Electronic Patient-Reported Outcomes and Toxicities During Radiotherapy for Head and Neck Cancer

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Introduction

Head-and-neck cancer and its treatment inflict a substantial burden on patients, including a variety of acute and late toxicities (1,2). Five-year survival rates between 34% and 70% (3) compound patient distress. To minimize this burden, providers must try to ameliorate adverse events (AEs) that impact quality of life (QOL) during radiotherapy (RT) or concurrent chemoradiotherapy (CCRT) for head-and-neck cancer. Although research has shown QOL to be analogous to other vital signs (4), many aspects of QOL may not be evident to the clinical team as they focus their efforts on treating the patient's disease. Physicians have begun to use patient-reported QOL (PROQOL) data in an effort to assess changes in QOL that might otherwise remain unaddressed. Using PROQOL data in the outpatient oncology setting improves physician-patient communication (4–6) and provides tangible benefits. For example, the use of PROQOL data can decrease the underestimation of depression and anxiety by physicians (7). Furthermore, for patients with head-and-neck

cancer, PROQOL data correlates with locoregional control (8), disease-specific survival (9), and overall survival (9–12).

Prospective longitudinal studies of RT alone and CCRT for head-and-neck cancer have shown worsening PROQOL over the course of treatment (1,13). Although improvements have been made by employing intensity-modulated radiotherapy (IMRT), an advanced technology to conform radiation dose more closely to the specific area intended for treatment, substantial symptom burden persists (13–19). A wide range of symptoms, both physical and psychosocial, become progressively worse during the course of radiation with or without chemotherapy. Overall QOL, nausea, vomiting, pain, dysphagia, dysphonia, anorexia, and insomnia typically improve within 6 months after treatment, whereas physical functioning, cognitive functioning, xerostomia, fatigue, anosmia, dysgeusia, depression, and anxiety recover over a longer period (13,20). Overall symptom severity has been shown to be worse for CCRT than for RT alone, particularly for fatigue, drowsiness, anorexia, dysgeusia, and mucus production (1,21).

Real-time, electronic patient-reported outcomes (ePROs) collected via a web-based system have shown promise for clinical benefit in outpatient medical oncology practice (22). In outpatient radiation oncology practices, patients frequently interact with providers over the course of RT or CCRT, typically at weekly on-treatment visits (OTVs), which provide an opportunity to monitor AEs. Real-time ePROs are a novel means to systematically monitor and address the aforementioned symptom burden at OTVs and have the potential to be integrated into outpatient radiation oncology practice (23). However, the use of ePROs at several time points during head-and-neck RT has not been evaluated. Therefore, we aimed to characterize QOL, AEs, and supportive care interventions over the course of head-and-neck RT using ePROs.

Methods

Study Design

We analyzed the subset of primary head-and-neck cancer patients who were enrolled in a larger study (23) evaluating the clinical significance of ePROs during RT at a National Cancer Institute–designated comprehensive cancer center. Patients could not have evidence of distant metastasis, needed to have received at least 5 weeks of RT with or without chemotherapy, and had to be able to use a desktop computer to complete ePRO questionnaires in English. The study was approved by the Mayo Clinic Institutional Review Board. Informed consent was obtained from all individual participants included in the study.

Data Collection

QOL Measures—The linear analog self-assessment (LASA) was used to measure 12 health-related QOL domains (overall QOL, mental well-being [WB], physical WB, emotional WB, social activity, spiritual WB, pain frequency, pain severity, fatigue level, level of support, financial concerns, and legal concerns) (24–28). The 12 LASA single-item assessments ask patients to rate each specific QOL domain from 0 to 10 over the past week (0 being as bad as it can be, 10 being as good as it can be). Although scores on the 0 to 10

scale may clump around the middle and the quartiles (29), patients have been shown to score along the entire spectrum from 0 to 10 without ceiling or floor effects or restriction of range (28). The 12 single-item LASA domains assessed herein have been validated and standardized to give general measures of QOL for patients in numerous oncology settings (24–28).

All patients completed the LASA electronically in the radiation oncology examination room by using a web-based application—before starting RT, before biweekly OTVs (ie, weeks 1, 3, and 5), and at the last week of RT (Figure 1). As part of the larger study, providers were randomized to having the ePRO data available for review before OTVs. The clinicians could view the ePRO data in either tabular or bar-graph format on their office computer or with the patient in the examination room. Clinically meaningful changes were color-coded in the tabular format to capture the attention of the clinicians viewing the data (Figure 2). To assist clinical decision-making related to LASA outcomes, clinicians could view algorithms based on the National Comprehensive Cancer Network distress management guidelines via a hyperlink that was embedded in the table of results for each patient.

