

## Neoadjuvant Chemotherapy in Locally Advanced Stomach Cancer: Our Experience

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### Abstract

**Background:** Neoadjuvant chemotherapy is standard of care in GE junction tumours; however their role in distal gastric cancer still needs to be evaluated. We aimed to evaluate the role of neoadjuvant chemotherapy in distal locally advanced gastric cancer

**Materials and methods:** Case data of patients treated with neoadjuvant chemotherapy in locally advanced gastric cancer were retrospectively reviewed in Mahavir Cancer Sansthan, Patna. 41% of patients were female and the mean age of study population was 46.92 years. All of them had distal gastric cancer as sub site.

**Results:** Around 58% of the patient progressed on neoadjuvant chemotherapy. 17% of patients had stable disease but could not undergo curative resection due to pancreatic head involvement. Rest patient who were operated had R0 resection along with D2 lymphadenectomy. The mean duration of tumor recurrence was 14 months.

**Conclusion:** Neoadjuvant chemotherapy improves resectability rate in locally advanced gastric cancer. Further studies needs to be done to adequately evaluate the role of neoadjuvant chemotherapy in distal gastric cancer.

**Keywords:** Distal gastric cancer; Neoadjuvant chemotherapy

### Introduction

Stomach cancer is the fifth most common cancer in INDIA and second most common cause of cancer related death in young population between age group 15 and 44. Data from national cancer registries shows variable incidence, highest in north-eastern and southern states of India. The highest rate of age-adjusted incidence is reported in Chennai being 11.1 per 100,000 [1]. Advanced stage at presentation is major concern in our population. The Mumbai registry reports mortality rate of 1.7 for females and 1.8 for males in 2005 [2]. The five year survival for stomach cancer is very poor in our country being reported as approximately 6% [3]. However a decline in incidence rate along with improvement in 5 year survival rate has been observed recently from Mumbai and Chennai based cancer registries.

Distal gastric cancer is still the most common site reported in our country contrary to the western data where a shift towards proximal site has been observed. Today the management of stomach cancer has shifted from surgery as only modality to multimodal treatment owing to advanced stage at presentation (T3-T4 or N<sup>+</sup>). The role of adjuvant radiotherapy and chemotherapy in locally advanced gastric cancer is well established. NCCN recommends peri-operative chemotherapy in clinically T2 or higher and any N<sup>+</sup> tumor. These recommendations are mostly based on the findings of MAGIC, and FNLC ACCORD 07 trial. Most of the patient selected these trial did not undergo adequate lymphadenectomy and only half of the patient could undergo treatment as per protocol. Furthermore in both MAGIC and ACCORD trial considerable number of patient had GE junction and lower

oesophageal adenocarcinoma. Next conclusive evidence on role of peri-operative chemotherapy in stomach cancer comes from EORTC study which strictly included only gastric cancer. However the study had insufficient statistical power [4].

### Materials and methods

We have retrospectively reviewed our data from January 2015 to August 2017. The patient diagnosed with locally advanced stomach cancer who underwent neoadjuvant chemotherapy was reviewed.

### Inclusion criteria

- Patient with biopsy proven and clinical T4 gastric cancer.
- Patient with diagnosed gastric cancer and having suspicious para-aortic nodes or clinically N2 on imaging.

### Exclusion criteria

- Patient with GE junction tumor.

A detailed clinical history and examination findings were recorded along with CT findings. All patients were subjected to neo-adjuvant chemotherapy in form of CapeOX. The total number of cycle was 6. Patients were evaluated after 4 cycles of chemotherapy to see for response and those having sufficient downsizing of lesion were subjected to surgery. Those not having sufficient response on CT were given additional 2 cycles and then subjected to surgery. Those who progressed during chemotherapy were subjected to palliative treatment.

