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RADIATION THERAPY AND RADIATION THERAPY INNOVATIONS IN COLORECTAL CANCER (P LEE AND A RALDOW, SECTION EDITORS)

Quality of Life After Radiotherapy for Rectal and Anal Cancer

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Abstract

Purpose of Review With advances in radiation therapy (RT) techniques for rectal and anal cancers allowing for the modulation of critical normal tissues, there has been an increased emphasis on improving the quality of life (QOL) for cancer survivors. Herein, we review the literature to examine the impact of RT on QOL and patient-reported outcomes (PROs) to better inform providers about the challenges of survivorship.

Recent Findings Large systematic reviews, recent studies, and long-term follow-up of pivotal clinical trials have shown that RT impacts QOL, particularly fecal continence and sexual function. Modern preoperative RT techniques, which allow for decreased dose to organs-at-risk, will likely improve QOL.

Summary RT, although critical in the treatment of rectal and anal cancer, can have a profound impact on QOL for some patients. Recent studies have included PROs and validated QOL metrics to better inform providers and patients.

Keywords Quality of life · Patient-reported outcome measures · Radiation therapy · Rectal neoplasms · Anus neoplasms · Cancer survivors

Introduction

Radiation has a well-established role in the treatment of rectal and anal cancers. Since the introduction of radiation therapy (RT) into treatment regimens, patients and clinicians have scrutinized the toxicities of these modalities as much as their benefits. Historically, clinicians primarily reported and estimated the toxicities of therapy on the patient; however, physician-reported toxicities fail to illustrate the level of toxicity that the patient experiences [1, 2]. Based on the technological improvements in radiation therapy design and delivery that permits improved organ sparing, a greater emphasis has been placed on using patient-reported outcomes (PROs) and quality of life (QOL) questionnaires. These tools have been shown to better categorize patient symptoms and can be used in shared decision-making to better educate patients and reduce treatment-related regret [3].

In 2018, Lawler et al. identified critical gaps in the colorectal cancer literature, particularly insufficient evidence regarding the QOL concerns of survivors [4]. A systematic review by Sodergren et al. similarly concluded that less than 10% of the literature reporting on anal cancer RT toxicity formally assesses QOL [5•]. The Core Outcome Measures in Anal Cancer initiative emphasized the need to include QOL metrics in clinical trials, a recommendation by which the PersonaLising Anal cancer radioTherapy (PLATO) trial, a three part protocol aiming to optimize RT doses for various stages of anal cancer, has adopted [6–8].

This review will outline the current knowledge and knowledge gaps regarding QOL factors relevant to clinical trials and practice. Herein, we review the literature with a focus on work published between 2014 and 2019 on PubMed, examine the current tools used to measure the QOL concerns of rectal and anal cancer survivors treated with RT, and describe the QOL outcomes in this population. Understanding QOL outcomes will improve informed decision-making in clinical practice.

This article is part of the Topical Collection on *Radiation Therapy and Radiation Therapy Innovations in Colorectal Cancer*

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Measuring Quality of Life

The key tools used to quantify QOL for rectal and anal cancers can be subdivided into general cancer questionnaires, disease-specific modules, and symptom-specific questionnaires. Examples of commonly used tools are presented in Table 1.

EORTC QLQ-C30

The European Organization for Research and Treatment of Cancer (EORTC) aimed to develop tools that could categorize the QOL concerns of patients enrolled in clinical trials. In 1993, the Quality of Life Questionnaire-Core 30 (QLQ-C30) was introduced [9]. The questionnaire was designed to be broadly applicable to all cancer clinical trials, allowing for standardized reporting. The 30-item questionnaire measures symptoms and concerns such as, functional status, respiratory symptoms, pain, constitutional symptoms, gastrointestinal symptoms, psychological stress, impact on relationships, and impact on finances. Concerns specific to each disease or treatment modality, however, are sometimes not included. For example, although QLQ-C30 does include symptoms such as nausea, vomiting, and diarrhea, it does not measure specific concerns about fecal incontinence. This limitation was the impetus for development of disease-specific modules such as QLQ-CR38.

