

# Short-term outcomes of laparoscopy-assisted gastrectomy with D2 lymph node dissection for gastric cancer: Experience from a single institution in central Vietnam

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## Abstract

**Introduction:** Laparoscopic-assisted gastrectomy (LAG) has become more popular and extensively developed for gastric cancer. However, LAG with D2 lymph node (LN) dissection has not been widely deployed because it is a complex technique and should be performed by experienced laparoscopic surgeons. This study aimed to confirm the feasibility and outcomes of the LAG with D2 dissection for gastric cancer.

**Patients and Methods:** The prospective intervention study included 72 patients with gastric cancer and underwent LAG with D2 LN dissection between April 2017 and October 2021. All patients were operated by the same surgeon who had experience with laparoscopy. LAG with conventional D2 lymphadenectomy is based on the Japanese gastric cancer treatment guidelines 2014 (ver. 4).

**Results:** The LAG includes 31 (43.1%) total gastrectomies and 41 (56.9%) distal gastrectomies. Conversion to open laparotomy was required in one patient (1.4%). The mean number of harvested lymph nodes was  $20.4 \pm 9.1$  (range 4 - 47). In 75.0% of the procedures, at least 15 lymph nodes were resected. The mean number of positive lymph nodes was  $4.2 \pm 5.7$  (range 0 - 21), and  $16.2 \pm 9.3$  negative lymph nodes (range 0 - 47). The mean operative time was  $231.8 \pm 38.1$  minutes (range 170 - 350). The mean time to first flatus was  $3.5 \pm 1.0$  days (range 2 - 7). The mean postoperative hospital stay was  $10.8 \pm 4.0$  days (range 7 - 30). The complications within 30 postoperative days occurred in 12 patients (16.7%).

**Conclusions:** Laparoscopy-assisted gastrectomy with D2 LN dissection was safe and feasible with favorable short-term oncological outcomes. However, this technique must be realized by experienced surgeons in specialized centers.

**Keywords:** Gastric cancer, Laparoscopy-assisted gastrectomy, D2 dissection, Vietnam

## Introduction

Gastric cancer was the 5<sup>th</sup> most common malignancy and the 4th leading cause of cancer death in the world, according to GLOBOCAN 2020 data. [1] Treatment with radical gastrectomy and adequate regional lymph node (LN) dissection improves the long-term survival rate. [2], [3] Since laparoscopy-assisted gastrectomy (LAG) was initially reported in 1994 by Kitano et al., this technique has become more popular and extensive because of the advantages of minimally invasive surgery. [4] Regional lymphadenectomy is considered an essential part of surgical resection for gastric cancer. [5] The extent of lymphadenectomy is performed differently by surgeons. The National Comprehensive Cancer Network (NCCN) guidelines recommend gastrectomy with D1 or modified D2 LN dissection in the United States. [6] Surgeons in eastern countries regularly performed gastrectomy with D2 lymphadenectomy. [7], [8]

According to the Japanese gastric cancer treatment guidelines ver.4, the extent of LN dissection is further described according to the Japanese gastric cancer treatment guidelines 2018. [5] LAG with D2 dissection was performed in Asia randomized controlled trials (RCTs) from the Korean Laparoscopic Gastrointestinal Surgery Study (KLASS-02), the Chinese Laparoscopic Gastrointestinal Surgery Study (CLASS-01), and the Japan Clinical Oncology Group Study (JCOG0912).[7], [8], [9] These studies have demonstrated that LAG, performed by experienced surgeons in specialized centers, is safe and feasible. Moreover, this technique is as effective as open surgery. The retrieval of at least 15 nodes in gastric cancer is recommended by the current National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines (2017).[6], [10]

In Vietnam, there were 17,906 new cases of gastric cancer per year, according to Globocan 2020, accounting for 9.8% of the new cancer cases, ranking 4th after liver, lung, and breast cancer.[1] Although

laparoscopic gastrectomy with D2 LN dissection has been widely implemented worldwide and in several major centers in Vietnam. However, in Vietnam, there has not been many researchs on this issue . Therefore, we studied the patients underwent the laparoscopic gastrectomy with D2 LN dissection to evaluate some pathological characteristics and results of this surgery.

