The Gulf Journal of Oncology

Indexed By PubMed and Medline Database

Issue 49, Sep. 2025
ISSN No. 2078-2101



The Official Journal of the Gulf Federation For Cancer Control

Table of Contents

Original Articles

Survival Outcomes of Penile Cancer Patients undergoing Primary Surgery: Experience from a Tertiary Cancer Care Centre in South India **07**
Ricky Koshy Benjamin, Sivaranjith J, Madhu Muralee, Aswin Kumar, Jagathnath Krishna K. M

Incidental Radiation Exposure to the Internal Mammary Lymph Nodes in Breast Cancer Patients Undergoing Intensity–Modulated Radiation Therapy: A Retrospective Analysis **16**
Vishwadeep Mishra, Shashank Shekhar, Sudeep Bisht, Rachita Chatterjee, Laxman Pandey, Archana Pandey

Safety and Outcome Analysis of Preoperative chemoradiation in Esophageal carcinoma **22**
Shuchita Pathak, Santhosh KD, Parikshith J, Rasmi Palassery, Vinayak V Maka

Impact of size of ovoids with Intra–cavitary Brachytherapy on dose to point A in patients with Cancer Cervix **28**
Dr. Tanvir Pasha, Dr. Nikhila Radhakrishna, Dr. Rekha Reddy Buchapudi, Dr. Saritha Sunny Pullan, Dr. Hamsini R S, Dr. Elna Jerod, Dr. Naveen Thimmaiah, Dr. Sridhar Poojar, Dr. Uday Krishna, Dr. Siddanna Rudrappa Palled, Dr. Thejaswini B, Dr. Lokesh Viswanath

De novo mutation of the RET proto–oncogene revealing multiple endocrine neoplasia type 2A: a sporadic case from Western Algeria **35**
Amina Chami, Pauline Romanet, Fatima Mohammedi, Nadia Benabadji, Narimane Habour, Dalia Derkaoui, Tewfik Sahraoui

Predictors of Recurrence and Long–Term Outcomes of Intracranial Meningiomas: A Retrospective Multicenter Study from Saudi Arabia **40**
Afnan Alkhotani, Rothaina Saeedi, Haneen Alomar, Fahad Alghamdi, Joudah Almaghrabi, Mohammed Binmahfoodh, Saleh Baeesa

Quality of Life (QoL) using EORTC QoL–C30 and BN20 among Patients who Underwent Brain Tumor Resection in a Tertiary Care Center in Saudi Arabia **53**
Rana H. Moshref, Leena H. Moshref, Fatemah A. Alhalawani, Masaheer A. Aljehani, Noor M. Shibriq, Wafa A. Saber, Ahlam B. Khojah, Rawan M. Alsayed, Razan Daghistani , Khalid M. Bajunaid, Mohammed A. Alyousef, Abdulrahman J. Sabbagh, Saleh S. Baeesa

Is there a Correlation between estrogen receptor expression level and early breast cancer survival? A Retrospective Study **65**
Ayman Rasmy, Ahmed Zeeneldin , Walid Abozeed, Saeed Al–Ghamdi and Shereef Elsamany

Efficacy and Safety of Paclitaxel Plus Ramucirumab as Second–Line Therapy in Advanced Gastric Cancer: A Retro–Prospective Single–Centre Study **75**
Varun Goel, Arpit Jain, Nivedita Patnaik, Dharmistha Basu, Shaifali Goel, Akanksha Jaju, Vineet Talwar, Shivendra Singh

Single Centre Experience of Treating Children with Cancer in the United Arab Emirates **80**
Mehnaz Aabideen, Arya Ashokan, Dr.Sagar Mohan Nivargi, Dr. Mohammed Ramzan, Dr. Deepthi Boddu, Dr. Fouzia Aboobacker, Abdullah Odat, Mohammed Taher, Dr. Rawia Mohamed, Dr. Rajasekhar Cingapagu, Prof. Dr. Humaid O. Al Shamsi, Dr. Zainul Aabideen