EORTC QLQ-CR29

The first colorectal cancer module from the EORTC, QLQ-CR38, was designed in 1999 to be administered after the QLQ-C30 [10]. This tool was then revised in 2007 because it was less applicable to advances in treatment, such as chemoradiation and RT. The new questionnaire, QLQ-CR29, includes 29 questions for disease-specific complaints (e.g., have you had leakage of stool) and subheadings for patients living with and without a stoma [11]. The questionnaire also measures urinary symptoms, hair loss, dry mouth, self-image, health anxiety, concerns, and sexual symptoms.

FACT-C

The Functional Assessment of Cancer Therapy-Colorectal (FACT-C) was first introduced in 1999 [12]. The FACT-C is an iteration of the Functional Assessment of Cancer Therapy-General (FACT-G), with an additional section that addresses concerns related to colorectal cancer. There are 27 general questions that assess physical well-being, social/family well-being, emotional well-being, and functional well-being that are common to the FACT-G and FACT-C. The FACT-C also includes 9 questions measuring specific gastrointestinal complaints, self-image, and two questions for those living with ostomy (embarrassment and burden of caring for ostomy).

Table 1 QOL questionnaires for rectal and anal cancer

Questionnaire name	Area of focus	Development	Description
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)	General cancer	Validated	Functional status, respiratory symptoms, pain, sleep, fatigue, weakness, gastrointestinal symptoms, psychological stress, relationship impact, financial impact
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Module for Colorectal Cancer (EORTC QLQ-CR29)	Colorectal Cancer (delivered with EORTC QLQ-C30)	Validated	Urinary symptoms, Gastrointestinal symptoms, hair loss, dry mouth, self-image, health anxiety, stoma concerns, sexual symptoms
The Functional Assessment of Cancer Therapy – Colorectal (FACT-C)	General cancer with colorectal cancer	Validated	*Physical well-being*: constitutional symptoms, gastrointestinal symptoms, family concerns, pain, side effect concerns; *social well-being*: relationship concerns, support, sexual concerns; *emotional well-being*: affect, coping, future outlook; *functional well-being*: functional status, self-image, psychological concerns; *additional concerns*: gastrointestinal symptoms, self-perception, ostomy-specific questions
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Module for Anal Cancer (EORTC QLQ-ANL27)	Anal cancer (delivered with EORTC QLQ-C30)	In development	Gastrointestinal symptoms, skin symptoms, lifestyle adjustments, stoma concerns, sexual symptoms
Wexner Incontinence Scale	Fecal incontinence	Validated	Solid, liquid, and gas incontinence; pad requirement, lifestyle alternation
Fecal Incontinence Quality of Life Scale (FIQL)	Fecal Incontinence	Validated	Lifestyle adjustments, coping habits, impact of bowel leakage, self-perception, social stress, embarrassment

EORTC QLQ-ANL27

Sodergren and colleagues have characterized the paucity of QOL information in anal cancer patients and have led the phase I–III development of an anal cancer-specific QOL questionnaire [13]. The QLQ-ANL27 includes 27 questions to be delivered after the QLQ-C30; items include gastrointestinal symptoms, skin symptoms, lifestyle adjustments, stoma concerns, and sexual symptoms. This questionnaire is being used as an end point in the PLATO trial [14]. The QOL concerns specific to anal cancer have been largely overlooked in prior studies [5].

Fecal Incontinence Scales

Two commonly used fecal incontinence scales are the Wexner Continence Grading Scale and the Fecal Incontinence Quality of Life Scale (FIQL) [15, 16]. The Wexner Scale improved on previous grading systems because it measured the type of incontinence (solid, liquid, gas) and the lifestyle impact of symptoms (wearing pads and lifestyle alteration) with five questions rated on a scale of 0 (never) to 4 (always). Similarly, the FIQL assessed the impact of fecal incontinence using 29 questions in four domains: lifestyle, coping/behaviors, depression/self-perception, and embarrassment. These tools used in conjunction with other QOL questionnaires provide specificity to the common complaints of rectal and anal cancer survivors.

