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PATHOLOGICAL EVALUATION OF POST NACT/NACRT CHANGES IN OESOPHAGECTOMY SPECIMEN IN A TERTIARY CARE CANCER CENTER

Oncopathology

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ABSTRACT

Esophageal carcinoma is an aggressive malignancy with multifactorial etiology. Even with radical surgery, a significant percentage of patients with esophageal cancer can experience residual disease the impact of which can be determined by pathological evaluation of resected specimen.

Aims:

1. To observe the pathological changes both macroscopically and microscopically in oesophagectomy specimen receiving NACT/NACRT.
2. To determine the proportion of PCR (Pathological Complete Response) in post NACT/NACRT (Neoadjuvant chemotherapy/Neoadjuvant chemoradiotherapy) oesophagectomy cases.

Materials and Methods: A prospective study of 60 patients with esophageal carcinoma, operated between January 2024 and December 2024 is included. Clinical parameters such as tumour length, thickness, tumour site and histopathological parameters such as tumour grade, Lymphovascular invasion (LVI), Perineural invasion(PNI) is studied in relationship to the post NACT/NACRT oesophagectomy cases. Evaluation of tumour regression is done using Modified Ryan Score (Tumour Response Grade, TRG). **Results:** The study has showed a male to female ratio of 1:5:1, with age ranging from 40 yrs to 74 yrs (median age is 57 yrs). The most common site involved is mid thoracic oesophagus with squamous cell carcinoma as the most common histology type. Also, it has been observed that PCR is not associated with tumour size, since in this study the largest tumour size is 6.5X2X0.1 cm but it is associated with PCR. LVI, PNI, was also noted in the study. Association of LVI doesnot any show any correlation with PCR, whereas PNI has seen to be associated with incomplete pathological response with a p value of 0.001. Also, patient having squamous cell carcinoma histological type has good prognosis than adenocarcinoma with a p-value of 0.0002. **Conclusions:** Preoperative CT/CTRT followed by surgery currently represents the standard approach for esophageal carcinoma. Assessment of tumor response to neoadjuvant treatment followed by surgery is done by using parameters like tumour site, length, thickness, LVI,PNI, ENE, grade. In our present study 40% cases showed complete pathological response.

KEYWORDS

Squamous Cell Carcinoma, NACRT, PCR.

INTRODUCTION

Esophageal cancer remains a formidable global health challenge, with an estimated 604,100 new cases and 544,100 deaths reported in 2020. The disease is particularly prevalent in Eastern Asia and parts of Africa, while regions like Western Africa and Central America report lower incidence rates.[1,2]Characterized by rapid progression and poor prognosis, esophageal cancer primarily affects individuals aged 50–70 years. In India, it ranks as the sixth most common cancer, with a notably higher incidence in males and a concentrated burden in the North-Eastern states of Assam, Mizoram, and Nagaland—collectively termed the "esophageal cancer belt." [3]The disease manifests in two main histological subtypes: esophageal squamous cell carcinoma (SCC), which accounts for over 85% of global cases and is strongly associated with tobacco and alcohol use, and esophageal adenocarcinoma (EA), linked to obesity, smoking, and gastro-esophageal reflux disease. Both subtypes exhibit dismal survival rates, averaging around 13–14 months.[4,5]

The two primary histological types, squamous cell carcinoma (SCC) and esophageal adenocarcinoma (EA), demonstrate poor mean survival rates of 13.95 ± 11.2 months and 13.22 ± 10.23 months, respectively.[6]

Esophageal and gastroesophageal junctional cancers are highly aggressive, often diagnosed at an advanced stage with widespread lymph node involvement. Surgery remains the primary treatment, but recurrence is common within two years, and median overall survival is typically just 15–18 months. Due to the locally advanced nature of the disease, complete resection is frequently not possible, making prognosis especially poor.[7]

Surgical resection remains the cornerstone of treatment, yet recurrence within two years is common due to the aggressive nature and frequent lymphatic spread of the tumors. The advent of neoadjuvant chemotherapy (NACT) and chemoradiotherapy (NACRT) has significantly improved outcomes by enhancing tumor resectability and survival rates.[8] Notably, pathological complete response (PCR)—achieved in up to 45% of SCC cases and 30% of EA cases—serves as a critical prognostic marker, underscoring the importance of multimodal treatment strategies in managing this lethal disease.[9,10]

