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Original Article

Assessment of Health-Related Quality of Life after the Second Cycle of Chemotherapy in Esophageal Cancer Patients: A Prospective Cross-Sectional Study

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ABSTRACT

Aim: To evaluate early changes in symptom-specific Health-Related Quality of Life (HRQoL) among Esophageal cancer patients receiving chemotherapy up to the second cycle and to assess demographic and treatment-related differences in early responses. **Materials and Methods:** A total of 56 patients with histologically confirmed Esophageal cancer were evaluated prospectively before chemotherapy initiation and after the second cycle. HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Esophageal Cancer (EORTC QLQ-OES25). Domain scores were linearly transformed to a 0-100 scale according to the EORTC scoring manual, and changes from baseline to the second cycle were analyzed using paired t-tests and Pearson correlation. **Results:** The majority of patients were aged 45-64 years (57%) and male (66%). Stage III disease was most common (48%), and 77% received palliative chemotherapy. The mean overall symptom-specific HRQoL score improved modestly from 59.75±16.48 at baseline to 61.80±17.18 after the second cycle (p=0.032). Younger patients (25-44 years), females, and those receiving adjuvant therapy showed the greatest improvements. The correlation between baseline and post-cycle scores was strong (r=0.88, p<0.001). The highest symptom burden was noted in pain, odynophagia, and eating restriction domains. **Conclusion:** Early improvements in symptom-specific HRQoL were observed after two chemotherapy cycles, especially among younger and adjuvant-therapy patients. Routine early-cycle HRQoL monitoring using the EORTC QLQ-OES25 may help assess treatment tolerance and patient adaptation. Larger multicenter studies with longer follow-up are warranted.

Keywords: Chemotherapy, European Organisation for Research and Treatment of Cancer, Health-Related Quality of Life, Squamous cell carcinoma.

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INTRODUCTION

Esophageal cancer remains a major global health challenge characterized by late presentation, aggressive local progression, and considerable variation in incidence and subtype distribution across regions (Siersema, 2008). Two histologic types Squamous Cell Carcinoma (SCC) and adenocarcinoma dominate the clinical landscape, each with distinct etiologies, geographic patterns, and implications for prevention and treatment (Layke and Lopez, 2006). Overall survival has improved modestly with advances in multimodality therapy, but outcomes remain poor for many patients because the disease is frequently diagnosed at an advanced stage (Yu *et al*., 2009). Recent comprehensive reviews emphasize that progress in early detection, risk stratification, and access to standardized treatment pathways is essential to reduce mortality (Waters and Reznik, 2022).

Well-established environmental and behavioral risk factors, including tobacco use, alcohol consumption, dietary deficiencies, chronic mucosal irritation, gastroesophageal reflux disease, and obesity for Esophageal adenocarcinoma interact with host genetic susceptibility to drive carcinogenesis (Huang and Yu, 2018). Molecular and genetic studies have begun to clarify pathways involved in tumor initiation and progression, opening opportunities for biomarker-driven risk assessment and targeted therapies, although many genetic associations require further validation across populations. These insights help explain geographic hot-spots of disease and support tailored prevention strategies. Management of Esophageal cancer has evolved toward

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multidisciplinary, stage-directed care that integrates endoscopic assessment, accurate staging with cross-sectional imaging and endoscopic ultrasound, and combined-modality therapy (surgery, radiotherapy, and systemic therapy) when indicated. For localized disease, multimodal approaches (neoadjuvant chemoradiation±surgery) improve local control and survival in selected patients; systemic therapy and palliative interventions remain central in advanced cases. However, optimal strategies differ between SCC and adenocarcinoma and continue to be refined as new systemic agents and immunotherapies are evaluated (Yang *et al*., 2024).

Resource constraints substantially influence real-world outcomes: low- and middle-income settings face challenges including limited access to diagnostic endoscopy and imaging, fewer specialized surgical and oncology services, and barriers to delivering multimodality therapy, all of which necessitate context-adapted management algorithms and pragmatic public-health interventions. Strengthening early detection, domain-appropriate treatment pathways, and supportive care is therefore a priority to reduce the global burden of esophageal cancer (Mwachiro and White, 2022).