Adverse Events—Toxicities and AEs, as detailed by providers in the institutional medical record, were collected for baseline, biweekly intervals (ie, weeks 1, 3, and 5), and the last week of RT. AEs were graded retrospectively by using the Common Terminology Criteria for Adverse Events (National Cancer Institute, version 4.0, May 28, 2009) (30).

Clinical Characteristics and Supportive Care Interventions—Institutional medical records were used to retrospectively review all patient charts and collect data on patient demographic characteristics, tumor characteristics (histologic diagnosis, TNM stage, primary tumor site), RT course, and chemotherapy. Patient weight was recorded before RT was started, before biweekly OTVs, and at the last week of RT. Events that occurred during RT, including intravenous (IV) hydration, transfusion, feeding-tube placement, an emergency department (ED) visit without hospitalization, and emergent hospitalization at our institution were noted.

Statistical Measures—Patient demographic characteristics, tumor characteristics, RT course, chemotherapy information, and patient weight were summarized and compared between cohorts by using Wilcoxon rank sum, χ^2, or Fisher exact tests, as appropriate. All LASA item scores were transformed to a 0 to 100 point scale, with 100 being the best possible score. Area under the curve (AUC) summary statistics for each patient were calculated for each LASA item by using all available scores (31). The AUC was transformed to an average prorated AUC score, preserving the 0 to 100 range. Changes from baseline for each LASA item were also calculated at each time point. Prorated AUC scores, individual item scores at each time point, and all changes from baseline scores were compared between cohorts by using normality testing via the Shapiro-Wilk procedure followed by the Wilcoxon rank sum test for nonnormal distributions or the 2-sample t test for normal distributions (32,33). Comparison of the percentage of patients in each cohort who reported a clinically meaningful improvement or decrease (10 or more points on the 0 to 100 point scale) (34) was carried out by using χ^2 tests (35). The Wilcoxon rank sum test was used to compare the

AE grades between cohorts. All hypothesis testing was completed by using a 2-sided alternative hypothesis and a 5% type I error.

Results

Sixty-five patients met the inclusion criteria. The study population was primarily elderly (mean [range] age, 65.3 [32–89] years; SD, 12.6) white (92.3%), and male sex (80%). Patients who had CCRT (CCRT patients) were younger than patients who had RT alone (RT patients) (61.4 years, CCRT vs. 71.5 years, RT; *P*=.002). RT patients were more often treated in the adjuvant setting (80.0%, adjuvant RT vs 52.5%, adjuvant CCRT; *P*=.03). Table 1 displays patient characteristics of the CCRT cohort, the RT cohort, and the total population, including details of staging, the primary tumor site, histologic diagnosis, and type of systemic chemotherapy. Tumors were most commonly stage IV (59.9%) squamous cell carcinoma (78.5%).

Patient compliance with completing the ePROs averaged 93.8% (96.9% at baseline, 95.4% at week 1, 89.2% at week 3, and 93.8% at week 5). The patients completing 7 weeks of RT had a 94.4% compliance rate at week 7. At study completion, 94.7% of patients said they would participate in the study again.

Figure 3 shows the overall scores for each LASA item for the entire cohort over the course of treatment. During CCRT and RT alone, most patients had a clinically meaningful decrease (10 points from baseline on a 0–100 scale) in all QOL domains except for level of support, financial concerns, and legal concerns. The QOL domains for which patients most commonly experienced clinically meaningful decreases were fatigue (75.4% of patients; 95% CI, 62.9%–84.9%), social activity (70.8%; 95% CI, 58%–81.1%), and overall QOL (70.8%; 95% CI, 58.0%–81.1%). At the last week of CCRT or RT alone, the mean LASA score was worse than baseline in all QOL domains except level of support and financial concerns.