This study investigates the pathological changes in esophagectomy specimens following neoadjuvant chemotherapy (NACT) or neoadjuvant chemoradiotherapy (NACRT) in patients with esophageal carcinoma treated at a tertiary care cancer center. By examining histopathological features such as tumor grade,

lymphovascular invasion (LVI), and perineural invasion (PNI), along with clinical parameters like tumor size and anatomical site, the research aims to assess the extent of tumor regression and determine the proportion of patients achieving pathological complete response (PCR). Understanding these changes is crucial for evaluating treatment efficacy, guiding postoperative management, and refining prognostic models. The findings may offer valuable insights into the biological behavior of esophageal tumors post-therapy and help optimize therapeutic strategies for improved patient outcomes.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Oncopathology at a tertiary care cancer center from January 2024 to December 2024. A total of 60 patients diagnosed with esophageal carcinoma and who underwent esophagectomy following neoadjuvant chemotherapy (NACT) or neoadjuvant chemoradiotherapy (NACRT) were included in the study.

Clinical parameters such as tumour length, thickness, tumour site and histopathological parameters such as tumour grade, LVI, PNI is studied in relationship to the post NACT/NACRT oesophagectomy cases.

The tissue was processed, sections made of 3 micrometre thickness and then stained with Haematoxylin and Eosin stain.

Evaluation of tumour regression is done using Modified Ryan Score and pathological complete response (PCR) is assessed.

Statistical analysis was conducted using the Fisher-Freeman-Halton Exact Test to assess associations between variables, as the assumptions for Pearson's Chi-Square test were violated due to zero cell counts. This non-parametric test ensures validity by calculating p-values through all possible permutations under the null hypothesis. A significance level of $\alpha = 0.01$ was applied to minimize Type I error. All analyses were performed using the RVaideMemoire and ggplot2 libraries in R version 4.5.0.

RESULTS AND OBSERVATION

A total of 60 patients underwent oesophagectomy, post NACT/NACTRT from January 2024 to December 2024.

The demographic profile and baseline characteristics of the patients are in Fig 1. Fulfilled the inclusion criteria as per stated were enrolled during the study.

The age of the patients varied from 21 to 76 years with peak incidence in the 6th decade around 51.6%. 36(60%) patients were male and 24 (40%) were female . The male: female, M: F ratio is 1.5:1. The mean age of the patient was 54.7 years.In the present study, the age group 51-60 had the highest number of cases followed by age group 61-70. The youngest case was 23 years old female and the eldest case was 76 yrs old male.

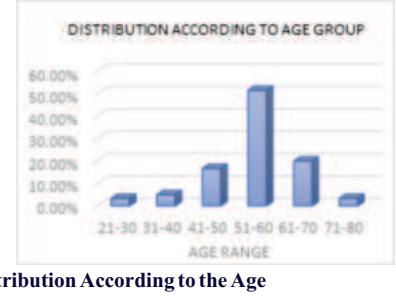

Fig: 1 Distribution According to the Age

The distribution of the Oesophagectomy cases was done according to the most common site involved. In this study, the most common site involved was the mid 1/3rd of the oesophagus: 34 (57%) cases, followed by the lower 1/3rd of the oesophagus: 15 cases (25%).

In our study the upper1/3rd of oesophagus is seen to be 10% (6 cases) of the total cases followed by the GEJ junction 8% (5 cases). (Table 1)

The number of cases were studied according to the site involved and were correlated to the complete PCR and incomplete PCR. These findings were than correlated using Modified Ryan Score, in which we are calculating the TRG (Tumour Response Grade).

It has been seen that the most common site is the mid 1/3rd of oesophagus where highest number of cases falls into the TRG score of 0 i.e 26 out of 33 number of cases(78.7%) in the mid 1/3rd portion and highest number of cases in TRG III can be seen in the GEJ 4 out of 6 (66.6%) cases.(Table 1)

Table 1: Therapy Response of the Cases According to the Site and the Associated with P-value

SITE	NO OF CASES		p-VALUE
	COMPLETE RESPONSE	INCOMPLETE RESPONSE	
UPPER	4(6.7%)	2(3.4%)	0.0009
MID	26(43%)	7(11.7%)	
LOWER	6(10.1%)	9(15%)	
GEJ	1(1.7%)	5(8.4%)	

In Table 1 we are observing the significance of complete PCR (p value) associated with the site of involvement.