## Patients and methods

### Study design

Between April 2017 and October 2021, the prospective intervention study included 72 patients diagnosed with gastric cancer and treated surgically with LAG with D2 LN dissection at the Department of Digestive Surgery, Hue University of Medicine and Pharmacy Hospital, Hue City, Vietnam. The inclusion criteria were that all selective patients had primary locally advanced gastric cancer, confirmed pathologically by endoscopic biopsy, and no evidence of Bulky lymph nodes and distant metastasis. A preoperative work-up included upper gastrointestinal endoscopy, computed tomography, and endoscopic ultrasound. Exclusion criteria included pregnancy patients, an American Society of Anesthesiologists (ASA) score > 3, previous neoadjuvant chemotherapy or radiotherapy, previous upper abdominal surgery, and other malignant diseases. All patients were treated by a single surgeon who had experience with laparoscopy. The ethical committee approved the study of Hue University of Medicine and Pharmacy. All patients were informed about the possible risks, and written informed consents were obtained.

Patients characteristics, including age, gender, body mass index (BMI), American Society of Anesthesiology (ASA), and comorbidities, were analyzed. According to the 7th and 8th editions of the American Joint Committee on Cancer (AJCC), the disease was diagnosed with pathological stage, location, size, and differentiation of tumors. Intraoperative variables included surgery types (proximal gastrectomy, total gastrectomy, distal

gastrectomy) and reconstruction procedures. The specimens were retrieved to count the number of regional lymph nodes (LNs). The selection of gastrectomy with D2 lymphadenectomy was based on version 4 of the Japanese gastric cancer treatment guidelines. The surgeons experience determined the type of reconstruction. LNs were separately dissected by the surgeons at the end of the procedure and identified by specialized pathologists to examine microscopically for metastases.

The operative outcomes included operative times, time to first flatus, first oral feeding, postoperative hospital stay, and postoperative complications. Morbidity and mortality were followed for 30 days after surgery.

### **Surgical procedures**

The patients are placed in a supine position under general anesthesia. The surgeon and the assistant holding the laparoscope stand on the patients right side. The other assistant stands on the left. An initial 12-mm trocar for a 30° laparoscope is inserted below the umbilicus and pneumoperitoneum at 12 mmHg. The liver and the peritoneal cavity are inspected to rule out metastasis. A 12-mm port can be placed in the right upper quadrant, a 5-mm trocar is inserted at the contralateral side, and the other 5-mm trocar is placed in the left upper quadrant.

LAG with conventional D2 lymphadenectomy is based on the Japanese gastric cancer treatment guidelines version 4. The D2 lymphadenectomy includes Nos. 1-7, 8a, 9, 10, 11p, 11d, 12a for total gastrectomy and Nos. 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p, 12a for distal gastrectomy. The first portion of the duodenum is stapled and sectioned about 2cm below the pylorus with an Endo-GIA stapler (US Surgical Corporation, Norwalk, CT, USA) through the 12-mm port. A small incision is performed in the middle of the upper abdomen. The incision length was about 4 - 6 cm for distal gastrectomy and 6 - 8 cm for total gastrectomy. The surgeons experience determines the type of reconstruction. Gastrectomy and anastomosis are extracorporeally performed

using a handsewn method or Endo-GIA stapler (US Surgical Corporation, Norwalk, CT, USA). In the case of distal gastrectomy, anastomosis is carried out by Billroth II or Roux-en-Y reconstruction. The choice of gastrojejunostomy depends on the surgeons and the age of the patients. We often use Roux-en-Y anastomosis in the case of distal gastrectomy for young patients in the early cTNM stage. By contrast, total gastrectomy is always used in the Roux-en-Y anastomosis. In these cases, an end-to-side esophagojejunostomy is constructed using an EEA™ circular stapler (US Surgical Corporation, Norwalk, CT, USA). The Roux limb was closed with a linear stapler, and a 70-cm Roux limb was created to construct the proximal anastomosis using the handsewn technique.

The abdominal drainage was placed near the duodenal stump or esophagojejunostomy, a place with a high risk of anastomosis leakage. Finally, the laparotomy was sutured with layered closure.

### **Statistical Analysis**

The statistical analysis in our study were performed using SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The data were presented as the means  $\pm$  standard deviation (SD) and range of continuous variables. Categorical variables were expressed as the number of patients (n) and percentages (%).