The European Organisation for Research and Treatment of Cancer (EORTC) developed disease-specific instruments to assess Health Related Quality of Life (HRQoL) in cancer populations, including the esophageal-specific module EORTC Quality of Life Questionnaire - Oesophageal Cancer Module (QLQ-OES25) which evaluates swallowing, pain, reflux, eating restrictions, and related symptoms. While most studies have explored long-term HRQoL outcomes after surgery or chemoradiation, there is limited evidence on short-term, chemotherapy only HRQoL changes.

While several studies have evaluated HRQoL after multimodality or surgical therapy, data focusing on early-chemotherapy cycle but HRQoL changes using the EORTC QLQ-OES25 remain limited, particularly in Indian patient populations.

Hence, the present study aimed to evaluate early changes in symptom-specific HRQoL among esophageal cancer patients receiving chemotherapy up to the second cycle, using the EORTC QLQ-OES25 and to correlate the findings with demographic and treatment-related variables.

MATERIALS AND METHODS

Study Design

A prospective observational study was conducted from October 2023 to March 2024 at Department of Medical Oncology, Karnataka Medical College and Research Institute, Hubballi, Karnataka, India. A pilot study was initially performed to determine the sample size. Subsequently, the research comprised 56 histologically confirmed Esophageal cancer patients who were planned for chemotherapy and met the study eligibility criteria.

Study population

Inclusion Criteria

- Adult patients aged 18 years and above.
- Histologically confirmed cases of Esophageal carcinoma.
- Patients who were planned for chemotherapy any intent: palliative, adjuvant, definitive, or neoadjuvant.

Exclusion Criteria

- Patients receiving concurrent radiotherapy along with chemotherapy.
- Patients with any other active malignancy.
- Patients who were unwilling or unable to complete the HRQoL questionnaire (EORTC QLQ-OES25).

Participants

Patients were categorized based on age (18-24, 25-44, 45-64, ≥65 years), gender, disease stage (I-IV), treatment type (palliative, adjuvant, definitive, neoadjuvant), and histopathology (well, moderately, or poorly differentiated SCC).

Treatment and Assessment

HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Esophageal Cancer Module (EORTC QLQ-OES25) at baseline and after the second chemotherapy cycle. The EORTC QLQ-OES25 is a 25-item, disease-specific instrument designed to evaluate the symptom profile and quality of life in patients with esophageal cancer. Each item is scored on a 4-point Likert scale ranging from 1 ("Not at all") to 4 ("Very much").

The questionnaire covers major symptom domains, including dysphagia, eating restrictions, reflux, pain, odynophagia, and dry mouth, along with single items assessing coughing, choking, taste alteration, weight loss, and difficulties in talking or eating in public. Scores for each domain were linearly transformed to a standardized 0-100 scale according to the EORTC scoring manual, where higher scores indicate greater symptom burden.

The study focused on symptom-specific HRQoL using the EORTC QLQ-OES25 alone. The core EORTC QLQ-C30 questionnaire was not applied, as the objective was to assess early, chemotherapy-related changes in esophageal-specific quality of life rather than overall functional status.

Statistical Analysis

Descriptive statistics summarized patient characteristics. Paired t-tests compared mean domain scores before and after treatment. Pearson's correlation assessed associations between baseline and second-cycle HRQoL scores, with $p<0.05$ considered statistically significant.

RESULTS

Patient Demographics

The majority of patients (57%) were middle-aged (45-64 years), reflecting the typical age of presentation of Esophageal cancer. Only 13% were younger adults (25-44 years), while nearly one-third were elderly (>65 years). No patients were in the 18-24 age group, indicating the rarity of Esophageal cancer in very young populations. Males predominated in the study (66%), consistent with global epidemiological trends where Esophageal cancer is more common among men. The smaller female proportion (34%) still provided an important comparative subgroup for response analysis. Nearly half of the patients (48%) presented with stage III disease, followed by stage IV (23%). This highlights the late presentation pattern of Esophageal cancer in many clinical settings. Only 9% were detected at stage I, suggesting limited opportunities for early intervention. Most patients (77%) received palliative chemotherapy, reflecting the advanced disease burden at presentation. A smaller group (14%) underwent adjuvant therapy, while only a handful were treated with definitive (7%) or neoadjuvant (2%) approaches. This distribution again underlines the predominance of late-stage disease in the cohort. Among the 56 patients, no additional procedures were performed in (n=42, 75%), radiation therapy alone was received by (n=1, 1.8%), surgery alone was undergone by (n=10, 17.9%), and both surgery plus radiation were received by (n=3, 5.4%) (Table 1 and Figure 1).

