

Total laparoscopic resection for advanced gastric cancer is safe and feasible in the Western population

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Abstract

Background There is debate surrounding the use of laparoscopic resection for advanced gastric cancer in the Western population. Here we aim to assess the feasibility and short-term outcomes of laparoscopic gastrectomy in consecutive patients in a Western population.

Methods From 2012 to 2014, retrospective review of 28 patients with clinically staged advanced gastric cancer ($\geq T3$ or $\geq N1$) treated with laparoscopic resection.

Results Sixty-one percentage of patients were male. Median age was 67 years (range 35–86). Median BMI was 26.5 (range 19.4–46.1). Resection types were proximal ($n = 2$), distal ($n = 14$), and total ($n = 12$). Twenty-six (93 %) patients underwent D2 lymphadenectomy. Four patients underwent conversion to open. Median blood loss was 125 mL (range 30–300). Median LOS was 7 days (range 4–16). Of postoperative complications, five were minor: arrhythmia ($n = 1$), surgical site infection ($n = 3$), in-hospital fall ($n = 1$); and four were major (intra-abdominal abscess, stricture, PE, and anastomotic bleed). T stages were Tx ($n = 1$), T2 ($n = 3$), T3 ($n = 18$), and T4 ($n = 6$). N stages were N0 ($n = 4$), N1 ($n = 8$), N2 ($n = 1$), and N3 ($n = 15$). Median tumor size was 5.8 cm (range 0–9.5). Median lymph node yield was 22 (range 6–53). All margins were negative. Median follow-up was

12.8 months (range 2–27). Six patients have died of progressive disease.

Conclusion Following total laparoscopic resection for advanced gastric cancer, oncologic endpoints, postoperative course, and early cancer-specific follow-up are excellent. The results demonstrated here support the routine use of these techniques in the Western patient population.

Keywords Advanced gastric cancer · Total laparoscopic resection · Laparoscopic gastrectomy

There are approximately 22,220 new cases of gastric cancer diagnosed per year with an estimated 5-year survival of 28.3 % [1]. Patients commonly present with advanced disease as identified by CT scanning or endoscopic ultrasound (EUS). Advanced gastric cancer (AGC) patients ($\geq T2$ or $\geq N1$) are frequently recommended for neoadjuvant chemotherapy or adjuvant chemoradiotherapy due to improvement in survival outcomes [2–4].

While there has been previous debate as to the survival benefit of a D2 lymphadenectomy in these patients, currently many experienced centers perform a spleen and pancreas preserving D2 lymphadenectomy due to a trend toward improved survival [5–8]. There has been hesitancy to accept minimally invasive techniques for the definitive management of gastric cancer given concern for the adequacy of oncologic resection including lymphadenectomy using laparoscopic approaches. Laparoscopy is widely accepted for gastric cancer staging and demonstrates metastatic disease in approximately one-third of patients with a sensitivity of 84 % [9]. With the increased incidence of gastric malignancy in Asian countries, there is more experience with both open and minimally invasive surgical approaches in this region. There are numerous reports

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supporting the use of laparoscopy or laparoscopic-assisted procedures in the management of early gastric cancer [10–17]. Initial studies into the use of a laparoscopic approach for AGC suggested a “laparoscopic-assisted” approach with conversion to an open procedure after initial exploration, mobilization, and lymphadenectomy for resection and subsequent reconstruction [12, 16–22]. There have been several combined trials with both early and AGC comparing laparoscopic to open approaches and some reports on the use of laparoscopic approaches for AGC [23–33]. The majority of these studies are from the Eastern world with a few more recently from Italy and the USA [23, 24, 27–30, 32, 33]. Nevertheless, there remains a paucity of data from North America, and the oncologic feasibility and safety of laparoscopic gastrectomy with D2 lymphadenectomy for AGC in this patient population is unknown. Here we present one of the largest experiences with total laparoscopic proximal, distal, and total gastrectomy for AGC in consecutive patients from a North American population with the aim to assess feasibility and short-term outcomes over the 2-year time period.

Materials and methods

Patients

Institutional review board approval was obtained prior to study initiation. Retrospective review was completed on 28 patients with clinically staged AGC ($\geq T3$ or $\geq N1$) who underwent a total laparoscopic resection from 2012 to 2014. During this time frame, all consecutive patients with gastric cancer involving the gastric cardia, body, or antrum, regardless of the clinical stage, were offered a minimally invasive resection with the exception of one patient who had a previous margin positive distal gastrectomy for presumed ulcer disease at a referring hospital 4 months prior to repeat resection for AGC. Those patients clinically staged as $\leq T2$, N0 disease were excluded from analysis. Procedures were performed at Roswell Park Cancer Institute (Buffalo, NY) and University of Florida (Gainesville, FL) by two independent, experienced laparoscopic surgeons. Ethnicity was collected and assigned by the clinical team at the time of intake history and physical examination.

