Background
The overall 5-year survival of patients with gastric cancer has not changed significantly over the past three decades and remains at 10-15% (U.I.C.C. report). The consistently poor results of surgical treatment have led to the conduct of several adjuvant chemotherapeutic trials. Cytotoxic drugs have also been used for advanced carcinoma of stomach where surgery is not undertaken either due to contraindication for surgery or patient’s refusal. Though the results of chemotherapy are not encouraging, still many cytotoxic regimens are under study throughout the world. India being a poor country, mass screening is quite expensive is not possible. Therefore, the management of advanced carcinoma of stomach has become important. This study has been designed to evaluate the incidence of advanced gastric carcinoma in surgical ward of M.K.C.G. Medical College and Hospital, Berhampur, over a period of 2 years including period of follow up.

Methods
The present work is an observation on the different modalities of management in case of advanced carcinoma of stomach admitted to the surgical wards of MKCG Medical College Hospital, Berhampur, for a period extending from July-2017 to June-2019 including period of follow up. Seventy-five cases of carcinoma of stomach were admitted to the surgical wards of M.K.C.G. Medical College, Berhampur from July 2017 to June 2019. All of them were in the advanced stage of the disease and were taken into consideration in the present study, after confirmation of diagnosis on the basis of presenting symptoms, physical sign and investigations.

Results
Only 44 cases were studied in the initial one-year i.e. between July 2017 to June 2018 so one year follow up was done and median survival for one year follow up was maximum for partial gastrectomy with SFU (8.7 months) followed by combined ECF regimen group (6.3 months). Single drug chemotherapy SFU group and palliative GJ + SFU group had almost similar survival rates (5.1 months).

Conclusions
The patients were followed up till the end of study period and their medium duration of survival found out. 10 patients who were getting 5 F.U. as single agent therapy and were available to the follow up showed a medium survival time of 5.1 months. 16 patients were followed up who were getting ECF regimen and median duration of survival in this group was 6.3 months. Median survival duration of 8.7 months was found in 6 patients who were getting 5 F.U. after palliative partial gastrectomy and were available for follow up. Median duration survival of 5.1 months was found in 20 patients who were getting 5 F.U. after gastrojejunostomy and available for follow up.

Keywords
Carcinoma, Stomach, Cytotoxic Drugs
BACKGROUND

Though various factors have been advocated as the causative agents of carcinoma stomach, the aetiology remains largely obscure. Endeavours are being made from the very early time to fight against this dreadful disease, but no satisfactory results have been yet achieved. The disease is curable only it its early stage. So, the sheet anchor of treatment is early detection of the disease. Unfortunately, there are rarely symptoms associated with ‘early’ carcinoma of stomach and when symptoms occur, they are quite vague and nondescript. So, when the patients present with the symptoms, the disease is advanced and do not pose any diagnostic problem. In this stage the patient is beyond the scope of surgical cure. Hence rightly speaking the first against cancer is a fight for early diagnostic and thus for earlier radical treatment.¹

Objectives

This study has been designed to evaluate:

1) The incidence of advanced gastric carcinoma in surgical ward of M.K.C.G. Medical College and Hospital, Berhampur within a period of consecutive 2 years including period of follow up.

2) To study different modalities of treatment for advanced stomach carcinoma and find the best type of treatment to achieve good quality of life of patient and also survival benefit.

Pathophysiology

Advanced gastric cancer denotes lesion beyond muscularis propria. It exhibits deep invasion, serosal involvement, invasion of adjacent organs, extensive nodal metastasis ends secondary deposits usually, within the peritoneal cavity. So, they are often not amenable to curative resection, unfortunately most of the patients have reacted this stage when first diagnosed by definition these tumours always exceed 2 cm in diameter²,³

Borrman, in 1926, classified advanced adenocarcinoma of stomach into 4 types.

Group-I: Circumscribed, solitary polypoid carcinomas without ulceration.

Group-II: Ulcerated carcinomas with wall like mercinal elevation and sharply defined border.

