

## MANAGEMENT OF GASTRIC CARCINOMA; COMPARATIVE ANALYSIS OF VARIOUS TREATMENT MODALITIES

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**ABSTRACT ... Objective:** (1) To find the best treatment modality for carcinoma stomach. **Design:** Case series study. **Setting:** Combined Military Hospital Rawalpindi. **Period:** From January 1996 to December 1999. **Patients and methods:** 42 cases of gastric carcinoma are included in this study. The mode of treatment predominantly remained surgical with the aim to cure the patient of this disease. **Results:** The disease occurred mostly above the age of 50 years. Common clinical features were unexplained weight-loss, malnourishment and anaemia, respiratory tract infections. No specific etiological factor was detected except that, out of 42 patients 35 were smokers or had quit smoking during the past six years. Nearly all were having at least 8-10 cups of hot tea per day. Adenocarcinoma was the most frequently encountered histological type. 03 patients could not be operated upon because of extremely poor prognosis due to multi-organ failure. 12 patients were selected for surgery curative resection was carried out, whereas the remaining 27 were subjected to palliative resections. Five patients died during or within one month of surgical intervention. Out of the remaining 34, only 21 patients reported for follow up. In most of the patients in whom curative resection was performed, the quality of life was reasonably good. At the end of one year, another eight patients had died of tumour dissemination and cachexia, three patients developed tumour recurrence at the anastomotic site, and one patient developed stricture at anastomotic site. Patients with recurrence were sent for radiotherapy. **Conclusions:** It is concluded that for carcinoma of stomach the only possible treatment is surgery either alone or in combination with radiation and chemotherapy, the most common, preventable etiological factor is smoking, probably in combination with hot beverages in excess. The most common presentation remains weight loss with dyspepsia or weakness and anorexia, commonly effected age group is middle and old age, preoperative nutritional build-up achieves good postoperative results, palliative surgical procedures made the quality of life of the patient better. The prognosis remains extremely poor, in terms of morbidity and mortality.

**Key words:** Carcinoma stomach, Billroth I gastrectomy

### INTRODUCTION

Avicenna (980-1037) gave the first account of carcinoma of stomach<sup>1</sup>. Morgagni was the first to write a detailed note on malignant lesions of stomach in 1761<sup>1</sup>.

Recent advances in the detection techniques have led to the conclusion that gastric carcinoma is one of the leading cause of cancer mortality in the world.

It is 95% of all tumors. Despite improvement in surgical techniques and modernization of equipment no worthwhile gain in the prognosis has been achieved.

Although the incidence of gastric carcinoma has reportedly declined steadily through most parts of the world<sup>2</sup> yet it remains prevalent in others such as Japan, Finland, Austria and Britain.

The distressing outlook of the disease has been best challenged by the Japanese with experience over the

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past 50 years evidenced by improved overall 5 year survival following resection. Although a large number of series reported are retrospective but the Japanese are also conducting prospective studies and clinical trials. Many western observers remain critical of these and describe the differences in survival to ill-defined differences in biological aggressiveness of gastric cancer occurring in Japan as opposed to the west<sup>2</sup>.

The consistently poor results of surgical treatment, in the west, have led to several adjuvant chemotherapy trials. Radiotherapy so far has been shown to be ineffective.

Overall 5-year survival ranges from 10-25 percent with surgical resection. When resection is carried out for apparently localized disease it ranges from 25-50% and when cancer is confined to mucosa or submucosa, 5 year survival rate is as high as 90%<sup>3</sup>. Laparotomy offers little or no prospect of cure in advanced disease, although palliative resection or bypass procedures may improve quality of life when performed for obstruction<sup>4</sup>.

LASER Palliation, Intraluminal Brachytherapy and intubations have been tried with no significant effect on prognosis<sup>5</sup>.

Combination regimens have been evaluated primarily in patients with squamous cell carcinoma. Because this is an uncommon malignancy, most studies include patients treated preoperative as well as those with recurrent and metastatic disease. Kelsen and colleagues at Memorial Sloan-Kettering Cancer Centre have the largest single institution experience testing combination chemotherapy. His group first evaluated cisplatin and infusional bleomycin in patients with squamous cell carcinoma observing a 17% response rate. Subsequent trials are testing the 3-drug regimens cisplatin, bleomycine and vindesine. MGBG, vindesine yielded response rates of 31% and 40%, respectively. Three-drug cisplatin-based regimens tested by other investigators confirmed the response rate of 30% to 40%<sup>6</sup>. Toxicity was primarily a moderate myelo-suppression. 5-FU may be more effective when administered by continuous infusion and has demonstrated synergism with cisplatin. The

regimens currently being used mostly as Neo Adjuvant therapy are, ECF (Epirubicin, Cisplatin, 5-florouracil) and FMA (5-florouracil, andriamycin, Mitomycin C)<sup>7,8</sup>.