It has been observed that the there is significant association of the complete PCR with the carcinoma arising according to the site. Most of the carcinoma which has occurred in the mid thoracic oesophagus has the highest complete PCR in compared to that of the other site with a p value of 0.0009 which is statistically significant.

The next parameter we are observing is the size of the tumour and its correlation with the pathological complete response and its associated significance. (Table 2).

Table 2: Tumour Size and its Correlation with TRG and its p-value

Tumour Size (greatest dimension)	TRG 0	TRG I	TRG II	TRG III	p-value
0.5 cm- 1.4 cm	3	3	0	9	0.0235
1.5 cm- 2.4 cm	7	2	0	2	
2.5 cm- 4.4 cm	9	0	4	5	
> 4.5 cm	8	3	0	5	

A total of 15 cases can be seen in the tumour size, ranging from 0.5cm to 1.4cm, out of which most of the cases are associated with TRG grade III (60%) whereas the tumour size of >4.5 cm, 8 out of the 16 cases have a TRG grade 0. Also p-value of 0.023 was observed which did not associate with tumour response and is statistically not significant.

In Fig 2: It has been shown that size of the tumour is important in nodal involvement and distant metastasis. As the tumour size increases, there is presence of nodal involvement and metastasis which is not seen in tumour sizes <0.5cm.

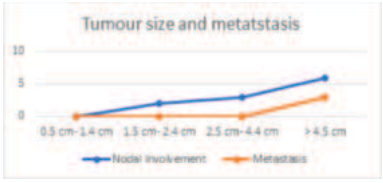

Fig 2: Tumour Size and Metastasis Correlation

Next we observe the length of the tumour. Out of 12 cases of tumours having a length of 3 cm, 50% of the cases (6 cases) fall into TRG0, 25% of the cases each fall into TRG1 and TRG2, respectively.

Whereas with tumour length >6 cm, out of 21 cases, 57% of the cases (21 cases) fall into TRG3, whereas only 23% of cases (5 cases) fall into TRG0.(Fig 3)

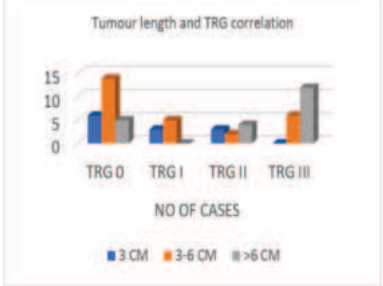

Fig 3: Tumour Length with TRG Correlation

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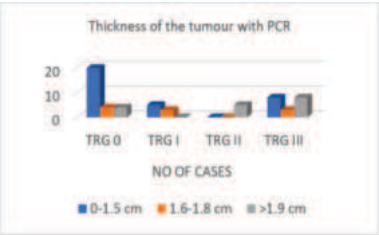

Fig 4: Tumour Thickness and TRG Correlation

The thickness of the tumour and its correlation with pathological complete response are observed. It has been seen that when the thickness of the tumour increases, the tumour becomes less responsive to NACRT/NACT, as a result, the TRG score increases.

In this study it has been observed that when the thickness of the tumour is >1.9 cm out of 17 cases, 47% (8 cases) has a TRG3 and only 23% of cases (4 cases) has a TRG score0, whereas tumour with thickness of 0-1.5 cm, 66% of cases (20 cases) has a TRG score0 and 26% of cases (8 cases) has a TRG3. (Fig 4)

The thickness of the tumour is directly correlated with the PCR, and it is statistically significant with a p-value of 0.0016.

Fig. 5: Shows that the PCR varies according to the histological type of the tumour. In Squamous Cell Carcinoma, out of 47 cases, 7 cases are of Well Differentiated Squamous Cell Carcinoma, 30 cases are of Moderately Differentiated Squamous Cell Carcinoma, and 10 cases are of Poorly Differentiated Squamous Cell Carcinoma.

We had 10 cases of adenocarcinoma, out of which 1 case was Well Differentiated Adenocarcinoma,3 cases were Moderately Differentiated Adenocarcinoma, and 6 cases were Poorly Differentiated Adenocarcinoma. 3 cases have Neuroendocrine (NEC) features: Residual PDSCC with focal neuroendocrine differentiation, Residual Mixed NEC +Non NEC (ADENO), and Small Cell NEC.

