



Patterns Of Care, Prognostic Factors and Survival in Carcinoma Esophagus at Tertiary Care Hospital

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Abstract

Background: Esophageal cancer is one of the common malignancies in Kashmir, and the optimal treatment for it is still debatable. Our aim was to document the current patterns of care along with the associated outcome in form of survival in esophageal cancer at tertiary care institute. Various prognostic factors for carcinoma esophagus and its effect on the survival was studied.

Method: It was a retrospective study for a period of four years. The data was collected from the files at regional cancer center at tertiary care institute.

Results: The total of 1416 patients were included in our study out of total 1609 registered patients over a period of four years. It was seen that most of the patients were in 5th to 6th decade of life with slight male preponderance. Patients without comorbidities and good performance status had better survival. Use of tobacco and related products, advanced age had bad prognostic effect on survival. Well differentiated and mid esophageal lesions had better survival. Higher the stage at presentation worse was the outcome. Most of the patients presented in stage III (66.1%) followed by stage IV (23.6%). Radiation alone as treatment modality was used in maximum patients (37.78%). Concurrent chemoradiation was received by 421 patients (29.73%) with a 3year survival of 24.7%. Patients receiving triple modality (chemotherapy/radiation /surgery) accounted for 11.22% of the total patients and had 3-year survival of 45.28%.

Conclusion: Chemoradiation alone or combined with surgery has been increasingly used in the management of carcinoma esophagus. Chemoradiation prolonged survival when it was used as definitive treatment or combined with surgery. Out of total 1609 patients 193 patients defaulted, the reasons for which remain unknown. Comprehensive prospective patterns of care studies are needed to further refine the management in these cancers, which include major proportion of cancer burden in our population.

Keywords: Esophageal Carcinoma, CA Esophagus, Patterns of Care, Survival in CA Esophagus, Chemoradiation, Radiotherapy, CA Esophagus in Kashmir

INTRODUCTION

Esophageal cancer is one of the common malignancies of the gastrointestinal tract (GI). As per the World Health Organization (WHO), Globocon 2018, esophageal cancer is the 7th most common cancer (3.2%) in the world, and 6th most common cause of cancer related mortality (5.3%).[1] Among the malignancies of the GI, esophageal cancer accounts for 3.2% of all the newly diagnosed cancer patients in

the world, which is behind colorectal (10.2%) and stomach (5.7%) cancer.[1] Esophageal cancer accounts for about 5% (407,000 deaths) of all cancer deaths annually in the USA.[2],[3] In India, as per WHO, Globocon 2018, esophageal cancer is the 6th most common cancer with incidence of 5.04%. It is 5th most common cancer in males and 6th most common cancer in females.[1] The male to female ratio in India

is 2.4:1.[1] Incidence of esophageal carcinoma in Kashmir is 12per lakh population as per PBCR 2019(unpublished data).

Squamous cell carcinoma (SCC) and adenocarcinoma (AC) are the two main histological types of esophageal cancer. The most common form of esophageal cancer worldwide is SCC. About 90% of the esophageal carcinoma in the residents of Asia, Africa, and Eastern European countries is SCC.[4] In the western world, the incidence of SCC has declined steadily over the past three decades while AC has increased simultaneously. AC is now the most dominant histological type in the western world.[5] Studies from India show that the proportion of AC varies from 6% to 54% of all esophageal cancers.[6],[7],[8],[9] Some studies identify the upper third while others, the middle third as the most common site for SCC.[10] Esophageal cancer is a disease of advanced age, peaking in the seventh and eighth decades of life.

Primary treatment modalities include surgery, radiation, chemotherapy or combined modality treatment depending upon stage of the disease.

Patterns of Care studies provide important information on the receipt of cancer therapies, data on radiation therapy, immunotherapy, and chemotherapy. Data gathered through the patterns of care studies are used in a number of ways. For example, the data help investigators examine disparities in cancer treatment among age, racial/ethnic groups, and urban/rural residents. They also provide information about the dissemination of new therapies into community practice.

Till date not much information has been provided regarding the topic of research, its conflicts in theory, methodology, evidence and conclusion. As the topic is important for the management of patient at the level of tertiary care so needs to be well reviewed, and has been put under as subject of research to improve the standards of management.

Aim and objective

- 1) To provide an idea of pattern of care in esophageal cancers.
- 2) To define length & quality of survival in relation to anatomic site, clinical stage & aspects of types of treatment.

- 3) To show time trends in proportions of early to late stages at time of diagnosis.

MATERIAL & METHODS

The study was conducted retrospectively, in which patient record was retrieved from the files in regional cancer centre at the tertiary care institute. Out of total 1609 histologically proven esophageal cancer patients 1416 were included in the study. Clinical profile of the recruited patients was studied thoroughly, which included:

- Patient profile: Age, sex, performance status, co-morbidities, habits.
- Tumor related factors: Histopathology, differentiation of carcinoma, site of disease, stage of disease,
- Treatment received: radiation-therapy,chemotherapy,surgery.
- Disease status at 6 months was evaluated, and in case of progression of disease or residual disease the modality of treatment used was studied.
- Survival for types of treatment modalities received was studied.
- Survival for each of the parameters was evaluated at 1 year and then at 3 year.

Inclusion criteria

All the histologically proven cases of esophageal cancer who received treatment in the institute.

Exclusion criteria

The patients who registered with RCC but refused treatment/defaulters.

