

## Clinical Management of Esophageal Carcinoma in Tertiary Care Centre

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### Abstract

**Background:** Carcinoma esophagus is one of the least studied and deadliest cancers worldwide because of its extremely aggressive nature and poor survival rate. Overall, at the time of presentation, more than 50% of patients had metastatic disease, near 30% had locally advanced disease and less than 20% had a localized stage that could be cured.

**Aims and Objectives:** To document and analyse: (1) Various modalities of treatment in esophageal carcinoma. (2) Surgical interventions with particular emphasis on postoperative events and their outcomes.

**Materials and Methods:** All patients with esophageal carcinoma presented to the surgical wards of KRH Mysuru from January 2019 to June 2020 for 18 months with clinical / pathological / radiological endoscopic / CT / MRI features of esophageal carcinoma. A total of 33 patients were included in the study and had undergone curative resection. This was a hospital-based cross-sectional study. Routine blood investigation, x-ray chest, abdominal pelvic ultrasound, upper GI endoscopy, HPE of biopsy, CT chest and abdomen done and patient planned accordingly into primary surgery or CRT. Postoperative complications were identified promptly and managed accordingly. Patients after recovery were followed on an OPD basis and examined thoroughly for complications.

**Results:** The incidence of carcinoma esophagus in our institution by our study was 33/645 (5.1%). The most common age group was 51 to 60 years and males outnumbered females (5.6:1). The most common location was in the middle 3<sup>rd</sup> and squamous cell carcinoma was the most common histological variant. Out of 33 cases, 14 (42%) cases were early cancer and 19 (56%) were locally advanced cancer. And 7 cases (21%) underwent NACT, and 26 cases (78%) underwent primary surgery. 21 cases (63%) got discharged within 10 days of hospital stay. 15 cases (45%) had respiratory complications. The number of postop mortality was 4 cases. Gastroesophageal reflux and dysphagia were the commonest complications during follow-up.

**Keywords:** Metastatic disease; Curative resection; NACT; Postoperative mortality; Gastroesophageal reflux; Dysphagia.

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## Background

Squamous cell carcinoma accounts for most esophageal cancers. The prevalence of adenocarcinoma is more in the USA. In squamous cell carcinoma, male to female ratio is 3:1 and it is 15:1 in adenocarcinoma.

It is usually seen in the fifth decade of life and is rare before the age of 30 years. Squamous cell cancers arise from the squamous epithelium of the esophagus. Major risk factors are smoking and alcohol. Nitrosamines, achalasia, vitamin A deficiency, long-term ingestion of hot liquids, zinc deficiency, bulimia, and Plummer Vinson syndrome are also causative factors.

Obesity, GERD, western diet, proton pump inhibitors, and lower sphincter relaxing medications are all specific risk factors for adenocarcinoma [1].

*H. pylori* is shown to be protective against esophageal adenocarcinoma. Substantial reduction in morbidity and mortality has been achieved in recent years due to the improvised standard of investigations, surgical technique and perioperative care.

Early diagnosis can't be done in a lot of patients due to late presentation; because of its biological behaviour, the study of esophageal carcinoma is interesting. It infiltrates locally, involves adjacent lymph nodes, and metastasizes widely by haematogenous spread.

The prognosis and survival rates are poor. Carcinoma esophagus ranks as the 8th most common cancer and 6th among all cancers in mortality and it is one of the least studied and deadliest cancers worldwide because of its extremely aggressive nature and poor survival rate.

The overall 5 year survival rate is 17 percent.

Reasons for this poor survival outcome stand on the fact that it is diagnosed at a rather later stage.

Overall at the time of presentation, more than 50% of patients had metastatic disease, near 30% had locally advanced disease and less than 20% had a localized stage that could be cured [2].

## Aims and Objectives

To document and analyse:

Various modalities of treatment in esophageal carcinoma.

- Surgical interventions with particular emphasis on postoperative events and their outcomes.

