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GERIATRIC ONCOLOGY (AR MACKENZIE, SECTION EDITOR)

Health-Related Quality of Life in Older Adults with Colorectal Cancer

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Abstract

Purpose of Review Health-related quality of life (HRQoL) is a topic of great importance among older patients with cancer. Here we review the literature on HRQoL in older patients with colon and rectal cancer.

Recent Findings HRQoL in older cancer patients with colon and rectal cancer can be impacted by care delivery model, use of selected treatments (i.e., chemotherapy), and the trajectory of the patient after surgery for colorectal cancer (CRC).

Summary HRQoL is an important outcome for older cancer patients. Greater numbers of older patients are undergoing treatment for CRC and may experience wide variations in quality of life during and after treatment. Trials should be developed with HRQoL as a primary outcome, and interventions need to be developed to maintain or improve HRQoL in older patients with cancer.

Keywords Colon cancer · Rectal cancer · Quality of life · Geriatric oncology · Older adults

Introduction

The population in the USA is rapidly aging. The Centers for Disease and Prevention Control predicts that the number of adults 65 years of age and older will rise to approximately 89 million by 2050, a 100% increase from the number of older adults currently living in the USA [1]. It is widely recognized that, with aging, there is an increase in cancer prevalence and incidence [2]. According to the National Cancer Institute, the group with the largest percentage of new cancer diagnoses was 65–74-year olds at 27.6% (SEER21 2012-2016, All Races, Both Sexes). The percent of new cases diagnosed in all patients over 65 was 54%. [3] Colorectal cancer (CRC), in particular, is largely a disease of aging. According to the SEER database, the median age at diagnosis is 67, and over half of all diagnoses are in patients over 65.

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In 2013, the Institute of Medicine (IOM) delivered a report entitled, "Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis" [4]. This report recognizes the critical need for high-quality cancer care, with an emphasis on the complex needs of our aging population. A central tenet to the delivery of high-quality care in the geriatric population is to consider quality of care from the perspective of the patient and caregivers. The first priority in the IOM's report is to develop a system of engaged patients, in which patient preferences and values play a central role in shared decision-making.

Senior adult oncology (SAO) patients (over 65 years of age) present unique challenges to the treatment team. In these patients, a greater understanding of cancer in the context of aging is necessary. Life expectancy may be limited even in the absence of the cancer, meaning the choice of treatment may be driven less by cure and prolongation of life, and more by maintenance of functional status and health-related quality of life (HRQoL). [5–7] As patients age, traditional outcomes such as overall survival and tumor response may fade to the background as other outcomes, freedom from pain, for example, become increasingly important. Incorporating patient reported outcomes into clinical research is especially crucial in this population. Quality of life is one such outcome that deserves attention.

Quality of life can be defined in several ways. Broadly, it encompasses a person's physical health, psychological health, level of functioning, social relationships, and personal beliefs

[5, 6]. Quality of life is affected by illness or health conditions, and treatment of those conditions may have an impact upon quality of life [8]. Quality of life is recognized as an important outcome in oncologic research [9, 10, 11••, 12–16], but the definition of HRQoL in SAO patients is not concrete. Little is known what factors are associated with HRQoL in the SAO population [5–7, 9].

In the general geriatric population, HRQoL is correlated positively with: mobility, good physical health, lack of sensory deficits, low frequency of pain, intellectual well-being, coping skills, and autonomy. It is correlated negatively with ageism, isolation, depression, and environmental barriers (e.g., lack of grab bars in public places, heavy doors, poor lighting) [17, 18, 19•]. Age alone is not associated with low HRQoL and should not be the sole determinant of perceived HRQoL in the healthcare setting. A study of the "oldest old" (age 90–99) demonstrated fairly high levels of self-reported HRQoL regardless of cognitive function [19•].