Comparing Effectiveness of Tools

Recent studies have compared the efficacy of the aforementioned tools through analyses of questionnaire responsiveness. Responsiveness is a metric defined as a tool's ability to detect clinically significant changes. A prospective study investigating EORTC QLQ-C30, EORTC QLQ-CR38, and FACT-C in rectal cancer survivors found QLQ-C30 to be significantly more responsive than QLQ-CR38 and FACT-C, despite the fact that QLQ-C30 was not designed particularly for the colorectal cancer population [17]. However, the responsiveness of QLQ-CR29, the subsequent iteration of QLQ-CR38, has yet to be extensively investigated. A study comparing abdominoperineal resection (APR) and sphincter-sparing surgery detected patient-reported differences in body image and micturition through the use of EORTC QLQ-CR38 but found no significant differences with FACT-C [18]. Furthermore, a systematic review showed that the FACT-C was the most extensively evaluated questionnaire but that the EORTC-CR38 had the most positive ratings across all metrics (e.g., hypothesis testing, validity, and internal consistency) [19].

There are many additional validated tools that assess QOL. Other commonly used instruments include the Medical Outcomes Study 36-Item Health Survey (SF-36) and Medical Outcomes Study 12-Item Health Survey (SF-12), European Quality of Life Questionnaire (EuroQol; EQ-5D), the Memorial Sloan Kettering Cancer Center Bowel Instrument, Anal Sphincter Conservative Treatment Questionnaire, an abbreviated version of the Functional Living Index-Cancer (Quick-FLIC), and the EORTC Proctitis Module [20–26]. The decision to include any given questionnaire is largely investigator dependent. However, using a combination of general cancer questionnaires and disease – and symptom-specific questionnaires, allows for a breadth of information to characterize the QOL of survivors.

Quality of Life After Rectal Cancer Treatment

Standard Curative Rectal Cancer Treatment

Standard curative rectal cancer treatment employs neoadjuvant (chemo)radiotherapy and total mesorectal excision (TME). The advances made in improving local control of disease may have come with the cost of reduced QOL after treatment. Some of the most common QOL concerns reported involve fecal incontinence, sexual dysfunction, and overall health status, primarily in the years after radiation therapy.

Data from the Dutch TME trials have been evaluated longitudinally to establish the benefits and toxicity of preoperative radiotherapy using short-course radiotherapy (SCRT) (25 Gy/5 Gy in 5 fractions). Men and women receiving SCRT experienced both a reduction in sexual activity and worse overall sexual functioning relative to the surgery alone group in the short term (3 to 24 months after surgery) [27]. This effect persisted at 14 years of follow-up [28•]. In the Medical Research Council (MRC) CR07 and National Cancer Institute of Canada (NCIC) Clinical Trials Group C016 trial, SCRT (25 Gy/5 Gy in 5 fractions) and TME after 7 days were compared with surgery and selective postoperative chemoradiotherapy (50.4 Gy/1.8 Gy in 28 fractions with concurrent 5-fluorouracil). While study showed that SCRT was associated with better local control and disease-free survival, the SCRT group also experienced worse sexual dysfunction at 6 months and 3 years. This effect is possibly related to the larger fraction sizes delivered, perhaps resulting in more late effects, in contrast with the long-course treatment [29]. Even though female patients from this study were also surveyed about sexual function, few completed the sexual function questions [30].

Subsequent studies, however, have included analyses of the impact of RT on female patients. Although both male and female survivors experience sexual dysfunction, male sexual enjoyment may be preserved, while female sexual enjoyment wanes as sexual dysfunction persists. This discrepancy is possibly related to hormonal changes as radiation will ablate ovarian function in premenopausal patients.

Importantly, sexual interest was not decreased in either men or women, further validating the importance of addressing sexual dysfunction to improve QOL [31]. In addition to RT, the presence of ostomy is also an independent risk factor for sexual dysfunction in men and women [32, 33•]. The contribution of physiological symptoms of sexual dysfunction as well as concerns about body image to overall QOL will likely be the subject of future investigation. Although one of the benefits of preoperative RT is the ability to enable sphincter preservation and avoidance of a permanent colostomy, this benefit may come at the cost of impacting sexual function [34].