## Materials and Methods

This was a hospital-based cross-sectional study conducted among patients with esophageal carcinoma presenting to the surgical wards of Krishnarajesndra hospital, Mysuru during the study period (January 2019 to June 2020) with clinical/pathological/ radiological endoscopic/CT/MRI features of esophageal carcinoma.

## Methods of Data Collection

Patients' data were collected from those attending department of General surgery, Krishnarajesndra hospital, Mysore Medical College and Research Institute, Mysuru as inpatients irrespective of their age, gender, background, and socioeconomic status. The patients were evaluated and followed up according to protocol. A detailed history of the patient was entered in the proforma. A complete haemogram, blood urea, serum creatinine, LFT and serum electrolyte were sent and the results were obtained. A preliminary x-ray chest and abdominal ultrasound were done. Preliminary upper GI

endoscopy and biopsy were taken and sent for histopathological examination. The patients were put on the conservative line of management. They were informed about any surgical procedure and consent was taken.<sup>TM</sup> Patients were operated on after adequate resuscitation. With the facilities available in our hospital, transhiatal esophagectomy was done for all the patients.

Postoperative complications were identified promptly and managed accordingly. Patients after recovery were followed up on an OPD basis and examined thoroughly for complications.

### Inclusion Criteria

All patients attending Krishnarajesndra Hospital diagnosed with esophageal carcinoma by either endoscopy or histopathological biopsy.

### Exclusion Criteria

Patients presenting with metastatic disease for palliative therapy

### Sample Size

The calculated sample size was 33 with the level of significance (alpha) of 5% and absolute error (d) =14 and the prevalence of carcinoma esophagus among carcinoma GIT being 21%.

### Statistical Methods

Descriptive statistics employed in the present study- mean, standard deviation, frequency and percentage. Inferential statistics employed included chi-square test, and Crosstabs (Cramer's V) Cramer's V test.

All the statistical methods were carried out through the SPSS for Windows (version 20.0)

### RESULTS

The incidence of carcinoma esophagus in our institution by our study was 33/645 (5.1%).

**Table 1: Demographic Distribution**

Age Group (Years)	Number of Cases	Percentage			
<30	0	0			
31 to 40	1	3			
41 to 50	5	15			
51 to 60	16	48.5			
61 to 70	9	27.5			
71 to 80	2	6			
Total	33	100			
Age group distribution					
Gender	Number of Patients	Percentage	Mean	Standard Deviation	Standard Error Mean
Male	28	84.8	57.7143	8.78069	1.65939
Female	5	15.2	55.0000	7.87401	3.52136
Total	33	100.0			
Gender distribution					

**Table 2: Independent Samples Test**

t-test for Equality of Means				
t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
.645	31	.524	2.71429	4.20885

**Table 3: Distribution of tumour according to the site of the tumour**

Location	Number of Cases	Percentage
Middle 1/3	22	66.7
Lower 1/3 and GEJ	11	33.3
Total	33	100

Various studies have documented a major shift in the histological pattern of the cancer esophagus, with a double-fold rise from a traditional SCC to adenoma over the last few decades. But, observations made in our study do not correlate well with the changing trend as far as the histological pattern is concerned.

The commonest histological pattern was still squamous cell carcinoma in our institution.

**Table 4: Procedure**

Procedure	Number of Cases	Percentage
Neoadjuvant chemoradiotherapy	7	21.21
Primary surgery	26	78.8
Total	33	100

### Surgery

Open transhiatal esophagectomy was the procedure done for all 33 cases. A gastric conduit was used in all cases. Patients were selected for curative surgery according to their general condition, scope findings, the extent of disease, and histological grade of the lesion, without any metastases and complications. Out of 33 cases, 14 were early-stage cases for whom surgery was the primary option. Later on, followed by chemoradiation. Another 19 cases were locally advanced cases, out of which 7 underwent neoadjuvant chemoradiotherapy and the remaining 12 underwent primary surgery followed by chemoradiotherapy.