Review Articles:

Histopathological and Molecular Features of the Mammary Sclerosing Adenosis Lesions and Their association with breast carcinoma: Review of literature **85**
Rabab Ahmed Mohammed, Amina Ismaeel, Fayek Al Hilli

Conference Highlights/Scientific Contributions

- **News Notes** **93**
- **Advertisements** **96**
- **Scientific Activities** **97**

Original Article

Safety and Outcome Analysis of Preoperative chemoradiation in Esophageal carcinoma

Shuchita Pathak[1], Santhosh KD[2], Parikshith J[3], Rasmi Palassery[2], Vinayak V Maka[2]

[1]Dayanand Medical College & Hospital, Ludhiana, Punjab, INDIA
[2]MS Ramaiah Medical College, Bengaluru, Karnataka, INDIA
[3]Mohandai Oswal Hospital, Ludhiana, Punjab, INDIA

Abstract

Background: The incidence of esophageal cancer (EC) is increasing now–a–days and the management of EC has changed dramatically with the widespread adoption of mixed modality therapy. Although many Indian centres use combined modality therapy with neoadjuvant chemoradiation (nCRT), published data are scarce. This study assessed the feasibility of trimodality therapy in terms of safety and pathological complete response (pCR) among newly diagnosed patients with EC.

Patients and Methods: This ambispective study included the retrospective data of patients with locally advanced resectable carcinoma of the middle and lower thoracic oesophagus who were diagnosed and treated between January 2018 and December 2020 along with the prospective data of patients who were diagnosed between January 2021 and January 2023. The clinicodemographic details, radiation technique delivered along with the total dose planned, the dose received and chemotherapy details along with haematological toxicities and non–haematological toxicities were noted. The surgical details and aspects such as the interval between completion of neoadjuvant chemoradiation and surgery, postoperative mortality, pulmonary and cardiac complications, anastomotic leaks and length of hospital stay were recorded. The main outcome was the pCR of patients who received nCRT and underwent surgery.

Results: Out of 250 cases retrieved, 100 eligible cases were included, in that, 50 patients received nCRT. About 84% of them underwent surgery after receiving nCRT and 30 patients (60%) post–surgery develop pCR. There were no grade 3 or 4 haematological toxicity noted and only few pateints developed non–haematological toxicities. Also, 16 patients developed postoperative complications. The median follow–up was 24 months, and the 1–year overall survival rate was 62 % among patients who received nCRT followed by surgery.

Conclusion: Neoadjuvant chemoradiotherapy followed by surgery was tolerable and safe in the majority of patients with locally advanced EC with lower incidence of Grade 3 and 4 haematological, non–haematological toxicity and post–surgical complications.

Keywords: Esophageal cancer, Neoadjuvant chemoradiotherapy, trimodality therapy, pathological complete response, haematological toxicities

Introduction

Esophageal cancer (EC) is one of the most prevalent gastrointestinal cancers globally, alongside stomach, pancreas, hepatobiliary, and colorectal cancers. According to the recent GLOBOCAN 2022 estimates, EC ranks as the 11th most commonly diagnosed cancer and the 7th leading cause of cancer death worldwide, with an estimated 511,000 new cases and 445,000 deaths. In India, there were 70,637 new cases of EC with the incidence being 5% of all new cancer cases, and 66,410 (7.2%) deaths due to EC.[1] Further, the incidence of EC varies significantly by geographic region, with notable differences between the two most common histologic subtypes: squamous cell carcinoma and adenocarcinoma. These subtypes have distinct etiologic factors contributing to their development where smoking and alcohol are major risk factors for squamous cell carcinoma and adenocarcinoma is associated with excess body weight, gastroesophageal reflux disease and Barrett esophagus.[2,3]

Corresponding author: Dr Vinayak V Maka, Senior Professor–Medical Oncology, MS Ramaiah Medical College, Bengaluru, Karnataka, INDIA.
E–mail: vinayakvmaka@gmail.com

