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STAGING LAPAROSCOPY AND NEOADJUVANT CHEMOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED CANCER STOMACH: A PROSPECTIVE STUDY

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ABSTRACT

Aim: To study the value of staging laparoscopy and neoadjuvant chemotherapy (NACT) in the treatment of locally advanced gastric cancer (LAGC). **Methods:** 32 Patients of radiologically proven locally advanced gastric cancer were enrolled for the study. All were subjected to staging laparoscopy, of whom 6 patients were excluded from the study after detecting occult metastasis. The patients were then subjected to 4 cycles of neoadjuvant chemotherapy and were then restaged radiologically, laparoscopically and pathologically. **Results:** Staging laparoscopy helped in averting unnecessary laparotomy in around 19% by detecting occult metastasis in them. No primary residual tumor (R0 resection rate) was found in 85%. Pathological complete response was seen in 15.38% of the cases and ypT0 - 2 was seen in 61.53%, thereby showing significant downstaging post neoadjuvant chemotherapy (P-value= 0.005). Conclusion: Laparoscopy is an effective tool in staging of locally advanced cancer stomach, and Neoadjuvant chemotherapy proves of great significance in downstaging of the disease.

KEYWORDS: - Staging laparoscopy, Neoadjuvant chemotherapy, R0 resection, Pathological complete response.

INTRODUCTION

Stomach cancer ranks fifth for incidence and fourth for mortality among all the cancer worldwide, with over one million new cases in 2020 and around 0.77 million deaths (one in every 13 deaths worldwide). Hence remains an important topic of concern among cancers. The incidence of stomach cancer is 5.6% and accounts for 7.7% total cancer mortality, with incidence rates among men being double than women (7.1%:4%).[1] Stomach cancer is amongst the first five cancers in the Kashmir Valley, with male predominance (Male: Female– 3.17: 1).[2] About 74.5% of new diagnosis of stomach cancer and 74.7% of deaths from the disease worldwide took place in Asia; more than half of cases reported from China alone. Japanese Classification of Gastric Carcinoma 15th edition, and the UICC TNM classification 8th edition recently revised the staging system of the gastric cancer.[3] Staging laparoscopy stands as a recommended step of the preoperative work-up in most of the previously published guidelines.[3-9] Ramos et al.[10] conducted a meta-analysis which included five studies with a total of 240 patients, showing that the pooled overall sensitivity was 84.6% (95 CI, 74.7 –91.8%), while specificity was 100% (97.7–100%). False negative rates reported in recent reviews ranges from 0% to 17.2%.[11]

MATERIAL AND METHODS

This was a prospective observational study, conducted in the Department of General Surgery, Government Medical College, Srinagar over a period of 2 .5 years, from June, 2019 to December,2021 after obtaining ethical clearance from the institutional ethical committee. The study was conducted on a series of 32 patients of histologically and radiologically documented locally advanced gastric cancer. During this study, we subjected the patients of locally advanced cancer stomach for staging (radiological and laparoscopic) to know the nodal status and rule out distant spreads and peritoneal seeding, after which they were subjected to neoadjuvant chemotherapy, four cycles of FLOT; fluorouracil, leucovorin, oxaliplatin, docetaxel. Restaging (radiological and laparoscopic) was done post neoadjuvant chemotherapy (NACT) treatment before proceeding to curative resection, followed by pathological staging after resection. Our study included the patients who were previously untreated, had biopsy and radiologically proven locally advanced

adenocarcinoma of proximal and distal stomach (T3-4 any N M0 or any T N1-3 M0), non-pregnant, having adequate bone marrow function, renal function, liver function tests respectively. Following set of patients were excluded from the study: early gastric cancer (T1-2 N0 M0), distant spread (M) including proven peritoneal carcinomatosis (PC), episodes of severe tumor bleeding, medically unfit for NACT, prior surgery to stomach, secondary malignancies, previous history of chemoradiotherapy.

OBSERVATION AND RESULTS

A total of 32 patients of radiologically proven locally advanced gastric cancer (LAGC) were enrolled for the study. The age of the patients ranged from 34 to 75 years, with the maximum number being in the range of 51 -60 years (Mean ± SD = 54.3±9.1). Males predominated in the study in numbers with male: female ratio of 4.3:1 (n=16) [Table 1].

Table 1: Age distribution (n=32).

Age (years)	Male	Female
31-40	0	2
41-50	4	4
51-60	14	0
61-70	6	0
>70	2	0

All the patients were subjected to staging laparoscopy. Staging laparoscopy (SL) could detect distant metastasis/ adjacent organ involvement in 6 cases (18.75%) and the said number of patients was dropped from the study as they did not meet the selection criteria of our study, reducing the number to 26 (Table II, Fig.1). All 26 patients were able to complete 4 cycles of NACT and were taken for curative resection 2-3 weeks after completion of last cycle. None of the patients in our study showed progression during or after NACT, with no serious adverse events due to same.

Table II: Pre NACT staging (n=32).