**Table 5: Postoperative Period**

Postoperative Hospital Stay(days)	Number of Cases	Percentage
Up to 10 days	21	63.6
10 to 20 days	9	27.3
More than 20 days	3	9.1
<b>Postoperative hospital stay</b>		
Complications	Number of Cases	Percentage
Wound infection	10	30.3
Anastomotic leak	2	6.1
Respiratory complications	15	45.5
Wound dehiscence	2	6.1
Cardiac complications	3	9.1
Anastomotic stricture	1	3
Death	4	12.1
<b>Complications</b>		
Mortality	Number of Cases	Percentage
In-hospital mortality	4	12.1
<b>Mortality</b>		

A total of 4 deaths occurred in our study. One death occurred in early-stage cancer (IIA) due to cardiac complications. Out of 3 deaths in locally advanced cancer (III to IV), 2 cases were with anastomotic leak and were on conservative management and 1 case died due to respiratory complication.

### Follow-Up

Out of 33 patients, death occurred in 4 patients and among the remaining 29 cases, 5 cases lost follow-up. Patients who got enrolled earlier in the study had longer periods of follow-up while some patients who came later were still on follow-up. As this period was not uniform and no patient was randomized to any particular form of treatment, the information obtained from this may not be accurate. However, the mean duration of follow-up was 9 months. The longest follow-up was done in a postoperative patient who died after 17 months of follow-up due to recurrence. During follow-up visits, patients were subjected to investigations to

find out any recurrence and any evidence of metastases. Those patients were referred to the chemoradiotherapy department in our hospital for further management. Since the study period was 18 months, a longer survival rate could not be calculated with the above data.

Recurrence was found in 2 patients during follow-up and both patients died in spite of chemoradiation. After a mean follow-up of 9 months, the following results were obtained.

### Survival Rate

After a mean follow-up of 9 months, 2 cases died due to recurrence. 5 cases lost follow-up. 22 cases were left behind. Among them, 15 cases had disease-free survival (68.2 %) and the remaining 7 cases had a recurrence and were subjected to investigations followed by chemoradiotherapy. All the patients who had recurrence during follow-up were locally advanced at the time of initial presentation to the hospital.

**Table 6: Chi-Square Test**

	Sex	Histology	Early stage cancer	Locally advanced cancer	Prior neoadjuvant crt	Primary surgery	Wound infection	Respiratory complications	Anastomotic leak	Wound dehiscence	Cardiac complications	Stricture	Mortality	In hospital mortality
Chi-Square	16.0 30 <sup>a</sup>	3.6 67 <sup>a</sup>	.75 8 <sup>a</sup>	.75 8 <sup>a</sup>	10.9 39 <sup>a</sup>	10.9 39 <sup>a</sup>	5.1 21 <sup>a</sup>	.27 3 <sup>a</sup>	25.4 85 <sup>a</sup>	25.4 85 <sup>a</sup>	22.0 91 <sup>a</sup>	29.1 21 <sup>a</sup>	10.9 39 <sup>a</sup>	18.9 39 <sup>a</sup>
Df	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Asymp. Sig.	.000	.05 6	.38 4	.38 4	.001	.001	.02 4	.60 2	.000	.000	.000	.000	.001	.000

a. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 16.5.

## Discussion

There was a male predominance in our study compared to females. Around 85% were males and 15% females. M: F ratio was 5.6:1. In Dhaval *et al* study 2020, it was 1.66:1 [3] And the most common age group was 51 to 60 years (48.5 percent) which is comparable to other studies. The predominant age group in Dhaval *et al* study [3] was 50 to 60 years. And also the nationwide incidence of the predominant age group as reported by Nayak *et al* was in the 6th decade.

The prominent histological type noted in our hospital was squamous cell carcinoma (66.7%). In Europe and America, adenocarcinoma is more prevalent. Observations made in our study also showed a rise in the incidence of adenocarcinoma (33.3%).

Esophageal cancer is usually located in the middle third about 50% and in the upper and lower third esophagus contributes only less [4].

