

## Research Letter

# Patient-Reported Outcomes After Chemoradiation in Patients With Anal Cancer: A Qualitative Analysis



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## Abstract

**Purpose:** Pelvic chemoradiation therapy (CRT) is the curative therapy for non-metastatic anal cancer, resulting in excellent survival rates. However, anal cancer survivors may experience diminished quality of life (QOL) due to late toxicities from pelvic CRT. Few studies use patient-reported QOL, and few include thematic analyses of the patient experience in their own words. We conducted a survey study with qualitative analysis of free-text responses to explore themes of patient perceptions of their QOL during and after pelvic CRT to inform future interventions, reform patient education, and improve outcomes.

**Methods and Materials:** We surveyed 248 patients with anal cancer treated with definitive intensity modulated radiation and concurrent chemotherapy from 2010 to 2018 who were alive and without recurrence. The survey included the Functional Assessment of Cancer Therapy General 7 item version, questions about satisfaction with preparation and patient education, and an optional free-text response question. Survey free response data were analyzed using the constant comparative method of qualitative analysis. Representative themes were generated.

**Results:** One-hundred and twelve patients (45%) completed surveys. Of these respondents, 84 (75%) answered the free-text question. The median (interquartile range) Functional Assessment of Cancer Therapy General 7 item version score for survey responders (N = 112) was 21 (range, 15-24). Three themes most mentioned by respondents were persistent toxicity effecting QOL (82%), insufficient upfront information about CRT (56%), and gratitude toward care received (35%).

**Conclusions:** Patients described late toxicities that affect QOL after pelvic CRT for anal cancer. This may be partially due to insufficient preparative information and post-treatment support. This study contributes to the literature supporting improved patient education and side effect management to augment long-term QOL for survivors of anal cancer.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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## Introduction

Despite excellent cure rates for patients with anal squamous cell carcinoma,<sup>1</sup> survivors may have diminished quality of life (QOL) due to the late toxicities of definitive pelvic chemoradiation (CRT).

Some studies have reported the incidence of late toxicities in anal cancer survivors,<sup>2-4</sup> with one meta-analysis showing that severe late gastrointestinal toxicities occur in one-third of patients with anal cancer who receive pelvic CRT.<sup>5</sup> However, few studies include a formal assessment of patient-reported QOL.<sup>6</sup> The Actions Concertées dans les Cancers Colorectaux et Digestifs prospective trial analyzing CRT in patients with anal cancer reported QOL using validated patient-reported outcome (PRO) questionnaires, showing overall improved QOL 2 months after CRT completion compared with before treatment.<sup>7</sup> However, there has been no report on long-term QOL. Thus, we performed a survey study to characterize long-term patient-reported bowel, urinary, and sexual function as well as QOL after pelvic CRT.<sup>8</sup> We included questions about preparedness and support for late toxicities as well as open-ended questions to develop a more comprehensive understanding of anal cancer survivors. The objectives of this study were to: (1) report QOL outcomes in long-term anal cancer survivors; and (2) describe the most prevalent themes resulting from our qualitative analysis of patient free-text responses.

## Methods and Materials

We received Institutional Review Board approval for this project. We contacted all patients who completed definitive intensity modulated radiation and concurrent chemotherapy for non-metastatic anal squamous cell carcinoma at a single institution between January 1, 2010 and September 1, 2018 and had at least 2 years follow-up without recurrence. For patients interested in participating in our larger project using PROs to assess functional outcomes after definitive treatment for anal cancer,<sup>8</sup> we administered a PRO survey containing several instruments, including the Functional Assessment of Cancer Therapy General 7 item version (FACT-G7).<sup>9</sup> Notably, this study administered the FACT-G7 as a single questionnaire at one timepoint, which is not how the survey was designed and validated.<sup>10</sup> Our survey also contained questions regarding preparedness and support for late toxicities and an optional free-text response that allowed patients to share additional thoughts about their general QOL. For all study participants, informed verbal consent was obtained using telemedicine at the time of initial contact and informed written consent was obtained at the time of PRO initiation on the first page of the survey.

