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Long-term health-related quality of life in esophageal cancer survivors: a literature review

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Introduction and objectives

Long-term survival after esophageal cancer has increased substantially over the past few decades.^{1,2} Esophageal cancer is the eighth most commonly diagnosed cancer worldwide with more than 0.6 million new cases each year.^{3,4} Approximately 1 in 10 people diagnosed with esophageal cancer today are predicted to survive their disease for at least 10 years.^{5,6} While the increasing survival of patients clearly indicates improvements in clinical management, it is not the only measure of treatment success. Overall survival remains the gold standard clinical trial endpoint, yet it alone may not be the outcome most relevant to patients. Therefore, as the survivorship of patients with esophageal cancer increases, the quality of that survivorship is becoming more relevant to fully capture the remaining unmet need in this population. Evidence of health-related quality of life (HRQoL) is required to understand the patient experience during and after treatment and into survivorship to appreciate the complete impact of the current standard of care on a patient's life. Together with survival, we cannot only measure how long patients are living but if they are living well. We aimed to conduct a literature review of long-term HRQoL in esophageal cancer survivors to understand how current clinical management impacts patients after they are cured and what aspects matter to patients and most affect their wellbeing.

Methods

We conducted a targeted literature review to identify longitudinal studies assessing the HRQoL of esophageal cancer survivors, using the key terms "esophageal cancer", "survivors", "HRQoL", and "long-term". Searches were conducted on PubMed (Jan 2019-Dec 2023). Identified articles were screened based on relevance against predefined inclusion and exclusion criteria. "Long-term" outcomes were defined as those measured at least 1 year after treatment was completed. "HRQoL" was defined as any patient- or caregiver-reported outcomes. No restriction on the stage, type, or treatment for the esophageal cancer was imposed.

Results

The literature search identified 16 relevant studies that assessed HRQoL ≥1 year after treatment was completed. Of these studies, six assessed HRQoL for \geq 10 years. The majority of studies recruited patients who had undergone curative surgery with or without neoadjuvant/adjuvant treatment.

All studies, except one, measured HRQoL using EORTC QLQ-C30 and 12 also utilized either EORTC QLQ Oesophago Gastric 25 or EORTC QLQ Oesophageal 18 (Figure 1).



Figure 1: HRQoL measures utilized across esophageal cancer survivor studies

Abbreviations: EORTC QLQ C30, European Organization for Research and Treatment of Cancer Quality of Life questionnaire-C30; FACT-E, Functional Assessment of Cancer Therapy-Esophagus; HRQoL, health-related quality of life; OES18, Oesophageal 18; OG25 Oesophago Gastric 25; SCNS-SF34, Supportive Care Needs Survey-Short Form 34; SF36, Short Form 36; LASER, Lasting Symptoms After Esophageal Resection; SF-HLQ, Short-Form Health and Labour Questionnaire

Most common symptoms and comorbidities affecting HRQoL were dysphagia and eating difficulties, reflux, dyspnea, fatigue, pain and discomfort, appetite loss, weight loss, and dry mouth. Over 80% of the studies agreed that symptom burden persisted into long-term survival (Figure 2).

Four studies compared the HRQoL of esophageal cancer survivors with the general population. Of these, two studies found esophageal cancer survivors to have comparable to improved HRQoL compared with the general population; however, all four studies highlighted that a high proportion of esophageal cancer survivors had long-term symptoms related to the digestive tract that negatively impacted their HRQoL up to 20 years after curative surgery. One of the four studies found that nearly half of these patients had a persistently poor or deteriorating HRQoL trajectory.

Studies disagreed on whether long-term global HRQoL was decreased in esophageal cancer survivors; however, functioning specifically was more likely to be affected including physical, role, and social functioning (Figure 2).



Figure 2: Long-term HRQoL results in esophageal cancer survivor studies

Five studies found that patients who had postoperative complications were associated with worse HRQoL for several years after surgery compared with those who did not. These data show that the incidence of major postoperative complications is high in this patient group, up to 69% in some patient cohorts depending on the type of surgery, and that longitudinal HRQoL is highly dependent on the management of and recovery from these complications. Other vulnerable populations identified (those likely to have worse HRQoL) were those with a more advanced tumor stage, those who received postoperative chemotherapy, and those of a younger age.

One study specifically investigated how esophageal cancer survivors were impacted at work. Using the Short-Form Health and Labour Questionnaire (SF-HLQ), investigators found that 51% of patients who worked before diagnosis were still working and, of those, 44% reported reduced work pace, 33% reported a self-imposed need to work in seclusion, and 28% reported concentration problems.

Another study investigated psychological comorbidities in patients with esophageal cancer. An increase in psychological distress disorders was seen after treatment compared with before treatment was initiated. The highest rate of increase after treatment was noted for stress reaction/adjustment disorder compared with anxiety, depression, or substance abuse. However, a comparison in the incidence of these psychological disorders in esophageal cancer survivors compared with the general population over time was not made.

Conclusions

Esophageal cancer survivors often have a high symptomatic burden, principally dysphagia and eating difficulties, and deterioration in long-term HRQoL, particularly associated with functioning. The evidence indicates that symptoms can be life-long and can worsen over time, meaning continuation of healthcare follow-up is vital.

Both the EORTC Quality of Life Questionnaire-Oesophageal 18 (QLQ-OES18) and EORTC QLQ Oesophago Gastric 25 (QLQ-OG25) capture many of the gastrointestinal symptoms experienced by esophageal cancer survivors. Importantly, QLQ-OG25 also includes broader HRQoL aspects such as worries about weight loss and attractiveness. However, to ensure a comprehensive view of the patients' HRQoL is captured, these questionnaires should ideally be used with the EORTC QLQ-C30.

Of note, both the QLQ-OES18 and QLQ-OG25 also include the question "do you have difficulty talking?", indicating that patients may have preferred ways of communicating and these should be offered when conducting studies to improve data collection.

Further longitudinal studies are required to understand the specific factors contributing to long-term impairment of HRQoL in order to improve treatment strategies and achieve high quality survivorship. Evidence gaps include the impact on survivors' work life and mental health and studies evaluating carer burden. Most of the studies identified analyzed patients who had undergone curative surgery, with few undergoing radiotherapy. Radiotherapy is known to have significant short-term side effects, but the prevalence and HRQoL impact of long-term side effects has not been sufficiently assessed in this patient population. Identification of subpopulations at higher risk of deterioration in quality of life is also of great importance to ensure personalized and patientcentered follow-up care is offered by healthcare systems.

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