

Esophageal Malignancy – Endoscopic and Clinicopathologic Patterns Study and Their Outcome in a Tertiary Hospital in South India

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ABSTRACT

Objectives: The aim of this study is to define epidemiological, clinicopathological and prognostic factors in patients with esophageal cancer.

Methods: This study was conducted in JSS Medical college & Hospital, Mysuru and the study period was from January 2020 to January 2023. All the patients who were diagnosed to have carcinoma esophagus were included in study. These patients were allowed to undergo necessary diagnostic work up and treatment. They were called for follow up at regular intervals. Data thus collected were analyzed and studied for understanding the pattern of the disease presentation, efficacy of the diagnostic modalities and management which includes Surgery, chemotherapy and radiotherapy.

Results: 71 patients with esophageal cancer were included. The mean age of esophageal malignancy was 62 years. Males were more than females (56 % v/s 44%). In our study, chronic smokers were 51%. Twenty three percent patients were alcoholics. Upper third of esophagus was found to be most common site. 82 % of patients had squamous cell carcinoma while 18% had adenocarcinoma. Out of 71 patients, surgery was done as therapy for 5(7%) patients. 60% underwent combination Chemoradiotherapy. The longest duration of follow-up was one and a half years in a post-operative patient. Among surgical patients two patients were alive at 1 and 1.5 years. The remaining were in their 2nd to 8th postoperative months and were still on follow-up and all are keeping well.

Conclusion: Carcinoma esophagus is one of the common gastrointestinal cancer in our hospital. Early diagnosis offers the only chance of cure in these patients. Unfortunately, 50 % of patients with this disease are already in advanced stage at presentation, so prognosis continues to be very poor. Chemo radiation therapy has made a real impact on current management strategies and improved survival with low morbidity in carefully selected patients.

Key words: adenocarcinoma, chemotherapy, surgery

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INTRODUCTION

Cancer of the esophagus ranks twelfth among the major cancers and seventh in the number of cancer death. Its high mortality rate makes it a major concern. Overall survival rate is 62.5% at 1 year, 42.4% at 2 years, 30% at 5 years (1).

Early stages of the disease are only found serendipitously or during screening of precursor lesion. As a result, the typical patient presents with locally advanced disease with lymph node involvement (2).

Esophageal malignancies are diagnosed by UPPER GI ENDOSCOPY with multiple biopsies. CT scan is needed to identify lung and abdominal metastases. It also helps in assessing the local invasion of the growth by delineating the invasion into mediastinal structures and for assessment of response to neoadjuvant therapy in patients with esophageal cancer. FDG PET seems to be a promising noninvasive tool for assessment of neoadjuvant therapy in patients with esophageal malignancy (3).

Surgery remains the best option for these patients providing the only chance of cure (4). Combined modality therapy including radiotherapy and chemotherapy has raised hope for improvement of survival with promising preliminary data.

Finally, for palliation of dysphagia in those patients with advanced disease endoscopic management remains standard of choice.

MATERIAL AND METHODS

It is a longitudinal study conducted in the Department of Medical Gastroenterology, JSS Medical College and Hospital, Mysuru, Karnataka – a tertiary care hospital. Study duration was from January 2020 till January 2023. A total of 71 patients who were diagnosed with Esophageal malignancy were included in the study. They were called for follow up at regular intervals.

Inclusion criteria

Patients of all ages, sex or occupation primarily

diagnosed in out patients/in patients department and later confirmed by radiological/histopathological reports were included in the study.

Exclusion criteria

Patients excluded from study were;

1. Where multiple concurrent tumors were found on CT scan in other parts of GIT.
2. Patients who were bound to be lost in follow up.
3. Patients insisting on having treatment from other hospital, other city and abroad.