Fecal incontinence is another major toxicity of RT that can negatively impact QOL. Although EORTC questionnaires were not available at the start of the Dutch TME trial, ratings of fecal incontinence were measured using various instruments at 0–2 years, 5 years, and 14 years. There were higher rates of fecal incontinence in the SCRT followed by TME group than the TME alone group, and, although there were higher levels of fecal incontinence in both groups, the TME alone group's rates improved more with time [28, 35]. Multivariate analysis of a recent cohort study revealed higher incidence of fecal incontinence in those receiving SCRT and long-course chemoradiotherapy (LC-CRT) [36]. A recent population study in the UK similarly demonstrated worse bowel-related symptoms in patients receiving preoperative SCRT and LC-CRT and surgery vs surgery alone [33]. A recent meta-analysis incorporating 11 studies that used the low anterior resection syndrome (LARS) score reported that SCRT and LC-CRT are independent risk factors for LARS, a constellation of symptoms common after the eponymous procedure, including fecal incontinence and urgency, diarrhea, and clustering of bowel movements [37–39]. Patients from the TME trial were surveyed at 14 years after therapy, and it was found that age < 75 years and receiving SCRT were risk factors for major LARS and decreased QOL [40•]. Interestingly, LARS might be the strongest factor related to overall QOL [41].

Despite mounting evidence of decline in bowel and sexual function after SCRT and LC-CRT, some aspects of overall QOL may be improved by RT. A study of patients from the Cancer Care Outcomes Research and Surveillance Consortium CanCORS showed that overall QOL scores of patients treated for stage II/III rectal cancer with neoadjuvant LC-CRT were superior to those patients treated with adjuvant RT and surgery alone [42]. At 14 years after treatment on the Dutch TME trial, patients treated with neoadjuvant SCRT demonstrated similar scores to those undergoing TME alone for overall function and global health [28•].

Qualitative studies capture important data that might even be missed by collecting PROs. These data describe the actual impact on survivors. In a qualitative study of cancer survivors' responses to information on the long term and late effects of pelvic radiotherapy 1–11 years post treatment, survivors wished that they knew more about the prolonged nature of the side effect profile [43]. These patients suggested that providers should remind them and destigmatize/normalize their late side effects throughout recovery and the survivor process; having the conversation only at the onset of diagnosis when determining the treatment course might not provide adequate reassurance or information. Respondents also said that while being counseled on the risks and benefits of RT, they are not listening as intently to the side effects; their primary focus is the impact on survival [43]. Using a consent aid that visually describes the risks of treatment and facilitates discussion could improve patient comprehension and retention of the potential acute and late toxicities [44].

Short-Course Radiotherapy vs Long-Course Radiotherapy

In 2007, Pietrzak et al. published one of the first phase III studies comparing SCRT with immediate surgery versus LC-CRT (45–50.4 Gy/1.8 Gy in 25–28 fractions with 5-fluorouracil and leucovorin boluses) with delayed surgery. There were no significant differences in sphincter preservation, survival, local recurrence rates, incidence of distant metastases, and late toxicity. However, SCRT was associated with lower early toxicity [45]. Data from long-term follow-up of patients receiving LC-CRT was also compared with historical data from patients receiving SCRT in the Dutch TME trial. Patients receiving LC-CRT had lower levels of satisfaction with their urinary function, but other QOL metrics were about the same [46]. LC-CRT was associated with a notable decline in QOL in the short term, but over time, this effect gradually diminished [47]. Another study suggested that SCRT and LC-CRT had similar effects on QOL and that surgical variables likely have a more significant impact on QOL [48].

There is, however, some evidence that suggests that SCRT may be inferior to LC-CRT for QOL. A population study from the UK demonstrated that patients receiving LC-CRT had better bowel control than those receiving SCRT; however, there were no differences in other outcomes [33•]. QOL outcomes were also worse in patients receiving SCRT followed by sphincter-sparing surgery than historical controls receiving LC-CRT with sphincter-sparing surgery or sphincter-sparing surgery alone [49].

Ultimately, because patients receiving LC-CRT can result in improved downstaging and may require different surgeries than patients receiving SCRT, the impact of RT on quality of life must be taken into context of the patient's whole treatment regimen. Similarly, because SCRT was traditionally employed with immediate surgery without time for tumor downstaging, future studies must clarify impact of the time delay of surgery. This is particularly important as advances are made in minimally invasive and organ-sparing surgeries.

