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Original Article

Laparoscopy Assisted Distal Gastrectomy Versus Open Distal Gastrectomy for Patients with Gastric Cancer in A Middle Resources Country

Anwar Tawfik Amin*, Hussein Fakhry and Badawy M Ahmed

Surgical oncology department, South Egypt Cancer Institute, Assiut University, Egypt

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ABSTRACT

Background: Laparoscopic surgery with a small laparotomy has several advantages over conventional open surgery, including less invasiveness, less pain, earlier recovery, and better cosmesis. The aim of this study was to compare technical feasibility and early clinical outcomes of laparoscopy-assisted distal gastrectomy in comparison with open distal gastrectomy for gastric cancer in a developing country.

Patients and methods: In this retrospective study, patients with distal gastric cancer were divided into two groups (a) patients underwent laparoscopy assisted distal gastrectomy (LADG) (21 patients) and (b) open distal gastrectomy (ODG) (21 patients). For the postoperative pathologic results, the tumor-nodal-metastasis (TNM) stage, grade of tumor differentiation, distal and proximal margins, the number of harvested lymph nodes were evaluated. Staging was done according to the 7th edition of the UICC tumor, node, and metastasis (TNM) classification. D1/D2 lymphadenectomy with curative R0 intention was attempted in all cases. Perioperative mortality and morbidity were assessed.

Results: The time to initiate oral intake, and postoperative hospital stay were significantly shorter in the LADG group than in the ODG group ($P < 0.001$). The operative time in the LADG group was significantly less than that of the ODG group ($P = 0.05$). Blood loss and blood transfusion frequency were significantly lower ($P < 0.0001$) in the LADG group in comparison to ODG group.

Conclusion: Laparoscopic-assisted distal gastrectomy for distal gastric cancer could be safe and feasible technique alternative to open gastrectomy in a middle income country, with at least similar short term surgical and oncological results. However, laparoscopic gastric surgery is in need to adequate training and technical support especially in D2 lymphadenectomy.

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Introduction

Laparoscopic gastrectomy for gastric cancer was reported for the first time by Kitano et al. in 1994, and since then the use of laparoscopy for gastrectomy in early gastric cancer (EGC) has increasing popularity for surgical treatment of EGC particularly in Japan, Korea and China [1]. In comparison to open gastrectomy, minimally invasive laparoscopic gastrectomy has many advantages that include early recovery, minimal blood loss, reduced postoperative complications and a shortened hospital stay [2-4]. It also maintains the short and long oncologic outcome as conventional open surgery [4, 5]. In the last two decades, highly advanced laparoscopic surgical instruments such as vascular sealing

devices have been developed lead to the advancement of laparoscopic surgical techniques. Therefore, extended lymph node dissection (D2) and total gastrectomy can now be performed laparoscopically [5, 6].

Laparoscopic gastrectomy indications have been extended by some institutions to highly selected patients with locally advanced gastric cancer (AGC). Recently many centers in Japan, Korea and China were interested in conducting several randomized controlled trials evaluating the feasibility and safety of laparoscopy assisted distal gastrectomy (LADG) for gastric cancer [7-9]. Despite the evidences from retrospective as well as prospective randomized trials reporting the

*Correspondence to: Anwar Tawfik Amin, Department of Surgical Oncology, South Egypt Cancer Institute, Assiut University, Egypt; Tel: +20-88242-1204; Fax: +20-88-234-86; E-mail: anwar71@oita-u.ac.jp

benefits of laparoscopic distal gastrectomy for cancer; except for Japan and Korea, low adoption rate of laparoscopic gastrectomy has been reported. Furthermore, because of the shortage of expertise and equipment high cost, the integration of advanced laparoscopic techniques in low and middle income countries is challenging [10]. To the best of our knowledge, there is no reported studies comparing the safety, feasibility and short-term outcomes of laparoscopy assisted distal gastrectomy (LADG) to those of open distal gastrectomy (ODG) in developing countries. Furthermore, randomized controlled clinical trials evaluating these two modalities have not yet been reported there. Therefore, this study has been conducted comparing the short-term outcomes achieved by LADG and ODG to investigate the efficacy of the laparoscopic approach for patients with gastric cancer in a developing country. The results may provide evidences supporting LADG procedure so that randomized controlled clinical trials as a further step could be conducted in our circumstances.

