comorbidity in this study, there was no significant difference in the overall survival rate between the two groups (p=0.774) (Figure 1E); for patients with comorbidities, the overall survival rate of the elderly group was lower than that of the non-elderly group, without statistical difference (p=0.068) (Figure 1F).

Discussion

In recent years, surgical treatment for elderly patients with GC has been widely developed in East Asia, such as China, South Korea and Japan

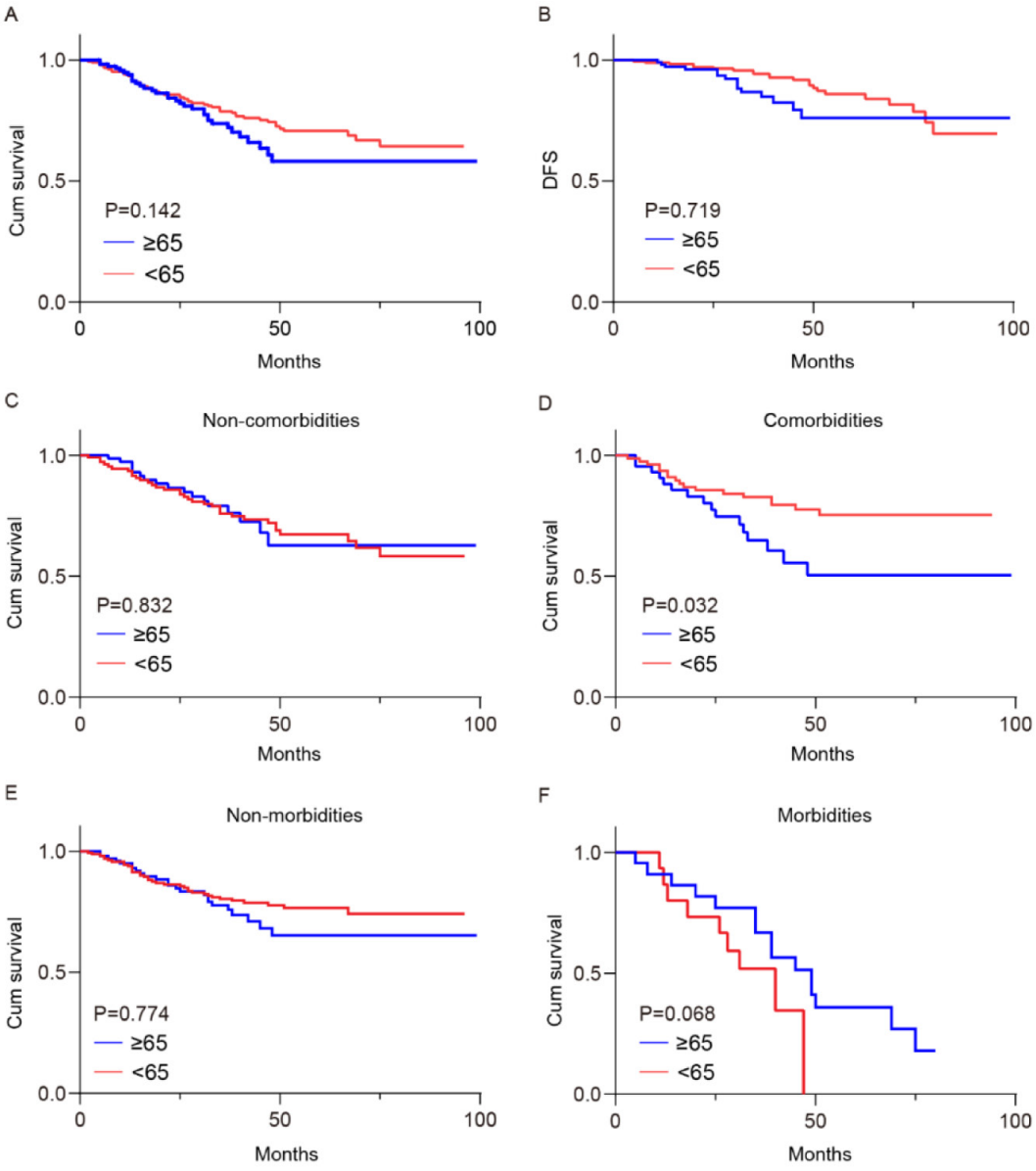

Figure 1. The survival status in the elderly group and the non-elderly group **A,B:** There was no significant difference in 5-year overall survival between the elderly group and the non-elderly group. **C,D:** In patients with comorbidities, the overall survival of elderly patients was significantly lower than that of non-elderly patients. **E,F:** For patients with comorbidities, the overall survival rate of the elderly group was lower than that of the non-elderly group, but without statistical difference.

[17]. There is also an increasing need for radical surgery in elderly patients with GC. A previous study suggested that advanced age was an important factor affecting the occurrence of postoperative comorbidities, thus more attention should be paid to the influence of advanced age in clinical outcomes, but the age was not a contraindication in operation [18]. Saif et al [19], through a meta-analysis on surgical treatment of elderly patients with GC, found that age alone was not the determinant for carrying out radical or palliative treatment for elderly patients with GC; furthermore, it was believed that physical state, organ function, social relationship and mental state of patients were also important factors. Another study [20] found that, for the elderly patients with GC, minimally invasive surgery could also achieve the same effect of radical resection of tumor as traditional open surgery, and had higher safety and economic efficiency. Takemura et al [21] also advocated that the age limit should be abandoned, and minimally invasive surgery was applicable for elderly patients who met surgical indications.