Quality of Life After Preoperative Chemoradiation and Organ-Sparing Surgery (Local Excision)

Although TME is the standard of care for rectal cancer, organ-sparing surgeries have been employed to reduce surgical morbidity and are gaining interest particularly to avoid APR and the resultant permanent colostomy [50, 51]. Some studies have demonstrated that LC-CRT and transanal local excision increase the risk of post-surgical morbidity and hospital readmission, while others have suggested that these complications are not unexpected and do not increase rates of reoperation [52–54]. Some data has also suggested that using preoperative LC-CRT with local excision might compromise the benefits of less invasive surgery, because the QOL related to anorectal and sexual function was no different from controls who received APR [55]; however comparing groups of patients who receive entirely different treatments can be difficult to interpret.

The data regarding anorectal QOL is equivocal for local excision procedures after LC-CRT. One study suggested that average fecal incontinence symptoms were stable at 1 year after LC-CRT and transanal excision or transanal endoscopic microsurgery, but this was because some patients deteriorated, and others had improved symptoms. Even with somewhat stable symptoms, the QOL related to anal function was decreased in the self-perception and embarrassment domains for this same cohort. Interestingly, the degree of incontinence symptoms reported to the physician did not correlate with the QOL indicators, which further validates the use of instruments that capture the impact on patients [56•]. One study found that patients receiving LC-CRT and intersphincteric resection had worse fecal incontinence scores but similar QOL when compared with patients who only underwent local excision [57]. Another study suggested a worse impact of preoperative LC-CRT on anorectal function compared to sphincter-sparing surgery alone. Incontinence scores were drastically worse in patients receiving LC-CRT at 2 years and improved to below the levels of sphincter-sparing surgery alone at 5 years. This same cohort also reported worse QOL related to fecal incontinence [58]. One study found an association between incidence of radiation proctitis and worsening anorectal function [59]. On the other hand, Coco et al. suggested that even though there might be a trend toward increased short-term morbidity in patients receiving preoperative LC-CRT, there was no difference in sphincter function; this study, however, did not include data regarding patient impact, potentially biasing toward a null result [54].

Irrespective of anorectal function, physical function QOL scores were actually similar in patients receiving LC-CRT and transanal endoscopic microsurgery (TEM) vs TEM alone. This same cohort did show a decrease in mental scores, which may characterize the psychological impact of treatment toxicities [58]. Other studies have shown that patients receiving LC-CRT and TEM or local excision have improved emotional well-being [60, 61•].

Some studies have better characterized how different radiation regimens have impact on QOL. For example, a trial by Arezzo and colleagues studied neoadjuvant SCRT followed by TEM. The study showed that SCRT was associated with more complications and reduced QOL vs matched patients that received TEM alone or preoperative LC-CRT and TEM; the study was interrupted because of high toxicity [49]. In the coming years, data from clinical trials including the Radical Surgery Versus Adjuvant Chemoradiotherapy After Local Excision for Early Rectal Cancers (TESAR) and Saving the rectum by active surveillance or TransAnal surgery after (chemo)Radiotherapy versus Total mesorectal excision for early Rectal Cancer (STAR-TREC) trials will better characterize the impact of adjuvant therapy and RT on QOL after organ-sparing surgery [62, 63].

Quality of Life for Nonoperative Management

Nonoperative management for rectal cancer aims to avoid the associated morbidity and decreased QOL after an operation. Understanding the QOL concerns of these patients can also improve our broader understanding of the impact of chemoradiation alone on QOL, as the surgical operation has been removed from the equation.

Habr-Gama et al. demonstrated that patients receiving LC-CRT and nonoperative management had better QOL outcomes than those receiving LC-CRT and TEM. The study enabled patients with a complete clinical response to avoid surgery and compared their outcomes nearly 3 years after treatment. Compared to the nonoperative management group, the Cleveland Clinic Incontinence Index scores were significantly worse in the TEM group, and the Fecal Incontinence QOL scores were significantly worse for all metrics (lifestyle, coping behaviors, depression/self-perception, and embarrassment) [64]. This study is an improvement on past work which used colostomy-free survival as a proxy for improved QOL [65].