In the oncologic arena, elderly patients have been found to weigh HRQoL as more important than a gain in survival when compared with younger patients [6]. Given this, a greater understanding of the factors influencing HRQoL is necessary for the oncologist, primary care provider and all members of the treatment team in order to provide therapy in the appropriate context to SAO patients. Multiple well-vetted patient-directed generic quality of life questionnaires exist, including the "Short Form-36" [20] and "EQ-5D" (EuroQol five dimension) tools [21]. There are also multiple cancer-specific questionnaires that are more applicable to the cancer population such as Functional Assessment of Cancer Therapy—General (FACT-G) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Q30 (EORTC QLQ-Q30). [21–25]

Colorectal Cancer

CRC is the fourth most common cancer and second leading cause of cancer death in the USA. There were 145,600 estimated new cases in 2019. With the widespread use of colon cancer screening and thus, earlier detection, this is one of the few cancers with a relatively robust 5-year survival rate (64.4%) [26]. This means that there are hundreds of thousands of Americans who are survivors of this disease and many of these patients are over the age of 65. By 2040, it is estimated that over 70% of cancer survivors will be 65 and over [27]. Early detection, coupled with advances in treatment efficacy, translates into more patients living with the sequelae of both the disease itself and treatment toxicities. In this setting, quality of life considerations are paramount.

As mentioned, there are a variety of generic quality of life measurement tools. Table 1 summarizes some of the validated questionnaires useful for assessing quality of life in various cancer settings. Of these tools, there is a specific colon-cancer tool called the "FACT-C" which focuses on the metrics that most impact colon cancer patients (Fig. 1). This tool includes assessments along axes such as physical, functional, social, and emotional. The low anterior resection (LAR) syndrome score was also developed specifically to assess bowel function after LAR for rectal cancer on the basis of symptoms and impact on quality of life [28]. In patients ≥ 70 years, the EORTC QLQ ELD15 questionnaire was developed to supplement the QLQ-30 and has been validated with all cancer types.

Treatment of CRC

There are consensus guidelines for the treatment of CRC in older patients from the International Society of Geriatric Oncology (SIOG) [31]. This 2014 document focuses on treatment recommendations based on level of fitness as determined by geriatric assessment. This paper highlights the following: (1) quality of life is an important outcome for older patients with cancer. (2) because treatment toxicity can so profoundly affect quality of life in older patients, especially those who are not fit, assessment of functional status is crucial. A 2015 paper from Millan et al. provides a review of CRC cancer treatment in the elderly. Concerns over frailty and ability to tolerate treatment are examined, with review of the role of the comprehensive geriatric assessment [32].

Measuring HRQoL

There have been several studies of variable size that have examined quality of life in CRC cancer survivors. There is a fairly standardized set of well-defined quality of life metrics—though less agreement on how CRC cancer affects the individual as a whole. For instance, a 2013 paper on quality of life in CRC examined several factors that are determinants of quality of life in the cancer care continuum [33]. The authors divided quality of life determinants into 5 groups: socio-demographic, health-related, cancer- and surgery-related, lifestyle, and other factors. Physical problems related to surgery and postoperative management seemed to be the most common. Socioeconomic status and comorbidities were identified to have clear impact on quality of life. In this study, age was found to have variable impact on HRQoL. Some studies cited in this paper report no significant role of age in HRQoL, whereas others report a decline in HRQoL with increasing age. Also notable in this paper was a higher prevalence of distress, depression, and anxiety in CRC patients compared with the general population. These authors delve into the interventions possible to improve quality of life, citing age as a non-modifiable risk

Table 1 Validated questionnaires useful for assessing quality of life in cancer patients [28–30]

Full name of tool	Acronym	Intended population	Number of items in questionnaire	Additional notes
Functional Assessment of Cancer Therapy	FACT or FACT-G	Multiple cancer types	27	Widely used, well-validated
Functional Assessment of Cancer Therapy—Colorectal	FACT-C	Colorectal cancer	36	Relatively short addition to general form
EORTC Quality of Life Questionnaire (core)	EORTC QLQ-C30	Multiple cancer types	30	Widely used, well-validated
EORTC Quality of Life Questionnaire (colorectal)	EORTC QLQ-CR29	Colorectal cancer	29	Multiple versions of varying length with updates for newer treatments
EORTC Quality of Life Questionnaire (elderly)	QLQ-ELD15 or QLQ-ELD14	Cancer patients over age 70	ELD15:15 ELD14: 14	One of the only tools targeted to older cancer patients
Low Anterior Resection Score	LARS	Rectal cancer patients after LAR	5	Score divided into no LARs (0–20), minor LARS (21–29), and major LARS (30–42). High sensitivity (72.54%) and specificity (82.5%) for major LARS.

factor. However, the interventions listed such as educational programs, cognitive behavioral therapy, coping mechanisms, exercise, and diet may be just as valuable in the older survivor as the younger when attempting to improve quality of life. Research focusing on the specific needs of the older CRC patient is crucial, since older cancer patients age in such a heterogeneous fashion.