Detection of early gastric cancer by comprehensive screening program by the Japanese have shown promising statistics for this disease. World wide prognosis is very poor.

The prognostic determinants are as follows;

- Age and sex have no significant effect.
- Longer duration of symptoms is associated with better prognosis.
- Prognosis for carcinomas of cardia and fundus is worse, and for carcinomas of antrum and pylorus it is fairly good.
- The size of tumour is inversely proportional to the prognosis. Lesions less than 3cm in size show 5-year survival of 52.5% while more than 3cm showed only 17%.
- Polypoidal and ulcerative growth have better prognosis than infiltrative growths. (Linitus plastica has very bad prognosis).
- Diffuse tumours have poorer prognosis compared with intestinal variety.
- Survival decreases as the number of involved lymph nodes increases.
- The depth of invasion of the wall is important factor. Survival for mucosal carcinoma in Japan is 100%, for submucosal carcinoma 80-87%, for muscularis propria 70-75% and for the lesions involving serosa survival is 34-40%.

Most significant determinant, of 5-year survival of gastric carcinoma, is its stage<sup>9</sup>.

Stage	5-years Survival
Stage I	70%
Stage II	30%
Stage III	10%
Stage IV	0%

Detection of early gastric carcinoma is only way to improve prognosis. This requires a vigorous approach to the symptoms of dyspepsia, starting in middle-aged, with careful radiology and endoscopic examination and critical follow up of doubtful abnormalities.

Japan is considered as the trend-setter for the management of gastric carcinoma. This is due to the fact that the disease is prevalent there, the general population is having awareness about it, Japan has well developed screening programs, and an aggressive approach towards management. Latest reports from Japan indicate over 60% overall 5-year survival for gastric carcinoma, attributable to frequently performed gastroscopic examination, detection of early resectable lesions and aggressive therapeutic approach<sup>10</sup>.

Helicobacter Pylori has been implicated as one of the preventable causes of gastric carcinoma and therefore it is recommended that H. Pylori eradication should be done in all cases of peptic ulcer<sup>11</sup>. It has also been suggested that in patients with carcinoma stomach who are negative for H pylori, tumour-specific immune responses might be downregulated and these patients should be followed up carefully because of a poor outlook<sup>12</sup>.

## OBJECTIVES

Carcinoma stomach is a major cause of morbidity and mortality through out the world and also one of the prime killers in Pakistan. The purpose of this study was to assess treatment modalities for various histological types, specifically sited Carcinoma stomach in different age groups of patients. Another purpose was to highlight the use of palliative modes to relieve the distress of the patient with advanced carcinoma.

## STUDY DESIGN

Case series study.

## MATERIALS AND METHODS

A retrospective study of 42 cases of gastric carcinoma was carried out during January 1996 to December 1999 at Combined Military Hospital Rawalpindi. This study

included patients with the diagnosis of Carcinoma Stomach treated during this time. Patients of all age groups were included. Detailed history with specific reference to obstructive symptoms, feeling of lump in epigastrium, weight loss and past history with reference to dyspepsia, gastric ulcer and hematemesis or any other gastric disease was taken.

Local and general physical examination was carried out and recorded to evaluate their fitness for various treatment modalities. A series of routine investigations (blood complete picture, urine routine examination, chest X-Ray) were done. Other investigations to assess physical fitness included electrocardiography, liver function tests, blood urea and electrolytes, ejection fraction and pulmonary function tests. Endoscopy and barium studies were done in all cases to confirm diagnosis. Endoscopic biopsies were also done in a limited number of patients.

The treatment predominantly remained surgical with an aim to cure the patient of this disease, except in those cases who refused surgical treatment or were found unfit for surgery, these patients were given radiotherapy and chemotherapy.

Palliative surgery in the form of de-bulking surgery and by pass procedures was mostly reserved to cure obstructive symptoms in cases that had wide spread metastasis.

