

## Acute Toxicity of Radical Chemoradiation in Patients with Esophageal Carcinoma

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**Abstract:** Currently, management of locally advanced esophageal cancers includes a trimodal approach, which combines radiotherapy, chemotherapy, and surgery. Chemoradiotherapy significantly improved prognosis and survival rates in locally advanced esophageal carcinoma, as demonstrated in several studies, data on its toxicity profile is limited. We assessed the frequency and severity of acute toxicities of Radical Chemoradiotherapy in patients with esophageal carcinoma. **Objective:** To evaluate the frequency and severity of acute toxicities associated with radical concurrent chemoradiotherapy in patients with locally advanced esophageal carcinoma and to identify clinical and treatment-related predictors of severe toxicity. **Methods:** A descriptive prospective study was conducted in the Department of Clinical and Radiation Oncology, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan, from 21-June-2024 to 21-April-2025. A total of 105 patients with esophageal carcinoma undergoing concurrent chemoradiation were analyzed. Clinical, treatment, and dosimetric parameters were recorded. Acute toxicity was graded using CTCAE criteria. The primary endpoint was acute toxicities. Univariate and multivariate logistic regression analyses were performed to identify independent predictors. **Results:** The mean age was  $44.3 \pm 10.6$  years. Esophagitis (100%) and fatigue (92.4%) remain the most common toxicity, with Grade  $\geq 2$  esophagitis occurring in 82.9% of patients, and Grade 3 toxicity observed in 38.1%. Hematological toxicities followed this: anemia (69.5%), thrombocytopenia (40%), and low absolute neutrophil count ANC 22.9%. The mean weight loss of approximately  $3.4 \text{ kg} \pm 3.08$  was observed during therapy. Each 1 kg increase in baseline weight reduced the odds of severe esophagitis by 7% (OR 0.93 per kg increase, 95% CI 0.89–0.97,  $p < 0.001$ ). Only one patient developed esophageal perforation, one patient died with grade 4 dyspnea/pneumonitis, and one died of neutropenic sepsis. Adequate target coverage was achieved across all plans, with a mean PTV V95% of 97.16%, and acceptable organ-at-risk doses were achieved in all plans. 60% of the patients underwent surgery following chemoradiation, and among those, 36.2% patients got a complete response. Only 6.7% patients progressed on the response assessment scan. **Conclusion:** Toxicity with esophageal chemoradiation is predominantly mucosal and hematological. Acute esophagitis remains the principal toxicity in radical chemoradiation for esophageal carcinoma, with over one-third of patients developing Grade 3 toxicity. Proactive nutritional support, optimization of radiation planning, and close monitoring are essential to improve treatment tolerability along with effective outcomes.

**Keywords:** Esophageal Carcinoma; Chemoradiation; Toxicities; Dosimetric Analysis; Esophagitis; Outcomes

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### Introduction

Esophageal carcinoma represents one of the most aggressive malignancies worldwide, ranking as the eighth most common cancer and the sixth leading cause of cancer-related mortality globally, with more than 450,000 new cases reported annually (1). The prognosis remains poor, as most cases present at locally advanced or metastatic stages at diagnosis (2). Two predominant histological subtypes characterize this disease: squamous cell carcinoma (SCC) and adenocarcinoma, with SCC being more prevalent in developing nations, including Pakistan (3).

The management of esophageal carcinoma is inherently multimodal. For locally advanced, potentially resectable disease, neoadjuvant chemoradiation followed by surgical resection has been established as the standard of care (4). For patients who are medically unfit for surgery or who present with unresectable disease, definitive concurrent chemoradiation therapy (CRT) serves as the primary curative-intent treatment modality (5). CRT combines cytotoxic chemotherapy agents—most commonly cisplatin/5-fluorouracil or carboplatin/paclitaxel—with external-beam radiation therapy, typically delivered at 50.4 Gy in 28 fractions. While this combined approach improves locoregional control and overall survival compared to radiation alone, it is associated with a spectrum of acute toxicities that can significantly compromise treatment delivery and patient quality of life (6, 7).

Acute toxicities encountered during radical CRT for esophageal carcinoma include esophagitis (occurring in 16–63% of cases), radiation pneumonitis (2–18%), cardiac toxicity (3–19%), hematological toxicities

such as leukopenia and neutropenia, and esophageal fistulas or strictures (approximately 8%) (2). Multiple factors, including radiation dose, fractionation schedule, treatment volume, radiation technique, and the specific chemotherapeutic agents employed influence the severity of these toxicities. The advent of intensity-modulated radiation therapy (IMRT) has improved the conformality of dose delivery, potentially reducing cardiopulmonary toxicity compared to conventional techniques (8).