Preoperative evaluation and management

The standard recommendations for the evaluation, staging, and management of gastric cancer were utilized including EUS and CT scans [34]. Diagnostic laparoscopy and peritoneal washings were used for the evaluation of locoregionally advanced disease in patients being considered

for neoadjuvant therapy as a separate procedure. All patients were discussed at a multidisciplinary tumor conference and considered for neoadjuvant or adjuvant therapy. Patients received therapy according to two different treatment strategies determined by patient and physician preferences. Patients were offered either neoadjuvant chemotherapy followed by surgery with the possibility of additional adjuvant chemotherapy or surgery followed by adjuvant chemoradiotherapy [3, 4]. During the later time frame of this report, more patients were directed toward neoadjuvant and adjuvant chemotherapy to avoid the use of postoperative radiotherapy.

Surgery

Participating surgeons had fellowship training in minimally invasive surgery or surgical oncology; both routinely perform more than 150 advanced, laparoscopic operations per year. All operations began with the intent for a completely laparoscopic approach with intracorporeal anastomosis. Laparoscopic proximal, distal, and total gastrectomies were included. Proximal gastrectomy was not frequently offered secondary to less optimal outcomes; however, in older patients with proximal lesions who were felt less likely to tolerate total gastrectomy, a proximal gastrectomy was felt to be a better alternative. When appropriate, laparoscopic distal gastrectomy with D2 lymphadenectomy was completed as previously described [35]. For total gastrectomy, the technique for creation of the anastomosis was completed with either the use of an Orvil stapling device or a laparoscopic side-to-side stapling technique. D2 lymphadenectomy involved resection of nodal tissue based on tumor location according to the Japanese Gastric Cancer Association [36]. Conversion to an open procedure was performed when necessary to complete a R0 oncologic resection.

Results

Patient characteristics

Median patient age was 67 years (range 35–86). Sixty-one percent of patients were male. Median BMI was 26.5 (range 19.4–46.1). The majority of patients, 71 %, were Caucasian. Sixty-one percent of patients had previous abdominal surgery. Forty-three percent of patients had a smoking history, and 39 % of patients had a history of clinically significant alcohol use. Ninety-six percent of patients had at least one medical comorbidity; 61 % of patients had three or more medical comorbidities. Fourteen percent of patients received neoadjuvant therapy only, 39 % of patients received adjuvant therapy only, 29 % of

patients received both neoadjuvant and adjuvant therapy, and 18 % of patients received neither neoadjuvant or adjuvant therapy (Table 1). In five patients, reasons for not receiving either neoadjuvant or adjuvant therapy included advanced age (≥ 80 years) and/or comorbidities.

Details of surgery

Seven percent of patients underwent a proximal gastrectomy, 50 % of patients underwent a distal gastrectomy, and 43 % of patients underwent a total gastrectomy. Ninety-three percent of patients underwent a D2 lymphadenectomy. Two patients did not undergo a D2 lymphadenectomy due to advanced age and/or comorbidities. Twenty-four of 28 patients underwent successful laparoscopic resection with laparoscopic intracorporeal anastomosis.

Table 1 Patient demographic information

Patient demographics	
Age, median (range)	67 (35–86)
Sex	
Male	17 (61 %)
Female	11 (39 %)
Race	
Caucasian	20 (71.4 %)
African American	5 (17.9 %)
Hispanic	2 (7.1 %)
American Indian	1 (3.6 %)
BMI, median (range)	26.5 (19.4–46.1)
Previous abdominal surgery	
Yes	17 (61 %)
No	11 (39 %)
Smoking history	
Yes	12 (43 %)
No	16 (57 %)
Alcohol use history	
Yes	11 (39 %)
No	17 (61 %)
Medical comorbidities	
0	1 (3.6 %)
>1	27 (96.4 %)
>3	17 (61 %)
Type of therapy	
Neoadjuvant only	4 (14 %)
Adjuvant only	11 (39 %)
Both	8 (29 %)
Neither	5 (18 %)

Unless otherwise noted, information is presented as number of patients and percentages

Four operations were converted to an open procedure. Reasons for conversion were: tumor adherent to pancreas, inability to identify an appropriate point for margin negative transection of the stomach, to obtain additional esophageal margin after intraoperative proximal margin was positive during minimally invasive approach, and to assist with anvil placement into the esophagus during total gastrectomy. Median operative time was 328.5 min (range 232–481). Median estimated blood loss was 125 mL (range 30–300) (Table 2).