RESULTS-

Over a period of four years 1609 histologically confirmed esophageal cancer patients were registered with regional cancer center, out of which 1416 patients fulfilled the inclusion criteria and were included in our study. These patients were studied with respect to following parameters:

Age: 682(48.16%) were in the age group of 41-60 years, followed by 632(44.64%) in the age group of 61-80 years. There were 73(5.16%) patients in the age group of 21-40 years and only 29(2.04%) patients > 80 year. There was no patient below 20 years. Maximum

survival was seen in age group of 41-60 years with survival of 56.60% at 1 year and 32.55% at three years. The results are summarized in Table 1 & Figure 1.

Gender: 793(56.08%) were male with a survival of 52.08% at 1 year and 24.84% at 3 years. 622(43.92%) patients were female with a survival of 54.66% at 1 year and 25.08% at 3 years. The combined survival at 1 and 3 year was 53.18% and 24.9% respectively. (Table 2 & Figure 2)

Performance status: Maximum survival of 73.24% and 35.2% at 1 year and 3 years respectively is seen in the patients with performance status of 1, whereas least survival of 4.8% and 0.60% at 1 year and 3 years respectively in patients with performance status of 3. (Table 3 & Figure 3)

Co-morbidity: Patients without any co-morbidity had an overall survival of 57.76% at 1 year, whereas survival was least in patients with multiple comorbidities. (Table 4 & Figure 4)

Personal habits: It was seen that those patients who didn't smoke or snuff had a survival of 75% and 35.27% at 1 year and 3 years respectively (Table 5 & Figure 5). Those patients who were cigarette smoker had least survival of 31.11% and 16.9% at 1year and 3year respectively, to be followed by hukka smokers and snuffers respectively. Among smokers, 33.9% were male and only 2.7% were female (Table 6 & Figure 6).

Location of tumor: According to location of esophageal tumor, upper and lower esophageal tumors had lower survival at 1 year and 3 years as compared to tumors located in the middle esophagus (Table 7 & Figure 7).

Histopathology: 1291 patients had squamous cell carcinoma with survival of 51.35% at 1year and 23.31% at 3year, 123 patients had histologically proven adenocarcinoma with survival of 72.39 at 1year and 41.4 at 3year and 2 patients had neuroendocrine carcinoma (Table 8 & Figure 8).

Tumor differentiation: Patients who had well differentiated tumor (19.2%) had a survival of 64.44% and 33.33% at 1 year and 3 years respectively (Table 9 & Figure 9) as compared to poorly differentiated tumor (24.8%), where the survival at 1 year and 3 year was 41.59% and 20.80% respectively.

Stage of disease: Maximum survival at 1year (93.1%) and 3year (75.17%) was seen in patients with stage II disease, as compared to patients with stage IV disease, where survival was 18.86% and 0.59% at 1 year and 3 years respectively (Table 10 & Figure 10).

Treatment modality received: Patients who received triple therapy with surgery plus chemo-radiation, survival was 70.44% and 45.28% at 1 year and 3 year respectively. 535 patients received radiation as sole modality with survival of 40.56% at 1 year and 15.5% at 3 years. 421 patients received definitive concurrent chemo-radiation with survival of 67.93% at 1 year and 24.7% at 3 years (Table 11 & Figure 11)

Dose of radiotherapy: 1285 patients received radiotherapy (Table 12 & Figure 12) out of which most patients (495) were treated with 50.4Gy

Disease status at 6 months: After receiving various treatment modalities, disease status was studied at various intervals, at 6 months (Table 13 & Figure 13) in 9.1% patients, NED was seen while as residual/regression was seen in 28.6% of patient. Disease progression was seen in 24.5% patients and a total of 8.1% patients expired.

Treatment modality used for progression or residual disease: Those patients with residual disease 3.2% received chemotherapy and 6.5% received radiotherapy as shown in Table 14 & Figure 14

Vital status at 1year and 3year: At 1 year it was seen that 53.2% patients survived while as 23.7% expired and status of 23.1% was unknown (Table 15 & Figure 15). Further survival at 3 year is shown in Table 18. It was seen that 24.9% (353) were alive at 3 years, while as 49.9% (706) died and 25.1% (356) were among those whose status was unknown as shown in Table 16 & Figure 16.

DISCUSSION

In our study 1416(46.35%) cases of oesophageal cancer were studied, out of which maximum patients that is 48.16% were in age group of 40-60 years followed by 44.64% in age group of 61-80 years, which correlates with the study done by Gomi *et al*¹¹ where median age of the patients was 62.3year. A male preponderance was seen among the patients (56.08%) as compared to female; same trend was reported by MP Barman *et al*¹² (67% male against 33% female). The survival declined in older age group and with

associated co-morbidity. Survival was seen to be better in patients with performance score 1 and earlier stages of disease (I and II) as was seen by Gomi et al¹¹ and LR Coia et al¹³ and Polee et al¹⁴. Smoking was associated with lower survival in our study; smoking has been established to be risk factor for development of oesophageal cancer in various studies. Kamangar et al¹⁵ in their study found that more than 90% cases are attributed to smoking and alcohol consumption in developed countries while as in less developed countries lower consumption of fruits, vegetables, selenium, zinc and vitamin E, poor oral hygiene are associated with higher incidence of oesophageal cancer. In Kashmir particularly smoking is common in the form of hukka smoking and cigarette smoking, which may be an important factor in development of oesophageal cancer. Kamangar et al¹⁵ compared incidence of oesophageal cancer across various continents and found that oesophageal cancer to be eighth most common cancer in world with incidences two-fold higher in less developed countries. Incidence was found to be two to three folds higher in male population.