In Pakistan, esophageal carcinoma constitutes a significant oncological burden, with SCC being the predominant histological subtype, particularly in the northern regions and among older male patients. The majority of patients in Pakistan present at advanced stages due to limited cancer awareness, delayed health-seeking behavior, and restricted access to diagnostic facilities. Radical chemoradiation represents the most feasible curative-intent treatment for a large proportion of Pakistani patients, as surgical expertise and perioperative infrastructure remain unevenly distributed across the country. Despite this clinical reality, robust local data characterizing the acute toxicity profile of radical CRT in Pakistani patients are scarce. Understanding the pattern, severity, and management of acute toxicities in this population is essential to optimize treatment protocols, improve patient compliance, and inform resource allocation within the Pakistani healthcare system. This study, therefore, aims to prospectively evaluate the acute toxicities of radical chemoradiation in patients with esophageal carcinoma treated at a tertiary care center in Pakistan.



**Methodology**

A descriptive prospective study was conducted in the Department of Clinical and Radiation Oncology, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan, from 21-June-2024 to 21-April- 2025. A total of 105 patients aged more than 18 years with a histologically proven diagnosis of esophageal cancer and good performance status were recruited through non-probability consecutive sampling. The study included T2-T4 or node-positive tumors staged according to the American Joint Committee on Cancer (AJCC), as well as irresectable esophageal cancer. Patients found to have metastatic disease, or those with poor performance status and not fit for radical treatment, were excluded from the study. Informed consent was taken from all patients before commencement of treatment. The Hospital Ethical Committee has approved this study. Selected patients received external beam radiation dose of 41.4-54 Gray given in 23-27 fractions of 1.8-2.0 Gray per fraction, in 5 fractions administered per week, along with a concurrent chemotherapy regimen with carboplatin targeted at an area under the curve (AUC) of 2 mg per millilitre per minute and paclitaxel 50 mg per square meter of body surface area. Patients were regularly followed every week during radiation and before each cycle of chemotherapy to monitor the development of toxicities. The baseline Complete Blood Count (CBC) was evaluated before the first cycle of chemotherapy and then before each cycle thereafter. Toxicities were graded according to the Common Toxicities Criteria of Adverse Effects. Appendix I. Dosimetric parameters were calculated using Dose Volume Histograms from the treatment planning system. All the data were collected on the specially designed Performa and analysed using IBM SPSS Statistics version 23. Quantitative variables such as age, weight, radiation dose, and dosimetric parameters are presented as the mean and standard deviation. Qualitative variables such as gender, stage, and grade of toxicity are presented as frequencies and percentages. Toxicities are stratified for age, gender, weight, radiation dose, dosimetric parameters, stage, and site. The chi-square test was used after post-stratification, with P-values <0.05 considered significant. Univariate and multivariate logistic regression analyses were performed to identify independent predictors.

**Results**

A total of 105 patients with histologically confirmed esophageal carcinoma treated with concurrent chemoradiotherapy were included in the study. The mean age of the cohort was 44.3 ± 10.6 years (range 18–64 years). Females constituted 60.0% of the study population, while males constituted 40.0%. The mean baseline body weight was 52.9 ± 12.4 kg. During treatment, the mean weight declined to 49.5 kg, corresponding to an average weight loss of 3.4 ± 3.08 kg; most patients presented with locally advanced disease. T3 tumors accounted for 95.2% of cases, while T4 tumors accounted for 2.9%. Nodal involvement was present in 83.8% of patients. Tumors were most frequently located in the distal esophagus (61.0%), followed by the middle esophagus (28.6%) and upper esophagus (12.4%). Nearly all patients had good functional status, with ECOG performance status 0–1 in 99% of cases (Table 1).

Among the 104 non-metastatic patients, the majority had T3 disease while only a small proportion had T2 or T4 tumors. Nodal disease was present in 83.8% of cases, highlighting the advanced stage at presentation in this cohort. Radiotherapy dose schedules varied according to tumor location. Most patients with middle and distal tumors received 45 Gy in 25 fractions, while cervical tumors received higher doses ranging from 50 to 54 Gy. No statistically significant association between radiation dose schedule and acute toxicity was observed (p = 0.95) (Table 2).