Figure 4 presents all LASA items over the course of therapy for the CCRT and RT alone cohorts. The addition of systemic chemotherapy significantly impacted QOL domains. By week 3 of treatment, CCRT patients had a significantly worse change from baseline in pain frequency compared with RT patients (–15.1, CCRT vs +6.7, RT; *P*=.02) and in pain severity (–16.0, CCRT vs –0.5, RT; *P*=.04), with a nonsignificant tendency toward worse fatigue (–13.7, CCRT vs +3.3, RT; *P*=.09). By week 5, CCRT patients reported a significantly worse change from baseline in social activity than did RT patients (–21.9, CCRT vs –1.9, RT; *P*=.001). At the last week of treatment, the following 3 domains continued to have significantly worse changes from baseline for CCRT patients as compared with RT patients: social activity (–19.4, CCRT vs –0.9, RT; *P*=.006), pain frequency (–23.8, CCRT vs +1.7, RT; *P*=.009), and pain severity (–19.4, CCRT vs – 3.5, RT; *P*=.048). Over the course of treatment, CCRT (compared with RT) was associated with a statistically greater incidence of clinically meaningful, decreased overall QOL (80.0% [95% CI, 63.9%–90.4%] vs 56.0% [95% CI, 35.3%–75.0%], *P*=.02), decreased physical WB (80.0% [95% CI, 63.9%–90.4%] vs 48.0% [95% CI, 28.3%–68.3%], *P*=.004), and increased pain frequency (80.0% [95% CI, 63.9% –90.4%] vs 52.0% [95% CI, 31.8%–71.7%], *P*=.02).

Table 2 lists the maximum grade for each AE a patient experienced during the course of CCRT or RT alone and also summarizes the overall maximum AE grade each patient experienced. For brevity and relevance, Table 2 presents only AEs of grade 3 or grade 4 that occurred more than once or AEs of any grade that showed a statistically significant difference between CCRT and RT alone. Grade 3 AEs occurring once included dyspnea, pleuritic pain, and urinary tract infection among RT alone patients versus cardiomyopathy, delirium, port-a-cath infection, and soft-tissue infection among CCRT patients. All except 1 patient experienced dermatitis, with the majority of events being a grade 2. Grade 1 or 2 dysgeusia was diagnosed in 82.5% of CCRT patients vs 56.0% of RT patients (P=.09, not presented in Table 2). Mucositis occurred in 97.5% of CCRT patients vs 64.0% of RT patients (P<.001); nausea, 82.5% of CCRT patients vs 28.0% of RT patients (P<.001); odynophagia, 97.5% of CCRT patients vs 60.0% of RT patients (P<.001); and xerostomia, 80.0% of CCRT patients vs 48% of RT patients (P=.01). All patients experienced at least 1 grade 2 AE during treatment. Overall, 35.4% and 3.1% of patients experienced grade 3 and grade 4 AEs. One patient who had adjuvant CCRT had a grade 4 acneiform rash, and 1 patient who underwent definitive CCRT experienced grade 4 respiratory failure. As compared with RT patients, CCRT patients experienced significantly worse maximum-grade AEs (50.0%, grade 3 and 5%, grade 4) than RT patients (12.0%, grade 3 and 0, grade 4) (P=.002). Patients' mean (range) weight loss was 5.5 kg (1.9–18.7) (SD, 4.4): 6.9 kg, CCRT and 2.8 kg, RT (P<.001). IV hydration was needed in 52.3% of patients: 77.5%, CCRT and 12.0%, RT (P<.001). Three CCRT patients required a transfusion of packed red blood cells (4.6% overall). At the discretion of the radiation oncologist, a feeding tube was placed in 40.0% of patients: 57.5%, CCRT and 12.0%, RT (P=.001). Of all patients, 10.8% had ED visits that did not require hospitalization. For the entire cohort, 37.5% of CCRT patients were admitted emergently to our hospital (5.0% hospitalized twice) versus 12.0% of RT patients (P=.04 for the difference between RT and CCRT hospitalization rates).

Discussion

Over the course of head-and-neck cancer radiotherapy, we assessed a variety of PROQOL outcomes, recorded AEs, and found widespread, clinically meaningful decrements in fatigue, social activity, and overall QOL with frequent grade 3 AEs, weight loss, IV hydration, feeding tube placement, ED visits, and hospitalization, particularly among CCRT patients. Multiple previous studies have assessed PROQOL outcomes and AEs in head-and-neck cancer (1,13–16,36,37). However, the previous studies used paper-based assessments and did not include provider-reported AEs and supportive care interventions. In contrast, our study is unique in that we evaluated multiple time points during therapy with real-time, web-based ePROs and subsequently collected provider-reported AEs and objective measures, such as weight loss and the need for interventions (IV hydration, transfusion, feeding tube placement, ED visit, and hospitalization).