In our study survival of patients with squamous cell carcinoma was found to be lower than adenocarcinoma, which is in agreement to the study done by Siewert et al¹⁶ in which they found survival better in adenocarcinoma patients and identified adenocarcinoma as a favourable independent predictor of long-term survival. Survival also correlated with the differentiation of tumour, as we found that well differentiated tumour had better survival as compared to poorly differentiated tumour. Location of the tumour was also seen to have effect on survival in our study, both upper and lower esophageal tumours have seen to have lower survival as compared to tumours in middle third of esophagus.

We found that most of the patients of carcinoma esophagus were treated by radiotherapy alone either because of low performance status or because of advanced stage, in which case it was given with palliative intent (to relieve symptoms or haemostasis).

Maximum survival was seen in patients receiving triple therapy with surgery followed by chemotherapy, as was observed in the study conducted by Shao et al¹⁷ but there were only 159(11.22%) patients who received this treatment. Concurrent chemoradiation was the second highest form of

treatment modality received by our patients of carcinoma esophagus and the survival was also better in these patients (67.93% at 1year and 24.7% at 3 year) when compared to patients who received radiotherapy alone. Similar results were obtained by Cooper et al¹⁸, LR Coia¹³ and Rebecea et al¹⁹. Gebiski et al²⁰ compared Ten randomised comparisons of neoadjuvant chemoradiotherapy versus surgery alone (n=1209) and eight of neoadjuvant chemotherapy versus surgery alone (n=1724) in patients with local operable oesophageal carcinoma, this comparison indicated a 2-year absolute survival benefit of 7%. In our study survival was also found to be better in patients receiving triple therapy as compared to surgery alone. Chemotherapy alone was given in palliative settings. The possible reason for better results in multimodality therapy, in this study, is due to selection of therapy with curative intent in these patients, whereas in radiotherapy only and chemotherapy only groups the primary intention of treatment mostly remains palliative, either due to advanced disease or poor performance status.

When disease status at 6 months was evaluated, it was found that only 9.1% had no evidence of disease (NED), 28.6% had residual disease, 24.5% had progression and 8.15% had expired. Status of 29.2% patients was not known because they were lost to follow up and could not be contacted for assessment of disease status. Since this study was retrospective, there was a significant proportion of patients who were lost to follow-up and their records could not be retrieved. Since, in esophageal cancer, most patients need relief of local symptoms, mostly in the form of dysphagia, therefore the possible reason for employing radiotherapy more often than chemotherapy in case of progression of disease or residual disease.

Hence it can be said that earlier the disease is treated better are the chance of survival of the patient and use of multimodal treatment is more effective than use of single therapy.

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Age	Frequency	% age	Survival 1yr	% survival 1yr	Survival 3yr	% Survival 3yr
≤20	0	0	0	0	0	0
21-40	73	5.16	36	49.31	19	26.03
41-60	682	48.16	386	56.60	222	32.55
61-80	632	44.64	321	50.79	112	17.72
>80	29	2.04	10	34.48	1	3.44
Total	1416	100	753		353	

TABLE 1: Effect of age on survival in carcinoma esophagus

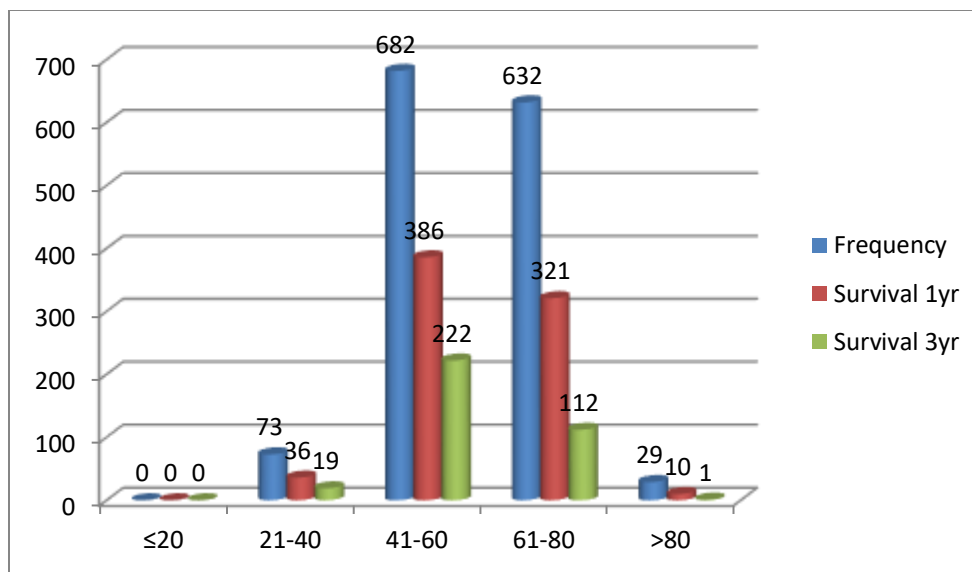


FIGURE 1: Effect of age on survival in carcinoma esophagus

Gender	Frequency	% age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Male	793	56.08	413	52.08%	197	24.84%
Female	622	43.92	340	54.66%	156	25.08%
Total	1416	100%	753	53.18%	353	24.9%

TABLE 2: Gender distribution and gender specific survival in carcinoma esophagus.