A regular follow-up was advised to all patients; however the turn-up remained low and less than half the original number was regularly followed for up to 1 year.

The majority of patients included in this study were male and only four females could be included in study. Being a military hospital any independent suggestion or proposal pertinent to the study could not be made to any patient regarding his treatment.

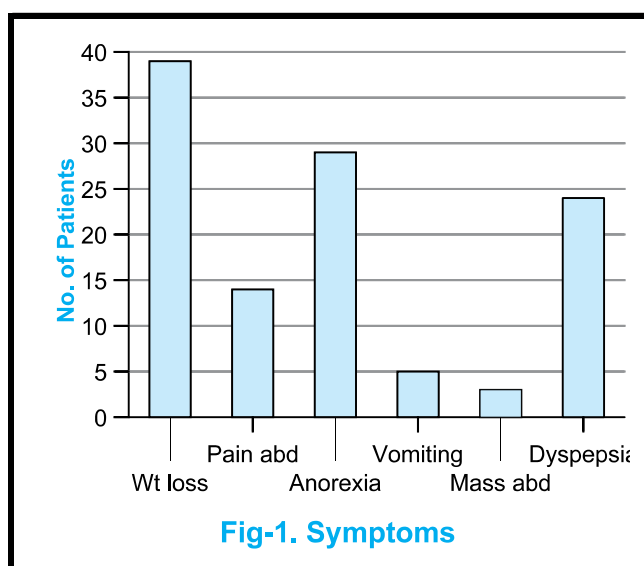
Some of the subjects included in the study were lost to follow up.

LASER palliation, Intraluminal Brachytherapy and

intubations were not carried out in our set up as the equipment was not available

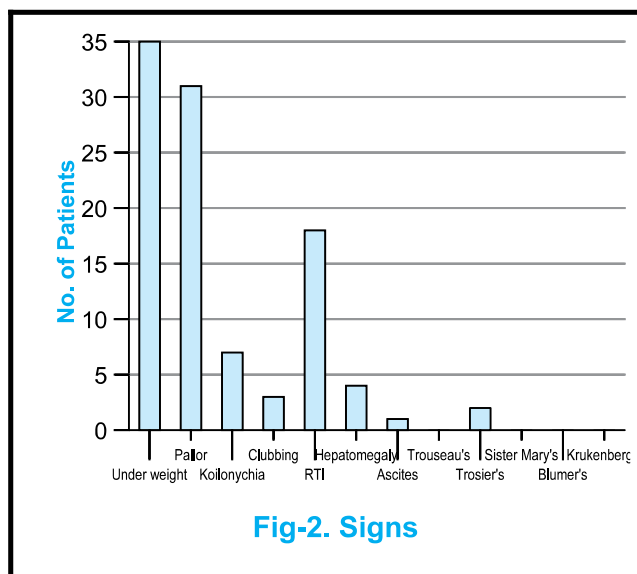
**RESULTS**

The disease occurred mostly over the age of 50 years. The youngest patient was 42 years old while the oldest patient was 81 years old, mean age being 57.60 years. The maximum incidence being in sixth and seventh decades of life. Most of the patients presented with unexplained weight-loss in the medical OPD and were referred to surgical department after endoscopy / barium studies revealed a gastric mass (Fig-1).