Patients and Methods

Patients who were diagnosed with primary distal gastric cancer and performed radical distal gastrectomy from January 2012 to October 2018 were assigned using a prospectively maintained gastric cancer database at South Egypt Cancer Institute, Assiut University, Egypt. The inclusion criteria were settled as follows: histopathologically proven gastric carcinoma with no distant metastasis, tumors located in the antrum or pyloric region of the stomach, distal gastrectomy and an R0 resection with curative intent. Patients with the following criteria have been excluded: T4b staging or distant metastasis, neoadjuvant treatment with chemotherapy or radiotherapy, lacking pathological proof and palliative or emergency gastrectomy. Finally, 30 patients were treated with LADG, and 96 patients were treated with ODG. Study parameters included surgical technique, demographic details, blood loss, operative time, body mass index (BMI), length of hospital stay (LOS), post-operative morbidity and mortality, readmission rate and histopathological data.

Numbering of the perigastric lymph nodes was defined according to the 3rd English edition of the Japanese classification of gastric carcinoma [11]. Perigastric lymphadenectomy was performed according to the Japanese gastric cancer treatment guidelines [12, 13]. At least D1 +alpha lymphadenectomy with curative R0 intention has been performed in all cases. The 7th edition of the pathological (pTNM) classification of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) was the base of tumor staging. The Charlson comorbidity index was the guide to comorbidities staging [14]. Postoperative complications severity was defined according to the Clavien-Dindo classification system [15]. Patients obtained detailed explanation of each surgical method as well as the advantages and disadvantages of LADG versus conventional ODG and they informed of the possible complications. Prior to the surgery, informed consent was obtained. Adjuvant chemotherapy using 5-fluorouracil (5-FU)-based regimens was given to most of the patients with advanced gastric cancer.

I Surgical technique

Laparoscopy-assisted gastrectomy was done according to our previously published standard technique with some modifications as follows [16].

After putting the patients in lithotomy position under general anesthesia, the surgeon stood on the patient's left side and the first assistant and camera assistant on the patient's right side. Using an open technique, a 10 mm trocar for a 0 degree rigid laparoscope was inserted trans-umbilically. After the establishment of pneumoperitoneum at 12 mm Hg, 2 other surgical ports were introduced and another 4th port was used if necessary. First, laparoscopic staging followed by division of the greater omentum at the mid portion of the transverse colon about 4-5 cm from the gastroepiploic arcade toward the lower pole of the spleen using Ligasure (Lymph nodes 4s-N4s) was performed. Then, the omentum and the lymph nodes along the right gastroepiploic vessels (N4d) were dissected. The infra-pyloric nodes (N6) as well as the nodes of the superior mesenteric vessels (N14v, if visible) were dissected. Then supra-pyloric nodes (N5) were dissected. After that, the nodes along the left gastric artery (N7) and the nodes around the celiac artery (N 9) as well as the proximal splenic artery nodes (N 11p) were dissected. Finally, the nodes along the common hepatic artery (N 8a), the right cardiac nodes (N1) and the nodes along the lesser curvature (N3) were dissected either laparoscopically or outside after stomach extraction. A 5-cm midline supra-umbilical incision or an extension of the umbilical incision was done. Billroth I gastroduodenostomy, Billroth II gastrojejunostomy or Roux en Y anastomosis were performed extra-corporeally by a hand-sewing or stapler techniques.

II Statistical analysis

Using SPSS v16.0 for Windows (SPSS Inc., Chicago, IL), statistical analysis was performed. Categorical variables were analyzed using the Chi-squared or Fisher's exact test, whereas unpaired Student's t-test or the Mann-Whitney U tests were used for analyzing continuous variables. The propensity score for each patient was calculated using multiple factor logistic regression models and we imposed a caliper width of 0.02 of the standard deviation of the logistic of the propensity score. LADG patients were individually matched to patients in the ODG group using the nearest neighbor matching principle and the non-replacement principle (i.e., a single patient cannot be used several times). To identify risk factors and independent risk factors for postoperative morbidity, univariate and multivariate analyses were performed using binary logistic multiple regression tests. P values less than 0.05 were considered significant.

Results

I Characteristics of the patients

The clinical and pathological characteristics of the LADG and ODG groups are presented in (Table 1). Calculating the propensity scores were done using a logistic regression model to balance the following covariates: gender, age, body mass index (BMI), tumor location, tumor size, comorbidities, reconstruction method, histologic type, pT stage and pN stage. Then, 42 patients (21 patients who performed LADG and 21 patients who performed ODG) were selected for analysis. The selected patients after propensity score matching did not show significant difference for the balanced covariates between the two study groups.