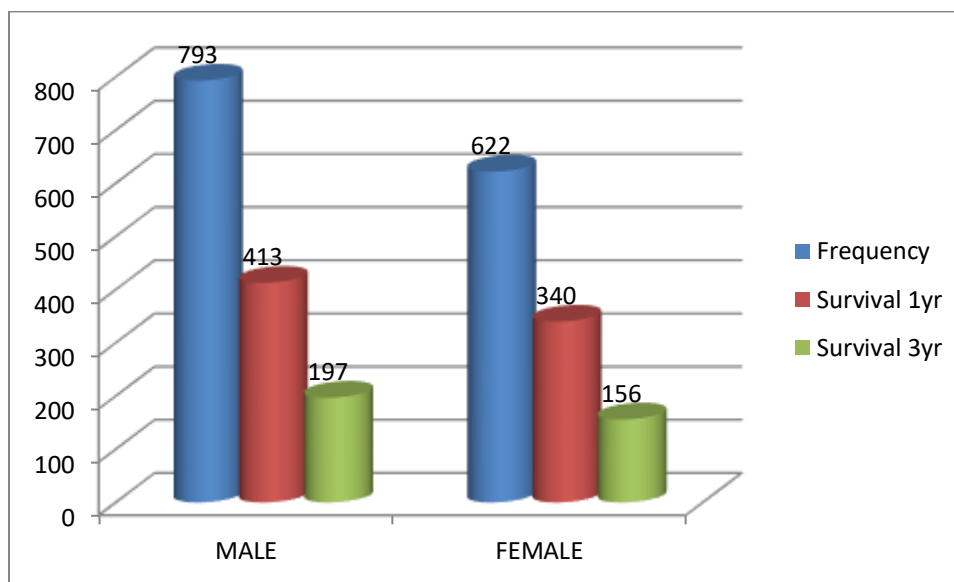


FIGURE 2: Gender distribution and gender specific survival in carcinoma esophagus.

Performance status	Frequency	Percent	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
0	0	0	0	0	0	0
1	699	49.1	512	73.24%	246	35.2%
2	551	39.3	233	42.28%	106	19.23%
3	166	11.6	8	4.8%	1	0.60%
4	0	0	0	0	0	0
Total	1416	100.0	753		353	

TABLE 3: Effect of performance status on survival in carcinoma esophagus.

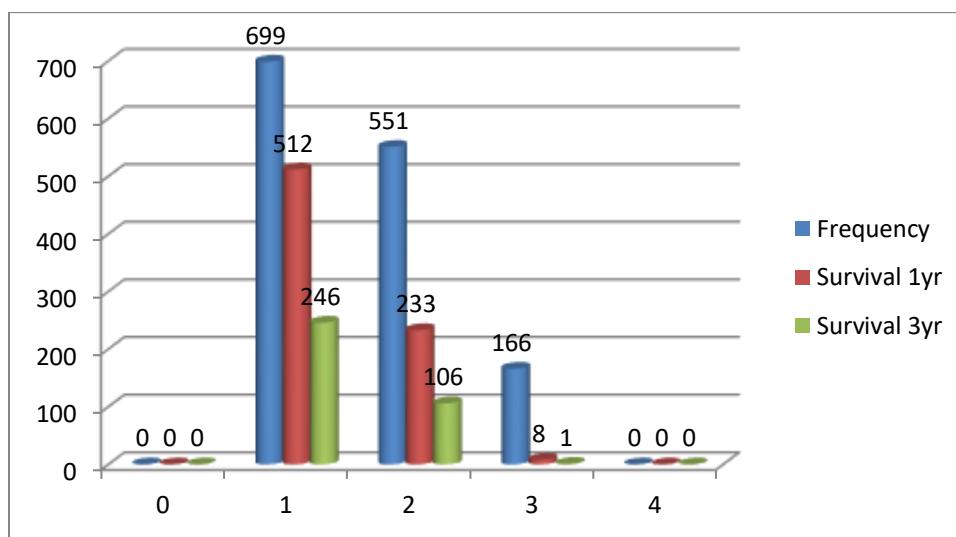


FIGURE 3: Effect of performance status on survival in carcinoma esophagus.

Comorbidity	Frequency	Percent	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Diabetes	16	1.12	07	43.75	3	18.75
Hypertension	466	32.9	219	46.99	128	27.46
Hypertension + diabetes	32	2.25	13	40.62	04	12.5
Not known	902	63.9	521	57.76	221	24.5
Total	1416	100.0	753		353	

TABLE 4: Effect of co morbidities on survival in carcinoma esophagus.

Habits	Frequency	%age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Hukka smoker	244	17%	93	38.11	42	17.21
Smoker (cigarette)	450	31.2%	140	31.11	76	16.9
Snuffer	140	9.7	82	58.57	29	20.71
Non smoker	584	41.2%	438	75.0	206	35.27
Total	1416	100.0	753		353	

TABLE 5: Tobacco habits and their effect on survival in carcinoma esophagus.

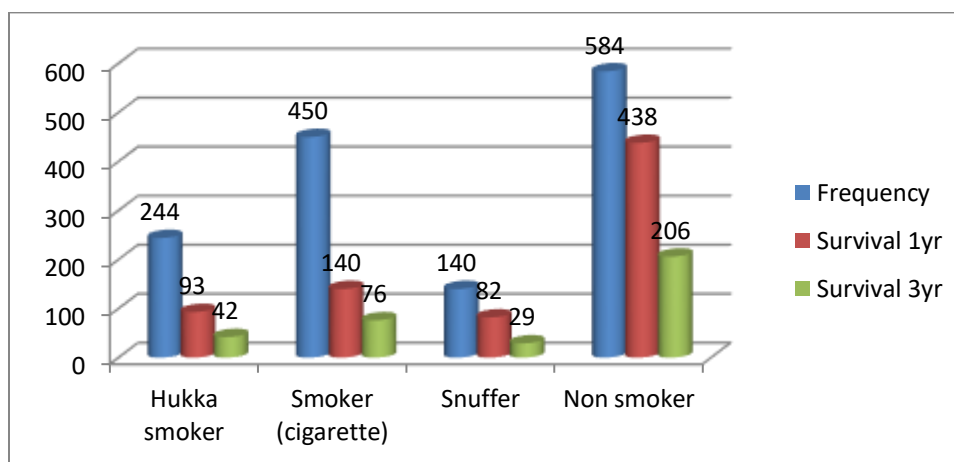


FIGURE 5: Tobacco habits and their effect on survival in carcinoma esophagus.