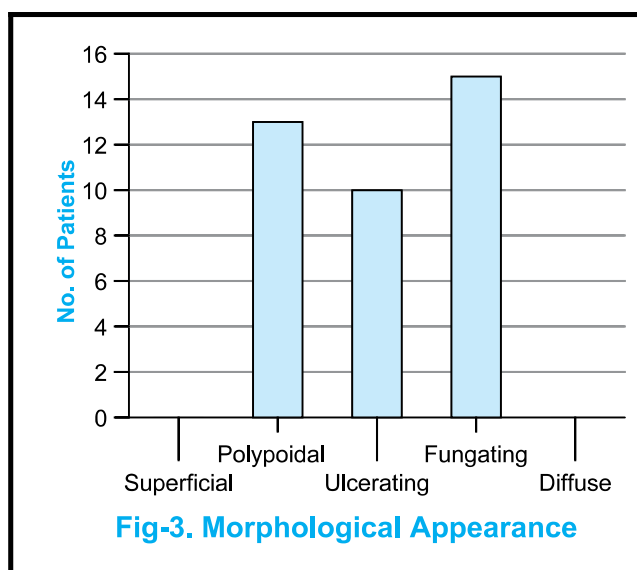


The patients almost always presented when the disease had advanced to catastrophic extents, with a mean duration of symptoms at presentation being 4.86 months. Common signs were malnourishment, weight loss and anemia. A significant number of these patients had concurrent gastric and respiratory tract infections. The signs observed in this disease are mentioned in the table (Fig-2). No specific etiological factor was detected except the facts that out of 42 patients included in the study 35 were smokers or had quit smoking during the past six years. An interesting fact pertaining to this section of patients was that nearly half of them were drivers. Nearly all of them were used to taking at least 8-10 cups of hot tea per day. Barium study and endoscopy were performed in all the patients and the diagnosis was confirmed by histopathology. The morphological

appearances observed in order of frequency were as shown (Fig-3).



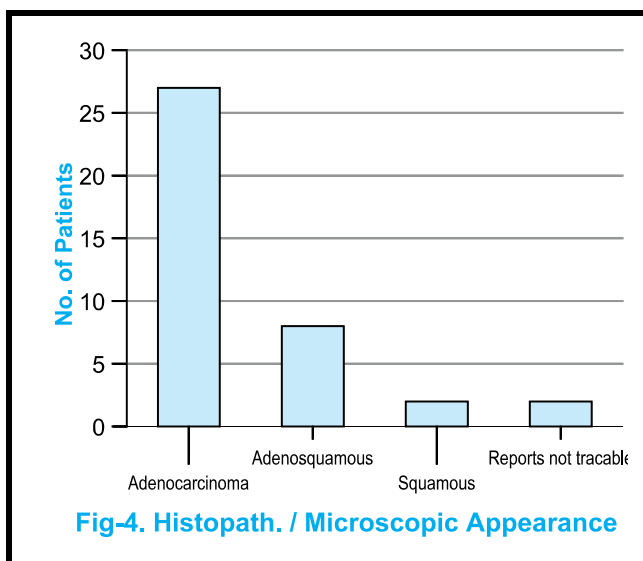
In 4 cases, despite a negative report from the endoscopist, surgery was performed on the basis of clinical symptoms and malignancy was detected on frozen section. Adenocarcinoma was the most frequently encountered histological type being 69.23 percent however two reports were lost. (Fig-4). A low level of haemoglobin was observed in 80.95 percent of the cases.



About 35 patients were found to be clinically malnourished and 34 had a haemoglobin level of less

than 10 gm/dl and thus required some sort of preoperative build up. It included high energy enteral feeding formulas, Total Parenteral Nutrition (TPN) and feeding Gastrostomies or Jejunostomies. Haemoglobin percentage was also improved by I/V blood transfusions of whole blood and Red Cell Concentrates (RCC) as required. Antibiotics were used to combat concomitant infections.

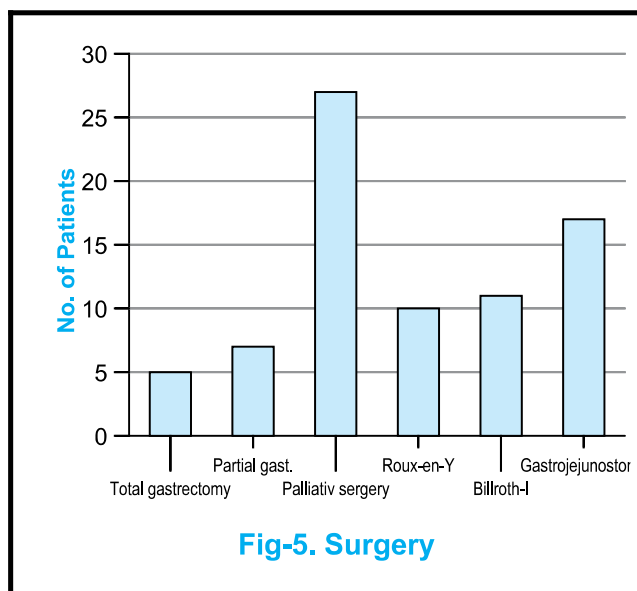
Out of 42 patients 39 were operable. 03 patients could not be operated upon due to multi-organ failure (MOF). One patient refused surgical treatment despite the fact that he was a candidate for curative resection.