### **Results**

Seventy-two patients underwent LAG with D2 LN dissection, including 49 male and 23 female patients, with a mean age of  $62.4 \pm 11.8$  years (range 36 - 83). Their mean BMI was  $20.9 \pm 1.7$  kg/m<sup>2</sup> (17.1 - 25.0). The pathological characteristics are presented in Table 1. The mean tumor size was  $3.8 \pm 1.7$  cm (range 1 - 8). According to the AJCC classification (8th edition), the pathological TNM stages were respectively 11.1%, 23.6%, 16.7%, 12.5%, 15.3%, 13.9%, and 6.9% for seven categories (Ia – IIIc stage).

There were 31 patients (43.1%) who had total gastrectomy, and 41 patients (56.9%) had distal

gastrectomy. Billroth II and Roux-en-Y were performed on 33 (45.8%) and 39 (54.2%) patients. Conversion to open laparotomy was required in one patient (1.4%) during surgery. The leading conversion causes were peritoneal adhesion and technical difficulties, with a 10cm incision length. The mean number of retrieved LNs was  $20.4 \pm 9.1$  (range 4 - 47). In 75.0% of the procedures, at least 15 LNs were resected. Additionally, the mean number of positive LNs was  $4.2 \pm 5.7$  (range 0 - 21) and  $16.2 \pm 9.3$  negative LNs (range 0 - 41).

The postoperative outcomes after LAG are shown in Table 3. The mean operative time was  $231.8 \pm 38.1$  minutes (range 170 - 350). The mean time to first flatus was  $3.5 \pm 1.0$  days (range 2 - 7), and the mean first oral feeding time was  $4.5 \pm 2.2$  days (range 2 - 18). The mean postoperative hospital stay was  $10.8 \pm 4.0$  days (range 7 - 30). The complications within 30 postoperative days occurred in 12 patients (16.7%).

Table 1: Clinical and pathological characteristics

Characteristics	n (%)
Age Mean (range)	$62.4 \pm 11.8$ (36 - 83)
Gender Male (%)	49 (68.1)
BMI Mean, kg/m <sup>2</sup> (range)	$20.9 \pm 1.7$ (17.1 - 25.0)
ASA I	43 (59.7)
ASA II	27 (37.5)
ASA III	2 (2.8)
Tumor location	
Upper third (%)	4 (5.6)
Middle third (%)	20 (27.8)
Lower third (%)	34 (47.2)
Overlapping lesion (%)	14 (19.4)
Tumor size Mean, cm (range)	$3.8 \pm 1.7$ (1-8)

Pathological Stage (8 <sup>th</sup> AJCC/UICC staging)	
IA	8 (11.1)
IB	17 (23.6)
IIA	12 (16.7)
IIB	9 (12.5)
IIIA	11 (15.3)
IIIB	10 (13.9)
IIIC	5 (6.9)
Tumor Grade	
Well-differentiated (%)	18 (25.0)
Moderately differentiated (%)	17 (23.6)
Poorly differentiated (%)	25 (34.7)
Unknown (%)	12 (16.7)

BMI: Body mass index; ASA: American Society of Anesthesiology

AJCC/UICC: American Joint Committee on Cancer/Union for International Cancer Control

Table 2: Intraoperative and retrieved lymph node variables

Characteristics	n (%)
Type of gastrectomy	
Total gastrectomy (%)	31 (43.1)
Distal gastrectomy (%)	41 (56.9)
Reconstruction	
Billroth II (%)	33 (45.8)
Roux-en-Y (%)	39 (54.2)
Incision length Mean, cm (range)	$5.5 \pm 1.1$ (4-10)
Conversion to Open	1 (1.4)
Adequacy of LN yield	
$\geq 15$ LNs (%)	54 (75.0)
$< 15$ LNs (%)	18 (25.0)
Number of retrieval LN (number)	1473

Retrieval LN Mean (range)	20.4 ± 9.1 (4 - 47)
Positive LN count Number, Mean (range)	304, 4.2 ± 5.7 (0 - 21)
Negative LN count Number, Mean (range)	1169, 16.2 ± 9.3 (0 - 47)

LN: lymph node.