Pathology

All patients had adenocarcinoma. The types of adenocarcinoma were: mucinous adenocarcinoma with a signet ring cell component (1), well differentiated (1), moderately differentiated (8), poorly differentiated without signet ring cell features (2), and poorly differentiated with signet ring cell features (15). One patient had no residual tumor following neoadjuvant therapy. Median tumor size was 5.8 cm (range 0.0–9.5). T stages were Tx($n = 1$), T1(0), T2(3), T3(18), and T4a(6). N stages were N0($n = 4$), N1(8), N2(1), and N3(15). Two patients were found to have metastatic disease on final pathology; one patient had periaortic lymph node involvement, and the other had a positive peritoneal biopsy recognized on final pathology only. Final pathologic stages were x(1), IB(1), IIA(3), IIIA(9), IIIB(9), IIIC(3), and IV(2). All patients had negative proximal and distal margins. Median number of lymph nodes harvested was 22 (range 6–53); median number of positive nodes was 9 (range 0–39, Table 3).

Table 2 Patient surgical details

Surgery	
Type of surgery	
Proximal	2 (7 %)
Distal	14 (50 %)
Total	12 (43 %)
D2 LAD	
Yes	26 (93 %)
No	2 (7 %)
Conversion to open	
Yes	4 (14 %)
No	24 (86 %)
Operative time ^a (min), median (range)	328.5 (232–481)
EBL (mL), median (range)	125 (30–300)

Unless otherwise noted, information is presented as number of patients and percentages

^a Operative time available for 14 patients

Table 3 Patient pathologic characteristics

Pathologic characteristics	
Type of cancer	
Well-differentiated adenocarcinoma	1 (3.6 %)
Moderately differentiated adenocarcinoma	8 (28.6 %)
Mucinous adenocarcinoma with signet ring cell features	1 (3.6 %)
Poorly differentiated adenocarcinoma without signet ring cell features	2 (7 %)
Poorly differentiated adenocarcinoma with signet ring cell features	15 (53.6 %)
No residual tumor	1 (3.6 %)
Tumor size (cm), median (range)	5.8 (0.0–9.5)
T classification	
Tx	1 (3.6 %)
T1	0 (0 %)
T2	3 (10.7 %)
T3	18 (64.3 %)
T4	6 (21.4 %)
N classification	
0	4 (14.3 %)
1	8 (28.6 %)
2	1 (3.6 %)
3	15 (53.6 %)
Total lymph nodes harvested, median (range)	22 (6–53)
Number of positive lymph nodes, median (range)	9 (0–39)
M classification	
0	26 (93 %)
1	2 (7 %)
Final pathologic stage	
x	1 (3.6 %)
IB	1 (3.6 %)
IIA	3 (10.7 %)
IIIA	9 (32.1 %)
IIIB	9 (32.1 %)
IIIC	3 (10.7 %)
IV	2 (7 %)
Margin status	
Negative	28 (100 %)
Positive	0

Unless otherwise noted, information is presented as number of patients and percentages

Postoperative outcomes

There were no immediate intraoperative complications, and no patients required reoperation. Median total hospital length of stay was 7 days (range 4–16). One patient required readmission within 30 days of discharge. There were nine complications in eight patients. There were five minor complications: arrhythmia (1), surgical site infection (3), and in-hospital fall (1). There were four major complications: intra-abdominal abscess (1), pulmonary embolism (1), anastomotic stricture requiring dilation \times 3 (1), and bleeding from anastomosis following initiation of anticoagulation requiring cessation of anticoagulation and

placement of an inferior vena cava filter (1). Clavien-Dindo classifications were I (3), II (2), and III (4). Median follow-up was 12.8 months (range 2–27). Six patients have died of progressive disease, one is alive with disease, and the remainder of patients is currently without evidence of disease (Table 4).

Discussion

Laparoscopy for staging and resection of early gastric cancer is widely accepted. Previous studies have demonstrated reduced blood loss, shorter hospital stay, and earlier

Table 4 Patient outcomes

Postoperative outcomes	
Total hospital LOS, median (range)	7 (4–16)
Reoperation	0 (0 %)
Readmission within 30 days	1 (3.6 %)
Complications	
Total	9 (32.1 %)
Arrhythmia	1 (3.6 %)
Surgical site infection	3 (10.7 %)
In-hospital fall	1 (3.6 %)
Intra-abdominal abscess	1 (3.6 %)
Pulmonary embolism	1 (3.6 %)
Anastomotic stricture	1 (3.6 %)
Anastomotic bleeding	1 (3.6 %)
Follow-up (months), median (range)	12.8 (2–27)
Outcome	
DOD	6 (21.4 %)
AWD	1 (3.6 %)
NED	21 (75 %)