Out of 39 cases selected for surgery curative resection was carried out in 12 patients, whereas the remaining 27 were subjected to palliative resections. The main reason for this low rate of curative resection was presentation of the patients at a late stage of the disease with presence of multiple distant metastases. In 7 cases out of 12, in which curative resection was performed, local resection of the tumour was complete, as judged by naked eye appearance. Proximal limit of the resection was 8-9 cm from the visible tumour.

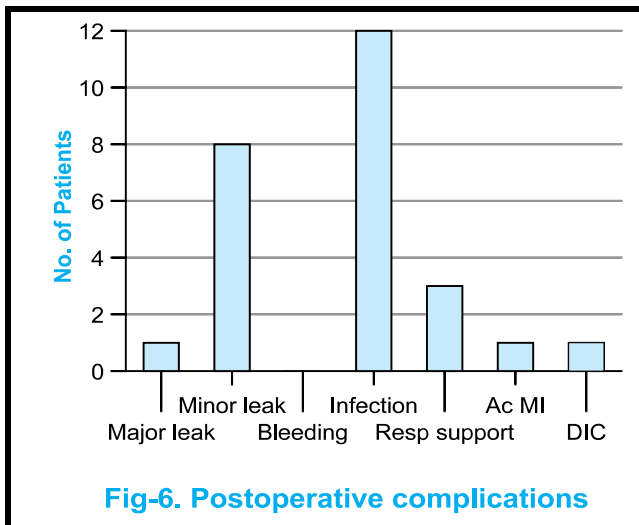
Partial resection of stomach with Billroth I reconstruction was done for tumours of distal stomach and pyloric region, where as total gastrectomy with Roux-en Y

reconstruction was performed for tumours of the body and proximal stomach. (Fig-5).

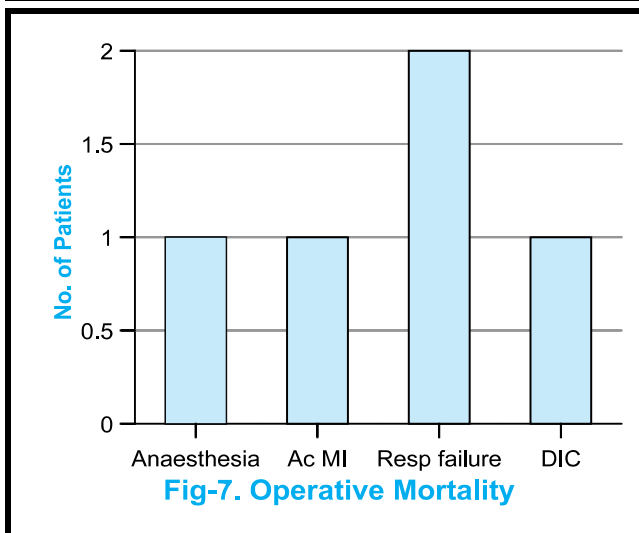


A number of postoperative complications were observed as shown in Fig-6. The operative mortality was 11.90%. (Fig-7). Out of 39 patients, on whom surgery was carried out, five died during or within one month of surgical intervention. Out of the remaining 34, only 21 patients reported in surgical out patient department for follow up. In most of the patients in whom curative resection was performed, the quality of life was reasonably good. At the end of one year, another eight patients had died of tumour dissemination and cachexia, three patients developed tumour recurrence at the anastomotic site, and one patient developed stricture at anastomotic site. Patients with recurrence were sent for radiotherapy. One patient who refused any type of surgical intervention was given radiotherapy and chemotherapy.

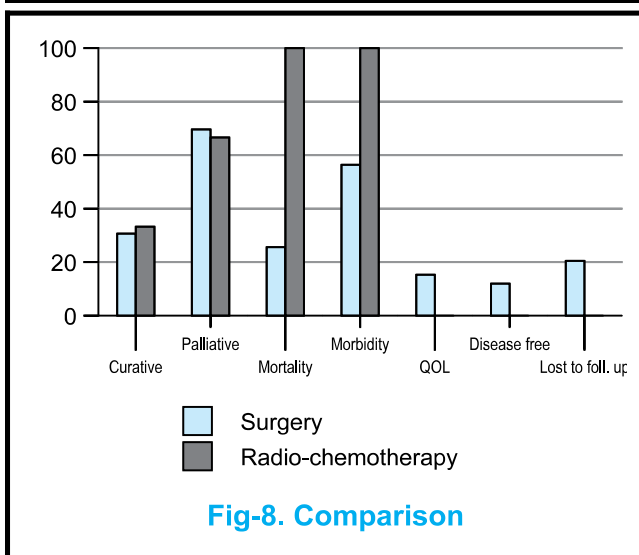
Newer modalities like LASER palliation, Intraluminal Brachytherapy and intubations were not tried due to non-availability of the equipment. Only surgery and radio chemotherapy were used as the mainstays of management. Therefore surgery and radio chemotherapy for both curative and palliative management were compared (Fig-8).