Statistical analysis

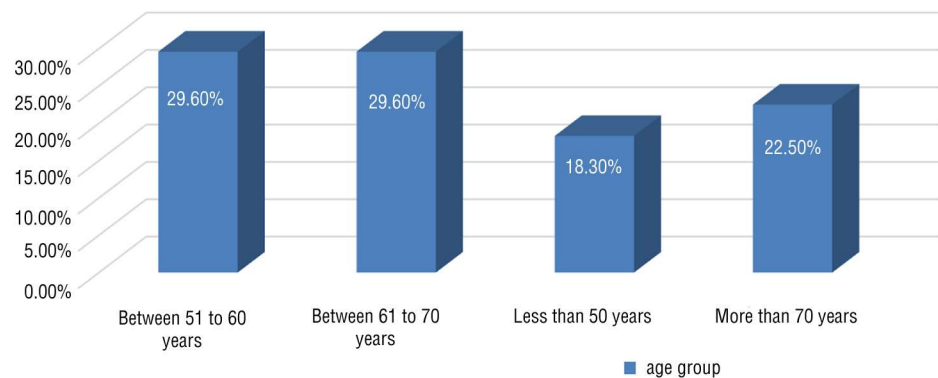
Data was collected and entered in Microsoft excel worksheet and analysed using SPSS V21 software.

RESULTS

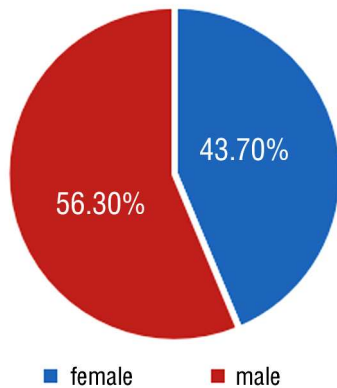
Total number of patients included in our study were 71 (*table 1*). Peak incidence of carcinoma esophagus occurred in the 5th and 6th decade of life. 29.6 % each in 5th & 6th decade (*fig. 1*). The mean age of esophageal malignancy was 62 years. Males were more than females (56 % v/s 44%) (*table 2, fig. 2*). In our study, chronic smoker was defined as a person who smokes more than 1 pack / day for at least 10 years (*table 4*). Among 40 men with the disease, 22 were smokers while women had the habit of tobacco chewing (*figs. 3, 4*). A patient was considered an alcoholic if he consumed 80gm of alcohol per week for atleast 5 years. Twenty three percent of patients were alcoholics. The average symptom duration was 8 weeks. Dysphagia was more to Solids & liquids than solids alone (94% v/s 6%) (*table 3*). Apart from dysphagia, loss of weight and appetite were the most prominent symptoms of the disease. Vomiting was present in 35% patients. Cough was associated in 9 % patients. Chest pain in 3%. Hoarseness of voice in 2 patients. On general examination, almost 60% patients had pallor. Except for general features like pallor and cachexia, the systemic examination was grossly normal in most of the patients.

Table 1 - Distribution of study subjects based on age group

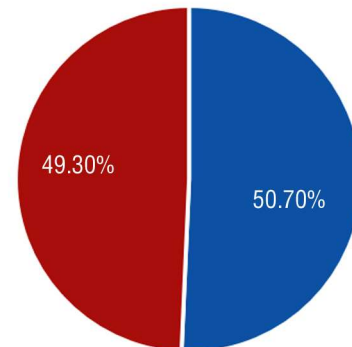
		N	%
Age Group	Between 51 to 60 years	21	29.6%
	Between 61 to 70 years	21	29.6%
	Less than 50 years	13	18.3%
	More than 70 Years	16	22.5%

Figure 1 - Graph wise distribution of study subjects based on age group**Table 2 - Distribution of study subjects based on gender**

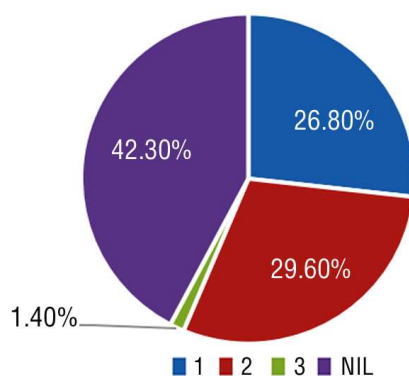
		N	%
Sex	Female	31	43.7%
	Male	40	56.3%

**Figure 2 - Graph wise distribution of study subjects based on gender****Table 4 - Distribution of study subjects based on smoking risk factor**

		N	%
Smoking	No	36	50.7%
	Yes	35	49.3%

**Figure 3 - Graph wise distribution of study subjects based on smoking risk factor****Table 3 - Distribution of study subjects based on dysphagia**

		N	%
Dysphagia	Both	28	39.4%
	Solids	4	5.6%
	Solids>Liquids	39	54.9%

**Figure 4 - Graph wise distribution of study subjects based on pack of cigarettes**

Diagnosis and management

Upper GI scopy was performed in all seventy one patients in our study. Three gross types of growths were identified in endoscopy. Ulcero-proliferative, Exophytic mass, Stricture (*table 6, fig. 5*). Upper third esophageal malignancy was found in 68% of patients (*table 7, fig. 6*). As noted in (*fig. 7, table 8*), 81.7% of patients had squamous variety of carcinoma while 18.3% of patients had adenocarcinoma.

