

Surgical management of gastric cancer: Single center experience from a developing country

Muhammad Kashif Khan, Aamir Ali Syed, Shahid Khattak, Syed Ather Kazmi, Aasim Yusuf

Abstract

Background: Geographical distributional of gastric cancer (GC), differences in stage at the time of presentation and varying surgical expertise have resulted in different management strategies around the world. The aim of this study is to determine postoperative morbidity/mortality and overall survival in patients with GC treated at a cancer hospital in Pakistan. **Patients and Methods:** A retrospective review of patients who underwent surgical resection with curative intent for GC from June 2006 to July 2012 was performed. Primary end point was overall survival after a minimum follow-up of 15 months. For categorical data, frequencies were calculated, and means were measured for continuous variables. Chi-square test was used to compare categorical data and Kaplan–Meir survival analysis was performed to estimate 5 years survival outcome using SPSS. **Results:** Majority of the patients were males with median age of 51 years. Perioperative chemotherapy was offered to 75 patients while upfront surgery was performed in 23 patients. In perioperative chemotherapy group 51 patients and 22 in the upfront surgery group ended up having curative resection. The 5 years survival ($n = 98$) was found to be of 37%. The 5 years survival of patients in perioperative chemotherapy group ($n = 75$) was 44% while those who had a curative resection ($n = 73$) had survival of 46%. **Conclusion:** Gastric adenocarcinoma is an aggressive disease. Perioperative chemotherapy works well in Pakistani population as the results at our institution are comparable with international data.

Key words: Gastric cancer, surgical management, survival

Introduction

Gastric cancer (GC) is the second most common cause of cancer-related deaths causing about 800,000 deaths worldwide/year.^[1] Although its incidence is on the decline in the developed world, it continues to be the “captain of the men of death” in developing countries. Outcomes of gastric resection and survival following multi-modality treatment has not been reported from Pakistan before.^[2]

Gastric cancer shows a wide variation in incidence worldwide, being highest in Korea and Japan. It is detected early in more than half of the cases due to the low threshold for upper gastrointestinal (GI) endoscopy and screening programs. In the rest of the world and particularly in developing countries, GC is advanced in most of the cases. This geographical variability in incidence and stage of disease at presentation coupled with controversies in extent and type of surgical resection make GC a unique disease to cure.^[3] Surgery remains the cornerstone of management. Excision with 4–5 cm resection margin is an established recommendation; however, the extent of lymphadenectomy continues to be a topic of controversy.

On a regional level, there is some data from India, but from Pakistan the data is scarce.^[2] The outcome of patients with GC is yet to be reported from this part of the world. Therefore, we have conducted this study to determine the outcomes of patients with GC undergoing multimodality treatment with curative intent.

Objectives

The aim of this study is to determine postoperative morbidity/mortality and overall survival in patients with GC treated at a cancer hospital in Pakistan.

Patients and Methods

A retrospective review of patients who underwent surgical resection with curative intent for GC from June 2006 to

July 2012 was performed. Patients with nonmetastatic resectable GC treated with curative intent were included while patients with <15 months follow-up were excluded. Patients were discussed in gastroenterology tumor boards as per hospital policy, and decisions were taken for the further treatment.

Patients with nonmetastatic resectable disease underwent staging laparoscopy. Those with no evidence of metastasis on staging laparoscopy were offered perioperative chemotherapy. These patients received three cycles of epirubicin, cisplatin and 5 fluorouracil (ECF) chemotherapy. They were restaged with computed tomography chest and abdomen before surgery to exclude disease progression and were operated 4–6 weeks after completion of chemotherapy. At the time of surgery, repeat staging laparoscopy was performed immediately prior to surgery, and if resectable and nonmetastatic only then surgeon proceeded with resection. Surgery was followed by three more cycles of ECF chemotherapy as per Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial protocol.^[4] However, patients with gastric outlet obstruction underwent upfront surgery (staging laparoscopy and proceed to gastric resection if resectable), followed by adjuvant chemotherapy. The study was approved by the institutional review board.