A total 17 patients meet the inclusion criteria during the study period. Their mean age was 46.92 years ranging from 27 years to 65 years. Seven were female. All of them had distal gastric cancer as sub-site of disease except two who had diffuse stomach involvement. Ill-defined planes with pancreas and liver along with para-aortic nodes on imaging were most common indication for NACT in the study group. Two patients had signet ring histology on biopsy and rest were having adenocarcinoma.

## Results

Three patients progressed during the treatment and were subjected to palliative treatment. One patient lost to follow up after few cycles of chemotherapy.

Total of 13 patients were subjected to surgery. Out of 13 patients 10 were subjected to surgery after 4 cycles of chemotherapy and 3 patients after 6 cycles of chemotherapy. A staging laparoscopy was done in each patient on the day of surgery.

Out of 13 patients who were subjected to surgery 7 had disseminated peritoneal metastasis on staging laparoscopy. Additional 3 patients were declared in-operable due to pancreatic head involvement. A palliative surgery in form of gastro-jejunostomy was done in 8 patient and feeding jejunostomy in two patient.

Three patients underwent curative surgery in form of distal radical gastrectomy with D2 lymphadenectomy. Two of them required en bloc transverse colon segmental resection. The final histopathology was yp T4N1 in one patient and yp T3N2 in other two patients. They completed the chemotherapy. Their median follow up was of 11 months. Two had recurrence in the tumor bed after a mean follow-up of 14 months. They died after 2 months of disease recurrence. One patient lost to follow after completion of chemotherapy.

## Discussion and Conclusion

Early gastric cancer when treated surgically has 5 year overall survival of 90%. When it comes to locally advanced gastric cancer a multimodal approach is required. This is the situation in our Centre where locally advanced stage is most common presentation. The 5 year survival rate of locally advanced gastric cancer when treated with surgery alone is only 25-35% [5]. In order to improve the result neoadjuvant and adjuvant chemotherapy with or without RT has been explored.

The role of neoadjuvant chemotherapy in locally advanced has been extensively studied. Landmark trials like MAGIC and FNLCLCC have established the role of peri-operative chemotherapy in locally advanced gastric cancer. Through our retrospective analysis we have tried to evaluate the role of neo-adjuvant chemotherapy in locally advanced and potentially unrespectable gastric cancer. Distal gastric cancer is the most common site in our study group and ill-defined planes with pancreas and/or para-aortic nodes were the most common indication of neo-adjuvant chemotherapy.

Out of 13 patients who underwent neo-adjuvant chemotherapy only three underwent curative surgery. Rest patient either progressed on chemotherapy or there was no significant downsizing. However the results need to be carefully interpreted since none of the patient underwent staging laparoscopy prior to the start of chemotherapy. So

we cannot conclusively tell that they progressed on chemotherapy or they already had metastatic disease.

All three patients who underwent surgery after neoadjuvant chemotherapy had D2 resection. Their final histopathology revealed T3/T4 and N1/N2 disease. All had R0 resection. Their median numbers of chemotherapy prior to surgery were 4 cycles. These findings suggest that neoadjuvant chemotherapy improves the resectability rate. Similar results were shown by Shahriyar et al. in their study on effect of neoadjuvant chemotherapy on locally advanced gastric adenocarcinoma [6].

The mean duration before tumor recurrence in surgically resectable patients was 14 months. Other researchers have found an average disease free survival of 25 months. Our poor results can be explained from the fact that most of our patient had distal gastric cancer compared to other researchers who had GE junction tumors also included in their study.

## Recommendation

- Neoadjuvant chemotherapy increases resectability rate in locally advanced gastric cancer.
- Larger randomized studies are needed to evaluate the role of neoadjuvant chemotherapy in locally advanced distal gastric cancer.
- The role of concurrent RT in neoadjuvant therapy needs to evaluate.

## Limitations of Study

- Single centre study with little number of patients.
- Lack of staging laparoscopy in staging prior to chemotherapy for adequate staging.
- Diagnostic peritoneal fluid cytology was not done in patient during surgery.

## Conflicts of Interest

The authors declared no conflict of interest.

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