Table 5 - Distribution of study subjects based on pack of cigarettes

		N	%
Packs of Cigarettes	1	19	26.8%
	2	21	29.6%
	3	1	1.4%
	NIL	30	42.3%

Table 6 - Distribution of study subjects based on endoscopic findings

	N	%
Endoscopy		
Ultero-Proliferative Growth in Upper Esophagus	18	25.4%
Ultero-Proliferative Growth in Lower Esophagus	15	21.1%
Post Cricoid Growth	11	15.5%
Mid Esophageal Growth	10	14.1%
Upper Esophageal Stricture	6	8.4%
Stricture In Mid Esophagus	4	5.6%
Postcricoid Growth	3	4.2%
Lower Esophageal Stricture	2	2.8%
Post Cricoid Growth With Fistula	1	1.4%
Mass With Sloughed Mucosa & Whitish Exudate In Pyriform Fossa	1	1.4%

Table 7 - Distribution of study subjects based on Location of tumour

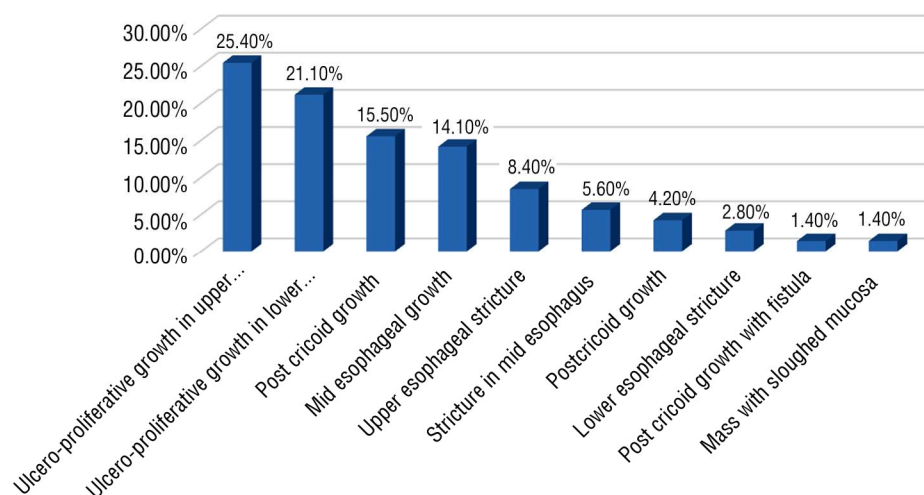
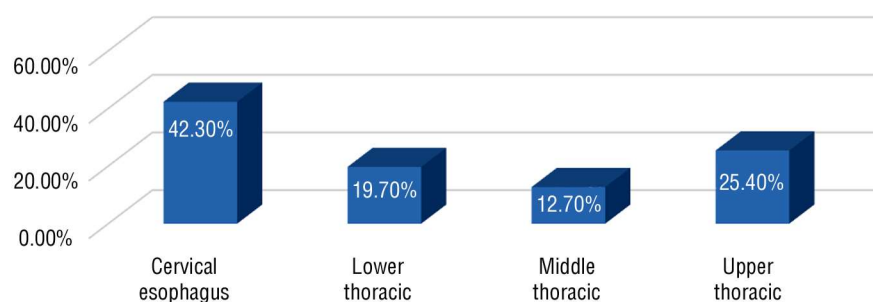
	N	%
Location of tumour		
Cervical Esophagus	30	42.3%
Lower Thoracic	14	19.7%
Middle Thoracic	9	12.7%
Upper Thoracic	18	25.4%

Table 8 - Distribution of study subjects based on type of tumour

	Count	Column N %
TYPE		
Adenocarcinoma	13	18.3%
Squamous Cell carcinoma	58	81.7%

Clinical staging

For accurate staging of early as well as locally advanced tumors according the current AJCC criteria, the role of endoscopic ultrasound is indispensable. Our patients had financial limitations and hence we had to strongly rely on CT scan for assessing tumor (T) characteristics like depth of invasion into the esophageal wall and infiltration into adjacent structures. Also for assessing mediastinal and abdominal adenopathy, CT scan was relied upon which does not have very good sensitivity and specificity. Hence our staging may be inaccurate and a proper staging evaluation may take the number of cases to higher stages (table 9).