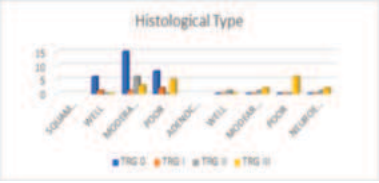

Fig 5: Correlation of Histological Type with PCR

All the cases were compared with Modified Ryan Score to observe how different histological types show the PCR.

Out of 47 cases of SCC, 72.3% (34 cases) of cases showed TRG0, whereas only 6% of cases showed TRG3. In Adenocarcinoma, out of 10 cases, all the cases showed incomplete PCR. 2 cases showed TRG2, and 8 cases showed TRG3. In oesophageal carcinoma with Neuroendocrine features 1 case showed TRG2 and 2 cases showed TRG3.

So in conclusion, SCC cases are significantly associated with higher rates of PCR in comparison to Adenocarcinoma or Neuroendocrine features with a p-value of 0.0002

Histological parameters such as LVI, PNI is correlated with complete PCR. In our study it has been observed when there is presence of LVI without PNI, most of the cases are seen in TRG0 (11 out of 13 cases, 84.6%. Secondly when PNI is present, LVI is absent most of the cases are associated with TRG3.

The p-value was calculated to see the statistical significance of LVI and PNI and was significant with a p-value of 0.0001.

Post therapy 63% of SCC remains in the same grade, whereas 21.2% improve and 14.8% deteriorates.

Similarly in Adenocarcinoma 40% of cases remain same and 60% of cases deteriorates post therapy. NEC remains same post therapy.

Photos:

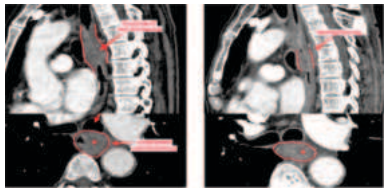

Fig: 6: Case of Esophageal SCC in Midthoracic Esophagus Which Decreased After NACRT