Much of the available data in quality of life is from the CRC surgery literature. This is likely due to easily defined postoperative metrics such as complication rates, pain, length

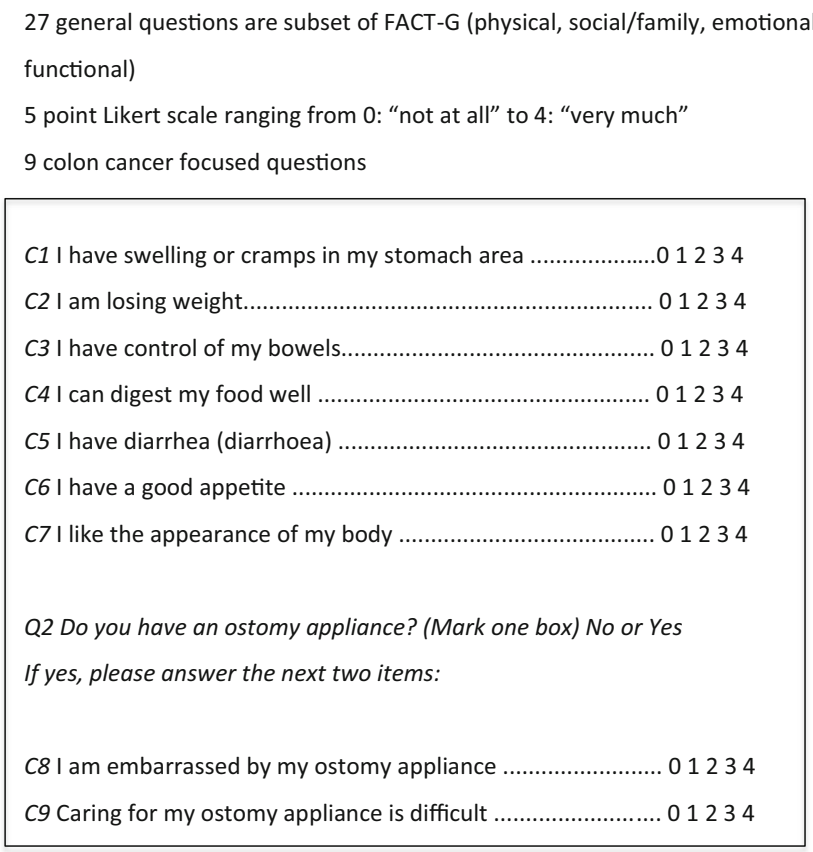

Fig. 1 Summary of FACT-C quality of life questionnaire [24]

of stay, ostomy issues, and incision appearance, all of which can influence one's quality of life. Outcomes of CRC surgery in elderly patients compared with younger ones are heterogeneous. Some studies have found that postoperative mortality increases with age [34] while other studies have found that postoperative complications or postoperative morbidity is not statistically significant [35, 36]. Follow-up to beyond 5 years highlights differences in short vs long-term symptoms that impact quality of life [37]. In the short-term, patients were more likely to report neuropathy and sleep disturbance. Long-term survivors complained of bowel problems, stress related to cancer, and depression. Although in this analysis most reviewed articles only assessed patients at a single point in time, these data are important for addressing patient concerns regarding quality of life throughout survivorship. Older patients may have greater comorbid conditions when going into treatment and may utilize post-acute care to a greater extent. In older cancer survivors, the incidence of post-acute care use up to 5 years following cancer therapy can be almost 17% among stage III patients. Patients who received chemotherapy and were of greater age (median age 77 years) showed increased short-term post-acute care needs. The need for assistive care in the older CRC patient population can be underestimated and should be acknowledged when discussing quality of life issues [38].