Descriptive statistics and frequency tables were used to summarize the survey scores. Three research team members (K.L.C., B.S.D., M.K.R.) independently reviewed survey free responses and identified dominant themes. The constant comparative method of qualitative analysis was then used to formulate themes

about the patient experience.<sup>11</sup> Topic expert EBH reviewed the final themes.

## Results

### Participant characteristics

One-hundred and twelve patients (45%) completed surveys. The median time from chemoradiation to survey completion was 50.7 months (interquartile range, 36.6-84.6 months). Of these respondents, 84 (75%) answered the optional free-text question. Table 1 describes demographic and clinical characteristics for those responding to the survey and providing free-text responses.

### Quality of life: FACT-G7

The median (interquartile range [IQR]) FACT-G7 score for all survey responders (N = 112) was 21 (15-24). The range of possible scores is 0 to 28, with higher scores indicating better QOL. Most patients reported that they “quite and bit” or “very much” are able to enjoy life (n = 78, 69.6%). However, nearly one-quarter (n = 25,

**Table 1 Demographic and clinical characteristics for patients treated with definitive chemoradiation for anal squamous cell carcinoma (N = 112)**

	No. (% or median IQR)
Time from chemoradiation to survey completion (mo)	50.7 (36.6-84.6)
Median age at diagnosis (y)	61.5 (53.8-66.0)
Sex	
Women	90 (80.4)
Men	22 (19.6)
Race	
White	106 (94.6)
Non-white	6 (5.4)
Ethnicity	
Hispanic	4 (3.6)
Non-Hispanic	108 (96.4)
T stage	
T1/T2	85 (75.9)
T3/T4	27 (24.1)
N stage	
N0	63 (56.3)
N1	49 (43.7)
<i>Abbreviation:</i> IQR = interquartile range.	

**Table 2 Responses from the Functional Assessment of Cancer Therapy-General 7 Item version for patients treated with definitive chemoradiation for anal squamous cell carcinoma (N = 112)**

	Not at all	A little bit	Somewhat	Quite a bit	Very much
	No. (%)				
I have a lack of energy	33 (29.5)	38 (33.9)	22 (19.6)	15 (13.4)	4 (3.6)
I have pain	55 (49.1)	23 (20.5)	22 (19.6)	10 (8.9)	2 (1.8)
I have nausea	92 (82.1)	17 (15.2)	3 (2.7)	0 (0)	0 (0)
I worry that my condition will get worse	46 (41.1)	37 (33.0)	12 (10.7)	13 (11.6)	4 (3.6)
I am sleeping well	17 (15.2)	18 (16.1)	24 (21.4)	33 (29.5)	20 (17.9)
I am able to enjoy life	8 (7.1)	5 (4.5)	21 (18.8)	39 (34.8)	39 (34.8)
I am content with the quality of my life right now	13 (11.6)	12 (10.7)	22 (19.6)	40 (35.7)	25 (22.3)

22.3%) of patients reported they were “not at all” or “a little bit” content with the quality of their life (Table 2).

**Themes**

We identified and described 3 themes that were most commonly addressed by survey respondents:

**Persistent toxicity affects QOL**

Sixty-nine (82%) patients described that the presence of a persistent or permanent late toxicity from CRT affected their QOL. Particularly, bowel function, urinary function, sexual function, and musculoskeletal function were mentioned. Representative patient quotations can be found in Table 3.

