RESEARCH ARTICLE

Comparison of the effects of perioperative and adjuvant chemotherapy on outcomes of operable gastric cancer: A retrospective cohort experience from a tertiary cancer center

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Abstract

Objective: To compare the overall survival and disease-free survival rates with perioperative or adjuvant chemotherapy regimens in operable gastric cancer cases.

Method: The retrospective, observational study was conducted at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, and comprised date from January 2015 to December 2020 of operable gastric cancer patients who had perioperative or adjuvant chemotherapy. Overall survival and disease-free survival were evaluated. Data was analysed using SPSS 23.

Results: Of the 108 patients in the aga range 27-80 years, 71(65.74%) were males. The overall median age was 49.50 years (interquartile range: 28 years). There were 69(63.88%) patients on perioperative and 39(36.12%) on adjuvant chemotherapy. The probability of 2- and 3-year overall survival was 68.20% and 57.32% in the perioperative group, and 51.09% and 45.43%, respectively, in the adjuvant group. The probability of 2- and 3-year disease-free survival was 55.45% and 49.30% in the perioperative group, while 2-year disease-free survival was 38.39% in the adjuvant group which had no patient reaching the 3-year mark. The median overall survival for the perioperative group was 49.29 months (interquartile range: 44.50 months) and for the adjuvant group it was 28.23 months (interquartile range: 25.00months) (p=0.07). The median disease-free survival was 35.46 months (interquartile range: 38.50 months) for the perioperative group and 10.19 months (interquartile range: 14.00months) for adjuvant group (p=0.16). The difference between the groups was not significant (p>0.05), but there was a trend suggestive of the superiority of perioperative chemotherapy over adjuvant chemotherapy.

Conclusion: In operable gastric cancer cases, the difference between the groups was not significant, but there was a trend suggestive of the superiority of perioperative chemotherapy over adjuvant chemotherapy with respect to overall survival and disease-free survival.

Keywords: Gastric cancer, Outcomes, Pakistan, Adjuvant chemotherapy, Perioperative chemotherapy, Survival.

(JPMA 73: 812; 2023) **DOI: https://doi.org/10.47391/JPMA.6390**

Submission completion date: 18-03-2022 **- Acceptance date:** 12-11-2022

Introduction

Gastric cancer is one of the leading causes of cancer death worldwide.[1] A lot of variations in incidence rate exists globally, and there is low prevalence in southern Asia compared to other parts of Asia.[2] Nonetheless, gastric cancer generally has poor prognosis with overall 5-year overall survival (OS) rate <20%.[3] The prognostic factors for poor outcomes are not only related to difficulty in making an early diagnosis, but also with frequent recurrences and metastasis.[4] In gastric cancer, the cornerstone for treatment is surgical resection along with lymph node (LN) dissection.[5] In Japan and South Korea, an extended LN dissection, which is commonly known as a D2 dissection for gastric cancer, is considered a standard surgical procedure. The D2 dissection consists of removing the stomach, the greater and lesser omentum, along with stage node 1 (N1) and N2 LN groups.[6] In the Western world, the standard procedure is partial gastrectomy or total gastrectomy with D1 LN dissection, in which peri-gastric LNs are removed.[7] To improve the prognosis besides curative surgery, perioperative chemotherapy and adjuvant chemotherapy have shown encouraging results.[8] In perioperative chemotherapy, patient receives preoperative chemotherapy followed by surgery and then postoperative chemotherapy. Perioperative chemotherapy for gastric cancer is given with the intention to downstage the disease, increase the rate of curative surgery, and eradicate the undetectable micro-metastases.[9] On the other hand, the goal of adjuvant systemic chemotherapy is to target residual micro-metastases after surgical resection. Both the modalities intend to increase disease-free survival (DFS) and OS.

Perioperative chemotherapy in the West, and post-surgery

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adjuvant chemotherapy in southeast Asia are established options for gastric cancer treatment. A trial showed better survival with perioperative chemotherapy compared to surgery alone.[10] Another trial demonstrated improved survival with adjuvant chemotherapy over surgery alone.[11] However, the matter of chemotherapy mode (perioperative vs adjuvant) in gastric cancer is still open for debate.

The current study was planned to compare OS and DFS rates with perioperative and adjuvant chemotherapy regimens in operable gastric cancer cases.