Figure 5 - Graph wise distribution of study subjects based on endoscopic findings**Figure 6 - Graph wise distribution of study subjects based on Location of tumour**

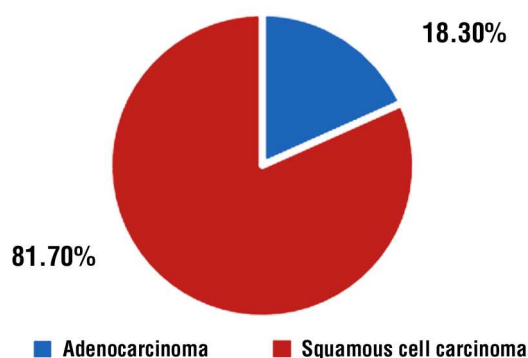


Figure 7 - Graph wise distribution of study subjects based on type of tumour

Treatment

The three main modalities of treatment offered in our hospital for cancer esophagus patients are surgery, chemotherapy and radiotherapy, often in combination. Patients are initially evaluated for operability. Surgery was the first treatment of choice in our hospital. In patients who are not fit or refuse surgery, radiotherapy was used.

Radiotherapy was used as a primary modality of therapy in patients with mediastinal invasion and for palliation of dysphagia. In a significant minority of patients who had widely disseminated disease and who were too sick for any form of anti-cancer therapy, supportive therapy was given.

Out of 71 patients, surgery was done as therapy for 5 patients (table 10, fig. 8). Actually, 13 patients were taken for surgery during the study. The remaining 8

Table 9 - Distribution of study subjects based on staging of tumour

		N	%
Staging	IA (T1N0M0)	1	1.4%
	IB (T2N0M0)	8	11.3%
	II A (T3N0M0)	4	5.6%
	IIB (T1N1M0)	1	1.4%
	IIB (T2N1M0)	20	28.0%
	III (T3N1M0)	2	2.8%
	III (T4N1M0)	1	1.4%
	IIIA (T4aN0M0)	12	16.9%
	IIIB (T4aN1M0)	8	11.3%
	IV	13	18.3%
	IVA(T3N2M0)	1	1.4%

Table 10 - Distribution of study subjects based on treatment

		Count	Column N %
Treatment	CT + RT	29	40.6%
	RT	23	32.4%
	Surgery + FJ + CT	4	5.6%
	Endoscopic dilatation + CT + RT	7	10%
	Endoscopic -Sems + CT + RT	7	10%
	Esophagectomy+CT	1	1.4%

patients had intraoperative findings that precluded resection. After postoperative recovery, Nine received combination chemotherapy and four received radiotherapy. Six patients had mucositis & three patients developed pulmonary complications, which were managed conservatively (table 11).

Figure 8 - Graph wise distribution of study subjects based on treatment

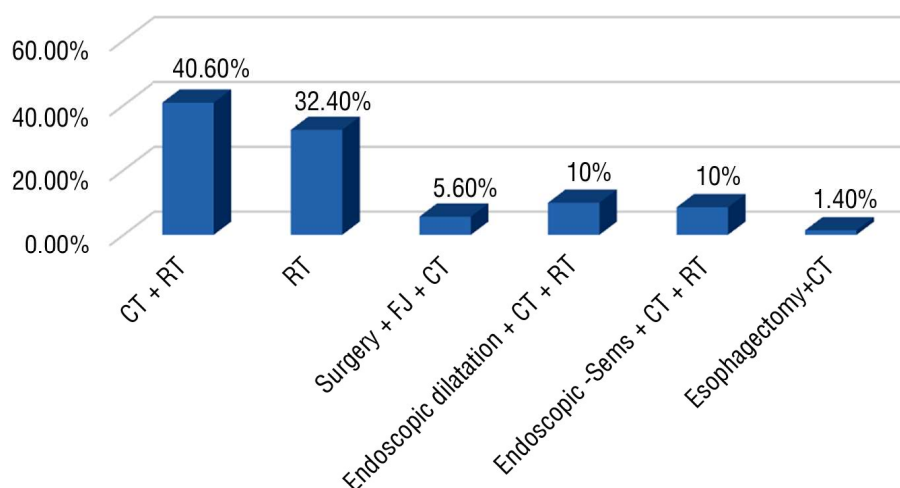


Table 11 - Distribution of study subjects based on treatment related complications

