Symptom Burden and Health-Related Quality of Life in Gastrointestinal Cancers: A Targeted Literature Review

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INTRODUCTION

- Gastrointestinal (GI) cancers, including colorectal, esophageal, and pancreatic cancers, make up more than 25% of global cancer cases; in 2023, it is projected that there will be approximately 1.96 million new cancer cases diagnosed in the United States and 609,820 cancer-related deaths (Siegel et al. 2023)
- The World Health Organization recommends screening for asymptomatic cases to facilitate early diagnosis and improve treatment effectiveness (WHO Guide to cancer early diagnosis)
- The influence of cancer stage on patient-reported outcomes is not well understood
- There may be a connection between advanced cancer stages, increased symptom severity, and a lower Health-Related Quality of Life (HRQoL), which can be measured using Patient-Reported Outcome Measures (PROMs)

OBJECTIVE

- The objective of this study was to understand the symptom impact and HRQoL impact by disease stage for patients with colorectal, esophageal, or pancreatic cancers

CONCLUSIONS

- Symptom impact varied across different GI cancer types, with advanced-stage cancer generally associated with worse HRQoL
- Both physical and mental components of HRQoL appear to be negatively affected by disease stage, highlighting the impact of stage and spread of disease on symptom burden
- Patients with advanced stage GI cancers reported greater symptom impact, particularly in general physical impairments such as pain and fatigue
- These data highlight the importance of early cancer detection to attenuate symptoms and minimize the overall negative HRQoL impact of cancer diagnosis

METHODS

- Literature searches were performed to identify studies reporting HRQoL and PROM outcomes stratified by cancer stage in colorectal, esophageal, and pancreatic cancer
- The primary search was performed using EVID PRO, an AI-assisted platform, which utilized disease-specific terms for each cancer type to identify journal articles published from January 2017 to December 2022. When fewer than 10 articles were identified in this timeframe, the search was extended to 10 years (from January 2012 to December 2022)
- The EVID PRO tool automatically identified articles containing specific acronyms, scales, and Patient-Reported Outcome (PRO) instruments
- Abstracts from key conferences were searched from January 2020 to December 2022
- The PICOS (Population, Intervention, Comparator, Outcome) criteria are shown in Table 1

Table 1. PICOS criteria

Element	Focus
Patients	Patients with staged cancer (e.g., AJCC): ○ Colon/ rectum ○ Esophagus ○ Pancreas Where a limited number of publications were identified that included information on staging, other studies were considered
Intervention/ comparator	○ Any
Outcomes	○ Severity and impact of cancer-related symptoms (e.g., pain, fatigue) by cancer type and stage, as assessed by standardized/ validated instruments (e.g., MDASI, EORTC-QLQ C30) ○ HRQoL/ PROs
Study types	○ Any
Timeframe	○ Literature published in the past five years. If less than 10 studies were identified, time limit was expanded to ten years
Geographic scope and language	○ United States (US) and European studies ○ English language abstracts
Databases to search	○ PubMed via EVID PRO ○ Hand searches ○ American Society of Clinical Oncology (ASCO) ○ European Society for Medical Oncology (ESMO) ○ Digestive Disease Week (DDW); GI cancers ○ Other conferences as appropriate for each oncology indication

KEY RESULTS: STAGE OF DISEASE HAS A SIGNIFICANT ROLE IN SYMPTOM BURDEN AS REFLECTED BY THE WORSE PHYSICAL HRQOL AND SYMPTOMOLOGY IN ADVANCED GI CANCERS

PATIENTS DIAGNOSED AT ADVANCED GI CANCER STAGES CONSISTENTLY REPORTED WORSE PROs RELATED TO SYMPTOM IMPACT AND HRQOL COMPARED WITH THOSE DIAGNOSED AT EARLIER STAGES

HRQoL/ PRO instruments utilized in identified studies

- Ten studies were selected from a combined pool of research on colorectal (n= 6 studies), esophageal (n= 2 studies), and pancreatic cancer (n= 2 studies). Detailed descriptions of the Patient-Reported Outcome (PRO) instruments utilized in these studies are shown in Table 3