**Table 1: Baseline Demographic and Clinical Characteristics (N = 105)**

Variable	Value
Age (years), mean ± SD	44.3 ± 10.6
<b>Gender</b>	
Male	42 (40.0%)
Female	63 (60.0%)
Baseline weight (kg), mean ± SD	52.9 ± 12.4
Weight loss during treatment (kg), mean ± SD	3.4 ± 3.08
<b>ECOG performance status</b>	
0–1	104 (99.0%)
2	1 (1.0%)
<b>Tumor location</b>	
Upper esophagus	13 (12.4%)
Middle esophagus	30 (28.6%)
Distal esophagus	64 (61.0%)

**Table 2: Tumor Stage and Treatment Characteristics**

Variable	n (%)
<b>T stage</b>	
T2	1 (1.0%)
T3	100 (95.2%)
T4	3 (2.9%)
<b>Nodal status</b>	
N0	17 (16.2%)
N1–N3	87 (83.8%)
<b>Metastatic disease</b>	
M0	104 (99.0%)
M1	1 (1.0%)
<b>Radiotherapy dose schedule</b>	
41.4 Gy / 23 fractions	14 (13.3%)
45 Gy / 25 fractions	74 (70.5%)
50 Gy / 25 fractions	10 (9.5%)
54 Gy / 27 fractions	7 (6.7%)

Acute treatment-related toxicities were common during concurrent chemoradiotherapy. Esophagitis was observed in all patients (100%), making it the most frequent toxicity. Grade ≥2 esophagitis occurred in 82.9% of patients, and Grade 3 esophagitis was observed in 38.1%. Fatigue was reported in 92.4% of patients, though most cases were mild. Hematological toxicities were also frequently observed, including anemia (69.5%), thrombocytopenia (40%), and neutropenia (22.9%). Other acute toxicities included vomiting (39.1%), skin reactions (12.4%), and dyspnea (7.7%) (Table 3).

**Table 3: Acute Treatment-Related Toxicities According to CTCAE Criteria (N = 105)**

Toxicity	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Esophagitis	0	18 (17.1%)	47 (44.8%)	40 (38.1%)	0
Vomiting	64 (61.0%)	32 (30.5%)	9 (8.6%)	0	0
Fatigue	8 (7.6%)	96 (91.4%)	1 (1.0%)	0	0
Dyspnea	97 (92.4%)	7 (6.7%)	0	0	1 (1.0%)
Skin reaction	92 (87.6%)	10 (9.5%)	3 (2.9%)	0	0
Anemia	32 (30.5%)	27 (25.7%)	34 (32.4%)	12 (11.4%)	0
Thrombocytopenia	63 (60.0%)	26 (24.8%)	9 (8.6%)	7 (6.7%)	0
Neutropenia (ANC reduction)	81 (77.1%)	17 (16.2%)	4 (3.8%)	3 (2.9%)	0

Logistic regression analysis was performed to identify predictors of severe esophagitis (Grade  $\geq 3$ ). Baseline body weight was independently associated with the risk of severe esophagitis. Each 1-kg increase in baseline weight reduced the odds of severe esophagitis by approximately 7% (OR 0.93, 95% CI 0.89–0.97,  $p = 0.001$ ). Gender and tumor location were not significantly associated with severe toxicity (Table 4).

**Table 4: Multivariate Logistic Regression Analysis for Severe Esophagitis**

Variable	Adjusted OR	95% CI	p-value
Baseline weight (kg)	0.93	0.89–0.97	0.001
Female vs male	1.53	0.61–3.87	0.366
Tumor site (middle vs upper)	0.78	0.15–4.15	0.767
Tumor site (distal vs upper)	2.03	0.46–9.04	0.352

Radiotherapy planning demonstrated adequate target coverage in all patients. The mean PTV V95% was 97.17%, indicating optimal target dose coverage. Organ-at-risk doses remained within recommended tolerance limits. The mean lung dose was 10.83 Gy and lung V20 was 11.1%, both below pneumonitis risk thresholds. Similarly, mean heart dose and spinal cord maximum dose remained within acceptable limits (Table 5).