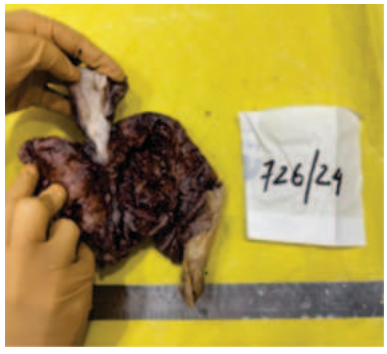

Fig: 7:Gross of Oesophageal Tumour in Lower Oesophagus

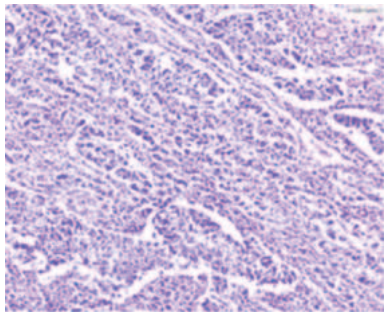

Fig 8: High Power view(40x) of NEC of Oesophagus

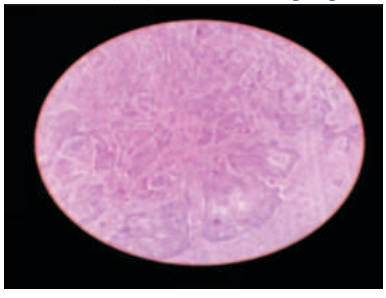

Fig: 9:High Power view(40x) of MDSCC of Oesophagus

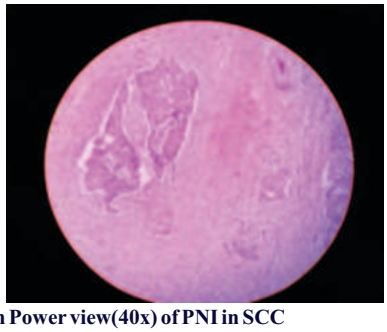

Fig 8: High Power view(40x) of PNI in SCC

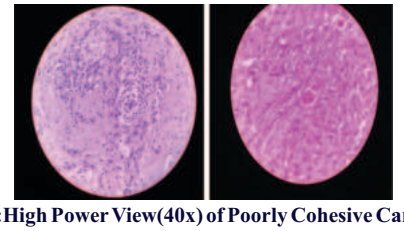

Fig: 10,11:High Power View(40x) of Poorly Cohesive Carcinoma

DISCUSSION

Esophageal carcinoma continues to pose a major global health burden, marked by high mortality rates despite evolving treatment strategies. The current standard for managing locally advanced, non-metastatic cases involves neoadjuvant chemoradiotherapy (NACRT) followed by surgical resection, which has shown significant improvements in R0 resection rates, disease-free survival (DFS), and overall survival (OS) compared to surgery alone.[6] In India, esophageal cancer ranks as the fourth leading cause of cancer-related deaths and affects both genders, with squamous cell carcinoma (SCC) comprising nearly 80% of cases. However, the incidence of adenocarcinoma is rising due to lifestyle changes. Regional variations in SCC etiology are notable, with tobacco use, alcohol consumption, hot beverages, and poor nutrition being key risk factors.[11] Particularly in Northeast India, the incidence of esophageal cancer is alarmingly high—up to ten times the national average—with age-adjusted rates ranging from 19 to 50 per 100,000. Although cultural practices such as the consumption of raw betel nut ('kwai') are widespread, their direct association with cancer risk remains unconfirmed.[12]

Esophageal cancer in India shows a clear male predominance, with most studies reporting a male-to-female ratio ranging from 1.8:1 to 2.5:1, and our study reflecting a similar trend at 1.5:1 with a median age of 57 years. This aligns with broader data indicating peak incidence in the sixth decade of life. Multiple studies, including those by Yang et al.[13], Swamik Das et al.[14], and Choksi et al.[15], reinforce this demographic pattern. Anatomically, the mid-thoracic esophagus emerges as the most commonly affected site, corroborated by both our findings and external research such as that by Yi Wang et al.[16], which highlights its vulnerability due to rich lymphatic drainage and carcinogen exposure. Therapeutically, mid-thoracic tumors tend to respond better to chemoradiotherapy, with higher rates of complete response and improved surgical accessibility, as shown in studies by Hamai Y et al.[17] Our data further supports this, with 78.7% of TRG 0 cases located in the mid-third of the esophagus, while the gastroesophageal junction (GEJ) showed a higher proportion of TRG III cases, indicating more aggressive disease and poorer response.

Tumor size, assessed grossly in our study and categorized into four subgroups—0.5–1.4 cm, 1.5–2.4 cm, 2.5–4.4 cm, and >4.5 cm—did not show a significant correlation with pathological complete response (pCR) when evaluated using the Modified Ryan Score. Interestingly, smaller tumors (0.5–1.4 cm) exhibited higher TRG scores compared to larger ones (>4.5 cm), suggesting that size alone may not be a reliable predictor of treatment response. This observation aligns with recent literature, including a meta-analysis in BMC Surgery (2025)[18]and studies in Diseases of the Esophagus (2023)[19] and the Journal of Thoracic Disease, all of which concluded that tumor size lacks independent prognostic value for pCR following neoadjuvant chemoradiotherapy. These findings emphasize the greater relevance of tumor biology, histologic subtype, and anatomical location in determining therapeutic outcomes, rather than relying solely on initial tumor dimensions.

The tumour size correlation with complete PCR in our study was statistically not significant with a p-value of 0.0235.

However, in our study it has been observed that larger is the tumour size, higher is the prevalence of nodal metastasis and distant metastasis.

In the current study size >4.5 cm, 6 cases are associated with nodal metastasis and 3 cases were associated with distant metastasis. Whereas cases of size 0.5-1.4 cm there is no nodal and distant metastasis.

Tumor size and thickness play a critical role in the progression and prognosis of esophageal cancer, with larger tumors often linked to increased risk of nodal and distant metastases. Studies such as those by Dubecz et al.[19] and guidelines from Cancer Research UK highlight that advanced T-stage tumors (T3–T4) frequently correspond with extensive lymphatic spread (N2–N3) and distant metastasis (M1). In our study, tumor thickness was found to significantly influence treatment response, with tumors (>1.9 cm) showing poorer outcomes—47% of cases had a TRG3 score, while only 23% achieved TRG0. In contrast, tumors (0–1.5 cm) demonstrated better response, with 66% achieving TRG0. These findings are supported by research from Wu and Li[20], who reported that a >40% reduction in esophageal wall thickness post-NCRT correlated with higher pCR rates and improved survival metrics. Wang et al. further emphasized that esophageal wall thickness measured via imaging could predict tumor stage, reinforcing its value as a non-invasive biomarker for assessing disease severity and therapeutic efficacy in ESCC.