Group-III: Partially ulcerated carcinoma with marginal elevation and partially diffuse spread.

Group-IV: Diffuse carcinoma

Spread of Carcinoma of Stomach⁴,⁵

The spread of gastric carcinoma occurs in the following ways.

1. Mucosa and Submucosa: The growth spreads mainly in the submucosa cost along the lesser and greater curvature, It the lesion destroys the pyloric ring, then spread occurs into the duodenum either by lymphatic permeation, direct spread or combination of the two, through submucosa. Oesophagus is involved in case of cancer or cardia, also in diffuse type of limitis plastics.

2. Lymphatic spread: Lymphatic spread occurs both by emboli and permeation. The retrograde spread via the lymphatics can occur if the onward flow through the lymphatics is obstructed. Lymph node metastasis is found in 60% of subtotal gastrectomies performed far carcinoma stomach. Lymph node metastasis occurs least when growth is situated on the anterior wall, on the greater curvature on in the region of fundus.

If the nodes in the portal fissure become involved, they may press upon and occlude the biliary passage giving rice to obstructive jaundice. Growth along the ligamentum teres spread towards the umbilicus around which it forms hard, knobby, bluish red tumour called "Sister Joseph's nodule". In very advanced cases the supraclavicular lymph nodes may be involved. It commonly occurs to the left supra-clavicular group (Troisier's sign) but the right supraclavicular group may also be involved in those cases where the thoracic duct divides into two branches into the right subclavian with the right lymphatic duct. Enlarged lymph nodes may not be always cancerous when they are soft, elastic and discrete due to inflammation where malignant nodes are hard and sometimes mated.⁶,⁷

3. Direct Spread: Direct spread may involve colon, pancreas, liver, gall bladder, spleen, duodenum & Jejunum.

4. Haematogenous: Spread via portal vein may involve liver or via systemic circulation occur to lungs, bones, pleura and skin.

5. Peritoneal spread: Peritoneal seedling from the involved gastric across occurs to the omentum & parietal peritoneum. Transcoelomic implantation to ovary cause Krukenberg's tumour or to the pelvis causing pelvic Cul-de-sac (Blumer's shelf).

6. Transplantation and transluminal implantation: Malignant cells may become implanted in the abdominal incision during operative procedure or may pass via the lumen to get implanted in the intestine lower down.

METHODS

The present work is an observation on the different modalities of management in case of advanced carcinoma of stomach admitted to the surgical wards of MKCG Medical College Hospital, Berhampur for a period extending from July-2017 to June 2019 including period of follow up. The selection of cases was done on the basis of their clinical symptoms and signs supplemented by routine and special investigations to arrive at a diagnosis. After confirming the diagnosis and assessing the extent of spread of disease the patients were grouped in different categories and the treatment instituted.
In this study advanced carcinoma of stomach is defined as where it is not possible to give a surgical cure. According to Japanese classification advanced gastric cancer is lesion beyond submucosa. So theoretically a curvature resection is possible in advanced carcinoma or stomach when the lesion remains confined within the wall of stomach without distant metastasis. In this series no case was within the scope of a curative resection.

Treatment Given to Patients
1. In case of mobile growth palliative partial gastrectomy was done.
2. In case of obstruction due to fixed prepyloric growth anterior gastro jejunostomy was done.
3. Postoperative chemotherapy with 5-FU given in all palliative operations.
4. Where palliative operation was not possible abdomen was closed taking biopsy from the mass from the lymph node and postoperative chemotherapy epirubicin + cisplatin + 5-FU.

Criteria for Palliative Operations
1. Features of obstruction like vomiting, dysphagia & visible peristalsis.
2. Palpable mobile lump in the distal part of stomach.
3. Haematemesis or Melena in a patient after 50 years of age.
4. Patient with intractable pain.
5. Absence of systemic disorders and metabolic diseases which precludes major surgery.