A controlled phase I gastric cancer trial (JCOG0912, KLASS-01) confirmed that there was no significant difference in the short-term clinical outcomes and postoperative comorbidities between LAG and open distal gastrectomy [22]. In this study, the incidence of 30-day postoperative comorbidities in the elderly group was higher than that in the non-elderly group, without statistical difference, indicating that LAG was relatively safe for the elderly patients. Although ASA classification and CCI score indicated that the elderly patients had decreased tolerance to the operation (Figure 2), there was no significant difference between the two groups in terms of time for postoperative recovery. In addition, in this study, elderly patients and non-elderly patients were similar in long-term outcomes. As previously reported, the tumor recurrence rate, the 5-year overall survival rate and 5-year tumor-free survival rate of GC patients undergoing LAG were 10-30%,

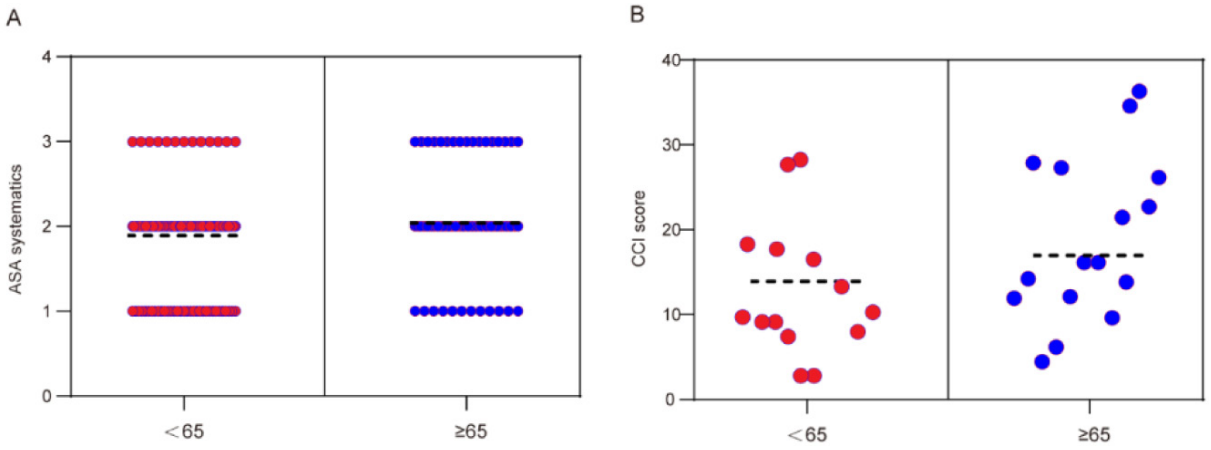

Figure 2. ASA classification and CCI score between two groups. **A,B:** ASA classification and CCI score indicated that the elderly patients had decreased tolerance to the operation, but there was no significant difference between the two groups in terms of time for postoperative recovery.

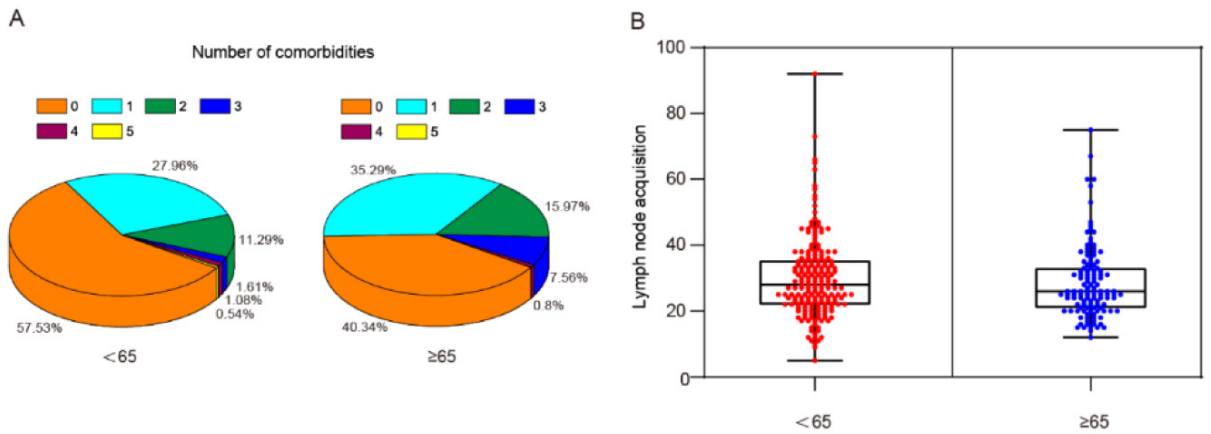

Figure 3. A: Number of comorbidities between two groups. **B:** Lymph node acquisition between two groups.

50-70% and 41-60% respectively [23], which were similar to our results. Concerning the long-term outcomes of LAG in the elderly patients with GC, previous evidence revealed that the overall 3-year survival rate was 55.8%. This study, for the first time, showed that elderly patients with GC receiving LAG could achieve similar long-term outcomes with the non-elderly patients.

In conclusion, with the improvement of laparoscopic equipment and operative technique of laparoscopic operation, laparoscopic-assisted radical gastrectomy for GC has been widely used in the clinic. Although the elderly patients with GC had higher risk in surgery and anesthesia due to the decline of physical function and more comorbidities (Figure 3). LAG, as a minimally invasive treatment, shows the advantages of light postoperative pain and fast recovery, without increase in surgical comorbidities, and it can achieve the same effect as open surgery in terms of radical resection of tumor [24]. Therefore, it is reliable and practical for the elderly patients with GC to carry out gastrectomy through the skillful cooperation of laparoscopic operation team and the reasonable nursing and treatment during the perioperative period.

Conclusions

In conclusion, LAG can be performed safely and successfully in the elderly population with acceptable postoperative and long-term results.

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Conflict of interests

The authors declare no conflict of interests.

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