The histological pattern that occurs in oesophageal cancer has also been observed. Out of 60 cases, 47 cases were of Squamous Cell Carcinoma, where 7 cases are of Well Differentiated Squamous Cell Carcinoma, 30 cases are of Moderately Differentiated Squamous Cell Carcinoma, and 10 cases are of Poorly Differentiated Squamous Cell Carcinoma.

We had 10 cases of adenocarcinoma, out of which 1 case was Well Differentiated Adenocarcinoma,3 cases were Moderately Differentiated Adenocarcinoma, and 6 cases were Poorly Differentiated Adenocarcinoma. 3 cases have Neuroendocrine features: Residual PDSCC with focal neuroendocrine differentiation, Residual Mixed Neuroendocrine (NEC) +Non NEC (SCC), and Small Cell NEC.

All the cases were compared with Modified Ryan Score to observe how different histological types show the PCR.

Out of 47 cases of SCC, 72.3% (34 cases) of cases showed TRG0, whereas only 6% of cases showed TRG3. In Adenocarcinoma, out of 10 cases, all the cases showed incomplete PCR. 2 cases showed TRG2, and 8 cases showed TRG3. In oesophageal carcinoma with Neuroendocrine features 1 case showed TRG2 and 2 cases showed TRG3.

So, in conclusion, in our study SCC cases are significantly associated with higher rates of PCR in comparison to Adenocarcinoma or Neuroendocrine features with a p-value of 0.0002

Recent research highlights nuanced differences in prognosis between esophageal squamous cell carcinoma (SCC) and adenocarcinoma (ADC, with some studies suggesting SCC may offer a survival advantage in specific clinical contexts. For instance, Kauppila et al.[21] (2018) reported higher 5-year survival rates for SCC than ADC in non-surgical cases, with female SCC patients showing notably better outcomes. Fan et al.[22] further demonstrated superior locoregional control and lower recurrence rates in SCC patients following neoadjuvant chemoradiotherapy, emphasizing the impact of histologic subtype on treatment response. Mariette et al.[23] (2005) also found slightly improved long-term survival for SCC after curative esophagectomy, particularly in locally advanced stages. However, contrasting evidence from Tustumi et al. (2021)[24] suggests that Adenocarcinoma may have the best long-term survival overall, with SCC trailing slightly behind but still outperforming neuroendocrine carcinoma (NEC) subtypes, which showed the poorest outcomes. These findings underscore the importance of considering histologic subtype when evaluating prognosis and tailoring treatment strategies for esophageal cancer.

Histological parameters such as lymphovascular invasion (LVI) and perineural invasion (PNI) appear to have distinct implications for treatment response in esophageal cancer. In our study, the presence of LVI without PNI was predominantly associated with favorable outcomes, with 84.6% of such cases falling under TRG0, indicating complete tumor regression. Conversely, when PNI was present in the absence of LVI, the majority of cases were linked to TRG3, suggesting poor response to neoadjuvant therapy. This pattern implies that while LVI alone may not serve as a significant prognostic factor, PNI could be indicative of more aggressive disease and reduced treatment efficacy. Supporting evidence from Singh et al. shows that LVI does not significantly impact overall or disease-free survival, whereas PNI correlates with increased morbidity and mortality. Similarly, Nusrath et al.[25] found no direct association between LVI and tumor regression post-NACT/NACRT, reinforcing the notion that PNI may be a more reliable marker of poor prognosis than LVI in esophageal carcinoma.

We have also observed the post-therapy changes of all the cases, where 63% of SCC remains in the same grade, whereas 21.2% improve and 14.8% deteriorate. Similarly, in Adenocarcinoma, 40% of cases remain the same, and 60% of cases deteriorate post-therapy. NEC remains the same post-therapy.

