

Research Article

Open Access, Volume 2

Evaluation of the efficacy of distal gastrectomy for the treatment of gastric cancer

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Received: Jan 27, 2022

Accepted: Mar 08, 2022

Published: Mar 11, 2022

Archived: www.jjgastro.com

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Abstract

Introduction: This work aims to evaluate the efficacy of distal gastrectomy and outcome of patients who underwent a distal gastrectomy for distal gastric adenocarcinoma.

Materials and methods: Case series with retrospective data collection of patients treated for distal gastric cancer from January 2013 to December 2017. The risk factors, histopathology, outcomes and long term follow up results were analyzed.

Results: Eighty six 86 patients were treated for gastric cancer, but only 44 had distal cancer and 30 were included in the study. The average age was 64 years, the sex ratio 1.5. Twenty eight patients underwent a distal gastrectomy and 2 patients underwent total gastrectomy. The median number of lymph nodes resected was 6 following distal gastrectomy versus 26 after total gastrectomy. Resection margins were clean except for three patients who underwent a distal gastrectomy. Postoperative complications occurred in 05 patients. They were mainly infectious, anastomotic leakage. Two (2) cases of postoperative mortality (<30 days) was noted. Metastasis was found in 3 patients with subtotal gastrectomy, two of whom had insufficient lymph node dissection.

Conclusion: The choice of the extent of surgery depends on several factors namely the location of the tumor, its size and its histological type. The total gastrectomy is often associated with a high morbidity thus the distal gastrectomy can be preferred for patients with morbidity or borderline for total gastric resection.

Keywords: gastric adenocarcinoma; laparoscopic gastrectomy; esophageal entero anastomosis.

Introduction

Gastric cancer is the fourth leading cause of cancer related death worldwide and its rate of median survival is less than 12 months for the advanced stage [1]. The curative treatment is based on surgical resection associated with complete lymph node dissection with/or without chemoradiotherapy. The technique of choice for surgery of distal adenocarcinoma of the stomach remains a controversial topic, due to the problem of oncologic safety and postoperative complications [2]. The aim of this study is to evaluate the efficacy of the subtotal gastrectomy for distal adenocarcinoma of the stomach in terms of oncology surgery, postoperative morbidity and mortality and patients overall survival. This manuscript is presented in line with process checklist 2020 Criteria [3].

Materials and methods

This is a retrospective study of patients operated for distal adenocarcinoma of the stomach by distal gastrectomy at Ibn Rochd University Hospital Center in Casablanca, in the service of digestive cancer surgery and liver transplantation from January 2013 to December 2017. Was included the patients with distal adenocarcinoma confirmed by histopathology.

Results

Thirty patients (30) were included in the study. The average was 61 year with the limits ages ranging from 41 to 78 years old and the sex ratio Male to Female at 1.5. Twenty eight (28) patients underwent distal gastrectomy and 2 patients underwent a total gastrectomy. Tobacco was the most common risk factor in our patients and was found in 39% of patients. However, no risk factor was noted in 9 patients (30% of cases). The mean time from onset of symptoms to diagnosis of gastric cancer for both groups was 6 months with extremes of 1 month and 12 months. The most frequent functional signs were epigastralgia, vomiting and Melena. The physical examination was normal in 15 patients (53%), epigastric tenderness in 11 patients (39%) and epigastric mass was found in 02 patients (7%). The esophagus fibroscopy has been performed in all patients and showed ulcerative bud tumor with a percentage of 75% and vegetative in 25%. The location was antru-pyloric in 57% and Antral in 43%. The tumor biopsies allowed us to set up histopathology diagnosis and revealed adenocarcinomas, including cell-independent adenocarcinomas for all patients. The table N°4 showed the differentiation of the cells tumors for our study. TAP CT was the imaging tool performed for tumor extension performed in all patients showing the site, the regional extension and the presence or not of distant metastases of the tumor and permitted us to classify our patients according to the classification UICC 2016, 8th edition. A celioscopic look was performed in 4 patients in the DG group, (13.3%) and was normal. The tumor markers were performed in 18 patients (64%) 4 patients had a positive ACE level, and two patients a positive CA19-9 level. The curative treatment was indicated during multidisciplinary consultation meetings at the end of this extension assessment. The cells count was performed and showed 5 patients had microcytic hypochromic anemia with a hemoglobin level <10 g/dl, requiring blood transfusion by 1 to 3GC. Neoadjuvant chemotherapy was performed in 05 patients, i.e. 16.6% of patients whose:

- A patient who received 3 courses of ECX and whose evolution was marked by tumor regression with a therapeutic response estimated at 90%.
- A patient who received 3 courses of EOX and in whom we noted a stagnation of the lesion with no therapeutic response detected subsequently.
- Two patients received ECX: one 2 doses with discontinuation of the third dose due to cardiac toxicity and other received 6 doses but still presented with a locally advanced tumor.