Moderately and well differentiated squamous cell carcinoma were equally common, each accounting for 43% of cases. Poorly differentiated SCC was less frequent (14%), which is clinically significant as poorer differentiation is often linked to more aggressive behavior (Figure 1).

A modest but statistically significant improvement in the overall OES25 symptom-related HRQoL score was observed after the second chemotherapy cycle (p=0.032). The change indicates early symptom relief and treatment adaptation (Table 2).

Domain-wise analysis showed significant reductions in pain, odynophagia, and reflux symptom scores following chemotherapy, suggesting early improvement in symptom burden. Other domains exhibited stable trends with minimal change.

All scores were transformed to a 0-100 scale according to the EORTC QLQ-OES25 scoring manual, where higher values represent greater symptom burden (Table 3).

Younger patients and those receiving adjuvant chemotherapy demonstrated the highest improvement in OES25 symptom-related HRQoL scores, while elderly and definitive-therapy groups showed smaller gains, likely reflecting disease burden and treatment tolerance (Table 4).

DISCUSSION

This prospective observational study assessed early changes in symptom-specific Health-Related Quality of Life (HRQoL) using the EORTC QLQ-OES25 among patients with esophageal cancer undergoing chemotherapy. Evaluation up to the second chemotherapy cycle demonstrated a modest yet statistically significant improvement in the overall OES25 composite score, from 59.75±16.48 at baseline to 61.80±17.18 after two cycles (p=0.032). These results indicate measurable, early symptom relief rather than a major functional gain. The most prominent improvements were noted in the domains of pain, odynophagia, and reflux, which represent core swallowing-related symptoms of esophageal malignancy. Stability in domains such as dry mouth and eating restrictions suggests that nutritional and salivary difficulties may persist despite early treatment response.

Younger patients, females, and those receiving adjuvant therapy demonstrated relatively higher HRQoL gains compared with older or palliative counterparts, emphasizing the influence of demographic and treatment intent on HRQoL trajectories. Similar subgroup trends have been reported in earlier prospective series where younger patients exhibited better tolerance to cytotoxic

Table 1: Age-wise distribution of participants (n=56).

Age Group	N	%
18-24 years	0	0
25-44 years	7	13
45-64 years	32	57
>65 years	17	30
Gender		
Male	37	66
Female	19	34
Stage		
Stage I	5	9
Stage II	11	20
Stage III	27	48
Stage IV	13	23
Category		
Palliative	43	77
Adjuvant	8	14
Definitive	4	7
Neoadjuvant	1	2
Procedure Performed Prior to or Subsequent to Chemotherapy		
None of The Above	42	75
Radiation	1	1.8
Surgery	10	17.9
Surgery + Radiation	3	5.4

Table 2: Overall symptom-related HRQoL (EORTC QLQ-OES25 composite score) before and after 2nd cycle.

Time point	Mean±SD	Mean change	*p*-value
Baseline	59.75±16.48		
After 2nd cycle	61.80±17.18	+2.05	0.032

Table 3: EORTC QLQ-OES25 domain scores (0-100) at baseline and after 2nd cycle.

Domain	Baseline Mean±SD	After 2nd cycle Mean±SD	Change	*p*-value
Pain	58.9±14.3	56.4±14.9	-2.5	0.041
Odynophagia	56.9±15.1	54.2±15.6	-2.7	0.047
Reflux	47.9±14.8	45.5±15.2	-2.4	0.028
Eating restrictions	37.5±13.9	35.1±14.2	-2.4	0.080
Dry mouth	26.8±10.9	26.0±11.1	-0.8	0.400

Table 4: Mean Overall OES25 Symptom-Related HRQoL Scores by Subgroup (Baseline and After 2nd Cycle).