Habits	Male		Female	
	Frequency	%age	Frequency	%age
Hukka smoker	126	15.6	118	18.9
Smoker (cigarette)	433	33.9	17	2.7
Snuffer	84	10.3	56	9.0
Non smoker	316	39.8	431	69.2

TABLE 6: Gender specific distribution of tobacco habits in carcinoma

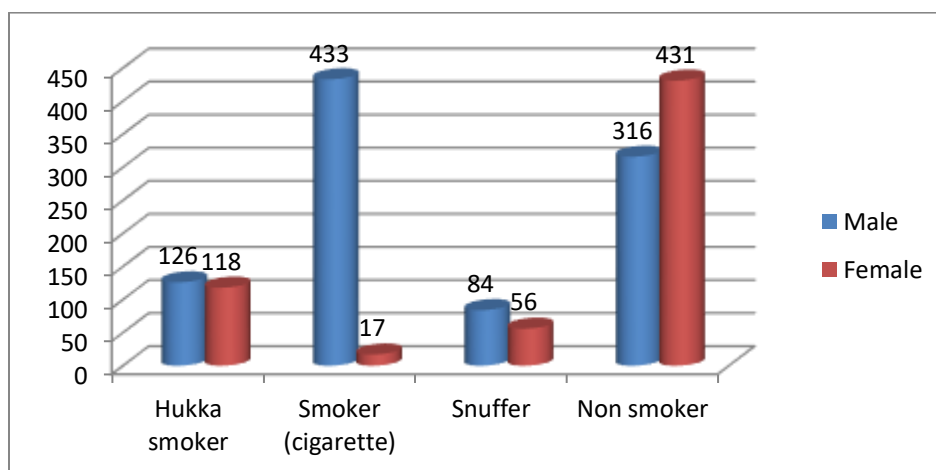


FIGURE 6 Gender specific distribution of tobacco habits in carcinoma

Location	Frequency	%age	Survival 1yr	%Survival 1yr	Survival 3yr	%Survival 3yr
Upper	132	9.3%	68	51.51	22	16.6
Middle	651	46%	359	55.1	158	24.27
Lower	633	44.7	326	51.5	173	27.33
Total	1416	100%	753		353	

TABLE 7: Location wise distribution of carcinoma esophagus & survival.

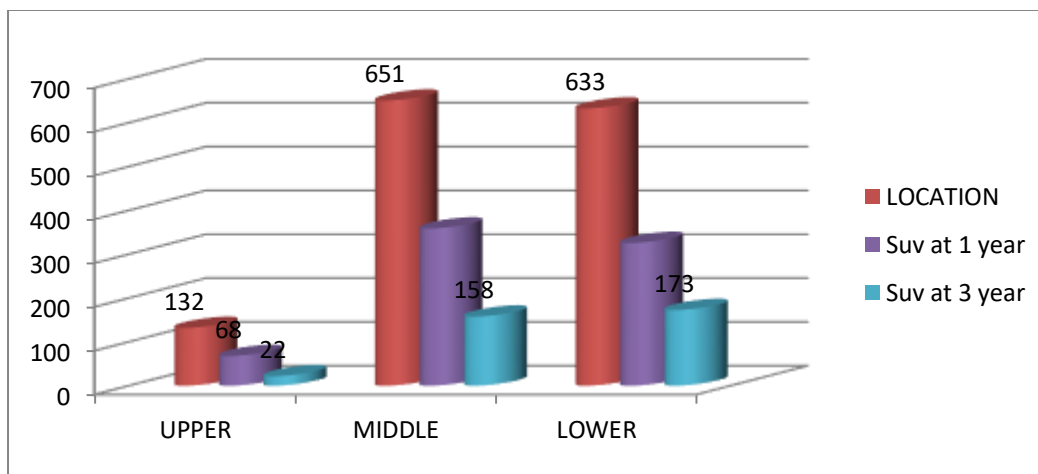


FIGURE 7: Location wise distribution of carcinoma esophagus & survival

Histopathology	Frequency	%age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Squamous cell carcinoma	1291	91.2	663	51.35	301	23.31
Adeno carcinoma	123	8.7	89	72.39	51	41.4
Neuroendocrine carcinoma	2	.1	1	50	1	50
Total	1416	100.0	753		353	

TABLE 8: Histopathology wise distribution of carcinoma esophagus & survival.