Although surgery is a typical treatment for locally advanced resectable esophageal cancer, the outcomes are often unsatisfactory. The 5–year survival rate following surgery is extremely low, and the majority of patients experience local recurrence or distant metastases.[4,5] Currently, neoadjuvant chemoradiotherapy (nCRT) is considered as the preferred treatment for local advanced resectable esophageal cancer, with a median overall survival (OS) of 49.4 months and a pathological complete response (pCR) rate of 29%, according to the CROSS trial and with the median OS of 100.1 months and a pCR of 43.2% as per NEOCRTEC 5010 trial.[6,7] Despite nCRT and surgery, the 5–year overall survival and progression–free survival (PFS) rates were around 47% and 44%, respectively, indicating that a significant proportion of patients still experience disease progression and death.[8] In addition, the safety of chemoradiation is an important concern since some patients cannot tolerate nCRT.[7] Furthermore, the applicability of trimodality approaches in developing countries like India has been a challenge. A spectrum of obstacles, such as limited infrastructure, financial access, acceptance of treatment and lack of a multidisciplinary team have hindered its adoption in our country.

In this ambispective study, we aim to assess the feasibility of trimodality therapy in terms of safety and pCR among newly diagnosed patients with locally advanced resectable carcinoma of the middle and lower thoracic oesophagus at a tertiary cancer centre in Southern India.

Patients and Methods

Patient Selection

In this study, the retrospective data of patients with locally advanced resectable carcinoma of the middle and lower thoracic oesophagus who were diagnosed and treated between January 2018 and December 2020 along with the prospective data of patients who were diagnosed between January 2021 and January 2023 were included. The inclusion criteria consists of patients aged 18 years and older, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 or 1, histologically proven squamous cell carcinoma or adenocarcinoma, clinical stage T1N1 to T3N1, tumour location in the mid and lower thoracic oesophagus with a tumour length less than or equal to 8 cm and a tumour width of 5 cm or above in diameter.

Procedure

The medical records of the included patients were reviewed, along with hospital outpatient consultation records, discharge summaries, surgical procedure notes and postoperative care and follow–up records. The clinicodemographic profile of patients was noted, which included age, gender, ECOG PS, histology and grade, tumour length, tumour width, and clinical stage. The radiation technique delivered along with the total dose planned, the dose received and any delay in radiation were ascertained. Chemotherapy details were also noted with the number of cycles received, calculated dose, dose received, and number of cycles missed, along with haematological toxicities and non–haematological toxicities such as alopecia, constipation, diarrhoea, esophagitis, fatigue, nausea, vomiting, and neurological symptoms as per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI– CTCAE) v5. The surgical details and aspects such as the interval between completion of neoadjuvant chemoradiation and surgery, postoperative mortality, pulmonary and cardiac complications, anastomotic leaks and length of hospital stay were recorded. The date of last follow–up and date of death, if applicable, were noted.

Outcomes

The primary outcome of this study was the pathological complete response rates (pCR) of patients who received neoadjuvant chemoradiation and underwent surgery. The secondary outcomes were the haematological, non–haematological, and postoperative toxicities of patients receiving trimodality therapy. The incidence of postoperative mortality within 1 month of surgery and overall survival were also ascertained in our study.

Sample size estimation

From a review of the literature, it has been observed that the pathological complete response is 29%.[6] In the present study, expecting similar results with a 95% confidence level and 15% absolute precision, the study requires a minimum of 35 subjects.

Statistical analysis

Descriptive statistics of pathological complete response rates, haematological and non–haematological toxicities, and surgical toxicities, along with the incidence of post–treatment mortality within 1 month, were described in percentage. Overall survival was analysed with Kaplan–Meier survival curves. A chi–square or Fischer's exact test would be used to compare pathological complete response, haematological, non–haematological, and surgical toxicity between gender, age, etc.