In a matched control study, evaluating the QOL using the EORTC QLQ-C30 and QLQ-CR28 and measuring defecation, sexual, and urinary problems, patients receiving LC-CRT and nonoperative management were compared with those who received LC-CRT and TME who were disease free at 2 years after treatment. Although these patients had a similar clinical outcome, QOL in those treated nonoperatively had better physical and cognitive functioning and roles with better global health status. However, general health perception was better in the TME group. Nonoperative management had fewer problems with defecation; fecal incontinence, LARS symptoms, and overall defecation problems were less severe in patients treated with nonoperative management. Patients receiving LC-CRT did experience LARS, albeit less frequently.

Patients treated with nonoperative management also have fewer urinary complaints and better sexual function [66].

Nonoperative management is a viable option for rectal cancer patients and is still under investigation for a select group of patients who achieve a complete clinical response and can be closely monitored for recurrence. Across a variety of QOL metrics, avoiding surgery seems to improve QOL. This is particularly important given the complications of surgery that are exacerbated by radiation such as wound dehiscence. Nonoperative management provides a promising alternative for patients and is currently under investigation.

Quality of Life After Radiation Therapy for Anal Cancer

From the extensive data in rectal cancer, it is expected that patients with anal cancers treated with (chemo)radiotherapy would also have complaints of fecal incontinence and other QOL measures. Anal cancer is typically treated with chemoradiation with concurrent 5-FU and mitomycin-C (MMC) in an effort to avoid APR and permanent colostomy. The ACT I trial was important in determining the benefits of adding 5-FU and MMC to radiation as well as characterizing the toxicities. LC-CRT was found to decrease the local failure rate and death rate from anal cancer, with an increase in short-term morbidity [67]. Followed up after 12 years, the ACT I trial further supported the use of LC-CRT to increase the rates of colostomy-free survival and showed that despite earlier data of increase short-term morbidity, late morbidities (clinician-reported) were no different between patients who received LC-CRT vs RT [68]. The ACT I trial, however, did not include PROs to characterize the impact on patients.

Ensuing trials, such as the randomized ACCORD 03 prospective assessment of early impact on the QOL, however, did utilize the EORTC QLQ-C30 and the Anal Sphincter Conservative Treatment Questionnaire. This study showed that 2 months after treatment, patients had improved emotional functioning, global health status, and intestinal satisfaction, with a corresponding decrease in pain, dyspnea, insomnia, appetite loss, and constipation. The improvement of QOL from before treatment is important in counseling patients regarding the benefits of seeking care; however, these data did not characterize the common complaints and drawbacks of treatment [69].

Bentzen et al. used the QLQ-C30 and QLQ-C29 to compare the QOL of anal cancer survivors to healthy volunteers. Across almost all metrics, anal cancer survivors reported a decrease in QOL, but these patients were not compared to a group of APR patients. Concerns included fecal incontinence and other bowel function concerns, as well as sexual interest and sexual function (impotence in men and dyspareunia in women) [70].

RT for anal cancer is associated with fecal incontinence, sexual, and other quality of life concerns, but more work is needed to characterize the extent of treatment toxicities. With the implementation of anal-cancer-specific questionnaires, future clinical trials can reliably measure meaningful PROs that can inform patients and providers.

IMRT and Quality of Life

Intensity-modulated radiation therapy (IMRT) can aid in reducing the dose to surrounding tissues while providing effective treatment. As IMRT has become the standard of care to treat anal cancer, more data has been published regarding the QOL impact.

The majority of the data supporting the use of IMRT does not include PROs but rather the clinician-reported toxicities using Common Terminology for Adverse Events (CTCAE). IMRT was found to have a significantly lower rate of severe acute skin toxicity and acute gastrointestinal toxicity [71]. Koerber et al. retrofitted the CTCAE v 4.0 into a questionnaire with additional questions from the Late Effect in Normal Tissue, Subjective, Objective, Management, Analytic (LentSoma) scales and compared patients receiving 3D conformal radiotherapy (3D-CRT) to those receiving IMRT. Sexual function and interest side effects might be improved with IMRT compared to 3D-CRT. Severe chronic vaginal dryness was experienced in more patients treated with 3D-CRT than IMRT. Although IMRT was associated with a 29% rate of severe loss of overall QOL, 3D-CRT had a rate of 43%, supporting the use of IMRT to reduce side effects and improve on QOL concerns of conventional treatment [72].