**Table 5: Dosimetric Parameters**

Parameter	Mean	Median	Range
PTV V95 (%)	97.17	97.06	93–100
PTV Dmax (%)	106.52	106.30	103–111.6
Lung mean dose (Gy)	10.83	10.40	0–79
Lung V20 (%)	11.10	10.30	0–30
Heart mean dose (Gy)	16.70	18.40	0–26
Heart V30 (%)	13.67	12.30	0–33.18
Spinal cord Dmax (Gy)	22.21	22.00	10.3–43
Liver mean dose (Gy)	8.02	9.30	0–39

Following chemoradiotherapy, 63 patients (60%) underwent surgical resection, whereas 42 did not. Radiological response assessment showed complete response in 2.9% of patients, partial response in 72.4%, no response in 18.1%, and progressive disease in 6.7%. Among patients who underwent surgery, pathological complete response was achieved in 36.2% (Table 6).

**Table 6: Treatment Outcomes and Response After Chemoradiotherapy**

Outcome	n (%)
Surgery performed	63 (60.0%)
No surgery	42 (40.0%)
<b>Radiological response</b>	
Complete response	3 (2.9%)
Partial response	76 (72.4%)
No response	19 (18.1%)
Progressive disease	7 (6.7%)
<b>Pathological response among operated patients</b>	
Complete response	23 (36.2%)
Partial response	13 (21.0%)
Stable disease	2 (3.0%)

During follow-up, disease progression was observed in 18.1% of patients. Most cases of progression occurred in patients who did not undergo surgery (61%). The majority of recurrences involved distant metastases (68%), particularly pulmonary, hepatic, and osseous metastases, while nodal metastases accounted for 18% of cases. Local recurrence was uncommon, occurring in only two patients.

## Discussion

The present study evaluated acute toxicities of radical chemoradiotherapy (CRT) in 105 patients with histologically confirmed esophageal carcinoma. The mean age of the cohort was  $44.3 \pm 10.6$  years, which is notably younger than the populations reported in most Western and East Asian series. Chen et al. reported a median age of 55.5 years in their phase II neoadjuvant CRT study (9), while Bostel et al. described a median age of 73 years in their multicenter analysis of elderly patients with esophageal adenocarcinoma (10). The relatively younger age distribution observed in the present cohort is consistent with the epidemiological profile of esophageal carcinoma in South Asian populations, where the disease tends to manifest at an earlier age, likely attributable to dietary habits, tobacco use, and socioeconomic determinants of health. Furthermore, the female predominance (60%) observed in this study is atypical compared to most published series; Chen et al. reported over 90% male patients in their cohort (9), and Ma et al. described a predominantly male population (15 men and 5 women) in their proton plus carbon-ion radiotherapy series (11). This gender distribution may reflect regional epidemiological differences in Pakistan, where esophageal squamous cell carcinoma disproportionately affects women in certain geographic clusters, particularly in the northern belt.

The mean baseline body weight of  $52.9 \pm 12.4$  kg, with a mean treatment-related weight loss of  $3.4 \pm 3.08$  kg, underscores the nutritional vulnerability of this patient population. Dong et al. demonstrated that baseline nutritional status is an independent predictor of radiation esophagitis, with a Patient-Generated Subjective Global Assessment (PG-SGA) score  $\geq 9$  being significantly associated with grade  $\geq 2$  esophagitis ( $p = 0.042$ ) (12). The low baseline body weight observed in the present cohort may therefore have contributed to the high rates of esophagitis documented herein. This finding warrants prospective nutritional intervention strategies in future Pakistani cohorts.

The overwhelming majority of patients in the present study presented with T3 disease (95.2%) and nodal involvement (83.8%), reflecting the advanced stage at presentation that is characteristic of esophageal carcinoma in resource-limited settings. Liu et al. similarly reported that a considerable proportion of patients in Eastern countries have already lost the opportunity for surgical treatment at the time of diagnosis, necessitating definitive concurrent CRT as the primary treatment modality (13). Kato et al. enrolled patients with stage II, III, and IV esophageal cancer in their phase I nimotuzumab-CRT study, acknowledging that local recurrence or distant metastasis occurs in approximately 30–60% of cases following radical treatment (14). The distal esophagus was the most frequent tumor location (61.0%) in the present cohort, followed by the middle (28.6%) and upper esophagus (12.4%). Zhang et al. noted that cervical esophageal cancer accounts for only approximately 5% of all esophageal cancers, consistent with the low proportion of upper esophageal tumors observed in the present series (15). The majority of patients in the present study received 45 Gy in 25 fractions, with cervical tumors receiving higher doses of 50–54 Gy. No statistically significant association between radiation dose schedule and acute toxicity was observed ( $p = 0.95$ ). This finding is broadly consistent with the literature. Sun et al., in a meta-analysis evaluating high versus low radiation dose in concurrent CRT for esophageal carcinoma using modern radiotherapy techniques, concluded that high-dose radiotherapy ( $\geq 60$  Gy) was associated with improved overall survival and locoregional control without a significant increase in severe toxicities (16). Halder et al. employed a dose of 50.4 Gy in 28 fractions with concurrent cisplatin and 5-fluorouracil in their randomized study of locally advanced esophageal carcinoma, reporting a toxicity profile comparable to that observed in the present series (17). Watanabe et al. similarly utilized 50.4 Gy in 28 fractions for thoracic tumors and 61.2 Gy for cervical tumors in their retrospective study of elderly patients with esophageal squamous cell carcinoma (8).