Results

A total of 250 cases with histologically proven oesophagal carcinoma were retrieved from the hospital

records over a period of 5 years from January 2018 to January 2023. In that, 100 patients with locally advanced carcinoma of the middle and lower thoracic oesophagus were included in the study as per the inclusion criteria. Out of these 100 eligible patients, 30 patients refused surgery as part of trimodality therapy and opted for definitive chemoradiation, and another 20 patients had disease extension above the level of the carina, which rendered them unresectable. Hence, 50 patients were included in the study (Figure 1).

The median age of the included subjects at the time of diagnosis was 56 years, and there was a female predominance noted in this study with 27 patients (54%) were females. The most common subsite was the lower thoracic oesophagus, which comprised 21 patients (42%). Squamous cell carcinoma was noted in 42 patients (84%) and a vast majority of patients, comprising 46 in number, were diagnosed with Stage III. About 34 patients (68%) presented with a history of weight loss.

Out of 50 patients who received neoadjuvant chemo–radiotherapy, 41 patients (82%) fulfilled the criteria for the same as per the CROSS Protocol, while 9 patients (18%) patients did not fulfil the criteria. The clinical and demographic characteristics are presented in Table 1. Thus, 50% of patients received the latest technique of radiotherapy with Intensity–modulated radiotherapy (IMRT) and 12 patients (24%) had radiation dose delays (>3 days). Also, 12 patients (24%) missed at least one cycle of planned chemotherapy during treatment.

In our study, there was no grade 3 and grade 4 haematological toxicities noted while 18 patients had grade 1 anaemia (36%), 6 patients (12%) had grade 2 neutropenia, and 2 patients (4%) had grade 2 thrombocytopenia. Half of the patients developed grade 1 alopecia. Among gastrointestinal toxicities, 15 patients (30%) had grade 2 constipation, while 1 patient (2%) had grade 3 diarrhoea. In addition, 5 patients (10%) had Grade 3 nausea, while 15 patients (30%) had Grade 3 vomiting. Grade 2 fatigue was seen in 26 patients (52%) (Table 2). There were no patients developed neurotoxicity. Of the patients who received neoadjuvant chemoradiotherapy, one developed oesophageal perforation.

About 42 patients (84%) underwent surgery after receiving neoadjuvant chemo–radiotherapy, while 8 patients (16%) were deemed unresectable after response assessment. All the patients tolerated the surgery well except only one patient (2%) died within 1 month of surgery was noted.

Among post–surgical toxicities, pulmonary complications were the most common, with 8 patients (16%) developing pleural effusion or pneumothorax. Moreover, myocardial infarction (2%), anastomotic leak (6%) and chyle leak (6%), chylothorax (2%), and vocal cord palsy (2%) were also noted.

Overall, 30 patients (60%) had a pathological complete response after neoadjuvant chemo–radiotherapy while 11 patients (22%) had residual disease (Figure 2). At a median follow–up of 24 months, the 1–year and 2–year overall survival (OS) rates were 62% and 41.2%, respectively, and the median OS was 15.6 months (95% CI, 11.1–18.23 months) as shown in Figure 3.