The Seattle CRC family registry published 2016 data that showed older patients had worse quality of life scores [39]. The study assessed 1,021 patients 5 years post-diagnosis in an attempt to identify characteristics associated with poor quality of life. While registry patients had long-term quality of life (> 5 years) similar to the general population, there appeared to be subgroups of CRC patients with decreased quality of life. Indeed, increased age was one risk factor for lower physical function scores as defined by reduced ability to complete daily tasks. This study was limited by the use of a general questionnaire (as opposed to cancer-specific tool), though it did allow for the benefit of comparison to the non-cancer patient population group.

In 2016, a quality of life study from France was launched that exclusively evaluated older CRC patients (> 65 years old) [40••]. The authors used the EORTC QLQ-C30 tool to examine health-related quality of life. This study demonstrated lower survival in patients with the following attributes: appetite loss and low "role" dimension scores (defined by hobbies, leisure, and daily activities). Although this study was limited by low response rate, it is ground-breaking in that it is the first of its kind to examine quality of life in the older CRC patient population, specifically. The major conclusion of this study is that "preserving older patients health-related quality of life should be a major management goal."

Patients who undergo LAR for rectal surgery face a unique set of challenges. The advent of sphincter-preserving LAR has allowed rectal cancer patients to avoid permanent colostomy. Unfortunately, such patients can develop bowel dysfunction resulting in bowel incontinence, urgency, and frequent bowel movements, called low anterior resection syndrome (LARS). [35]. Prior to the development of the LARS score, a validated questionnaire specifically designed to assess bowel dysfunction and the impact on quality of life after LAR, there was considerable heterogeneity in the assessment of such symptoms [36]. The LARS questionnaire consists of 5 questions regarding incontinence of flatus, incontinence of liquid stools, frequency, clustering, and urgency. The range (0–42) was divided into 0 to 20 (no LARS), 21 to 29 (minor LARS), and 30 to 42 (major LARS).

A recent meta-analysis that included only studies utilizing the LAR score as the primary collection tool found that the prevalence of persistent major LARS was 41% (95% CI 34–48) [41]. The two factors that had the greatest negative impact on bowel function following LAR were radiotherapy and low tumor height. Anastomotic leak and temporary ileostomy were also been identified as risk factors for the development of LARS. Longitudinal studies have found that the prevalence of major LARS did not change significantly with time and that nearly 50% of patients experienced majors LARS even 7 to 16 years after the surgery [41, 42]. Thus, LARS plays a significant and persisting impact on quality of life in both older and younger patients.

There are limited studies examining the effect of LAR specifically in elderly adults vs in younger adults. Some studies have found no statistically significant difference based on anorectal manometry and number of daily bowel movements, however, a small study may not be powered to detect a difference [41]. Older adults tend to have deterioration of pelvic diaphragm muscles and the external anal sphincter, leading to greater incidence of incontinence and defecation disorders, even in the absence of external factors [42]. Thus, it is conceivable that elderly adults would be affected to a greater extent than younger adults, contributed in part by age-related physiologic changes. There is also a suggestion that elderly (≥ 70 years) females may have worse coping skills and depression/self-perception compared with younger females and elderly males, which may contribute to poorer outcomes [43].

Given that older patients often have fewer remaining active life expectancy years, maintaining quality of life is crucial. There are a number of unique challenges facing older patients. Recovery and maintenance of functionality can be more difficult for the older patient undergoing treatment for colorectal cancer. Changes in nutritional status, increased incidence of sarcopenia, cognitive changes, and loss of mobility are all physical/functional impairments that contribute to psychosocial and emotional health [40••, 44]. Addressing these concerns is complex, but there are some studies that have tried specific interventions with varying degrees of success.