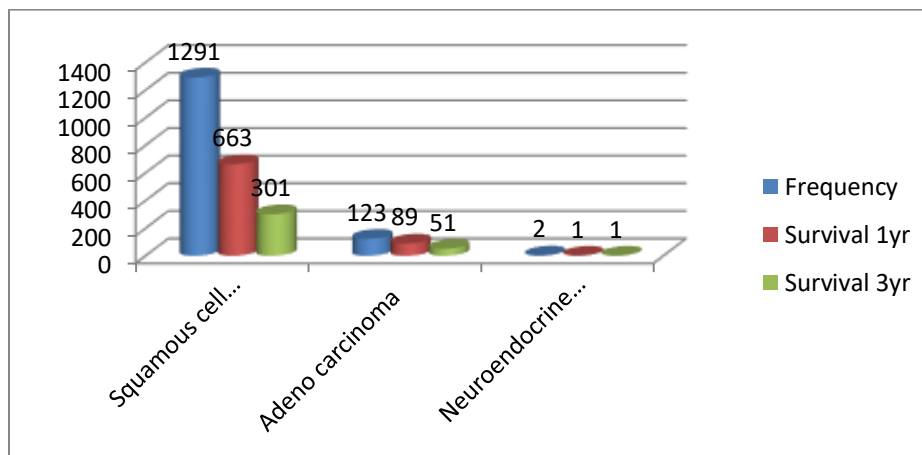


FIGURE 8: Histopathology wise distribution of carcinoma esophagus & survival.

Differentiation	Frequency	%age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Well differentiated	270	19.2	174	64.44	91	33.33
Moderately differentiated	795	56.1	433	54.46	189	23.77
Poorly differentiated	351	24.8	146	41.59	73	20.80
Total	1416	100.0	753		353	

TABLE 9: Survival pattern according to differentiation in carcinoma esophagus.

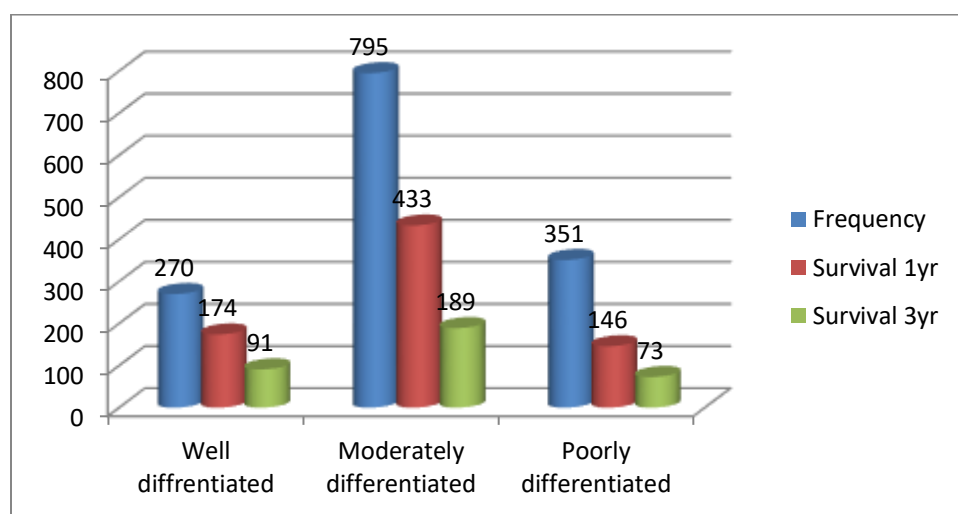


FIGURE 9: Survival pattern according to differentiation in carcinoma esophagus.

Stage	Frequency	%age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
I	0	0	0	0	0	0
II	145	10.2	135	93.1	109	75.17
III	936	66.1	560	59.8	242	25.85
IV	334	23.6	63	18.86	02	.59
Total	1416	100.00	753		353	

TABLE 10: Effect of stage on survival in carcinoma esophagus.

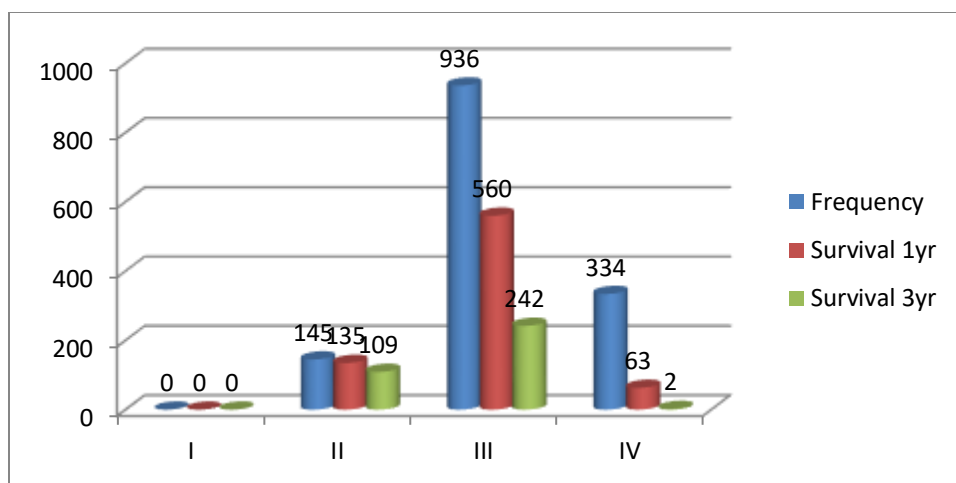


FIGURE 10: Effect of stage on survival in carcinoma esophagus.