Unless otherwise noted, information is presented as number of patients and percentages

LOS length of stay, DOD died of disease, AWD alive with disease, NED no evidence of disease

return to oral intake with laparoscopic compared to open gastrectomy [15, 18, 19, 21, 23]. Kim et al. [37] reported improved quality of life outcomes following laparoscopic compared to open gastrectomy for early gastric cancer with regard to patients' physical, emotional, and social function. Specifically, patients reported improvement in pain scores, and body image. Still the majority of the available literature supports a "combined" or "laparoscopic-assisted" approach to gastrectomy for advanced gastric cancer. This is a popular approach in Asia, where the gastric cancer incidence is much higher and experience with minimally invasive approaches is far greater for this disease [12, 18–21].

This combined procedure involves the completion of the lymphadenectomy laparoscopically through a 5-port technique. The procedure is converted to an open approach near completion of the lymphadenectomy for the remaining gastrectomy and anastomosis [18, 19, 21]. This approach has been shown to result in significantly longer operative times when compared to an open approach; but similar to previous reports in early gastric cancer, a laparoscopic-assisted approach also resulted in lower blood loss, analgesic use, and shortened recovery time [18, 19, 21]. The popularity of the combined approach results from the concern over the technical difficulty of an adequate lymphadenectomy when completed through a completely

laparoscopic technique [12]. Huscher et al. reported on a totally laparoscopic approach to the management of early and advanced gastric cancer. In their series of 100 patients, they reported acceptable outcomes in regards to oncologic resection, morbidity, and mortality.

There have been only a few studies from North America focusing on laparoscopic resection for gastric cancer [27, 29, 30, 32, 33]. In 2003 and 2006, Weber et al. [33] and Varela et al. [32], respectively, reported on their combined series of patients undergoing laparoscopic resection for gastric cancer. In total, nine patients presented with advanced disease (\geq Stage II) were treated with laparoscopic resection with acceptable outcomes. In 2009, Strong et al. [29] reported on their institutional series of subtotal gastrectomies for gastric cancer. Of the 30 patients treated with laparoscopic resection, 12 had AGC (\geq Stage II). Similar to other studies, laparoscopic resection was associated with longer operative time, decreased analgesic use, and shorter length of stay. Kachikwu et al. [27] also reported on their pilot series of 16 patients undergoing laparoscopic total gastrectomy, nine of whom had AGC (\geq Stage II). There were no conversions in their series with two patients requiring en bloc additional visceral resections. Both studies concluded that the minimally invasive approach was safe and adequate for gastric cancer patients.

Most recently, Kelly et al. [30] published their retrospective series of patients undergoing laparoscopic gastrectomy compared with patients treated with an open resection over the same time period. In this series, 87 patients underwent laparoscopic gastric cancer resection, with a minority ($n = 32$) of those patients treated for advanced gastric cancer (\geq Stage II). Overall, laparoscopic resection was associated with longer operative time, decreased blood loss, decreased analgesic use, shorter length of stay, and fewer minor complications. There was one 30-day mortality in the laparoscopic group and none in the open group. Of note, eight of the patients treated with laparoscopic resection had microscopically positive margins. The present report compares favorably to this series as there was a similar number of patients undergoing laparoscopic resection for AGC with a zero percent incidence of microscopically positive margins. Perhaps the zero margin positivity rate is related to appropriate conversion to an open procedure when concerned for adequate oncologic resection, evidenced by the 14 % conversion rate reported in this study.

Complete laparoscopic gastrectomy for AGC including proximal, distal, and total gastrectomies is feasible in the majority of patients and safe. Here we present a 28-patient series with eight patients experiencing a morbidity (28.6 %), four of which were minor. There were no patients experiencing a postoperative mortality. The

median length of stay in our patient population was 7 days (range 4–16). This compares favorably to previous reports from larger database analyses (NSQIP), which included primarily open approaches, where the median length of stay was 12 days [38]. Reflecting the predominant patient population in North America, BMI was elevated in our patient population which was predominantly Caucasian. Nevertheless, we feel the immediate and short-term oncologic outcomes of these techniques are comparable to open approaches with low morbidity rates. We believe laparoscopic approaches should be routinely considered and offered in North America and the Western population.

Compliance with ethical standards

Disclosures Drs. Rebecca Tuttle and Moshim Kukar have nothing to disclose. Drs. Steven Hochwald and Kfir Ben-David are consultants for Ethicon EndoSurgery.

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