Interventions to Improve HRQoL

Identifying factors that have a negative impact on quality of life in the older cancer patient is the first step in affecting change for these patients. A successful intervention is something of a grail. One Spanish study compared exposure with a multi-disciplinary team with regular care in older CRC patients to determine if quality of life is impacted by the use of a team approach [45]. Patients in the study group ranged in age from 80 to 84 years of age, and those in the control group were 75–79 years of age. The study used the Short Form-12, which analyzes quality of life on a 0–100 scale. The characteristics between the two groups were similar except that 45% of patients in the control group (no multi-disciplinary evaluation) received adjuvant chemotherapy versus 19.5% in the study group ($p = 0.0004$). Quality of life was similar between the two groups except for "physical function", which was higher in the study group. Overall survival was similar between the two groups and the discrepancy in adjuvant chemotherapy does not appear to have had an impact here. Although this study does not comment on whether the increased use of chemotherapy in the control group is correlated to the improved physical function scores, it is important to note that a multidisciplinary evaluation may be one way to maintain quality of life in older CRC surgical patients.

Treatment of cancer can play a role in either improving or worsening HRQoL in older patients. The type of treatment chosen may add burden with side effects or may palliate both the tumor and the symptoms. A recent phase II study examined the use of oral chemotherapy in the form of capecitabine in patients with advanced colorectal cancer over the age of 65. Patients on reduced dose capecitabine (750 mg/m2 vs. 1000 mg/m2) had overall improved HRQoL scores as measured by the FACT-G when compared with baseline scores. In addition, increased quality of life scores were significantly associated with improved progression-free survival and overall survival. This study demonstrates that not only can reduced dose chemotherapy improve HRQoL, it can improve survival in those patients with improved HRQoL [46].

In older CRC cancer patients who have undergone surgery for high-risk stage II or stage III cancer, there is the possibility of safely offering 3 months of adjuvant CapOX chemotherapy versus 6 months, with a non-inferior outcome. The incidence of pain, diarrhea, hand-foot syndrome, and peripheral neuropathy was significantly lower in the 3-month group. The median age in this trial was 65, and there was no subset analysis based on age, but this could be an alternative treatment regimen that will give both a survival and a quality of life advantage [47••].

A number of different interventions have been explored in rectal cancer patients to assess for improvement in LARS. Such interventions include percutaneous tibial nerve stimulation [48], sacral nerve stimulation [49, 50], pelvic floor rehabilitation [51, 52], transanal irrigation, probiotics, and 5-HT3 receptor antagonists. Unfortunately, these studies contain small numbers of patients and are not randomized. Given the significant impact of LARS on quality of life, its persistence even years after surgery, and lack of validated interventions, patients should be adequately informed prior to surgery of the longevity of these effects. It is not clear if these effects are more severe in older patients; however, any pre-existing comorbid conditions that might worsen LARS should be taken into account when developing treatment plans.

Clinical Observations

A key component to assessing and managing quality of life in older adult patients is discussing the patient preferences at the start of treatment. While it is ideal to perform a geriatric assessment prior to treatment initiation in all patients over 65, this is not generally feasible for the general oncologist in a busy clinic. A geriatric assessment can provide valuable information about the patient's possible tolerance to treatment and areas in which patients may be vulnerable to toxicity. Discussing patient preferences and asking about the patient's acceptable quality of life can help guide treatment recommendations and planning. In our senior adult oncology center, part of the assessment includes a discussion of patient preferences and an estimation of longevity in the absence of the cancer. If patients are expected to live for a number of years, and treatment can be utilized to improve quality of life, this is an important piece of information to share with the patient. Conversely, if patient life expectancy is predicted to be very limited, it is important to discuss if the treatment will add meaningful clinical benefit in the amount of time the patient has left to live. Life expectancy and mortality predictions can be estimated by using online calculators such as the Lee and Schonberg indices [53].

Conclusion

The aging colorectal cancer population in the USA has multiple implications for providers. Greater numbers of patients will be fit enough for treatment at older ages. Patients need individualized treatment plans to reflect not just the cancer but the patient as a whole. This includes an understanding of what may have both a positive and a deleterious effect on HRQoL. Various questionnaires have been validated to assess quality of life measures in the SAO, specifically in colon cancer patients (FACT-C) and rectal cancer patients (LARS score). The QLQ ELD15 questionnaire may be used in patients specifically ≥ 70 years. Optimally, oncologic providers will assess quality of life as a part of tailoring treatment plans in older adults.

Future research initiatives must include HRQoL as a primary endpoint for clinical trials, more rigorous assessment of HRQoL in older patients with cancer, and larger data sets on older adult patient preferences during and after treatment.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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