Subgroup	N	Baseline Mean±SD	After 2nd cycle Mean±SD	Mean change
Age 25-44 years	7	68.6±15.7	70.7±16.4	+2.1
Age 45-64 years	32	61.4±15.9	63.6±16.6	+2.2
Age ≥65 years	17	53.4±16.3	55.3±17.1	+1.9
Male	37	59.4±15.3	61.4±16.0	+2.0
Female	19	60.6±19.2	62.6±19.9	+2.0
Palliative	43	60.5±16.9	62.6±17.6	+2.1
Adjuvant	8	66.5±11.0	68.9±11.5	+2.4
Definitive	4	39.8±6.9	41.0±7.4	+1.2

therapy, quicker symptomatic recovery, and fewer comorbid limitations (Lv *et al.*, 2010).

Our findings are consistent with the QUINTETT trial (Malthaner *et al.*, 2022), which observed that treatment sequence and intent-particularly adjuvant regimens-had a major impact on early QoL outcomes, with adjuvant therapy associated with fewer acute toxicities and better symptom control. This reinforces that HRQoL changes during systemic therapy depend not only on treatment toxicity but also on patient adaptation, nutritional support, and psychosocial resilience. In contrast, studies evaluating multimodality or surgical management have shown substantial short-term deterioration in HRQoL following esophagectomy, with recovery occurring only after several months, underscoring the heavier QoL burden associated with surgical morbidity (Scarpa *et al.*, 2011).

Further comparison with indicates that long-term QoL outcomes differ across treatment types, with definitive chemoradiotherapy offering disease control but often at the cost of mucosal toxicity and dysphagia (Lv *et al.*, 2014). In contrast, the present short-term chemotherapy-only evaluation showed small but favorable improvements in swallowing-related symptoms, possibly reflecting early tumor shrinkage and improved esophageal patency. The strong correlation (r=0.88, $p<0.001$) between baseline and post-cycle OES25 scores mirrors findings (Boorn *et al.*, 2020) confirming that baseline HRQoL serves as a reliable predictor of post-treatment wellbeing and survival.

Recent international evidence has further supported the value of HRQoL monitoring during systemic therapy. The KEYNOTE-590 trial demonstrated that adding pembrolizumab to chemotherapy for advanced esophageal cancer maintained or improved HRQoL, especially in swallowing-related domains, using the EORTC QLQ-C30 and OES18 instruments. Similarly, a real-world cohort study from the Netherlands (Juloori *et al.*, 2014) involving patients on first-line systemic therapy reported sustained improvements in odynophagia and dysphagia domains measured by the QLQ-OG25. Although these studies used slightly different QoL modules, their findings parallel the present OES25-based results, confirming that systemic therapy can alleviate esophageal symptoms and maintain patient wellbeing even during active treatment.

Although the mean improvement of +2.05 points observed here was statistically significant, it remains below the 5-10-point threshold generally considered clinically meaningful (Pickard *et al.*, 2007). This suggests that the observed change represents early symptom stabilization and adaptation to chemotherapy rather than complete functional recovery. Nevertheless, even small improvements in swallowing and pain can translate into