Table 3: Short-term operative outcomes

Characteristics	n (%)
Operative time Mean, minutes (range)	231.8 ± 38.1 (170 - 350)
Time to first flatus Mean, days (range)	3.5 ± 1.0 (2 - 7)
Time to start a diet Mean, days (range)	4.5 ± 2.2 (2 - 18)
Postoperative hospital stay Mean, days (range)	10.8 ± 4.0 (7 - 30)
<b>Complications</b>	
Overall complications (%)	12 (16.7)
Wound infection (%)	3 (4.2)
Delayed gastric emptying (%)	4 (5.6)
Intra-abdominal abscess (%)	2 (2.8)
Anastomotic leakage (%)	3 (4.2)
Pneumonia (%)	2 (2.8)
Bowel obstruction (%)	1 (1.4)
Incisional hernia (%)	1 (1.4)

**Discussion**

The first LAG was reported by Kitano et al. in 1994. [4] Since then, LAG has been widely performed to treat gastric cancer, especially in Japan and Korea, where LAG was recognized as a safe and technically feasible treatment. [7], [8] The Japanese Gastric Cancer Association has presented complete D2 lymphadenectomy as the standard therapy for gastric cancer. [5] LAG with

D2 LN dissection was well accepted by Eastern Asian countries, such as three ongoing multicenter RCTs from JCOG0912, KLASS-02, and CLASS-01. [7][8][9] These studies focused on the safety and efficacy of LAG with D2 lymphadenectomy. [11], [12], [13] The patients undergoing LAG had a better postoperative recovery, quicker return of bowel function, and shorter hospital stay than those undergoing open surgery. [14], [15], [16]. However, many gastric surgeons commented that LAG with D2 LN dissection had not been widely deployed because it is such a difficult technique that only experienced laparoscopic surgeons should perform. [8], [16], [17] Our study confirms that the LAG benefits with D2 LN dissection measured by being technically feasible in terms of LN dissection range, open conversion rate, and early postoperative recovery can safely be performed in patients with gastric cancer.

The role of regional lymphadenectomy has been confirmed as important for pathological N-stage evaluation. [18], [19] Based on that result, a proper plan was established to treat gastric cancer. The NCCN recommended the harvest of at least 15 regional LNs to evaluate appropriate staging and avoid stage migration in gastric cancer. [6] In our study, 54 patients (75.0%) had ≥ 15 LNs retrieved as recommended by the NCCN. The mean number of harvested LNs ranged from 18.0 to 46.6 in previous studies, assessing the adequacy of LN yield. [7], [8], [12], [20 - 22] In the current study, the mean number of retrieved LNs was 20.4 ± 9.1 (range 4 - 47), which was similar to that conducted by Abdelhamid M.A. [12] in Egypt and Brenkman H.J.F. [22] in the Netherlands. However, our research data showed fewer retrieved LNs than studies conducted in East Asian countries. The KLASS-02 RCT trial reported a mean number of 46.6 ± 17.9 LNs. [8] The median number of LNs was 39 in the JCOG0912 trial. [7] The CLASS-01 also reported that the mean number of retrieved LNs was 36.1 ± 16.7. [9] The number of LNs retrieval may be influenced by the extent of

lymphadenectomy, tumor size, experience of the surgeon, examining pathologist, and the number of LNs in each patient. [23] In Japan, Shinohara T. [24] have recommended that the incidence of LNs metastasis of gastric cancer was higher in the suprapancreatic area. Their technique has been performed with meticulous dissection of the suprapancreatic LNs. Consequently, the number of LNs removed in their series exceeded 40. [24] In East Asian countries, the highly experienced surgeons have performed about 200 gastrectomy yearly in large centers. [2] In our department, approximately 20 cases of gastric cancer were operated each year. Among all retrieved LNs in our study, the mean number of positive LN counts was  $4.2 \pm 5.7$  (range 0 - 21) and  $16.2 \pm 9.3$  (range 0 - 47) negative LN counts. Numerous studies with large databases evaluated that there was an association of the increase in number of retrieved LNs and superior survival for gastric cancer. [2], [3] There was even an increase in negative LNs count that appeared to have therapeutic and prognostic value. [3]

Some studies reported a conversion rate ranging from 0.2% to 6.4%. [7], [8], [9], [12], [25] A potential reason for the higher conversion rate to open surgery was observed when the locally advanced cancers were intraoperatively diagnosed as stage T4. [7], [26] Other predictors for conversion were obesity, upper gastric cancer, and lack of surgical experience. [27] In our study, there was no case of obesity performed by a surgeon experienced in laparoscopic surgery. The conversion to open procedure was in one patient (1.4%), which was lower than seen in JCOG0912 (3.5%), KLASS-02-RCT (3.7%), CLASS-01 (6.4%), but higher than that noted in previous reports by KLASS-01 (0.9%). [7], [8], [9], [25] In this technical conversion, the advanced gastric cancer was stage T4b, which invaded the pancreas and was an aggressive tumor requiring total gastrectomy.