Table 2. PRO instruments and key findings by cancer

Cancer type	Instruments and key findings
Colorectal	**SCL-17, SF-12 PCS, FACT-C** ○ Advanced cancer stages were associated with greater symptom burden (stage II vs III, p=0.001) and worse physical (I-IV, p<0.05) (Reyes et al. 2017; Belachew, Reyes et al. 2020) or functional HRQoL (II vs III, p=0.004) (Ganz et al. 2022) **HADS, SF-12 MCS** ○ Prevalence of depression was significantly higher in patients with metastatic vs non-metastatic disease (p=0.015) (Varela-Moreno et al. 2022) ○ Advanced stages were associated with low mental wellness (I-IV, p<0.01) (Reyes et al. 2017) **SF-36 Vitality** ○ No significant differences by cancer stage (II vs III) were observed for patient energy (p=0.179) (Ganz et al. 2022) **Symptoms (PROMIS)** ○ Patients with stage IV disease reported higher symptom scores for pain interference (56.5 vs 52.1) and fatigue (56.5 vs 50.8) compared with patients with stage I/ II disease (p not reported) (Jensen et al. 2017)
Esophageal	**FACT-E, FACT-ECS** ○ Advanced clinical tumor stages were associated with worse HRQoL (T1-T4, p<0.05) (Kidane et al. 2018) ○ Patients diagnosed with Stage II/III exhibited elevated scores for pain (3.2 vs. 2.8) and fatigue (3.2 vs. 2.6) in contrast to patients with Stage IV disease (p-value not reported) (Doherty et al. 2018) **FACT-G** ○ No significant findings were reported (Doherty et al. 2018)
Pancreatic	**SF-12 PCS, MDASI** ○ Advanced cancer stages were associated with worse physical function (I-IV, p<0.001) (Deng et al. 2018) and increased symptomology (I/II vs III/IV, p not reported) (Ambai et al. 2021). **SF-12 MCS** ○ Cancer stage was not significantly associated with mental wellness (I-IV, p=0.16) (Deng et al. 2018)

Table 3. PRO instruments utilized in identified studies

Instrument	Details
Generic PRO instruments	
European Quality of Life Five Dimension questionnaire **(EQ-5D-3L)**	○ EQ-5D-3L consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/ depression), each with three levels (e.g., no problems, some problems, and extreme problems) (Rabin et al. 2001) ○ The combinations of answers may be reduced to a single health utility score ranging from 0 (poor health) to 1 (perfect health)
NSABP symptom checklist **(SCL-17)**	○ Symptom burden questionnaire consisting of scores which are the average of 17 items scored on a 0 to 100 range with higher scores representing greater symptom burden (Kopec et al. 2007)
Short-form survey-12 **(SF-12)**	○ Generic quality of life questionnaires that measure physical, functional, emotional, and social wellbeing (Ware et al. 1996) ○ Can be summarized into 2 indices: the Physical Component Summary (PCS) and the Mental Component Summary (MCS), describing patient physical and mental well-being, respectively ○ Higher scores indicate better QoL, scores ≥50 suggest above average HRQoL compared to the general population, while scores <50 suggest poor HRQoL
Functional assessment of cancer therapy-colorectal **(FACT-C)**	○ FACT-C is a colorectal cancer module consisting of 36 items (Wendy et al. 1999) ○ Total score ranges from 0-136 with higher scores representing greater quality of life ○ FACT-C TOI (trial outcome index) is derived from physical wellbeing, functional wellbeing, and colorectal cancer subscale scores. Scores range from 0-84, with higher scores indicating better QoL
Functional assessment of cancer therapy-sophageal **(FACT-E)**	○ FACT-E is a quality-of-life subscale of FACT-G, designed for patients with esophageal cancer (Darling et al. 2006) ○ FACT-E is comprised of five subscales: physical well-being, social/family well-being, emotional well-being, functional well-being, and esophageal cancer subscale
Functional assessment of cancer therapy-esophageal cancer subscale **(FACT-ECS)**	○ FACT-ECS is a disease specific module/subscale (score range 0-68) (Doherty et al. 2018; Kidane, et al. 2018)