Subtotal gastrectomy was performed for tumors of pylorus, antrum and distal body, with a surgical resection margin of at least 5 cm. Total gastrectomy was performed for proximal and mid GCs and patients with linitis plastica. D1 plus lymph node dissection (Japanese nodal stations 1–8) was performed. Splenectomy with or without distal pancreatectomy was labeled as total plus gastrectomy and performed only when indicated by disease involvement. Histopathological examination of the resected specimen was performed by dedicated GI pathologist using the American Joint Committee on Cancer

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Department of Surgical Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Correspondence to: Dr. Muhammad Kashif Khan, E-mail: kashifamc@gmail.com

staging for GC classification.^[5] Patients were followed up as per National Comprehensive Cancer Network guidelines.^[6]

Patients' sociodemographic disease and outcome-related variables were assessed. Short term outcome variables included duration of surgery, estimated blood loss, hospital stay and 30 days readmission and perioperative mortality. Perioperative mortality was defined as death occurring during the same admission irrespective of the cause or within 30 days of discharge attributable to surgical intervention. Overall survival was calculated from time of discussion to the time of death or last follow-up.

Data were analyzed using Statistical Package for Social Sciences Version 19 (SPSS by International Business Machines Corporation, New York, USA). Nominal data were provided as numbers (%) and continuous data as medians (range). Expected 5 years overall survival was calculated using Kaplan–Meier curve.

Results

A total of 98 patients with nonmetastatic resectable disease were included. A total of 23 patients were offered upfront surgery. Only one patient out of these had unresectable disease, whereas the rest underwent curative resection. The management details of patients undergoing perioperative chemotherapy (*n* = 75) is given in Figure 1.

A total of 73 patients underwent curative resection while six had palliative surgery. In 14 patients, surgery did not proceed beyond repeat staging laparoscopy. The perioperative details of patients undergoing curative resection are provided in Table 1.

The overall 5 years survival of the patients (*n* = 98) was found to be 37% after a mean follow-up of 26 months. Those patients who had resection with curative intent (*n* = 73) had 46% 5 years survival. The survival analysis details are provided in Table 2 and Figures 2-4. Statistically significant difference was present for the actual number of observed mortalities for patients with poorly differentiated carcinoma (*P* = 0.005) and extra-nodal extension (*P* = 0.002).

Discussion

There is a paucity of data from Pakistan on management of GC. The management protocols vary across Europe, America, and Japan. In Japan, D2 lymphadenectomy followed by adjuvant chemotherapy is considered as the gold standard.^[7] In the west, D2 lymphadenectomy is considered preferable but not mandatory, and consensus is on a minimum number of 15 lymph nodes required for proper staging. In United States of America surgery, followed by adjuvant chemoradiation is considered as standard of care.^[6] In most of the Europe,

perioperative chemotherapy is considered as the standard of care after the MAGIC trial.^[8] So the trials conducted in different parts of the world have provided their evidence for different management strategies.

The management of GC at our institute is also based on the findings of MAGIC trial; however, patients with gastric outlet obstruction are offered upfront surgery because of poor tolerance to chemotherapy. The mean age of our patients was 52 years, which indicates GC affects a relatively younger population in this part of the world as compared to the other parts of the world. In most of the cases, GC affected the gastric body. The perioperative chemotherapy was well-tolerated as only 4 of 75 patients were unable to complete the chemotherapy. The mean hospital stay in patients receiving perioperative chemotherapy was a little more than the patients undergoing upfront surgery while the rest of the parameters of perioperative morbidity are comparable. On the histopathological examination of the resected specimens, most of the adenocarcinomas were found to be poorly differentiated and extended to involve the overlying serosa in the majority of the cases. The 5 years and the median survival in the patients undergoing upfront surgery and perioperative chemotherapy were not much different. We believe that no survival advantage was observed in the chemotherapy group because the majority of patients who underwent upfront surgery had distal gastric tumors. The inherent favorable outcome of distal gastric tumors or early presentation with symptoms of gastric outlet obstruction might have resulted in improved survival potentially negating impact of chemotherapy in the other group.

In MAGIC trial, 503 patients with nonmetastatic and resectable adenocarcinoma of the stomach, gastroesophageal junction and lower 1/3rd of esophagus were randomly assigned to perioperative chemotherapy or surgery alone. The 5 years survival rate with perioperative chemotherapy was 36% when compared to the 23% with surgery alone.^[4] In our patients who underwent perioperative chemotherapy, the 5 years survival was 44%. Another phase III randomized controlled trial FNLCC ACCORD 07/FFCD 9703 was carried out in France to justify the rationale of perioperative chemotherapy. In this trial, 224 patients were randomized to receive perioperative chemotherapy or surgery alone. The 5 years survival was improved by 14% in the perioperative chemotherapy group (38% vs. 24%).^[9] The GC patients are offered perioperative chemotherapy at our institute on the basis of findings of these two trials.