According to the literature, LAGs operative time ranged from 217 to 288 minutes. [7], [8], [12], [21],

[16] In our study, the mean operative time was  $231.8 \pm 38.1$  minutes (range 170 – 350), which was longer than that of the study conducted in CLASS-01 (217.3 min), KLASS-02-RCT (227.1 min) but shorter than in JCOG0912 (278 min). These studies also demonstrated that the total gastrectomy had a longer operative time than the distal. In addition, LAG with total omentectomy and D2 LN dissection for gastric cancer increased the operative time. However, the duration of surgery has decreased with subsequent cases when the surgeons have gained more experience. [12], [14]

Some studies showed that LAG resulted in better short-term outcomes, including a shorter first flatus time, an earlier liquid feeding diet, and a shorter postoperative length of stay than open gastrectomy. [7], [8], [16] In the present study, the mean time to first flatus was  $3.5 \pm 1.0$  days (range 2 - 7), which was similar to the studies conducted in CLASS-01 (3.5 days) and KLASS-02-RCT (3.5 days). Some investigators reported that discharge at postoperative day 8 to 10.8 was possible in patients who received LAG. [8], [9], [12], [16], [20], [22] In our study, patients had a mean operative stay of  $10.8 \pm 4.0$  days (range 7 - 30), which is similar to the study performed in the CLASS-01 trial ( $10.8 \pm 5.9$  days) but longer than some studies in Korea, Egypt, and the Netherlands that reported a postoperative stay of 8.1, 8 and 8 days, respectively. [7], [8], [12], [22] Nursing facilities and rehabilitation centers are not well-developed in our country. Therefore, all patients were discharged from the hospital when they had completely recovered, resulting in a longer hospital stay.

Previous studies evaluated that the postoperative complication rates of LAG ranged between 6.4% and 25.4%. [7], [8], [9], [16], [28] This difference depended on the tumor characteristics, the extent of lymphadenectomy, and the surgeons experience with laparoscopic surgery. [28] In the present study, 12 patients (16.7%) developed postoperative complications. The CLASS-01 trial, KLASS-02 trial, and JCOG9501 trial reported a

complication rate of 15.2%, 16.6%, and 20.9%, respectively. [7], [8], [9] In the KLASS-02 trial, the common postoperative complications were wound problems (4.5%), pulmonary infection (2.7%), fluid collection (2.5%), and ileus (2.1%). [8] Two common postoperative complications in the CLASS-01 trial were pulmonary infection and anastomotic leakage, respectively 5.6% and 1.9%. [9] Anastomotic leakage, considered a major complication of LAG, was within the range of 0.2% to 4.0% reported previously. [7], [8], [9], [12] The mortality rate was from 0.0 to 0.4%, which reflected the safety of LAG. [7], [8], [9] In the present study, 3 patients (4.2%) were found to have anastomotic leakage. Among them, two patients with minor anastomotic leakage were managed by conservative treatment, and one required surgical intervention. The postoperative intra-abdominal abscess was detected in two (2.8%) patients who recovered after medical treatment. One patient (1.4%) developed intestinal obstruction from a trocar site incisional hernia. This case required reoperation, and recovered without further complications. The results of our study reflected the safety of the performed LAG with D2 dissection.

There were several limitations in our research. First, this was a single-center clinical trial which was limited by the small sample size. Second, we have not conducted a randomized controlled trial to compare laparoscopic and open gastrectomy. Finally, we did not evaluate a sufficient follow-up period to analyze long-term outcomes. However, the results have also contributed to evaluating the surgical safety of LAG with D2 LN dissection for gastric cancer.

## Conclusion

This study demonstrates the safety and feasibility of LAG with D2 LN dissection with favorable short-term oncological outcomes in Vietnam. However, only experienced surgeons in specialized centers should perform this surgical method. Based on the results of this study, we continue to evaluate a long-

term follow-up of LAG with D2 LN dissection for gastric cancer.

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