The therapeutic response was evaluated at 5%. The patient had received 3 doses of Folfox, without regression of tumor volume. The time between the end of neoadjuvant chemotherapy and surgery was 6 weeks, with limits of 9 weeks. An end to end gastro jejunal anastomosis according to Roux en Y was the most technique used with a percentage of 79% followed by the gastro jejunal anastomosis on an omega-mounted loop which was performed in 6 patients, in 21%. The average intervention time was longer in total gastrectomy than in distal gastrectomy (290 min versus 245 min). The median number of lymph nodes resected was 16 following distal gastrectomy versus 26 for the two patients with total gastrectomy. Resection margins were clean except for three patients who underwent a distal gastrectomy. Postoperative complications were observed in 05 patients operated with distal gastrectomy. They were infectious among patients who had a distal gastrectomy (postoperative peritonitis, anastomotic leakage, and the main complication observed in patients with total gastrectomy was anastomosis stenosis. In our study, there were 2 cases of immediate postoperative deaths (<30 days) among patients with distal gastrectomy and no immediate postoperative death occurred for the two patients with total gastrectomy. Three (3) cases of death were listed in our series, representing 10.7% of our patients. They were 2 early deaths:

- One due to septic shock at D10 postoperatively after surgical revision and other at home at D30 with unknown cause.
- 1 late death after 6 months of surgery in a patient who had presented with a colopariétal fistula in relation to peritoneal carcinosis (Table 1). The overall survival rate after 48 months was 40% for a follow up period of 48 months (4 years) (Table 2).
- Metastasis occurred in 3 patients with subtotal gastrectomy, two of whom had insufficient lymph node clearance:
 - Colonic location (1 case) after 6 months of surgery.
 - Peritoneal carcinosis (1 case) after 6 months of surgery
 - Osteolytic bone lesion (1 case) after 28 months of surgery.

During the follow-up 9 patients were lost to follow-up. The average follow-up of the patients with the DG group was 15 months with a maximum of 48 months. The two patients of TG were lost to follow-up after 12 months.

Table 1: Postoperative complications for patients of our study.

complications	DG		TG	
	Number	Date	Number	date
Urinary tract infections	1	D7	0	-
Lung infection	1	D3	0	-
Fistula	1		0	-
Death	3	-D 10 Septic shock infection -D 30 at home -6 months	0	-

Table 2: Overall survival for the patients.

OS	Minimum	Maximum	average
DG	2 months	48 months	15 months
TG	6 months	12 months	9 months

Table 3: Comparison of lymph node curage in studies according total or distal gastrectomy.

Study	TG	DG
Kim et al[2015]	38 nodes	33 nodes
Liu Z et al[2016]	27 nodes	24 nodes
Jeong et al[2012]	28 nodes	23 nodes
Our study	26 nodes	16 nodes

Discussion

Gastric cancer is the fourth after lung, breast and colorectal cancer. It is the fourth leading cause of cancer related death in women and the fifth in men [4]. Surgical resection is the standard of its curative treatment. The optimal surgery method should be based on R0 resection of the tumor and complete lymph node dissection with minimal complication and mortality, resulting in better long-term survival and quality of life improvement for the patient [5]. Many factors as patient comorbidities, tumor extension and experience of the surgeon can affect the choice of surgical decision since the more aggressive surgical strategy can affect the outcomes as regard survival, treatment related mortality and morbidity, and postoperative quality of life [6]. The indications for total and distal gastrectomy for gastric cancer have been subjects to debate for a long time and some criteria have been taken in considerations [7]. Total gastrectomy is indicated for gastric adenocarcinoma involving the entire or proximal stomach adenocarcinoma with signet ring cell due to the commonly encountered diffuse submucosal spread and difficulty in obtaining negative margins with a subtotal gastrectomy, or in patients with hereditary diffuse gastric cancer (CDH1 mutation carriers) who typically exhibit a multifocal pattern of involvement throughout the entire organ. The distal gastrectomy is indicated for tumors of the middle or antropyloric whom a 4-6 cm to proximal margin can be obtained. This offers an equivalent survival rate than total gastrectomy with less morbidity and better long-term quality of life [8]. Proximal margins of at least 3 cm is recommended for T2 or deeper tumors with an expansive growth pattern (types 1 and 2) and 5 cm for those with an infiltrative growth pattern (types 3 and 4). When these rules cannot be satisfied, it is advisable to examine the proximal resection margin by frozen section. For T1 tumors, a resection margin of 2 cm is required. When the tumor border

is unclear with difficulties of determination of limits resection, preoperative endoscopic marking by clips of the tumor border based on the biopsy results would be helpful. The tumor stage is an important criteria to consider when deciding the extent of the gastric resection especially for middle and antropyloric tumors to ensure a complete R0 resection and complete lymph node dissection. The clinical and pathology classifications (cTNM & pTNM) find here their rules [9]. For our study, 80% of patients have had a stage IIIb and 20% have had a stage IV with resectable tumors. Till now, D2 lymph node dissection is validated as the standard of lymphatic curage for gastric cancer. Node invasion has been shown to be an important prognostic factor [10].