Adjuvant radiotherapy alone does not result in survival benefit. Reports of improved survival with adjuvant

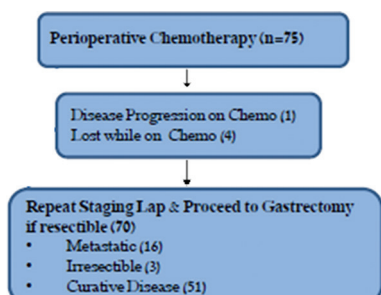


Figure 1: The management details of the patients receiving perioperative chemotherapy

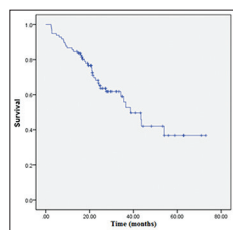


Figure 2: The intent to treat Kaplan–Meier survival curve of patients with gastric cancer (*n* = 98)

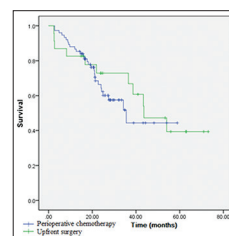


Figure 3: Kaplan–Meier survival curve comparison of patients undergoing perioperative chemotherapy (*n* = 75) and upfront surgery (*n* = 23)

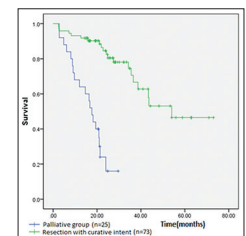


Figure 4: Kaplan–Meier survival curve comparison between patients undergoing resection with curative intent and palliative group

Table 1: The perioperative details of 73 patients who underwent curative resection

	Total	Upfront	Perioperative chemotherapy	P
Curative surgery	73	22	51	0.01
Subtotal gastrectomy	36	15	21	
Total gastrectomy	24	2	22	
Total plus gastrectomy	13	5	8	
Blood loss (ml): Mean (range)	297 (50-2100)	178 (50-600)	317 (30-2100)	0.14
Surgery duration (min): Mean (range)	234 (100-360)	206 (100-310)	240 (110-360)	0.036
Hospital stay (days): Mean (range)	11.74 (7-40)	10 (5-40)	11.5 (5-38)	0.91
30 days readmission (n) rates?	3	1	2	0.90
Perioperative mortality (n) rates?	2	1	1	0.90

Table 2: The survival analysis of patients with gastric cancer

Survival analysis	5 years survival (%)	Mean survival (months)	Median survival (months)
Overall (n=98)	37	43.24	38.63
Perioperative chemotherapy (n=75)	44	37.75	35.54
Curative resection (n=73)	46	50.91	54.0

chemoradiation led to a phase III randomized controlled trial (Intergroup 0116 study) in the United States ($n = 556$).^[10] In this study, 54% of the patients had D0 while rest underwent D1 resection. They reported 5 years survival of 50% in chemoradiation group when compared to 41% in surgery alone group. This study led to the strategy of adjuvant chemoradiation in United States but did not gain much popularity outside. In Japan, ACTS-GC trial randomized 1059 patients to receive surgery alone or surgery, followed by adjuvant chemotherapy. All these patients underwent D2 resection, and the 5 years survival increased from 61% to 72% with the addition of adjuvant chemotherapy. Japanese argue that their high survival rates are due to D2 resection.^[7] We performed D1 plus (Japanese nodal stations 1–8) dissection in our patients.

These trials have shown the superiority of adjuvant chemoradiation, adjuvant chemotherapy and perioperative chemotherapy over the surgery alone, but these modalities have not been directly compared. Of these different but internationally validated management strategies for management of GC, we have shown that perioperative chemotherapy in combination with D1 plus lymphadenectomy works well in our population.

Conclusion

Gastric adenocarcinoma is an aggressive disease. Perioperative chemotherapy works well in Pakistani population as the results at our institution are comparable with international data.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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