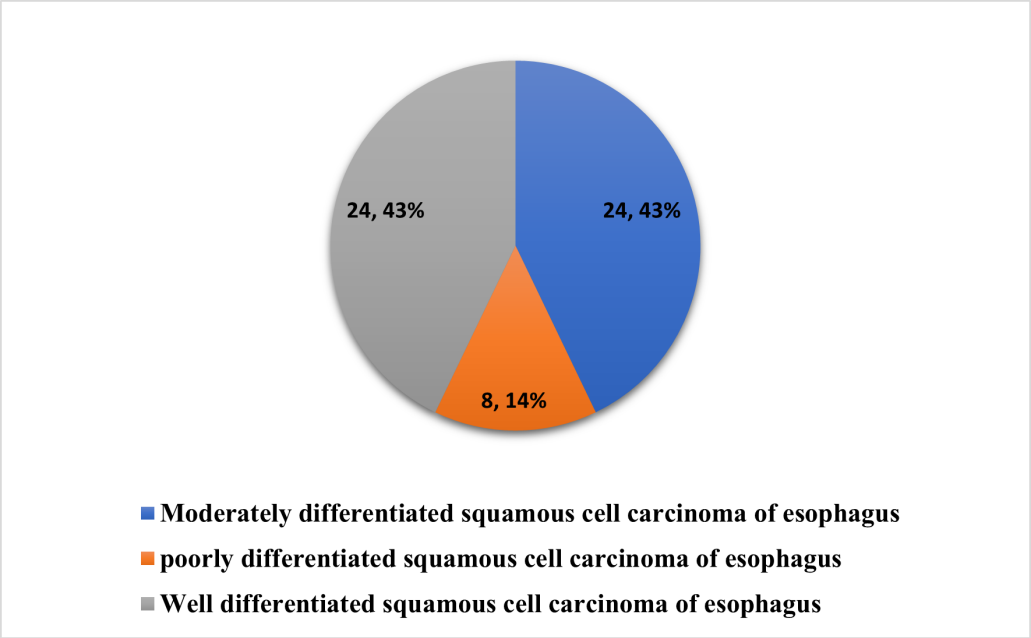

Figure 1: Histopathological distribution (*n*=56).

meaningful relief in nutritional intake, comfort, and treatment adherence.

From a clinical standpoint, this study highlights the importance of integrating EORTC QLQ-OES25-based HRQoL monitoring into routine chemotherapy follow-up visits. Regular assessment allows early identification of symptom aggravation, malnutrition, or dehydration-factors that can impact treatment continuity and dose tolerance. The OES25 tool, being concise and symptom-specific, can be administered easily in busy oncology clinics, providing a quantitative measure of subjective improvement parallel to tumor response.

Our findings also underline the value of timely supportive care-nutritional counseling, oral hygiene reinforcement, mucosal protection, and psychosocial support-in optimizing HRQoL outcomes. Incorporating multidisciplinary supportive interventions early during chemotherapy may help sustain patient comfort, compliance, and quality of life.

However, the present study has several limitations. It was conducted at a single tertiary center with a relatively small sample size and short follow-up limited to two chemotherapy cycles. Inclusion of only the OES25 module provided a detailed assessment of esophageal symptoms but excluded global and functional domains captured by the EORTC QLQ-C30. Future research should therefore combine both QLQ-C30 and QLQ-OES25 instruments, extend follow-up across all chemotherapy cycles, and include post-treatment assessments to determine whether early improvements persist and translate into long-term HRQoL and survival gains. Multicentric longitudinal studies would further strengthen external validity and allow adjustment for stage, histology, and treatment intent.

CONCLUSION

This study demonstrated modest but statistically significant improvements in symptom-specific Health-Related Quality of Life (HRQoL) among esophageal cancer patients after the second chemotherapy cycle, as assessed by the EORTC QLQ-OES25. Notable reductions were observed in pain, odynophagia, and reflux domains, indicating early symptomatic relief and improved treatment tolerance. Younger patients, females, and those receiving adjuvant therapy showed the most favorable changes, whereas elderly and definitive-therapy groups exhibited smaller gains. The strong correlation between baseline and post-cycle OES25 scores (r=0.88, $p<0.001$) suggests that early HRQoL assessments can help predict patient response and tolerance to chemotherapy. Although the observed mean improvement (+2.05 points) was statistically significant yet clinically modest, it reflects early symptom adaptation rather than full functional recovery. Integrating routine OES25-based HRQoL evaluation into chemotherapy follow-up could enhance patient-centered management and early supportive-care interventions.

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ABBREVIATIONS

HRQoL: Health-Related Quality of Life; **EORTC:** European Organisation for Research and Treatment of Cancer; **SCC:** squamous cell carcinoma.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

No specific funding was received for this study.

ETHICAL CONSIDERATIONS

The Institutional Ethics Committee (IEC) of KLE College of Pharmacy, Hubballi, approved and the Reference No. KLECOPH/IEC/2024-25/01. After providing detailed information about the study to the patients and their families, written informed consent was obtained from each participant.

AUTHORS CONTRIBUTION

Each author had equal responsibility for the study's conception, literature review's execution, manuscript writing and revision.

SUMMARY

Study demonstrated that chemotherapy alone can yield early, statistically significant, though modest improvements in esophageal symptom-specific HRQoL, particularly in domains directly related to swallowing discomfort. Early HRQoL monitoring using the EORTC QLQ-OES25 offers a practical framework for identifying responsive patients, guiding supportive care and ensuring more patient-centered chemotherapy delivery in esophageal cancer management.

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