**Fig-6. Postoperative complications**



**Fig-7. Operative Mortality**



**Fig-8. Comparison**

**DISCUSSION**

Carcinoma of stomach remains a formidable disease that poses a grave threat for the sufferers. Although not a common disease the affected suffers for long, and it makes the patient weak and emaciated. Usually the patients consult their doctors when the disease is at an advanced stage and the prospects of cure are limited. At this point the only help which a surgeon can provide to his patient is a palliative procedure to relieve his symptoms.

Management of carcinoma of stomach is multidisciplinary. Surgery, when possible is one of the primary modalities offering a hope of cure in this disease.

Surgery is the only treatment modality which produces effective relief of symptoms and permanent cure. The quality of palliation afforded by surgery is reasonably superior to chemotherapy.

Mortality from surgery varied in various institutions. Operative mortality was 11.90%. Radiotherapy used for palliation had poor outcome.

Preferable method of surgery is radical partial gastrectomy for lesions at distal end and total radical gastrectomy for lesions near proximal end of the stomach. The most dangerous complication in surgical management is anastomotic leak and duodenal blow-out. Newer technique of surgical stapling though considered safer was not practiced in our study. En-block or extended lymphnode dissection was used to improve the survival with good effect. .

Use of preoperative and postoperative radiotherapy or chemotherapy known as adjuvant therapy. Five of the patients included in our study in which curative resection was done from adjuvant chemoradiation with satisfactory results. It was also used as a palliative measure in some cases but with poor results. In un-resectable cases palliative bypass was done. LASER palliation, Intraluminal Brachytherapy and intubations were not carried out in our set up as the equipment was not available.

Advancements are being made in diagnostic investigations by procuring modern equipment thus offering curative treatment to an increasing number of patients. Screening and early detection of cancers is being made. Early diagnosis should be performed by screening the high-risk group of patients.

Due to limitations mentioned earlier, it is necessary to compare this study with other studies available locally<sup>13,14</sup> and internationally<sup>5,7,15,16,17,18</sup>, to get a panoramic view of the current trends in the management of carcinoma of stomach. Age group of patients affected is much younger in the studies carried out in Japan due to their effective screening program. The ratio of female patients was higher in other studies due to the limitations sited in our study. However the results of surgery are consistently better compared to the results of other modalities in both curative and palliative management<sup>19</sup>.

The results in terms of over all survival are relatively poor compared with the international studies, mostly due to late presentation and a relatively low standard of postoperative care. Increased incidence of gastric carcinoma in people consuming hot tea and smoking was also highlighted in our study, which may be due to the trend of smoking and drinking tea, which is generally seen in our population.

Over all complication rate quoted in local studies<sup>13,29</sup> is higher than international studies, but complications related to operative technique are comparable.

## CONCLUSION

It is concluded that the curative treatment possible for cases of carcinoma of stomach is surgery either alone or in combination with radiation and chemotherapy. The most common, preventable etiological factor is smoking, probably in combination with hot beverages in excess. The most common mode of presentation remains weight loss with dyspepsia or weakness and anorexia. Most commonly effected age group is middle and old age. Fungating and polypoidal appearance of the tumour is the commonest mode of presentation. Preoperative nutritional build-up, to improve general condition, gives

good postoperative results.

Palliative surgical procedures improved the quality of life of the patient. Careful selection of cases for surgery and good operative technique resulted in improvement in mortality. Despite every effort the prognosis of disease remains extremely poor, in terms of morbidity and mortality. Screening of high-risk patients and follow up of patients is usually not up to required standards due to poor health education and awareness of the general public.

The only means currently available by which prognosis can be improved is early detection, when it is at a curable stage should be investigated middle-age dyspepsia, with careful radiology and endoscopic examination. Early diagnosis, should be achieved by screening the high-risk group of patients.

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