**Table 3 Thematic analysis of free-text responses from patients treated with definitive chemoradiation for anal squamous cell carcinoma (n = 84)**

Theme	Frequency	Representative quotes
Persistent toxicity affects quality of life	n = 69 (82%)	Bowel toxicity: “The diarrhea is daily . . . I have to take Imodium the night before I travel the next morning. The bowel problems are horrendous and humiliating.” “Sometimes I wish I had a colostomy. The bowel incontinence and passing gas with no warning bothers me the most.” “Did not realize how life would revolve around my bowel movements. Must schedule all activity as to when I feel safe to leave home/bathroom.” Urinary toxicity: “I have to frequently urinate, I consistently drink water throughout the day. It gets to be very annoying as most days I will urinate about 3 times per hour and more depending on my water intake.” Sexual toxicity: “I have not had any sex with my husband. . . I wish I could have sex with him, but I am so afraid of the pain I may feel.” “I am a gay man and I like to be on the receiving end of sexual penetration. There was no information given to me on when or if I could ever do that again after radiation treatment.” Musculoskeletal toxicity: “Post treatment, I have experienced hip pain that has gradually prevented me from walking and exercising to the degree I did prior to treatment . . . losing my mobility is devastating.” “Radiation shattered my pelvic bone and it wasn’t discovered until the second-year mark . . . [I had to come in] for filling the cracks with medical cement.”
Insufficient upfront information about CRT	n = 47 (56%)	“All patients need to be counseled on exactly, step-by-step, what will take place prior, during, and after radiation.” “I had no idea that I would have lifelong ramifications after radiation.” “I wish I hadn’t had to discover ways to treat the side effects during treatment by myself.” “I was not aware of so many [of the late effects of radiation]. I cannot say because I was not informed; however, the focus is on beating cancer and the [concern for] long term toxicity does not arise until after survivor mode has passed.”
Gratitude toward care received	n = 29 (35%)	“The team approach that included both the radiation oncology and medical oncology department was reassuring, comforting, and informative!” “The radiation therapists were very compassionate and kind during my treatment.” “Thank you to my doctors and team who really took care of me. Very understanding, listened very patiently, and helped me to get through during cancer treatment.”

*Abbreviation:* CRT = chemoradiation therapy.

**Table 4** Responses to survey questions asking about patient education and support before and after definitive chemotherapy for anal squamous cell carcinoma (N = 112)

	Strongly disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
	No. (%)				
My physician/team prepared me well for the potential long-term side effects of radiation.	15 (13.4)	26 (23.2)	12 (10.7)	24 (21.4)	35 (31.3)
My physician/team supported me well in dealing with the long-term side effects of radiation.	15 (13.4)	21 (18.8)	14 (12.5)	16 (14.3)	46 (41.1)
Educational materials in the form of video or written materials would have been helpful to me before starting radiation.	5 (4.5)	7 (6.3)	28 (25)	31 (27.7)	41 (36.6)

### Insufficient upfront information about CRT

Forty-seven (56%) patients described that their care experience lacked adequate information regarding CRT. Some patients were unaware of the daily radiation treatment process and felt uncomfortable during their treatments, as one patient described the lack of modesty during treatments as a “psychological detriment.” Additionally, many patients were unaware of both the types and longevity of toxicities that they may face from CRT, characterized by feelings of shock: “I had no idea that I would have lifelong ramifications after radiation.” When addressing support for post-treatment anxieties, patients desired more help in dealing with treatment challenges both during and after CRT: “I wish I hadn't had to discover ways to treat the side effects during treatment by myself” (Table 3).

These responses largely agreed with 2 multiple choice questions included in the survey (Table 4). Over one-third of patients (n = 41, 36.6%) strongly disagreed or somewhat disagreed that their physician or team prepared them well for the potential long-term side effects of CRT. A majority of patients (n = 72, 64.3%) strongly agreed or somewhat agreed that further educational materials in the form of video or written materials would have been helpful before starting radiation therapy.

### Gratitude

Despite wanting more education about the treatment process and potential side effects, many patients were overall satisfied with their care experience. They described their physicians as “excellent, calm, and supportive” and had positive experiences with the entire radiation oncology team (Table 3).

### Discussion

In this study of QOL in long-term survivors of anal cancer after receipt of definitive pelvic CRT, FACT-G7 scores from our population (median [IQR] of 21 [15-24])

were similar to those reported for a sample of 4918 adult cancer patients (mean [standard deviation] of 19.1 [5.5]).<sup>9</sup> However, many patients in our study reported persistent or permanent side effects that they manage daily, which affects their QOL. Patients also described receiving insufficient upfront information regarding CRT as well as inadequate support managing post-treatment toxicities. Despite these challenges, many patients described gratitude toward their care teams and appreciation of their cancer-free status.