Parameters	CT staging	Staging laparoscopy	P value
Peritoneal carcinomatosis	0	6*	0.22
Ascites	8	16	0.27
Serosal involvement	16	22	0.47
Nodes	24	32	0.10

*Excluded from the study

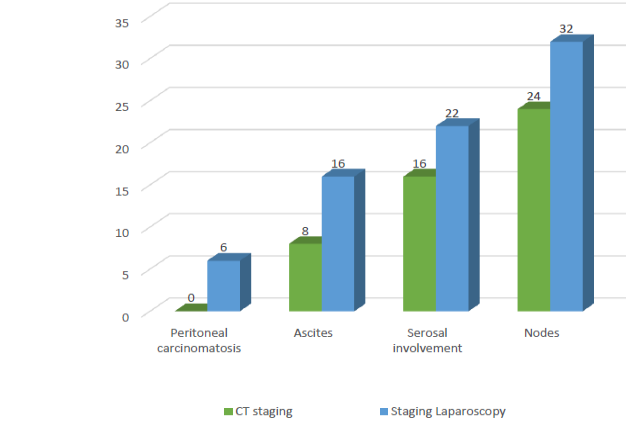

Fig. 1 Pre-NACT staging

Response to chemotherapy

The extent of R0 resection in our study as 85%, and the rest was R1 resection with involvement of proximal resection margin. None of the patients in our study had R2 resection. 4 patients (15.38%) showed pathological complete response, 10 patients (38.46%) partial response, 6 patients (23.07%) minimal response and 6 patients (23.07%) no response (stable disease) [Table III]. Disease progression was not seen in any of the patients in our study.

Histopathological classification

After NACT, higher percentage of patients belonged to pathological stage ypT0-2, constituting around 61.53% [16 patients, n= 26], and ypT3,4 =38.46% [10 patients] against cT3,4 of 68.75% hence showing significant downstaging (p-value =0.005) after NACT. The TNM stage after NACT and resection were as; stage I, stage II, stage III: 15.38% (4), 30.76% (8), 38.46% (10) respectively, and 15.38% (4) with no residual tumor in the specimen post NACT. Of total 864 Lymph nodes (LN) examined from 26 specimens, only 100 Lymph nodes were involved. The N0-1 percentage in our study was on higher side, constituting around 62%of all.

Table III: Response to chemotherapy.

Response to chemotherapy	Percentage (%)
Complete response	15.38
Partial response	38.46
Minimal response	23.07
No response/ stable disease	23.07

DISCUSSION

The results of our study showed the importance of the laparoscopy as a staging tool in the cases of LAGC. In our study, 18.75% of the cases were found to have occult metastasis on staging laparoscopy, after having been deemed operable on conventional CT staging, thereby preventing unnecessary resections/ laparotomies in them (p-value: 0.22). This result is slightly lower than the reports of previous studies conducted by Lowy et al,[12] Schuhmacher CP et al,[7] tourani SS et al[8] and Kakroo SM et al[9] with the percentage of detecting occult metastasis as 23%, 24%, 25%, and 28% respectively. The R0 resection has an impact on the overall survival of the patient and quality of life. R0 resection rate in our study was 85% which corresponds well with the results obtained by the previous studies, ranging from 79% to 91%.[13, 16-18] Pathological complete response (CR) was seen in 4 patients corresponding to 15.38% in our study. Similar results were observed by Biffi R et al,[17] Al-Batran et al,[19] Noronha V et al.[20] Our results are slightly higher than few other previous reports of histopathological response where the CR rate ranged from 0-12%.[12,21-25] In our study, the pathological T stage post NACT, ypT0, ypT1, ypT2, ypT3 and ypT4 were as 15.38%, 23.07%, 23.07%, 30.76% and 7.69% respectively. Higher percent of cases belonged to pT0-2 (61% P-value =0.005) which was statistically significant, thereby showing a significant downstaging of disease post NACT**.** Similar rates were observed by the studies conducted by Cunningham D et al,[26] Zhang Y et al,[18] Ychou M et al[16] and Schuhmacher CP et al[13] respectively on gastric cancer pre-treated with chemotherapy.

Lymph node (LN) metastasis is an important prognostic factor in patients of stomach cancer.Our study shows that NACT has a significant effect on LN metastasis, with ypN0 as 52%. 14patients in our study had ypN0 status. With only 11% of the total LN involved.

CONCLUSION

In conclusion, the present study demonstrated the benefits of laparoscopy in the staging of locally advanced cancer stomach in terms of detecting micro-metastasis/ peritoneal carcinomatosis, and, NACT proved to be of great advantage in downstaging of the locally advanced disease thereby increasing the percentage of R0 resection. However, the long-term oncological benefits cannot be evaluated as adequate data is missing and regular follow-ups couldn't be possible because of the Covid-19 pandemic.

Limitations

Relatively small sample size and short term follow up of the patients. Moreso, the rate of conversion surgeries couldn't be evaluated as the patients detected with peritoneal involvement on staging laparoscopy were dropped from the study.

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