It is well known that the stage of lymph node involvement is significantly affected by the number of nodes removed, so the stage of gastric cancer may be underestimated due to insufficient lymph node coverage. Therefore, at least 15 nodes should be removed for reliable staging according to the AJCC recommendations [11]. In several studies including Zhao and al, Z. shen and al [12], the results indicated that curage of more than 15 nodes had a better 5 year survival rate compared to insufficient curage regardless of node positivity or negativity. Li and al [13] suggested that patients who had insufficient lymph node curage and no lymph node involvement should be staged as N1 and not N0. These results indicate that TNM staging should be revised and adapted to the number of nodes removed in order to improve the survival rate in patients with insufficient lymph node coverage as well as the indication for postoperative chemotherapy which can be adjusted. Several studies comparing total and subtotal gastrectomy showed that the number of lymph nodes removed was higher in TG than GD. Indeed, in the study conducted in 2015 by Kim et al [14], the average number of nodes removed was 38 nodes for total gastrectomy versus 33 in case of distal gastrectomy, the same finding for the study by Liu Z et al [15], where the number of nodes removed was 27 vs 24 and for Jeong et al [16], 28 vs 23. The results of our study are in line with the other studies, in patients who underwent total gastrectomy, the average number of nodes removed was 26 compared with 16 nodes for distal gastrectomy. In addition, total gastrectomy allowed a lymph node curage >15 nodes in all patients, contrary to distal gastrectomy where the percentage of insufficient lymph node curage was 21.4% (Table 3). There is still no consensus regarding the best extent of gastrectomy for middle and lower-third gastric cancer [5]. For some authors, subtotal gastrectomy is the gold standard treatment for early-stage gastric cancer located in the distal third of the stomach [17]. Jin Qi find an overall survival rate for TG Vs DG of 49.6% (919/1852) vs 55.9% (721/1290) respectively and his meta-analysis revealed a favoring trend to DG procedure, with statistically difference between the two groups (HR = 0.91, 95% CI = 0.85–0.97, $p=0.006$) [18]. A retrospective study of liu et al. analyzed in 1262 distal gastric cancer patients with the range of follow-up from 0.17 to 76 months (mean, 29 months; median, 25.83 months). A 65.8% 5-year overall survival rate for the entire cohort was found. The 5-year overall survival rate of DG group was significantly higher than that of TG group (67.6% vs 44.3%, $P<0.001$, Figure 1). In his study, he emphasized on the importance of other risk factors for improving long overall survival rate for patients [15]. For our study, the overall survival was 40% after 48 months of follow up and it is in accordancy with literature.

The prognosis of gastric adenocarcinoma is very poor. The stage of the disease at the time of diagnosis is the main prognostic factor. In Japan, organized screening justified by the high incidence of gastric cancer allows for early diagnosis and consequently a much better overall prognosis of gastric cancer. In recent Western randomized trials including patients who underwent surgery without microscopic tumor residue (R0), 5 year survival ranged from 17%, 47% to 48% [99]. The most important poor prognostic factors after surgical resection are: age: A study done by J.Hallett et al [19] in 2017, with the aim to evaluate the association between advanced age and morbidity and mortality after gastrectomy for gastric cancer. This study included 4215 gastrectomies, 60.6% are older than 65 years. Morbidity increases with age 16.3% (<65 years) to 24.1 (>80 years). Increasing age is independently associated with morbidity RR=1.32 (76-80 years) and RR=1.49 (>80 years). A predictive model for morbidity included age, sex, BMI, surgical procedure, and comorbidities [100]. Compared to patients with age <65 years, the risk of morbidity increases by 18.6% between 75 and 80 years and 27.5% after 80 years, for the most complicated cases of total gastrectomy and by 11.6% and 17.2% for subtotal gastrectomy. For favorable postoperatives, the rates was 5.1% and 7.6% for total gastrectomy, and 11.5 and 17.1 for subtotal gastrectomy [19]. In conclusion, the age beyond 75 years is associated with increased morbidity after gastrectomy for cancer. The presence of neoplastic cells as well as a high CEA level in the peritoneal lavage fluid are predictive of the occurrence of peritoneal recurrence and poor survival prognosis [20]. The limitations of our study are the small number of patients in a single institution; the follow-up periods were insufficient to obtain longer survival data; and there was many lost to follow up, an important factor that affects survival, could create a hidden bias.

Conclusion

The global overall survival of gastric cancer remains poor. The choice of the extent of surgery depends on several factors and the postoperative complications might be kept taken in considerations when deciding the technique to perform during its treatment. Subtotal gastrectomy is a feasible technique with a survival benefits for stage III of gastric cancers especially for tumors of antru-pyloric location. Given the frequent complications and increased morbidity and mortality associated with total gastrectomy, surgeons should carefully consider the extent of gastrectomy for gastric tumors. Further studies are needed to clarify the benefit of subtotal gastrectomy with a new protocols for the treatment of adenocarcinoma of the middle and antru-pyloric gastric.

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