Colorectal cancer

- The primary stage for diagnosing colorectal cancer is often the regional stage, comprising 36% of diagnoses (SEER Incidence Rate, 2000-2020), and a smaller percentage of patients are diagnosed at the early (localized) stage (U.S. Cancer Statistics Data Briefs, No. 25, 2021)
- In comparison to patients with early-stage colorectal cancer, those with advanced-stage disease reported lower physical SF-12 scores in two separate studies (both p<0.05) (Reyes et al. 2017; Belachew et al. 2020)
- Mental SF-12 scores were significantly worse in advanced-stage disease in one study (p<0.01) (Reyes et al. 2017), while the second study did not find a significant association in this regard (Belachew et al. 2020)
- Patients diagnosed with stage III disease experienced significantly more symptoms (SCL-17, p=0.001) and a worse HRQoL (FACT-C, p=0.004) when compared to those with stage II disease (Ganz et al. 2022)
- Assessment of symptoms using the PROMIS PRO measurement system showed that patients with stage IV disease had higher symptom scores for pain interference and fatigue compared with patients with stage I/ II disease (score differences, 4.4 and 5.7, respectively) (Jensen et al. 2017)
- Additionally, depression was more prevalent among patients with metastasis compared to those without metastasis (p<0.015) (Varela-Moreno et al. 2022)

Esophageal cancer

- The predominant stage of esophageal cancer diagnosis occurs at the distant stage, representing 38% of all diagnoses (SEER Incidence Rate, 2000-2020)
- Considering a minimal clinically significant difference of 0.07 for EQ-5D utilities, patients diagnosed with stage IV esophageal cancer exhibited an inferior HRQoL in comparison to those with stage II/III disease (0.72±0.18 vs. 0.82±0.13, respectively) (Doherty et al. 2018)
- Furthermore, HRQoL, when stratified by tumor stage (T-stage), demonstrated significantly worse scores at higher T-stages (FACT-ECS, 58.7±9.1 vs. 44.5±15.4, T1 vs. T4; p<0.01) (Kidane et al. 2018)
- Assessment of symptoms using FACT-E-derived subscales revealed that patients diagnosed with Stage II/III disease exhibited higher symptom scores for pain interference and fatigue, with score differences of 0.4 and 0.6, respectively, when compared with patients with Stage IV disease (Doherty et al. 2018)

Pancreatic cancer

- The most common stage of diagnosis for pancreatic cancer is at the distant stage, constituting 51% of all diagnoses (SEER Incidence Rate, 2000-2020)
- For patients with stage III and IV pancreatic cancer, there was an increased risk of experiencing poorer SF-12 physical component scores when compared to those with stage I disease (1.80-fold and 2.32-fold increase, respectively; p-value for trend <0.001). However, there was no significant association observed with mental component scores (Deng et al. 2018)
- Measurement of symptoms (such as pain, disturbed sleep, numbness or tingling, and emotional distress) using the MDASI survey showed that patients with stage IV pancreatic cancer had greater symptom burden compared with patients with stage I/ II disease (mean MDASI score, 51.8 vs 47.3, p value not reported) (Ambai et al. 2021)

Table of Acronyms

Acronym	Definition
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire
EQ-5D-3L	European Quality of Life Five Dimension Questionnaire
FACT-C	Functional Assessment of Cancer Therapy-Colorectal
FACT-E	Functional Assessment of Cancer Therapy-Esophageal
FACT-ECS	Functional Assessment of Cancer Therapy-Esophageal Cancer Subscale
FACT-G	Functional Assessment of Cancer Therapy-General
HADS	Hospital Anxiety and Depression Scale
MDASI	MD Anderson Symptom Inventory
PROMIS	Patient-Reported Outcomes Measurement Information System
SCL-17	National Surgical Adjuvant Breast and Bowel Project Symptom Checklist
SF-12 MCS	Item Short Form Survey Mental Component Summary
SF-12 PCS	Item Short Form Survey Physical Component Summary
SF-12	Short-Form Survey-12
SF-36	Short Form-36

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Disclosures

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