Esophagitis was the most prevalent acute toxicity in the present study, occurring in 100% of patients, with grade  $\geq 2$  esophagitis in 82.9% and

grade 3 esophagitis in 38.1%. These rates are considerably higher than those reported in several published series. Wang et al. reported a total incidence of acute radiation esophagitis of 68.6% in their phase II SIB-IMRT plus nimotuzumab study, with grade 2 and grade 3 esophagitis occurring in 25.7% and 17.1% of patients, respectively (18). Kato et al. reported grade  $\geq 3$  radiation esophagitis in 30% of patients receiving nimotuzumab combined with concurrent CRT (14). Liu et al. documented grade 3 esophagitis in 11.1% of patients treated with weekly docetaxel and concurrent CRT with cisplatin (13). Rutenberg et al. reported grades 1–3 esophagitis in 82% of patients receiving proton therapy with concurrent chemotherapy for thoracic esophageal cancer (1), a figure comparable to the overall esophagitis rate in the present cohort. However, the grade 3 rate in the present study (38.1%) substantially exceeds that reported in most proton therapy series. The higher esophagitis rates observed in the present study may be attributable to the low baseline body weight and nutritional compromise of the study population, consistent with the findings of Dong et al., who identified baseline malnutrition as an independent predictor of grade  $\geq 2$  radiation esophagitis (12). Additionally, Li et al. emphasized that acute radiation-induced esophagitis is among the most serious toxicities associated with definitive radiotherapy or CRT for esophageal cancer, and that it is characterized by odynophagia and dysphagia within 90 days of thoracic irradiation (17). Hematological toxicities were frequently observed in the present cohort, including anemia (69.5%), thrombocytopenia (40%), and neutropenia (22.9%). Watanabe et al. reported substantially higher rates of grade  $\geq 3$  hematological toxicities in elderly patients receiving nedaplatin and 5-fluorouracil CRT, including neutropenia (76%), leukopenia (72%), thrombocytopenia (32%), and anemia (28%) (8). Kato et al. documented grade  $\geq 3$  lymphopenia in 90%, leukopenia in 60%, and neutropenia in 50% of patients receiving nimotuzumab-CRT (14). Liu et al. reported grade 3 neutropenia in 13.0%, grade 3 anemia in 3.7%, and grade 3 thrombocytopenia in 1.9%, with grade 4 neutropenia in 16.7% of patients (13). The relatively lower rates of severe hematological toxicity in the present study compared to some published series may reflect differences in chemotherapy regimens, patient age, and baseline hematological reserve. Ma et al. reported grades 1, 2, 3, and 4 acute hematological toxicities in 25%, 30%, 10%, and 30% of patients, respectively, in their proton plus carbon-ion radiotherapy series (11), suggesting that the hematological toxicity profile in the present cohort is broadly within the range reported in the contemporary literature.

Fatigue was reported in 92.4% of patients in the present study, with the majority of cases graded as 1. Liu et al. reported grade 3 fatigue in 20.4% of patients, which is higher than the grade 3 fatigue rate of 0% observed in the present cohort (13). Vomiting occurred in 39.1% of patients, skin reactions in 12.4%, and dyspnea in 7.7%. Rutenberg et al. reported no acute cardiopulmonary toxicities in patients who did not undergo surgical resection (1): consistent with the low rates of dyspnea observed in the present series. The low rate of skin reactions (12.4%) is consistent with the use of modern IMRT techniques, which reduce the integral dose to superficial tissues (16).