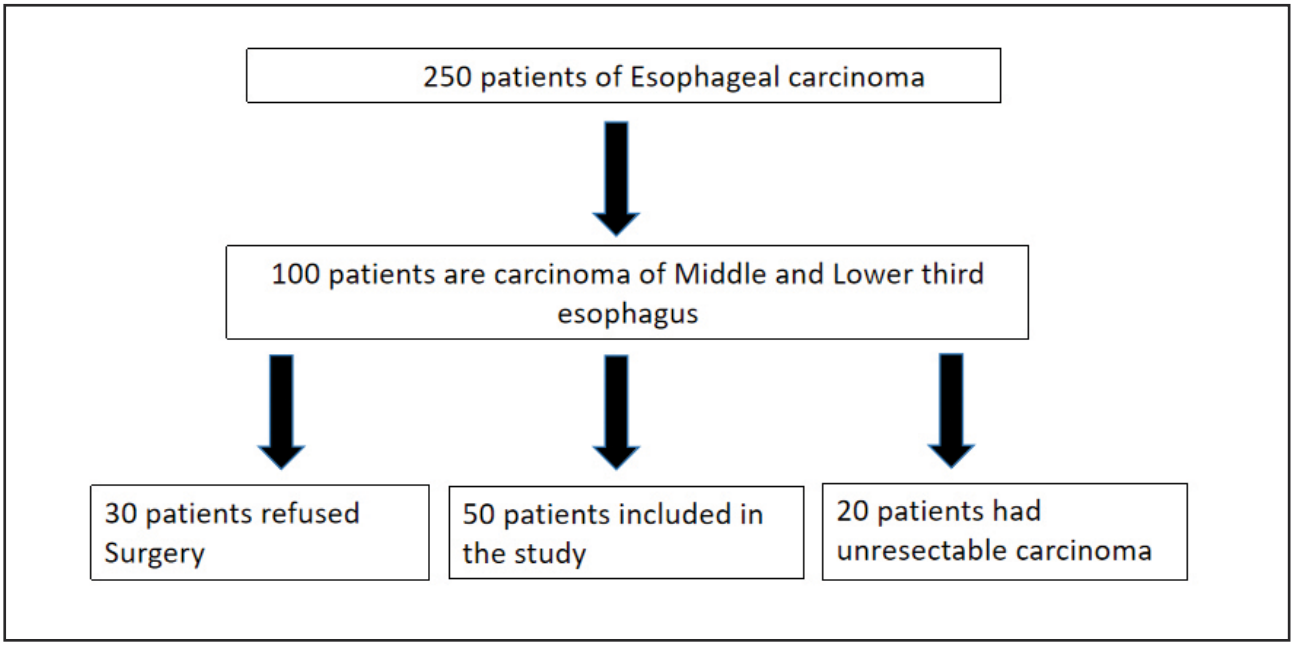


Figure 1. Selection of patients in the study

Variables	N=50
Age (years), median [range]	56 (24–60)
Sex, n (%)	
Male	23 (46%)
Female	27 (54%)
Tumour Site, n (%)	
Middle Third	19 (38%)
Lower Third	21 (42%)
Gastroesophageal junction	10 (20%)
Histology, n (%)	
Squamous Cell Carcinoma	42 (84%)
Adenocarcinoma	7 (14%)
Signet ring carcinoma	1 (2%)
Grading, n (%)	
Well Differentiated	9 (18%)
Moderately Differentiated	38 (76%)
Poorly Differentiated	3 (6%)
TNM, n (%)	
T1	1 (2%)
T2	9 (18%)
T3	35 (70%)
T4a	4 (8%)
T4b	1 (2%)
N0	15 (30%)
N1	30 (60%)
N2	4 (8%)
N3	1 (2%)
Clinical Stage, n (%)	
II	4 (8%)
III	43 (86%)
IVa	3 (6%)
Performance Score (ECOG), n (%)	
0	44 (88%)
1	6 (12%)
Cross Criteria Fullfilling, n (%)	
Yes	41 (82%)
No	9 (18%)

ECOG, Eastern Cooperative Oncology Group

Table 1. Clinico demographic characteristics of the study population

Discussion

The therapeutic landscape for resectable oesophageal carcinoma has been transformed since 2012 when Hagen et al.[6] published their CROSS Trial. This has since been incorporated across multiple countries and institutions.[9,10] However, its applicability in developing countries is questioned at times.[11] Our ambispective study performed from January 2018 to January 2023, is one the few studies from South India to ascertain the impact of Neoadjuvant Chemoradiation followed by surgery on outcomes.