Criteria for Chemotherapy
1. Fixed growth with distant metastasis without features of obstruction.
2. Patients unwilling for surgery.
3. Patients unfit for surgery.
4. Patients with deep jaundice.
5. Patients with tense ascites.

Seventy-five cases of carcinoma of stomach were admitted to the surgical wards of M.K.C.G. Medical College, BERHAMPUR from July 2017 to June 2019. All of them were in the advanced stage of the disease and were taken into consideration in the present study, after confirmation of diagnosis on the basis of presenting symptoms, physical sign and investigations. They were subjected to different modalities of treatment and the cases were studied during the period of stay in the hospital and were followed up after discharge from the hospital.

Laparotomy was done in 45 cases out of which in 9 cases (12%) the growth was distally situated and mobile for which palliative partial gastrectomy was done. In 36 cases (48%) the growth was distally situated but the growth was fixed to the posterior wall. So, in these cases anterior gastrojejunostomy was done. Thus in 60% of cases palliative procedure was undertaken.

Palliative operation was not done in 30 cases out of which 6 cases (20%) were having growth in the body extending to cardia. In 4 case (13.3%) the growth was present in the fundus extending to cardio-oesophageal junction. In these cases, palliative total gastrectomy is contraindicated. So, in these cases abdomen was closed without doing any surgery taking lymph node for biopsy. In 25% of cases patient were unwilling for surgery although, otherwise they were fit to undergo palliative surgery. In 30 cases (40%) the growth was fixed as assessed clinically and confirmed by investigation. So, these cases were given chemotherapy. The cases where only laparotomy was done (5 cases) those cases were given 5 F.U. after surgery. The patients who were unwilling to undergo surgery were also given chemotherapy. In 4 cases (10%) deep jaundice was present rendering the patient unsuitable for surgery. In these cases, chemotherapy was also given. 3 cases (7.5%) were in low condition with gross oedema of feet which rendered them unsuitable for surgery. In 3 cases (7.5%) tense ascites was present for which surgery could not be done. In all cases where palliative operation was done, single agent chemotherapy with 5 fluorouracil was given.

In 12 cases (16%) out of the total number of 75 cases single agent chemotherapy using 5 F.U. was given. In some number of cases combination chemotherapy with 5 F.U. cisplatin and epirubicin (ECF. regimen) was given. In these cases, the group getting ECF.

| Age Group in Years | No. of Cases | % |
|-------------------|--------------|---|
| 21-30             | 2            | 2.67 |
| 31-40             | 5            | 6.67 |
| 41-50             | 21           | 28  |
| 51-60             | 25           | 33.33|
| 61-70             | 22           | 29.33|
| Total cases       | 75           |      |

Table 1. Incidence of Gastric Carcinoma

| Biopsy Report | No. of Cases | % |
|---------------|--------------|---|
| Adenocarcinoma| 73           | 97.34%|
| Linitis plastica| 2         | 2.66%|

Table 2. Biopsy Report of Upper GI Endoscopy

| Type of Treatment | No. of Cases | % |
|-------------------|--------------|---|
| Palliative partial gastrectomy + SFU | 9 | 12 |
| Antecolic Gastro jejunostomy + 5FU | 36 | 48 |
| Single agent chemotherapy (SFU) | 12 | 16 |
| Combination Chemotherapy ECF regimen | 18 | 24 |
| Total Number of Cases | 75 |      |

Table 3. Various Treatments Given in Different Age Group

| Type of Treatment | No. of Patients | Follow up in Months | Median Survival in Month |
|-------------------|----------------|--------------------|-------------------------|
| SFU               | 7              | 6                  | 4-6                    | 7-9                     | 10-12                  | 5.1                     |
| Partial gastrectomy + SFU | 5          | 5                  | 5                      | 4                       | 3                       | 8.7                     |
| ECF               | 12             | 12                 | 9                      | 7                       | 4                       | 6.3                     |
| GI + SFU          | 20             | 16                 | 12                     | 8                       | 6                       | 5.1                     |
| Total No of Cases | 44            |                    |                        |                          |                          |                         |