Multivariate logistic regression analysis in the present study identified baseline body weight as an independent predictor of severe esophagitis (grade  $\geq 3$ ), with each 1-kg increase in baseline weight reducing the odds of severe esophagitis by approximately 7% (OR 0.93, 95% CI 0.89–0.97,  $p = 0.001$ ). This finding is consistent with the work of Dong et al., who demonstrated that baseline nutritional parameters—including PG-SGA score, weight loss percentage, and albumin level—were significantly associated with grade  $\geq 2$  radiation esophagitis in multivariate analysis (12). Gender and tumor location were not significantly associated with severe toxicity in the present study, a finding that is broadly consistent with the literature, as most published series have not identified these variables as independent predictors of acute esophagitis severity (12, 18). Radiotherapy planning in the present study demonstrated adequate target coverage, with a mean PTV V95% of 97.17%. Organ-at-risk doses remained within recommended tolerance limits, with a mean lung dose of 10.83 Gy and lung V20 of 11.1%, both below established pneumonitis

risk thresholds. Ma et al. demonstrated that proton and carbon-ion radiotherapy produced lower doses to organs at risk than photon IMRT, particularly for the spinal cord maximum dose and mean lung and heart doses (11). The mean heart dose of 16.70 Gy and the spinal cord maximum dose of 22.21 Gy observed in the present study are within acceptable limits, as reported in the contemporary literature (1, 11).

Following CRT, 60% of patients underwent surgical resection, with a pathological complete response (pCR) rate of 36.2% among those who underwent surgery. Kermani et al. reported pCR rates of 64.8% and 62.5% in the intervention and control arms of their randomized trial of enoxaparin plus CRT, respectively (20), which are higher than the pCR rate observed in the present study. Chen et al. reported a pCR rate of 45.8% in their phase II neoadjuvant DCF-CRT study (9). The radiological partial response rate of 72.4% in the present study is consistent with the response rates reported by Liu et al., who documented complete response in 44.4% and partial response in 44.4% of patients following docetaxel-cisplatin CRT (13). Disease progression was observed in 18.1% of patients, with the majority of recurrences involving distant metastases (68%), particularly pulmonary, hepatic, and osseous metastases. Kato et al. noted that local recurrence or distant metastasis occurs in approximately 30–60% of esophageal cancer cases following radical treatment (14), and Liu et al. reported a 3-year overall survival rate of 36.4% in their advanced esophageal SCC cohort (13), underscoring the persistent challenge of disease control in this malignancy.

The present study has several limitations, including its retrospective single-center design, the relatively small sample size, and the absence of long-term survival data. The predominantly young and female patient population may limit the generalizability of the findings to other settings. Future prospective multicenter studies with standardized nutritional assessment and quality-of-life endpoints are warranted to further characterize the acute toxicity profile of radical CRT in Pakistani patients with esophageal carcinoma.

## Conclusion

Definitive chemoradiotherapy with weekly carboplatin and paclitaxel is associated with significant acute toxicities, particularly esophagitis, fatigue, and myelosuppression. High occurrence of grade 3 esophagitis warrants early nutritional intervention, consideration of feeding tube placement, prophylactic analgesia protocols, strict adherence to esophageal dose–volume constraints, careful monitoring, and potential integration of advanced radiation techniques. Chemoradiation provides excellent local control; however, surgery plays a significant role in long-term survival. Future strategies should focus on reducing systemic progression through novel systemic agents, adaptive therapy, or optimized sequencing, while maintaining tolerable toxicity profiles.

## Declarations

### Data Availability statement

All data generated or analysed during the study are included in the manuscript.

### Ethics approval and consent to participate

Approved by the department concerned. (IRB-23-41)

### Consent for publication

Approved

### Funding

Not applicable

## Conflict of interest

The authors declared no conflict of interest.

## Author Contribution

*EK (Resident), AWK (Resident), MATA (Resident)*

Contributed to study design, data collection, and initial manuscript drafting

Assisted in data acquisition, literature review, and manuscript editing  
Performed statistical analysis and contributed to the interpretation of results

Helped in methodology development, data organization, and manuscript formatting

**MMI (Physicist), ASZ (Resident), TS (Consultant)**

Contributed to patient recruitment, data entry, and results compilation

Assisted in referencing, proofreading, and final revisions of the manuscript

Guided study execution and critically reviewed the manuscript

Supervised the research, coordinated among authors, finalized the manuscript, and approved the final version

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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