Collecting PROQOL data at multiple time points during therapy may create a concern regarding increased resource utilization. However, previous studies have shown the feasibility of incorporating PROQOL data into outpatient oncology practice without prolonging the clinical encounter or increasing the work burden of the care providers (4–6). In our institutional experience, collection of PROQOL data in a pilot setting only added an

average of 2.9 additional minutes to the clinical encounter (M. Y. Halyard, MD, unpublished data, August 2016). Electronic web-based data collection is convenient and allows simultaneous data entry. By collecting data at multiple time points during therapy, providers can track outcomes over time and respond to issues in real-time (38). In our institution, one of the medical oncology departments assesses the LASA overall QOL and fatigue domains for every patient at every clinic visit. As a result, patient concerns that would otherwise be unrecognized have been identified in 25% to 40% of visits (4). Snyder et al (22) also reported using real-time ePROs in outpatient medical oncology. Our study adds to the existing literature by demonstrating the feasibility of real-time ePRO collection at multiple time points in a head-and-neck radiation oncology practice. Our data also provide a picture of how patient-reported outcomes and provider-documented toxicities progress over the course of head-and-neck cancer therapy and document the supportive care interventions patients may need. This knowledge may allow patients and providers to anticipate and proactively address problems before they arise, and in the end, may even improve resource utilization.

The characteristics of our cohort matched those of the predominant patient population in the literature for head-and-neck cancer: men with advanced squamous cell carcinoma of the oral cavity or oropharynx (Tables 1 and 2). However, the mean age of our cohort was 5 to 10 years older than that of previously studied groups (1,13,36,39). This difference may reflect the characteristics of the patient population at our institution. In our cohort, CCRT patients were younger than RT patients. This could be due to providers being more apt to offer chemotherapy to younger patients who may be fitter and have fewer comorbidities. Radiotherapy alone followed surgery in an adjuvant manner more often than CCRT, and the median RT regimen delivered 60 Gy in 30 fractions, reflective of the standard-of-care postoperative regimen (40,41). The patients included in this report were treated with IMRT based on multiple randomized controlled trials that showed improved PROQOL and less toxicity with IMRT versus other radiotherapeutic modalities such as 3-dimensional conformal radiotherapy (13–16).

Our overall cohort's PROQOL data reflects the well-known, profound effects of head-and-neck cancer treatment on QOL (1,13–16,36,37). By the end of their radiotherapy, our patients' average QOL was diminished across nearly all domains, but especially for fatigue, social activity, and overall QOL (Figure 3). Level of support and financial concerns were the only domains that were not worse than baseline by the end of therapy. This may be accounted for by the patient population at our institution, which typically has a high level of social support.

The ePROs showed that the CCRT patients experienced greater impact on QOL than the RT alone patients. The mean baseline QOL was better for CCRT patients in all LASA items except emotional WB and financial and legal concerns (Figure 4). Despite these better baseline QOL scores, at the last week of treatment, the CCRT patients reported worse average scores than RT patients for all LASA items except physical WB. Data on the change from baseline for individual LASA items provides insight into this role reversal. Three weeks into CCRT, patients began to report decrements in pain frequency, pain severity, and fatigue that eclipsed their RT counterparts. Week 5 brought diminished social activity from

baseline for CCRT patients as compared with those who underwent RT alone. Changes from baseline that were statistically worse for CCRT than RT patients persisted into the last week of treatment for social activity, pain frequency, and pain severity. The CCRT patients also had more clinically meaningful worsening of overall QOL, physical WB, and pain frequency over the course of treatment. These findings reinforce those of other studies that reported increased symptom burden of CCRT as compared with RT alone (1,2,21). However, given the differences between the CCRT and RT alone groups in age, definitive versus adjuvant treatment, and radiation dose (Table 1), our findings must be weighed against these potential confounders.

Of particular interest, patients who underwent RT had significantly more fatigue at baseline (Figure 4). We hypothesize that this baseline difference between RT and CCRT can be attributed in part to the greater number of RT alone patients who had surgery before beginning their RT. Another possible contributory factor is that patients who received RT alone were also significantly older than patients who received CCRT (Table 1). This finding should be investigated further, because baseline fatigue level has been shown to predict overall survival among advanced head-and-neck cancer patients treated with RT (10).