Treatment	Frequency	%age	Survival 1yr	% Survival 1yr	Survival 3yr	% Survival 3yr
Surgery only	47	3.30%	17	36.17	7	14.8
Radiotherapy only	535	37.78%	217	40.56	83	15.51
Surgery +chemotherapy	38	2.68%	15	39.47	11	28.94
Surgery +radiotherapy	170	12%	98	57.64	76	44.7
Radiotherapy +chemotherapy	421	29.73%	286	67.93	104	24.7
Surgery +radiotherapy+ chemotherapy	159	11.22%	112	70.44	72	45.28
Chemotherapy only	46	3.24%	8	17.39	0	0
Total	1416	100%	753		353	

TABLE 11: Modalities of treatment received in carcinoma esophagus & its effect on survival

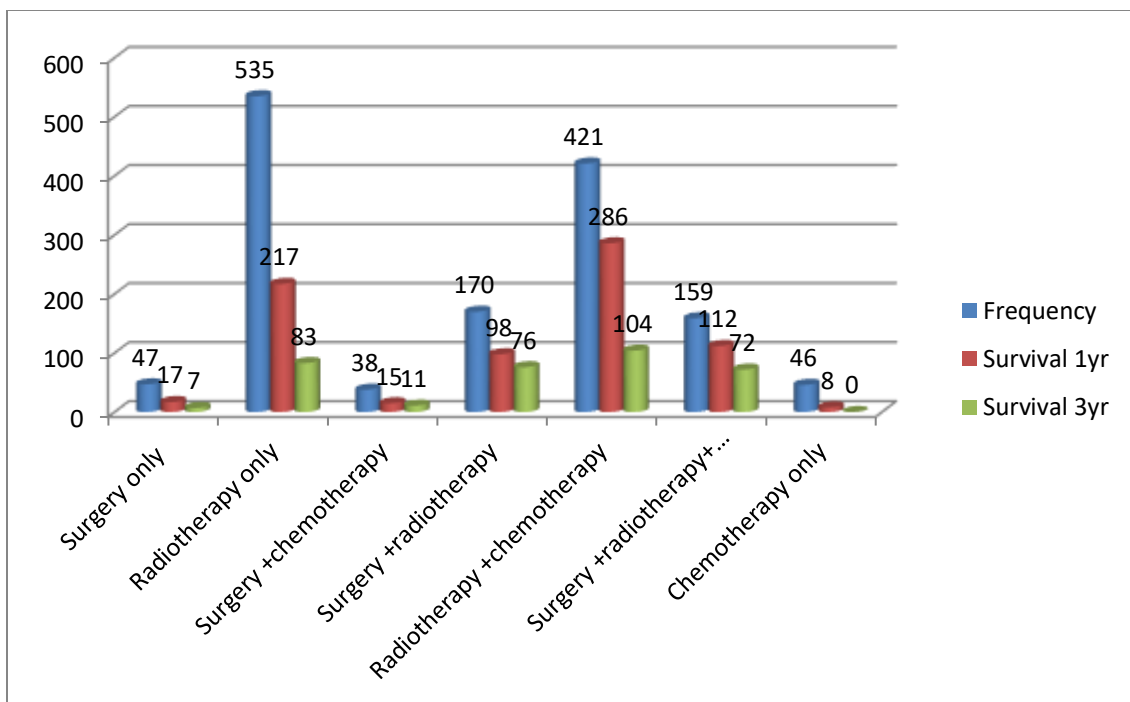


FIGURE 11: Modalities of treatment received in carcinoma esophagus & its effect on survival

Treatment	Frequency
All surgeries	414
All chemotherapy	664
All radiotherapy	1285

TABLE 12: Frequency of various modes of treatment received in carcinoma esophagus & survival

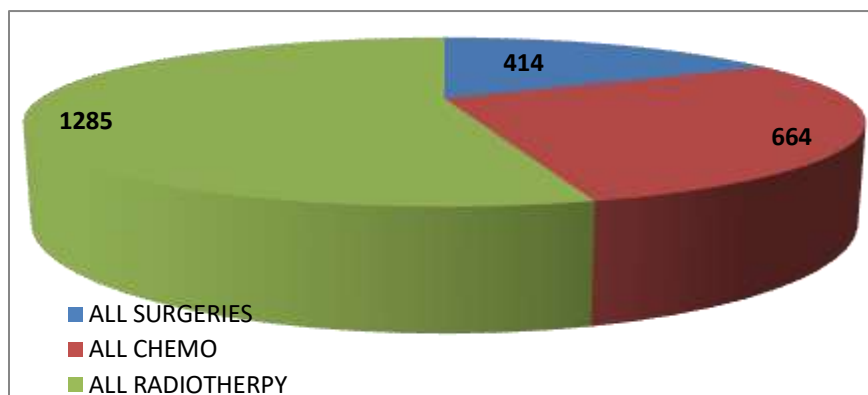


FIGURE 12: Frequency of various modes of treatment received in carcinoma esophagus & survival

Disease status at 6 months	Frequency	Percent
NED(No evidence of disease)	129	9.1
Residual/regression	408	28.6
Progression/recurrence	347	24.5
Expired	116	8.1
Unknown	416	29.2
Total	1416	100.0