		N	%
Treatment related complications	Mucositis	6	8.5%
	Nil	62	87.3%
	Pulmonary complications	3	4.2%

Follow-up & outcome

The mean duration of follow-up was 5.24 + 7 - 2.12 months. The longest duration of follow-up was one and a half years in a post-operative patient. Among surgical patients two patients were alive at 1 and 1.5 years. The remaining were in their 2nd to 8th postoperative months and were still on follow-up and all are keeping well. The patients who were found inoperable on table died on an average between 2 and 6 months following treatment.

Three out of 23 patients survived beyond one year. The remaining patients were lost to follow-up. Only one out of 29 patients who received chemotherapy as their primary therapy was surviving at the end of 1 year. Thirty-two percent expired at the end of 3 months while 56% died between 3-6 months (*table 12*). Ten percent did not survive beyond 6 to 12 months. Of the patients who were not treated by any modality, none survived beyond 6 weeks. Patients with poorly-differentiated cancers did not survive beyond 6 months.

DISCUSSION

Carcinoma esophagus is one of the most common gastrointestinal tract malignancies. The male: female ratio in our study was 1.4:1. Worldwide, esophageal cancer is much more common in males compared to females. The maximum occurrence of this malignancy in our study was found in the fifth and sixth decade of life which was similar to the nationwide incidence as reported by Pennathur et al (5).

Population-based studies demonstrate that tobacco and alcohol use are independent risk factors and their effects are multiplicative, as evidenced by the

association of the highest risk of developing esophageal cancer with heavy use of both agents. Cigarette smoking is also a risk factor in the development of carcinoma of the esophagus. Ninety percent of patients with adenocarcinoma in our study were heavy smokers. Although tobacco smoke contains known or putative carcinogens such as nitrosamines, 2-naphthylamine, benzopyrene and benzene, causative agents and their mechanisms of action for esophageal cancer have not been elucidated.

The consumption of alcoholic beverages is a major contributing factor in the increased risk of esophageal squamous cell carcinoma in Western countries. Although specific carcinogens may be present in a variety of alcoholic beverages, in all likelihood it is alcohol itself, either as a mechanical irritant, promoter of dietary deficiency, or contributor to susceptibility to other carcinogens, that leads to carcinogenesis. In our study, 16.0% of patients were alcoholics.

Gastroesophageal reflux disease has been implicated as one of the strongest risk factors for the development of adenocarcinoma of the esophagus. Chronic reflux is associated with Barrett's esophagus, the premalignant precursor of esophageal adenocarcinoma. Although no patients had documentation of either GERD or Barrett's esophagus in our study, 6 out of 13 adenocarcinoma patients had history that was strongly suggestive of GERD (6).

The overwhelming majority of esophageal malignancies may be classified as either squamous cell carcinomas or adenocarcinomas. Squamous cell carcinomas account for the vast majority of cancers arising in high-incidence areas throughout the world (7). Eighty two percent of our patients had squamous cell cancer while 18% had adenocarcinoma which is in sharp contrast to United States where only 40% were squamous variety. This reflects the difference in epidemiology and the fact that adenocarcinoma is not rising in incidence in less well-developed nations like ours compared to the West (8).

The symptoms most commonly associated with esophageal cancer are dysphagia and weight loss. Unfortunately, in most instances dysphagia signifies locally advanced disease or distant metastases or both.

Table 12 - Distribution of study subjects based on outcome

		TYPE			
		ADENOCA		SCC	
		Count	Column N %	Count	Column N %
Out come	Discharged	8	61.5%	40	69.0%
	Mortality	5	38.5%	18	31.0%

Chi Square = 0.267 p= 0.60

At presentation, patients usually describe progressive dysphagia, with difficulty initially in swallowing solids then liquids and in most extreme circumstances, their own saliva. In our study, all but one patient had dysphagia.