Materials and Methods

The retrospective, observational study was conducted at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, and comprised data from January 2015 to December 2020 of operable gastric cancer patients who had perioperative or adjuvant chemotherapy. After approval from the institutional ethics review committee, a research registry number (NCT04989764) was acquired, and medical records were retrieved related to patients with histologically proven gastric adenocarcinoma with operable disease status who had completed their prescribed perioperative or adjuvant chemotherapy cycles. Patients with early disease, asses by Tumour-Node-Metastasis (TNM) stage Tis or T1, node-negative, inoperable or metastatic disease, were excluded, and so were those who did not undergo adequate lymphadenectomy (<D2) or had R1 margins (cancer cells present microscopically at the primary tumour site) following surgery. Patients had undergone total gastrectomy, distal subtotal gastrectomy or proximal gastrectomy, as per the extent of the disease. The decision regarding perioperative or adjuvant chemotherapy was taken as per our hospital's multidisciplinary teams (MDT) recommendations.

Adjuvant chemotherapy had been offered to patients who had been referred from elsewhere within 8 weeks' post-surgery with adequate D2 lymphadenectomy. Patients who presented with tumour bleeding or perforation were also offered adjuvant chemotherapy after upfront gastric surgery. Similarly, to distal gastric cancer patients who presented with gastric outlet obstruction, upfront surgery was advised with adjuvant chemotherapy. All remaining patients were offered perioperative chemotherapy.

Regarding chemotherapy options, the patients in perioperative group A received Epirubicin, Cisplatin, Fluorouracil (ECF) or Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel (FLOT), while those in adjuvant chemotherapy group B received Capecitabine and Oxaliplatin (CAPOX) regimen. ECF[10], FLOT,[12] CAPOX[11] regimens were in line with literature.

The primary outcomes were OS and DFS. The OS was defined as the length of time from the date of diagnosis till the last follow-up or death, and DFS as the length of time from the date of last treatment to tumour relapse or death. The median OS or DFS was defined as the point at which 50% of the population had not encountered the event, which was death in case of OS and progression in that of DFS.

Data was analysed using SPSS 23. Since the data was skewed, continuous data was expressed as median and interquartile range (IQR), while categorical data was expressed as frequencies and percentages. Survival data was calculated using Kaplan-Meier survival to determine differences between the two groups. The end points of interest were death and progression for OS and DFS, respectively. Survival plot and Log rank test were employed using the Kaplan-Meier analysis. $P<0.05$ was considered statistically significant.

Results

Of the 520 cases of gastric cancer, 108(20.7%) formed the sample for the current study; 71(65.74%) being male subjects. The aga range was 27-80 years. The overall median age was 49.50 years (IQR: 28 years). There were 69(63.88%) patients in perioperative chemotherapy group A and 39(36.12%) in adjuvant chemotherapy group B (Table 1). At the time of analysis, in September 2021, the median follow-up for both groups was 28 months (IQR: 27.50 months).

There were 48(44.4%) patients who died; 17(35.41%) in group B, and 31(64.58%) in group A. Disease progression was found in 55(51%) cases; 23(41.81%) in group B and

Table-1: Clinicopathological characteristics of patients.

	Perioperative chemotherapy n(%) 69(63.88)	**Adjuvant chemotherapy n(%) 39(36.12)**
Age Overall	Median 49.50[28 IQR]	
Median -year	50[24.00 IQR]	50[27.50 IQR]
Range (Minimum-Maximum)	27-80	30-80
Gender		
Male	48(69.56)	23(58.97)
Female	21(30.43)	16(41.02)
Location of tumour		
Proximal	40(37.03)	10(9.26)
Distal	39(36.11)	19(17.59)
Preoperative TNM staging		
T2	19(17.59)	4(3.70)
T3	37(34.25)	20(18.51)
T4	13(12.03)	15(13.88)
N1	43(39.81)	4(3.70)
N2	16(14.81)	15(13.88)
N3	13(12.03)	19(17.59)

IQR: Interquartile range, TNM: Tumour-Node-Metastasis.

Table-2: Treatment-based survival outcomes.

	Perioperative chemotherapy n(%) 69(63.88)	Adjuvant chemotherapy n(%) 39(36.12)
Deaths	31(64.58)	17(35.41)
Progression	32(58.18)	23(41.81)
Overall survival		
Median [IQR] (months)	49.29[44.50 IQR]	28.23[25.00 IQR]
2-year Overall Survival	68.20	51.09
3-year Overall Survival	57.32	45.43
Disease-free survival		
Median (months)	35.46[38.50 IQR]	10.19[14.0 IQR]
2-year Disease Free Survival	55.45	38.39
3-year Disease Free Survival	49.30	Not achieved

IQR: Interquartile range.