Also, there is a suggestion that women experience greater sexual side effects than men after IMRT, which is critical to understand because the majority of patients diagnosed with anal cancer are women (5530 vs 2770 estimated new cases in the USA in 2019 for women and men, respectively) [73]. In a prospective study, women were found to have persistently elevated dyspareunia, whereas impotence scores were elevated after treatment but resolved after 12 weeks. Men and women had a similar decrease in sexual interest up to 6 weeks after treatment which is expected given that the acute toxicities are still resolving; however, the mean returned to baseline for both groups by 6 months after treatment [74]. Another study showed that impotence ratings might be worse in some male patients after IMRT [75].

Bowel symptoms in patients treated with IMRT usually fluctuate depending on the time since therapy. At baseline, many patients with anal cancer experience bowel symptoms such as rectal pain and blood or mucous in stool, and, during therapy, many of these symptoms worsen. However, at 12 months after treatment, bowel symptoms returned to baseline [74, 75].

Other symptoms that were worse in those treated with 3D-CRT as compared to IMRT included pubic hair loss and poor

urinary stream during treatment [72]. Urinary incontinence is not usually present at baseline, but IMRT increases rates of urinary symptoms [74]. Global health status and skin symptoms are worse by the end of IMRT treatment but improve to baseline after 3 months and remain stable. Interestingly, social functioning and appetite scores are better at 12 months [75].

IMRT is generally better tolerated than conventional RT techniques. For accurate assessment of the benefits of IMRT, QOL concerns need to be evaluated at baseline, throughout treatment, and at least at 12 months after follow-up because of the temporality of the side effect profile. This poses a challenge because many prospective studies have high attrition rates, which might bias the data. Understanding the time course of side effects and QOL concerns can help providers counsel patients and set expectations.

Summary

There is a wealth of information detailing the QOL that rectal and anal cancer survivors experience. However, there persists a scarcity of data providing direct comparisons between the QOL experienced by patients enduring each of many different treatment regimens. As more trials employ validated tools to measure QOL outcomes, the inextricable nature of this defining aspect of cancer survivorship will be further elucidated.

In patients treated for rectal cancer, QOL is often negatively impacted by RT. The role of radiation in treatment is to improve local control of disease, but this has been achieved at the cost of worsened anorectal and sexual function, as well as report of overall diminished QOL; however, no studies have clearly assessed the impact of tumor recurrence on QOL since recurrences are often symptomatic and difficult to cure. Still, in some subpopulations, QOL is improved; RT has the ability to downstage tumors to allow for organ-sparing surgery or, in some cases, nonoperative management that may provide an entirely different QOL profile compared to APR. Future studies will characterize the long-term QOL of patients treated with sphincter-sparing and nonoperative treatment strategies as well as intensified neoadjuvant therapy.

There is also a paucity of information regarding QOL after anal cancer treatment. However, in the past 5 years, the implementation of QOL questionnaires designed specifically for anal cancer survivors has begun. Efforts have simultaneously characterized the gaps in this literature and begun to supplement the field's knowledge through additional investigations specific to anal cancer survivors. The PLATO trial will answer important questions about modulating dose for anal cancer patients of various stages while providing the first evidence of the utility of the EORTC QLQ-ANL27 questionnaire. Future studies will employ a validated anal-cancer-specific QOL questionnaire to reliably assess new therapeutic strategies' impact on the QOL.

In short, physicians should carefully discuss the QOL challenges of survivorship when presenting treatment options, as toxicities such as fecal incontinence and sexual dysfunction may influence decision-making differently in each individual patient. With prudent consideration of QOL, physicians are better equipped to counsel patients on the risks and benefits of various treatment modalities.

Compliance with Ethical Standards

Conflict of Interest Shane S. Neibart, Sharon L. Manne, and Salma K. Jabbour each declare no potential conflicts 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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