Substantial weight loss accompanying dysphagia is seen in approximately 90% of patients with squamous cell carcinoma. In our study, 75% had significant weight loss. Approximately 20% of patients experience odynophagia (painful swallowing).

Esophagogastroscope allows precise evaluation of the extent of esophageal and gastric involvement and can precisely measure the distance of the tumor from the incisors to appropriately categorize the tumor's location (9). This is limited by the fact that negotiation into the stomach and duodenum will not always be possible because of totally occluding growths. In this study, 27% failure rate in negotiation into stomach was observed. Upper endoscopy also allows identification of "skip" lesions or second primaries as well as indicating the presence and extent of Barrett's esophagus (10).

On completion of the initial diagnostic workup and after a tissue diagnosis of esophageal cancer, pre-treatment staging procedures are essential to accurately determine the depth of esophageal wall penetration, the status of regional lymph node basins, and the presence or absence of distant metastases so that patients can be guided to the appropriate treatment options and provided with prognostic information (11). All patients should undergo a computed tomography (CT) scan of the chest, abdomen, and pelvis as the initial evaluation for extent of disease. CT scans are highly accurate (approaching 100%) in detecting liver or lung metastases and suggesting peritoneal carcinomatosis (ascites, omental infiltration, peritoneal tumor studding etc) (12). Accuracy for detecting aortic involvement or tracheo-bronchial invasion exceeds 90% (13).

CT is inaccurate in determining T stage, because it cannot define individual layers of the esophageal wall and will miss small T1 and T2 tumors (14). CT assessment of regional or distant lymph nodes is hindered by relatively low sensitivity (50% to 70%) due to its reliance on size criteria (larger than 1 cm) alone. Because lymph node involvement is frequently seen in small or normal-size lymph nodes, the false-negative rate is high, and despite a reasonable specificity of 85%, accuracy in determining lymph node involvement is limited (approximately 60%) (15).

The staging was done using TNM system according to the latest AJCC (16).

The goal of treatment for esophageal carcinoma

remains cure of the neoplasm for early stage, improvement of the disease-free and overall survival in advanced disease, relief from dysphagia, and improvement of quality of life for patients with metastatic disease and with minimal morbidity (17).

The following guidelines seem to be generally accepted:

- T1 or T2 tumors with no evidence of lymphatic metastases at endosonography (NO) or CT scan: surgical resection seems to be the treatment of first choice.
- T3 or T4 with nodal involvement (N +): inclusion into trials, surgical resection after preoperative radiochemotherapy may be preferable. Currently available data suggest that resection of the residual mass in responding patients are required for adequate tumor control (18-20).
- Patients with significant comorbidity considered unfit for major surgery should be treated by radiochemotherapy.
- Metastatic disease: palliative treatment only.

In our study, after initial endoscopic diagnosis, patients were assessed for operability. If ultrasound or clinical examination reveals metastatic disease, only palliative therapy was given. Following this resectability is assessed by CT scan of thorax and abdomen and patients are taken up for surgery if there is no invasion into major mediastinal structures.

CONCLUSION

Early diagnosis offers the only chance of cure in these patients. Unfortunately, 50 % of patients with this disease are already in advanced stage at their presentation, and so the prognosis continues to be very poor. Also, early diagnosis itself is difficult as dysphagia which is the cardinal symptom occurs relatively late in the course of the disease. Primary endoscopic screening is also impossible in our country as the cost benefit ratio of undertaking will not be acceptable (21).

However, advances have been made in the management of esophageal carcinoma; the key is to select the most appropriate combination for individual patients. Surgeons play a central role in direction treatment of this disease by advising on how best to integrate surgical resection with non operative programs. Our study shows very good survival rate in patients who underwent surgical resection which partly may be due to the stage at their presentation. Still, it is highly recommended to aim at improving the results further, so that low mortality rates for resections are used to compare with seemingly safer therapies (22).

Chemo radiation therapy has made a real impact on current management strategies and our study shows low morbidity in carefully selected patients. Distant metastasis remains a major problem even in the best centers and search is on for more effective systemic drugs. The challenge for future for us is to identify esophageal cancer at early stage & critically test our strategies in a scientific, unbiased manner and to explore other innovative treatment option.

Conflicts of interest

None declared.

Funding

None declared.

Ethical statement

Informed Consent taken, as well as Ethical Committee Approval.

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