II Surgical outcomes

The LADG group showed a significantly shorter mean operation time (149 ± 14.5 vs 165.8 ± 63.0 min, $P < 0.01$), less mean intraoperative blood

loss (90 ml vs. 209 ml, $P < 0.001$), a shorter mean time to first flatus (1.7 vs. 2.8 days, $P < 0.001$) and a higher number of retrieved lymph nodes (26.6 vs. 19.7, $P = 0.017$) than the ODG group (Table 2).

Table 1: Clinicopathological characteristics

Variables	LADG	OG	P value
Age:			
- Range	36 - 72	27 - 85	
- Mean	55.6 yrs.	57 yrs.	NS
Sex :			
- Male	14(66.7%)	14(66.7%)	
- Female	7(33.3%)	7(33.3%)	
BMI			
- Range	23 - 34	21.2 - 27.8	
- Mean	26.3	24.5	NS
Reconstruction:			
Bilroth-I	9(43.0%)	9(43.0%)	
Bilroth-II	12(57.0%)	12(57.0%)	
Tumor site:			NS
- Pylorus	13(62.0%)	13(62.0%)	
- Antrum	8(38.0%)	8(38.0%)	
Surgical margin:	All are free	All are free	
Grading:			NS
- Will diff	4(19.0%)	4(19.0 %)	
- Mod. Diff	9(43.0%)	9(43.0%)	
- Poorly diff	8(38.0%)	8(38.0%)	
Staging			NS
- Stage 1	2(9.5%)	2(9.5%)	
- Stage 2	16(76.2%)	16(76.2%)	
- Stage 3	3(14.3%)	3(14.3%)	

NS=Not Significant

Table 2: Surgical outcome and post-operative complications

variables	LADG	OG	P. value
Operative time (min.)	149±14.5	165.8±63	0.01
Blood loss (ml)	90±15.6	209±62	0.001
1 st oral feeding (Days)	3.8±1	6±2.1	0.05 0.05* _v
Hospital stay	9±2.7	14±5.3	0.0001
Harvested lymph nodes	26.8±6.3	19.9±3.9	0.03
Overall complications	28%	43%	0.03
Delayed gastric emptying	2(9.6%)	2 (9.6%)	
Pneumonia	3(14.3%)	3 (14.3%)	
Anastomotic leakage	1(4.8%)	2 (9.6%)	0.05
Wound dehiscence	0(0.0%)	2 (9.6%)	0.05

Table 3: Risk factors of postoperative morbidity

variables	Postoperative No(n= 27)	morbidity Yes(n=15)	Univariate analysis P	Multivariate analysis OR CI P
Age				
≤56	8	3	0.05	1.012 0.1
≥56	19	12		
Gender			0.14	
Male	15 (55%)	10 (67%)		
Female	12 (45%)	5 (33%)		
BMI (KG/M)	26±4	27±3	0.2	
Tumor location			0.32	
Antrum	17	9		
Pyloric	10	6		
Operative approach			0.01	0.6 0.02
LADG	15	6		0.05*
ODG	12	9		
Tumor size			0.5	
pT stage				
T1	6	2		
T2	9	7		
T3	12	6		
pN stage			0.6	
N0	8	5		
N1	13	7		
N2	6	3		
pTNM stage			0.3	
I	4	2		
II	9	5		
III	14	8		
Associated comorbidities			0.04	1.3 0.09
0				
1-2	12	5		
≥3	12	7		
	3	3		
Age Associated comorbidities			0.01	1.3 0.03
NO	19	3		
≤56	3	3		
≥56	5	8		
Operative time (min)	192±20	204±15		0.14
Estimated blood loss (EBL)	93±15.6	160±20		0.08

III Postoperative complication rate after LADG and ODG

The rate of postoperative complications at the LADG group and ODG group were 28.0% and 43% ($P = 0.03$), respectively. No one of the patients in the LADG group died, whereas one case was died in the ODG group (Table 2).

IV Postoperative morbidity associated risk factors

At univariate analysis, old age ($P = 0.05$), surgical approach ($P = 0.01$), comorbidities ($P = 0.04$) and age associated comorbidity ($P = 0.01$) were

closely related to postoperative complications. After multivariate analysis, the surgical approach ($P = 0.02$) and age associated comorbidities ($P = 0.03$) were independent risk factors for postoperative morbidity (Table 3).