Toxicity	n(%)
Anaemia	
Grade 0	32(64%)
Grade 1	18(36%)
Neutropenia	
Grade 0	24(48%)
Grade 1	20(40%)
Grade 2	6(12%)
Thrombocytopenia	
Grade 0	44(88%)
Grade 1	4(8%)
Grade 2	2(4%)
Alopecia	
Grade 0	25(50%)
Grade 1	25(50%)
Constipation	
Grade 0	21(42%)
Grade 1	14(28%)
Grade 2	15(30%)
Diarrhoea	
Grade 0	35(70%)
Grade 1	4(8%)
Grade 2	10(20%)
Grade 3	1(2%)
Esophagitis	
Grade 2	29(58%)
Grade 3	21(42%)
Fatigue	
Grade 0	1(2%)
Grade 1	23(46%)
Grade 2	26(52%)
Nausea	
Grade 1	8(16%)
Grade 2	37(74%)
Grade 3	5(10%)
Vomiting	
Grade 0	1(2%)
Grade 1	7(14%)
Grade 2	27(54%)
Grade 3	15(30%)
Oesophageal Perforation	
Grade 0	49(98%)
Grade 3	1(2%)

Table 2. Treatment–related adverse events

In our study, the median age of diagnosis was 56 years. The median age compared to 60 years in the CROSS trial, and 57 years in the study reported by Bhattacharyya T et al.[10] and 50 years in the study reported by Bajwa et al.[12] which was reported at a tertiary hospital in India. A female predominance was noted in our study which was not like other Indian studies.

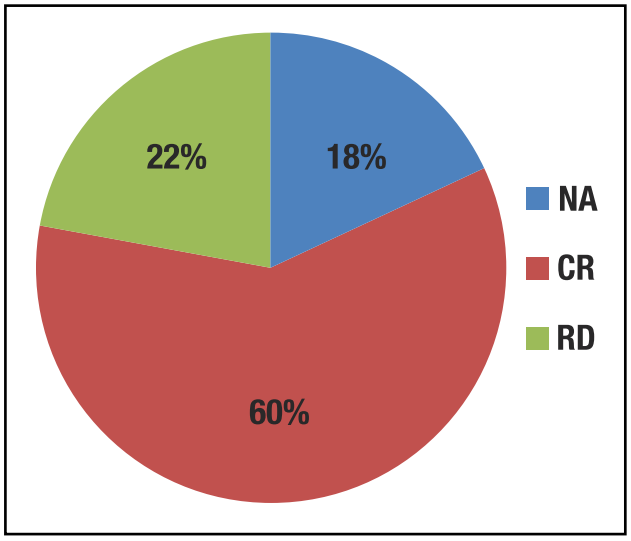


Figure 2. Clinical response to neoadjuvant chemo–radiotherapy.

assessment with upper esophagogastric endoscopy and PET–CT or CT, with 42 patients (84%) having PR and 3 patients (6 %) having progression. The median duration for completion of NACTRT to surgery was 35 days.

A pathological complete response rate of 30 patients (60%) was achieved in our cohort. Anap YS et al.[9] studied Western Indian data and showed a pathological complete response in 40% of cases while Bajwa et al.[12] studied a pathological complete response was seen in 39.6 % of cases and Bhattacharyya T et al.[10] study showed a pathological complete response of 41.3%. The overall survival of patients who underwent trimodality treatment was 18.5 months. Among 33 CROSS ineligible patients, 42.4% had pCR, in our study out of 9 patients cross ineligible, only 1 patient had pCR.