In our study, we found that the middle third carcinoma was contributing about 66.7%. The lower third and up to GEJ were about 33.3%. As reported by Anderson *et al*, approximately 60% of neoplasms were located in the middle 3rd of esophagus and 30% in the distal 3rd esophagus. Hence this study was comparable with our study.

In the past, esophageal surgery was burdened by high operative morbidity and mortality rates (Lauis *et al* 1983). There has been a remarkable reduction in these rates in the last 10 years.

In our study, once the diagnosis was made, patients were assessed for operability. After clinical examination and ultrasound, if there were metastatic cases, palliative treatment was given and excluded from our study. Following this, resectability was assessed by CT of the thorax and abdomen and patients

were taken up for surgery if there was no invasion into major mediastinal structures. All 33 cases underwent transhiatal esophagectomy with or without neoadjuvant chemoradiation.

The preoperative care for those who have to undergo transhiatal esophagectomy should include prophylaxis for any postoperative complications, mainly respiratory problems.

Cessation of smoking should be done at least 10 days before surgery. And in the presence of chest-related problems, physiotherapy is advisable. In the patients with malnutrition, nutritional correction should be done for a period of 7 to 10 days before surgery like the feeding of 2500 to 3500 calories per day [5].

Transhiatal esophagectomy without thoracotomy (Orringer *et al* 1993) has been performed by an increasing number of authors in recent years. It is performed by isolating the mediastinal esophagus through a cervicotomy and laparotomy (Orringer *et al* 1984, 1987) [6]. We at Krishnarajesandra hospital Mysuru, have adopted this technique in the selected patients, for so many years.

Akiyama *et al* 1978 [7] stated that the stomach is the viscus of choice to replace the esophagus resected for cancer. It is isolated tubulized before transposition.

According to this statement, stomach tubulization allows the removal of the lymph nodes located in the gastric vessels, a possible metastasis station, improves gastric vascularisation and avoids mediastinal encumbrance which is possible when the whole stomach is transposed. We have adopted the use of gastric conduit in our hospital for all cases.

Wong *et al* 1987 [8] identified that the anastomotic leak was the main postoperative

complication. The anastomotic leakage rate in our cases was well within our acceptable range which was about 6%.

Both patients were planned for conservative management. But unfortunately, both patients died because they had other complications and comorbidities.

In this study, postop mortality was observed in 4 patients. And the causes of postop mortality were an anastomotic leak and respiratory and cardiac complications.

Contrasting data regarding the resectability rates and the long-term survival rates are reported in the literature because of varying criteria for the selection of patients for different types of treatment, and the biological behaviour of the disease. From observations in our study, the postoperative mortality rate is about 12%.

Patients were followed up after discharge from the hospital. The mean duration of follow-up was 9 months. 5 cases lost follow-up. The longest follow-up was done in a postoperative patient who died after 17 months of follow-up due to recurrence. Most of the patients who underwent chemoradiation post-surgery were alive. Almost 15 cases had a disease-free survival rate during the follow-up period.

### Conclusions

The search for a cure for carcinoma esophagus is challenging. Treatment outcomes with combined mortality strategies are usually poor, likely due to diagnosis at advanced stages and propensity for metastasis.

The efficient management strategies of esophageal cancer should include methods both for local control and systemic therapy. The best clinical outcomes are usually observed when the treatments are related to early stages and surgery could be an optimal

choice for early-stage esophageal cancer as a local control method.

Surgeries for carcinoma esophagus are highly complex procedures involving more than one cavity. And they have high morbidity rates even in large volume surgical centres. Despite great advances in surgical technologies like minimally invasive esophagectomy and perioperative management including enhanced recovery after surgery, controversies remain regarding optimal surgical methods and postoperative care. Although still associated with high mortality and morbidity, esophagectomy with reconstruction using gastric conduit is feasible if performed by an experienced surgeon. Hence surgery continues to play a pivotal role in the treatment of disease in a combination of a multimodal approach.

The challenge for us in future is to critically test our strategies in a scientific, unbiased manner and to explore other innovative treatment options.

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