Although some studies have analyzed symptom-specific PROs in anal cancer survivors after completion of pelvic CRT,<sup>12</sup> few have focused on general QOL PROs or described how late toxicities affect daily functioning. As mentioned earlier, the Actions Concertées dans les Cancers Colorectaux et Digestifs study found improved emotion function, global health status, insomnia, pain, and satisfaction with intestinal function status at 2 months after CRT completion.<sup>7</sup> However, these data are not as informative for patients in long-term survivorship. Gilbert et al performed a comparative analysis between PRO scores in anal cancer survivors before and 1 year after CRT, and found that anxiety scores were improved at the 1-year surveillance visit.<sup>13</sup> With a median follow-up time of over 4 years, our results inform providers and patients about long-term, and likely permanent, toxicity expectations and their impact on daily life after pelvic RT for anal cancer.

Our findings emphasize the need for better and more standardized patient education regarding RT logistics as well as late or permanent toxicities from CRT. In 2012, Jagsi et al called for the development of strategies to help patients better understand RT and its effects, and for this to be a priority in radiation oncology research.<sup>14</sup> To date, a few studies have summarized sexual dysfunction risks<sup>15</sup> and strategies to minimize late side effects after CRT in patients with anal cancer<sup>16</sup>; however, publications on formal patient education initiatives have been lacking. For patients with anal cancer undergoing CRT, we recommend counseling on the following acute and late toxicities:

- Acute toxicities from pelvic CRT: diarrhea, pain with bowel movements, anal canal pain, skin irritation, dysuria, vaginal stenosis.
- Late toxicities from pelvic CRT: fecal incontinence or urgency, anal fistula, pelvic bone fracture, sexual dysfunction, infertility, skin telangiectasias.

In addition to better patient education, our results also suggest that patients with anal cancer need better post-treatment support. CRT results in specific acute and late toxicities for many patients,<sup>16</sup> resulting in significant stress and lifestyle changes. Moreover, fear of cancer recurrence is a well-described post-treatment phenomenon that occurs in up to 50% of patients with cancer.<sup>17,18</sup> Interventions to improve support for these post-treatment fears and anxieties are warranted, such as shorter time to follow-up and early initiation of cognitive behavioral therapy.<sup>17</sup>

Our study is one example of quantitative-qualitative mixed methodology research. Quantitative research uses numbers and data to explain changes in experimental variables through the scientific method. Qualitative research uses words from the study participant's perspective to explain or provide context for a phenomenon. Previously, qualitative research has rarely been used in radiation oncology, with few studies analyzing post-RT qualitative outcomes in head and neck cancer<sup>19-21</sup> and prostate cancer.<sup>22,23</sup> Recently, Shi et al published a mixed methodology study analyzing patient-reported pain response after palliative RT; the quantitative findings showed a numerical improvement in the pain score and the qualitative findings described which aspects of pain were improved.<sup>24</sup> Enhancing quantitative findings with qualitative research is an opportunity for better understanding of complex issues and the formation of interventions to address these issues and may be useful in future oncology research.

This study has several limitations, most notably its cross-sectional design and recruitment of patients from a single, large academic cancer center. Additionally, we did not have baseline symptom or QOL data for these patients. Finally, it was not a requirement to answer the open-ended questions in our survey and, therefore, we may have missed other relevant data.

## Conclusions

This is the first qualitative study to describe QOL after pelvic CRT for anal cancer from the patient's perspective. Many patients described a diminished QOL since receiving pelvic CRT, potentially due to insufficient pre-treatment education and post-treatment support. This study highlights the need for prospective studies to validate the impact of pelvic CRT on long-term QOL and for providers to encourage careful and consistent patient

education and improved support for late and permanent toxicities from pelvic CRT.

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