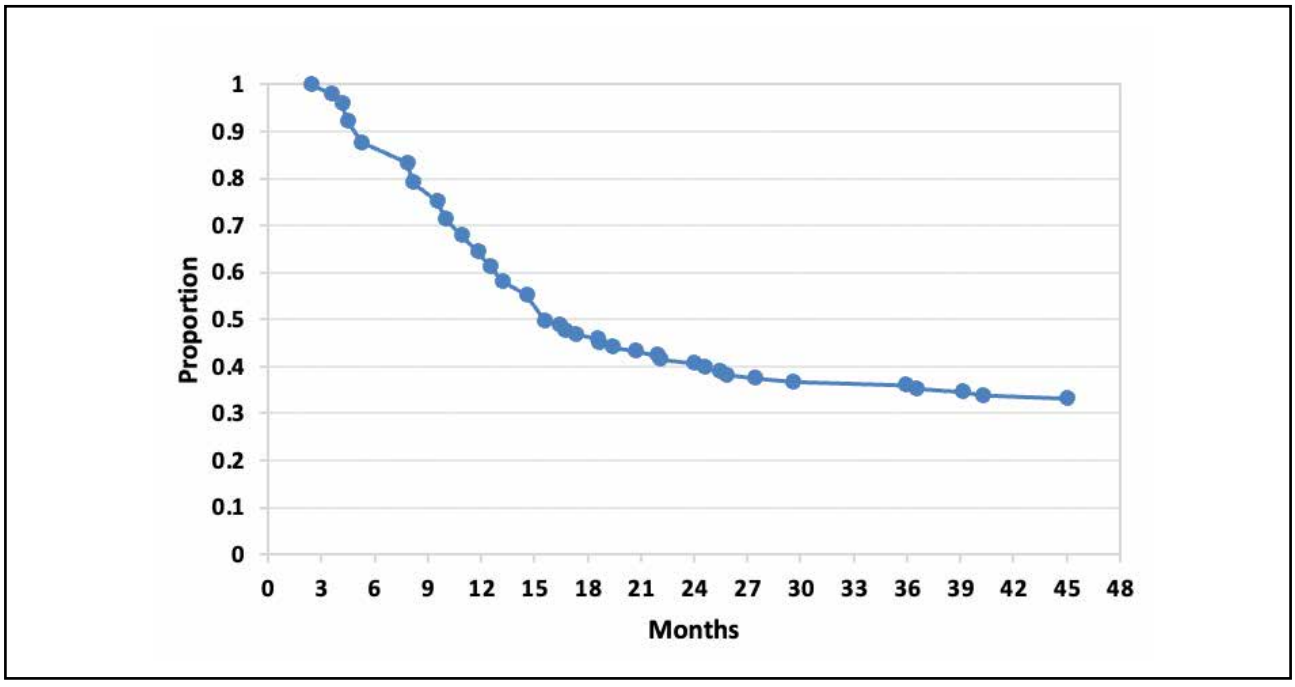


Figure 3. Kaplan–Meier survival curves for patients receiving NACT–RT

The most common histology was squamous cell carcinoma, which was seen in 42 patients (84%) and the lower third was the most common location which was similar to the rest of the Indian studies. The average tumour length was 5 cm.

Dose reduction was required in 1 patient (2%) during radiation, while in 3 patients (6%) patients during chemotherapy. 12 patients (24%) had radiation completion delay, with patient non–compliance being the most common cause of delay. No patients had therapy–related mortality during NACTRT.

Among the 50 patients in our cohort who completed NACTRT, 45 patients (90 %) underwent response

When analysed as per histology, 27 patients with SCC (90%) and 3 patients with Adenocarcinoma (10%) had pCR in our study. This is similar/higher/lower than pCR rates in CROSS which had pCR rates of 28 of 121 patients (23%) with adenocarcinoma and 18 of 37 patients (49%) with squamous carcinoma respectively. Bajwa et al.[12] study showed 44.7% of the resected squamous cell carcinoma achieved a pCR whereas only 20% of adenocarcinomas achieved a pCR.

The most common toxicities observed during NACTRT were fatigue, vomiting, and nausea. No grade 3/4 haematological toxicity was seen in our patients while in a study by Bhattacharyya T et al.[10], there were

grade 3/4 haematological toxicities noted. In addition, grade 3 or more severe form of neutropenia was seen in 11.3% of cases slightly higher than the CROSS study where 7% of cases suffered from grade 3 haematological toxicities. Among non–haematological toxicities, grade 3 gastrointestinal toxicity in our study was seen in 21 patients (42%). In a study by Bhattacharyya T et al., non–haematological toxicity was Grade 3 dysphagia was seen in 7.5% of cases.[10]

The incidence of perioperative and postoperative complications within 30 days such as pulmonary complications and chylothorax were noted in 17 patients. The incidence of these postoperative complications was lower compared to the Anap YS et al.[9] In our study, the pulmonary complication was seen in 8 patients, similar to the Anap YS et al., but vocal cord palsy and chyle leak rates were higher in 8 patients and 6 patients respectively. [9] In our study, one patient developed vocal cord palsy and 3 patients had chyle leak.