TABLE 13: Disease status at 6 months

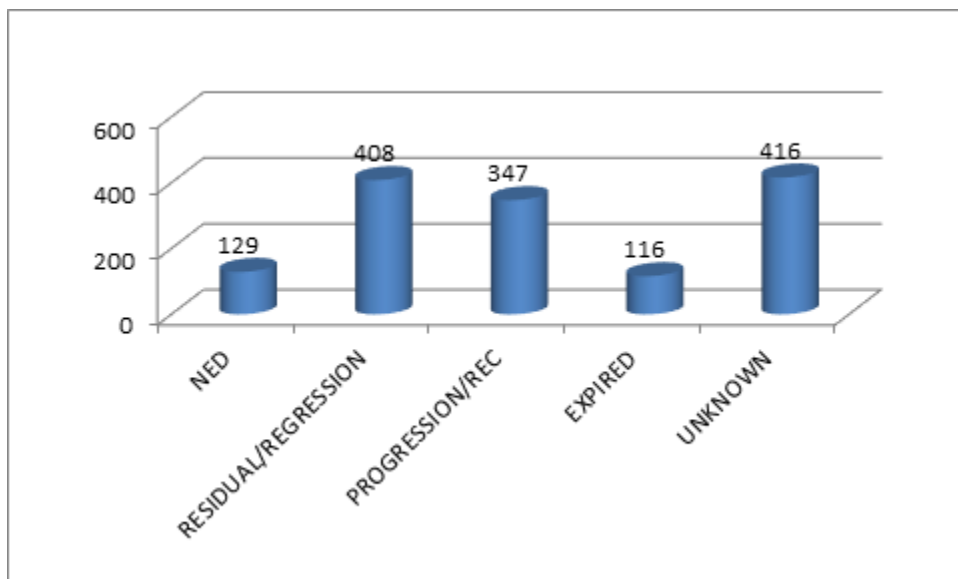


FIGURE 13: Disease status at 6 months

Treatment	Frequency	Percentage
Chemotherapy	46	3.2
Radiotherapy	93	6.5

TABLE 14: Treatment modality used for progression or residual disease

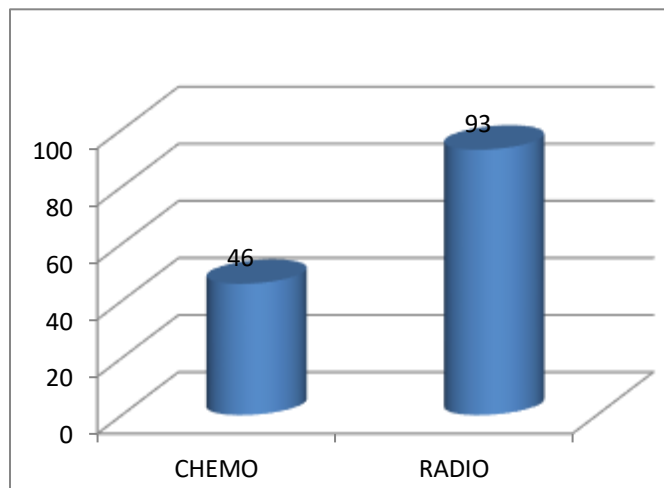


FIGURE 14: Treatment modality used for progression or residual disease

	Frequency	%age
Alive	753	53.2
Dead	336	23.7
Unknown	327	23.1
Total	1416	100.00

TABLE 15: Vital status at 1 year

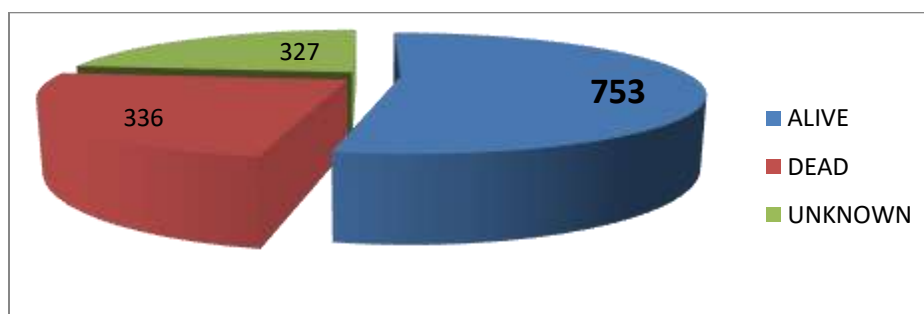


FIGURE 15: Vital status at 1 year

	Frequency	%age
Alive	353	24.9
Dead	706	49.9
Unknown	356	25.1
Total	1416	100.0

TABLE 16: Vital status at 3 years

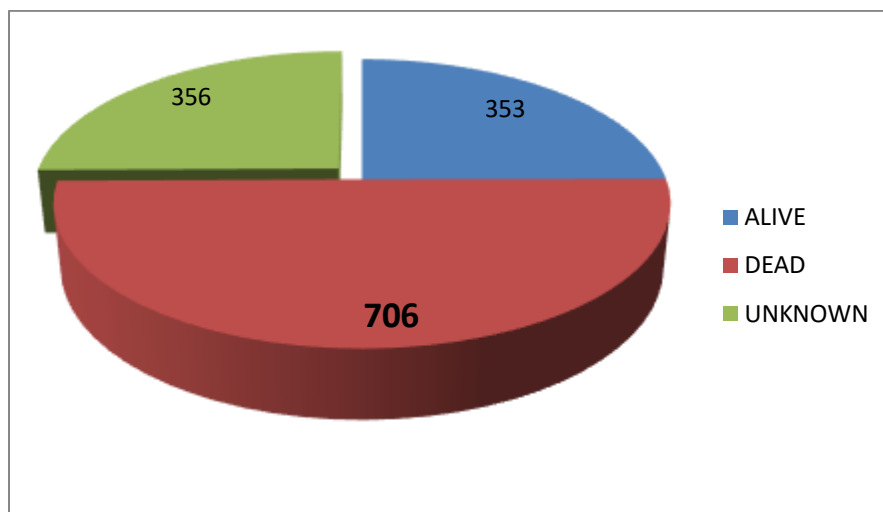


FIGURE 16: Vital status at 3year