While in a study a comparative analysis of pre- and post-therapy

differentiation status in esophageal cancers, 30% of squamous cell carcinoma (SCC) cases showed no change in differentiation following therapy, indicating greater stability. In contrast, only 2% of adenocarcinoma cases maintained the same differentiation status post-treatment. Interestingly, 4% of cases in both SCC and adenocarcinoma demonstrated improved differentiation, suggesting a partial therapeutic benefit. However, deterioration in cellular differentiation was observed in 8% of cases for both cancer types, which may reflect therapy-induced dedifferentiation potentially linked to increased tumor aggressiveness. These findings align with the principles of differentiation therapy, which aims to restore normal cellular behavior and reduce malignancy by targeting key molecular pathways involved in cell maturation and identity.[26]

CONCLUSION

Esophageal carcinoma remains a pressing health issue in India, with squamous cell carcinoma (SCC) being the predominant subtype, especially in high-incidence regions like Northeast India. The disease shows a consistent male predominance and peaks in the sixth decade of life, emphasizing the need for early detection and targeted interventions. Our study highlights the mid-thoracic esophagus as the most commonly affected site, with a high rate of complete pathological response (TRG0), while tumors at the gastroesophageal junction (GEJ) showed poorer outcomes. Although gross tumor size did not correlate significantly with treatment response, increased tumor thickness was associated with worse prognosis, making it a more reliable indicator. Histological analysis revealed that SCC had better treatment outcomes and greater post-therapy stability compared to adenocarcinoma and neuroendocrine carcinoma (NEC), which showed higher recurrence and dedifferentiation. Additionally, perineural invasion (PNI) was linked to poor response, whereas lymphovascular invasion (LVI) alone did not significantly affect regression. These findings underscore the importance of integrating anatomical, histological, and morphological parameters into personalized treatment planning for esophageal cancer.