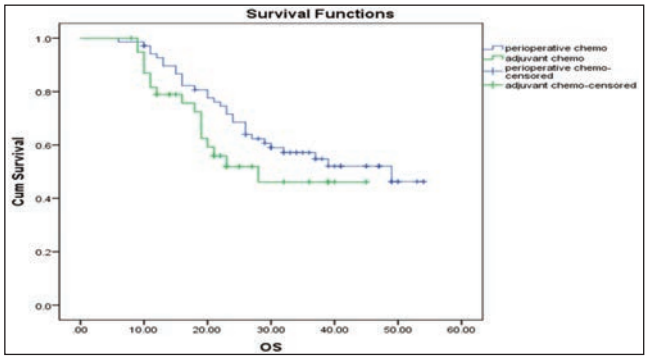

Figure-1: Kaplan-Meier Survival curves for gastric adenocarcinoma patients showing overall survival (OS).

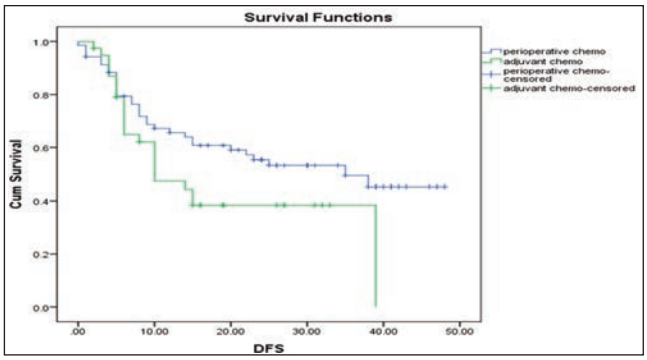

Figure-2: Kaplan-Meier Survival curves for gastric adenocarcinoma patients showing disease-free survival (DFS).

32(58.18%) in group A. The probability of 2- and 3-year OS was 68.20% and 57.32% in group A, and 51.09% and 45.43%, respectively, in group B. The probability of 2- and 3-year DFS was 55.45% and 49.30% in group A, while 2-year DFS was 38.39% in group B which had no patient reaching the 3-year mark. The median OS for group A was 49.29 months (IQR: 44.50 months) and for group B it was 28.23 months (IQR: 25.00 months) (p=0.07). The median DFS was 35.46 months (IQR: 38.50 months) for group A and 10.19 months (IQR: 14.00 months) for group B(p=0.16) (Table 2).

Kaplan-Meier survival curve for OS (Figure 1) and DFS (Figure 2) expressed similar data.

Discussion

Gastric surgery is the only curative treatment for locoregional gastric cancer.[13] Patients with resectable gastric adenocarcinoma are treated with perioperative chemotherapy or adjuvant chemotherapy to achieve downstaging and elimination of micro-metastasis, respectively. To the best of our knowledge, the current study is the first presenting local retrospective comparative data of perioperative and adjuvant chemotherapy in operable gastric cancer.

The findings demonstrated a trend towards better OS and DFS with perioperative chemotherapy, though it was not statistically significant. This goes well with data from Europe and North America.[14]

In a study, ECF and FLOT were compared and the median OS was 50 months, while 2- and 3-year OS was 59% and 48%, respectively, and the median DFS was 30 months.[12] The corresponding data in the current study was 49.29 months, 68.20%, 57.32% and 35.46 months. The difference could be due to younger age group in the current study and a smaller sample size compared to the earlier study.[12] Gastric cancer is a disease of younger age in Asia.[15]

Another study[10] showed superior results with perioperative ECF chemotherapy compared to the current study. Again, age of the subjects and the size of the sample could be the important variants.[16]

A meta-analysis reported statistically significant adjuvant chemotherapy benefits with respect to OS and DFS.[17] Another meta-analysis favoured perioperative group compared to the adjuvant chemotherapy group even though there was no difference in 1- and 2-year survival between the groups.[18]

One study reported better response in DFS terms when patients were given adjuvant chemotherapy along with surgery compared to those who had surgery alone.[11] The 3-year DFS for the adjuvant chemotherapy patients was 65%, while in the current study no patient in the adjuvant therapy group was able to reach the 3-year DFS point. The variance can be due to the difference between the sample sizes, as other study had 520 subjects[11] compared to 39 in adjuvant arm of the current study.

Another study compared perioperative chemotherapy with adjuvant chemotherapy,[19] with those in the perioperative group showing significant increase in OS and DFS compared to the adjuvant group, which is a finding similar to that of the current study.

There are limitations in the current study as the two groups were not equal in number and the sample size was limited. Also, the retrospective data has an inherent risk of bias. Ethnicity is a critical factor in this regard, but no comparable data could be found related to south Asian population. Moreover, treatment-related adverse events and dose reduction due to toxicity in both the arms of treatment were not documented in the current study.

A prospective, comparative study is recommended to further enhance understanding and improve the care of gastric cancer patients.

Conclusion

In operable gastric cancer cases, the difference between the groups was not significant, but there was a trend suggestive of the superiority of perioperative chemotherapy over adjuvant chemotherapy with respect to OS and DFS.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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