Discussion

In Japan, Korea and some other developed countries, laparoscopic gastrectomy became an acceptable alternative approach to open gastrectomy for patients with EGC. This is not only because of the established better early postoperative outcomes after laparoscopic distal

gastrectomy than those undergoing open gastrectomy, but also because of the similar survival and recurrence rate between the two procedures [4, 17-20]. Recently, several experienced institutions mainly from Japan, Korea and China have reported promising long-term oncological results as well as the improved technical feasibility and safety of LADG for the treatment of advanced gastric cancer in comparison with conventional open gastrectomy [21-23]. However, no reported studies examining LADG versus ODG in low to middle income countries and for the best of our knowledge this is the first research to do that. This study was conducted in our institute to evaluate the feasibility, safety and clinical efficacy of LADG in comparison to ODG in countries with low to middle resources before conducting randomized controlled clinical trials that evaluate the efficacy of LADG as a surgical approach for distal gastric cancer. To reduce bias of this retrospective study, the propensity score-matching method was used. Most of the previous studies of LADG versus ODG showed the main advantages of laparoscopic gastrectomy over conventional open surgery were less blood loss, less postoperative pain, a minimal skin incision, a shorter time to ambulation, a shorter time to oral feeding and a shorter postoperative hospital stay [7, 24]. One of obvious characteristics of laparoscopic approach is the ability to visualize finer structures due to laparoscopic amplification which results in fine dissection and more LNs yielding as shown in our results. Laparoscopic gastrectomy however, is also associated with disadvantages such as high cost, the need for surgeons skilled in laparoscopic techniques that mandates longer learning curve. These disadvantages are potential obstacles in developing countries [25]. Our study provides an evidence of the minimally invasiveness of laparoscopy assisted distal gastrectomy. Particularly, the LADG group in this study showed a significantly less estimated blood loss and a shorter time to flatus and oral feeding as well as short hospital stay compared to the ODG group. These results are similar to that reported from well experienced centers [17-25]. This may suggest that the advantages of LADG over ODG could be maintained even in developing countries provide that the basic laparoscopic facilities and skilled surgeons are present. In this study, the operative time of LADG is shorter than that of ODG. Some reported studies showed that the operation time was longer for laparoscopic gastrectomy than open gastrectomy [19-21, 24]. However, improvements in laparoscopic instruments, laparoscopic techniques, and the accumulation of experiences have reduced the operative time for laparoscopic gastrectomy [26]. Recently Hu WG et al. reported that the accumulation of laparoscopic experiences reduced the operation time of LADG [27]. The learning curve for LADG may need about 40 cases to reach the shortest operative time. Therefore, laparoscopic gastrectomy may not require longer time than conventional open gastrectomy when performed by an expert surgeon [28]. Our results showed that LADG group yielded more lymph nodes than ODG group. The average number of harvested lymph nodes was more than 19 in both groups. Provide that the surgeon is skilled in laparoscopy; laparoscopic surgery can aid the surgeon to dissect lymph nodes under critical anatomical structures as the laparoscope can amplify the fascia, vasculature, nerves and other structures [5]. Perioperative morbidity and mortality are essential parameters to evaluate the technical safety and feasibility. The rate of postoperative complications of LADG has been reported to vary from 2% to 32% [4, 6-8, 23]. In this study, the postoperative complication rates of the LADG group and ODG group were 28% and 43.0% respectively ($P = 0.03$).

At multivariate analysis of morbidity associate risk factors, operative approach and age associated comorbidities were found to be independent factors related to postoperative complications. Therefore, comorbidities specially when associated with old age may increase the postoperative complications rate which has been reported in previous studies [28, 29]. These results suggested that the safety and feasibility of LADG and ODG could be comparable

Our study however has some limitations that include relatively small sample size, only perioperative outcome has been evaluated due to difficulty in long term follow up and the retrospective nature of the study. Therefore, a prospective, randomized, controlled trial with clear indications in low source conditions is mandatory to overcome those limitations.

Conclusion

We cautiously suggest that LADG may be a feasible alternative to ODG when performed by experienced surgeons at high-volume institutions in low to middle income countries provided that adequate training and technical support are available. Conducting of a prospective, controlled, randomized trial with precised indications in low to middle resources conditions is mandatory to overcome the limitations of this study.

Disclosure

The Authors have no conflicts of interest or financial ties to disclose.

Author Contribution

Anwar Tawfik Amin contributed to the conception and design of the work. He made the data analysis and interpretation. Finally, he revised and drafted the manuscript. Hussein Fakhry contributed to the design and interpretation of the data for the work and in revising the manuscript. Badawy M Ahmed contributed to the analysis and acquisition of data and revising the manuscript. All the authors have approved this final version of the manuscript.

Conflicts of interest

None declared.

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