REFERENCES

1. Morgan E, Soerjomataram I, Rumgay H, Coleman HG, Thrift AP, Vignat J, et al. The Global Landscape of Esophageal Squamous Cell Carcinoma and Esophageal Adenocarcinoma Incidence and Mortality in 2020 and Projections to 2040: New Estimates From GLOBOCAN 2020. Gastroenterology. 2022 Sept 1;163(3):649-658.e2.
2. Cancer (IARC) TIA for R on. Global Cancer Observatory [Internet]. [cited 2025 June 27]. Available from: https://gco.iarc.fr/
3. Bora SK, Saikia AM, Chakraborty SS, Mahanta N. Dietary Risk Factors for Oesophageal Cancer: A Case Control Study from Assam, India. J Med Sci Health. 2023 Dec 30;9(3):304–9.
4. Kamangar F, Nasrollahzadeh D, Safiri S, Sepanlou SG, Fitzmaurice C, Ikuta KS, et al. The global, regional, and national burden of oesophageal cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020 June 1;5(6):582–97.
5. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the Future Burden of Esophageal Cancer by Histological Subtype: International Trends in Incidence up to 2030. Am J Gastroenterol. 2017 Aug;112(8):1247–55.
6. Coral RV, Bigolin AV, Coral RP, Hartmann A, Dranka C, Roehe AV. Metastatic lymph node ratio, 6th or 7th AJCC edition: witch is the best lymph node classification for esophageal cancer? Prognosis factor analysis in 487 patients. Arq Bras Cir Dig ABCD Braz Arch Dig Surg. 2015;28(2):94–7.
7. Ku GY, Ilson DH. 71 - Cancer of the Esophagus. In: Niederhuber JE, Armitage JO, Kastan MB, Doroshow JH, Tepper JE, editors. Abeloff's Clinical Oncology (Sixth Edition) [Internet]. Philadelphia: Elsevier; 2020 [cited 2025 July 10]. p. 1174-1196.e6. Available from: https://www.sciencedirect.com/science/article/pii/B9780323476744000712
8. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69–90.
9. Langer R, Ott K, Feith M, Lordick F, Siewert JR, Becker K. Prognostic significance of histopathological tumor regression after neoadjuvant chemotherapy in esophageal adenocarcinomas. Mod Pathol Off J U S Can Acad Pathol Inc. 2009 Dec;22(12):1555–63.
10. Zeybek A, Erdoğan A, Gülkesen KH, Ergin M, Sarper A, Dertsiz L, et al. Significance of Tumor Length as Prognostic Factor for Esophageal Cancer. Int Surg. 2013;98(3):234–40.
11. Samarasam I. Esophageal Cancer in India: Current Status and Future Perspectives. Int J Adv Med Health Res. 2017 June;4(1):5.
12. Harris C, Mawlong A, Tapkire R, Albert S, Jagtap V. 790. RISK FACTORS FOR ESOPHAGEAL CANCER IN NORTHEAST INDIA: A MULTI-CENTRIC CASE-CONTROL STUDY. Dis Esophagus. 2024 Sept 1;37(Supplement_1):doae057.386.
13. Yang Y, Huang X, Zhou L, Deng T, Ning T, Liu R, et al. Clinical use of tumor biomarkers in prediction for prognosis and chemotherapeutic effect in esophageal squamous cell carcinoma. BMC Cancer. 2019 May 31;19:526.
14. Das S, Kakoti L mudra, Ahmed S, Sarma A, Kataki A ch. Study of Serum CEA and Ca 19.9 in Esophageal Squamous Carcinoma and ROC Curve Analysis. Asian Pac J Cancer Biol. 2020 Dec 7;5(4):141–5.
15. Choksi D, Kolhe KM, Ingle M, Rathi C, Khairnar H, Chauhan SG, et al. Esophageal carcinoma: An epidemiological analysis and study of the time trends over the last 20 years from a single center in India. J Fam Med Prim Care. 2020 Mar;9(3):1695–9.
16. Wang Y, Huang Y, Zhao QY, Li XQ, Wang L, Wang NN, et al. Esophageal wall thickness on CT scans: can it predict the T stage of primary thoracic esophageal squamous cell carcinoma? Esophagus Off J Jpn Esophageal Soc. 2022 Apr;19(2):269–77.
17. Hamai Y, Hihara J, Emi M, Taomoto J, Aoki Y, Kishimoto I, et al. Treatment outcomes and prognostic factors for thoracic esophageal cancer with clinical evidence of adjacent organ invasion. Anticancer Res. 2013 Aug;33(8):3495–502.
18. Sun J, Sun C, Zhang Y, Jin Z, Witharana T, Li J, et al. Does pathological complete response after neoadjuvant chemoradiotherapy associate with long-term survival in esophageal cancer: A systematic review and meta-analysis. BMC Surg. 2025 July 16;25(1):295.
19. Dubecz A, Gall I, Solymosi N, Schweigert M, Peters JH, Feith M, et al. Temporal trends in long-term survival and cure rates in esophageal cancer: a SEER database analysis. J Thorac Oncol Off Publ Int Assoc Study Lung Cancer. 2012 Feb;7(2):443–7.
20. Change in Maximal Esophageal Wall Thickness Provides Prediction of Survival and Recurrence in Patients with Esophageal Squamous Cell Carcinoma After Neoadjuvant Chemoradiotherapy and Surgery - PubMed [Internet]. [cited 2025 Aug 1]. Available from: https://pubmed.ncbi.nlm.nih.gov/33758542/
21. Kauppila JH, Mattsson F, Brusselaers N, Lagergren J. Prognosis of oesophageal adenocarcinoma and squamous cell carcinoma following surgery and no surgery in a nationwide Swedish cohort study. BMJ Open. 2018 May 10;8(5):e021495.
22. Fan N, Wang Z, Zhou C, Bludau M, Contino G, Zhao Y, et al. Comparison of outcomes between neoadjuvant chemoradiotherapy and neoadjuvant chemotherapy in patients with locally advanced esophageal cancer: A network meta-analysis. EClinicalMedicine. 2021 Nov 6;42:101183.
23. Mariette C, Piessen G, Triboulet JP. Therapeutic strategies in oesophageal carcinoma: role of surgery and other modalities. Lancet Oncol. 2007 June;8(6):545–53.
24. Tustumi F, Marques SSB, Barros EF, Henriques AC, Waisberg J, Dias AR. THE PROGNOSIS OF THE DIFFERENT ESOPHAGEAL NEUROENDOCRINE CARCINOMA SUBTYPES: A POPULATION-BASED STUDY. Arq Gastroenterol. 2022;59(1):53–7.
25. Nusrath S, Thammineedi SR, Vijaya Narsimha Raju KV, Patnaik SC, Pawar S, Santa A, et al. Short-term Outcomes in Patients with Carcinoma of the Esophagus and Gastroesophageal Junction Receiving Neoadjuvant Chemotherapy or Chemoradiation before Surgery. A Prospective Study. Rambam Maimonides Med J. 2019 Jan 28;10(1):e0002.
26. Paul R, Dorsey JF, Fan Y. Cell plasticity, senescence, and quiescence in cancer stem cells: Biological and therapeutic implications. Pharmacol Ther. 2022 Mar;231:107985.