Table 4. Survival of Patients with Different Modalities of Treatment
DISCUSSION

Most of the Patients were between 51-60 years of age. These findings is very similar to the median age of 57 years noted by Halder SK et al in Kolkata. Among the Patients who underwent Palliative partial Gastrectomy with 5FU chemotherapy, the median survival noted was 8.7 months. Mariette, Bruyere et al. found a survival benefit after palliative surgery of 12.0 to 18.3 months. The next best option is palliative gastrojenuostomy followed by 5FU chemotherapy. In this study, the median survival noted was 5.1 months. This finding is very similar to Stupart et al who note a median survival important to 7 months with palliative GJ in unresectable gastric cancer patients with GOO. In groups where combination chemotherapy with 5 F.U. cisplatin and etoposide (ECF. Regimen) and single agent chemotherapy with 5FU was given, in these cases the group getting ECF. Regimen get better duration of survival in comparison to the group getting 5 F.U. alone that IS 6.3 and 5.1 months respectively. This study correlates with the study by David Cunningham and William.

CONCLUSIONS

In the present work an attempt has been made to study the management of advanced carcinoma of stomach and compare the results of different modalities of treatment. Laparotomy was undertaken in a limited number of patients where surgery was indicated. Palliative resection is better than simple bypass procedure as debulking increases response to adjuvant chemotherapy by reducing the tumor mass. Chemotherapy does not give any cure to the patient. It may halt the disease for some time but ultimately disease progresses. Adjuvant chemotherapy following palliative resection gives the best result by prolonging the survival time as has been observed in this series. A bypass surgery followed by single agent chemotherapy only improves the quality of life than improving survival time. Combination chemotherapy with ECF regimen although prolongs duration of survival, there is little difference in the duration of survival between ECF regimen and 5 F.U. given as single agent chemotherapy but ECF group had more incidence of chemotherapy toxicity. However, a large group of study and a long follow up is needed to comment on the overall result in advanced carcinoma of stomach. Efforts should be made to diagnose the disease in its early stage so as to give some hope of cure to this group of patients.

REFERENCES

[1] Ang TL, Fock KM. Clinical epidemiology of gastric cancer. Singapore Med J 2014;55(12):621-628.
[2] Jemal A, Bray F, Center MM, et al. Global cancer statistics. CA Cancer J Clin 2011;61(2):69-90.
[3] Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014. Gastric Cancer 2017;20(1):1-19.
[4] Sun Z, Zheng H, Yu J, et al. Liver metastases in newly diagnosed gastric cancer: a population-based study from SEER. J Cancer 2019;10(13):2991-3005.
[5] Reddavid R, Sofia S, Chiaro P, et al. Neoadjuvant chemotherapy for gastric cancer. Is it a must or a fake? World J Gastroenterol 2018;24(2):274-289.
[6] Gumus M, Kaya S, Eris S, et al. Neoadjuvant treatment in patients with locally advanced gastric cancer. J Clin Oncol 2019;37(4 Suppl):127.
[7] Sano T, Aiko T. New Japanese classifications and treatment guidelines for gastric cancer: revision concepts and major revised points. Gastric Cancer 2011;14(2):97-100.
[8] Halder SK, Bhattacharjee PK, Bhar P, et al. Demographic and clinico pathological profile of carcinoma stomach in a tertiary referral center of Eastern India. All Ameen J Med Sci 2012;5(4):398-402.
[9] Stupart DA, Panieri E, Dent DM. Gastrojenuostomy for gastric outlet obstruction in patients with gastric carcinoma. S Afr J Surg 2006;44(2):52-54.
[10] Mariette C, Bruyere E, Messager M, et al. Palliative resection for advanced gastric and junctional adenocarcinoma: which patients will benefit from surgery? Ann Surg Oncol 2013;20(4):1240-1249.
[11] Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355(1):11-20.