With a median follow–up of 24 months, the median OS was 15.6 months (95% CI,11.1–18.23 months). The 1–year and 2–year OS was 62% and 41.2%.

Our study is different from other studies as we have included patients who do not fit CROSS eligibility criteria, our study has shown a high pathological complete response with no grade 3/4 haematological toxicity and very few non–haematological toxicity with less incidence of post–operative complications Thus is safe and applicable for all the patients which are not included in cross criteria with prolong overall survival.

The limitation of the study is a small sample size with financial constraints and less compliance.

Conclusion

In our study, Neoadjuvant chemoradiotherapy followed by surgery was tolerable, safe and higher pathological complete response in the majority of patients with locally advanced esophageal cancer with lower incidence of Grade 3 and 4 haematological, non–haematological toxicity and post–surgical complications.

Acknowledgement

None to declare

Funding and Conflict of Interest

We have not received any funding. I hereby declare that there is no conflict of interest.

References

1. Ferlay J, Laversanne M, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Tomorrow (version 1.1). Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/tomorrow [Accessed on Jan 04, 2024].
2. McCormack VA, Menya D, Munishi MO, et al. Informing etiologic research priorities for squamous cell esophageal cancer in Africa: a review of setting–specific exposures to known and putative risk factors. Int J Cancer. 2017;140(2):259–271.
3. Blot WJ, Tarone RE. Esophageal cancer. In: Thun MJ, Linet MS, Cerhan JR, Haiman C, Schottenfeld D, eds. Cancer Epidemiology and Prevention. 4th ed. Oxford University Press; 2017:579–592.
4. Chen SB, Weng HR, Wang G, et al. Prognostic factors and outcome for patients with esophageal squamous cell carcinoma underwent surgical resection alone: evaluation of the seventh edition of the American Joint Committee on Cancer staging system for esophageal squamous cell carcinoma. J Thoracic Oncol. 2013;8:495–501.
5. Pennathur A, Gibson MK, Jobe BA, et al. Oesophageal carcinoma. Lancet (London, England). 2013;381:400–12.
6. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med. 2012;366(22):2074–84.
7. Yang H, Liu H, Chen Y, et al. Neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced squamous cell carcinoma of the esophagus (NEOCRTEC5010): A phase III multicenter, randomized, open–label clinical trial. J Clin Oncol. 2018;36(27):2796–803.
8. Shapiro J, van Lanschot JJB, Hulshof MCCM, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long–term results of a randomised controlled trial. Lancet Oncol. 2015;16(9):1090–8.
9. Anap YS, Tanawade PK, Matmaker MJ, et al. Preoperative Chemoradiation in Locally Advanced Resectable Carcinoma of the Esophagus in a Single Rural Cancer Hospital in Western India. South Asian J Cancer. 2020;9(3):158–162.
10. Bhattacharyya T, Arun Singh M, Chakraborty S, et al. Can the CROSS protocol be safely implemented in real–world scenarios with broader eligibility criteria? Experience from a tertiary care centre in India. E cancer medical science. 2021; 15:1291.
11. Puja K, Verma M, Kukreja D, et al. Cross Protocol for esophageal cancer in India: Reality or pipe dream? Annals of oncology. 2022;33(7):1112–1113.
12. Bajwa HK, Singareddy R, Alluri KR. High–dose–rate interstitial brachytherapy in oral cancer–Its impact on quality of life. Brachytherapy. 2016;15(3):381–386.