In concert with the ePRO data, the provider-reported AEs again reflect the intense impact of head-and-neck cancer treatment on patients (Table 2). Grade 2 toxicities are ubiquitous. The patients who underwent CCRT experienced more grade 3 toxicities than RT patients and had 2 grade 4 toxicities (Table 2). Although a prior randomized phase III study of advanced head-and-neck cancer found no significant differences in PROQOL between RT alone and RT with cetuximab (37), 8 patients who underwent CCRT in our study experienced the acneiform rash classic for cetuximab, 1 of which was a grade 4. This serves as a reminder that although previous studies may show no statistical difference between 2 treatment regimens, providers must nonetheless be prepared for the side effects possible with each regimen. A previous retrospective study of hypopharyngeal cancer found increased dry mouth and problems with swallowing among CCRT patients (36), findings that were reinforced by our data showing that CCRT was associated with increased xerostomia and odynophagia (Table 2). We also describe statistically higher-grade mucositis and nausea among patients who underwent CCRT compared with RT alone (Table 2). The only occurrences of pleuritic pain (2 patients), sinus crusting (3 patients), and thromboembolic events (2 patients) were among the RT alone cohort. It is certainly possible that these AEs can be attributed to the surgical procedures performed before the start of RT.

As previously reported (36), we found that CCRT was associated with increased weight loss. In addition, a significant proportion of patients, especially those undergoing CCRT, required IV hydration and feeding tube placement. Higher-grade dry mouth, problems swallowing, dysgeusia, mucositis, and nausea could account for the greater weight loss and the need for IV hydration and feeding tubes among CCRT patients. These issues may also play a role in the difference in hospitalization rates between CCRT and RT alone. Understanding this potential for weight loss, IV hydration, feeding tubes, and hospitalization for patients during therapy is important for both patients and clinicians in decision-making and in working to prevent AEs.

Our study has several limitations. Because of its size (N=65), the head-and-neck subpopulation used for our study has limited power. Our assessment of differences between CCRT and RT alone is also an unplanned subgroup analysis. Therefore, the CCRT and RT alone groups were unbalanced, introducing potential confounders. Furthermore, we retrospectively collected and graded AEs by using our institution's medical records. The AE data extraction was not double-coded, and a variety of providers contributed to the medical record, both of which potentially introduce ascertainment bias. Prior work has shown that AE reporting by cancer clinicians shows only moderate agreement between different clinicians (42). Moreover, physician- versus patient-reported AEs have shown only slight agreement (43). This emphasizes the need for patient-reported outcomes (PROs) in addition to clinician assessments to improve the ability to detect and subsequently address problems. Future studies that correlate PROs and AEs in head-and-neck RT will help to clarify the role PROs can play in addressing patient concerns and mitigating AEs.

To our knowledge, our study is the first reported use of real-time ePROs at multiple time points during the course of RT for patients with head-and-neck cancer. Real-time electronic collection of PROQOL data is feasible in RT for head-and-neck cancer and reveals QOL deficits that merit attention by providers. Given the significant impact of head-and-neck CCRT and RT on QOL, continued investigation for optimal incorporation of ePRO collection into the clinical practice should be a priority.

Acknowledgments

Abbreviations

AE	adverse event
AUC	area under the curve
CCRT	concurrent chemoradiotherapy ED, emergency department
ePRO	electronic patient-reported outcome
IMRT	intensity-modulated radiotherapy
IV	intravenous
LASA	linear analog self-assessment
OTV	on-treatment visit
PROs	patient-reported outcomes
PROQOL	patient-reported quality of life
QOL	quality of life
RT	radiotherapy

WB well-being

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Linear Analogue Self Assessment (LASA)

Please check the number (0-10) best reflecting your response to the following that describes your feelings during the past week, including today.

How would you describe:

1. Your overall Quality of Life? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

2. Your overall mental (intellectual) well being? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

3. Your overall physical well being? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

4. Your overall emotional well being? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

5. Your level of social activity? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

6. Your overall spiritual well being? (0=As bad as it can be, 10=As good as it can be)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

7. The frequency of your pain? (0=No pain, 10=Constant pain)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

8. The severity of your pain, on the average? (0=No pain, 10=Pain as bad as you can imagine)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

9. Your level of fatigue (weariness, tiredness) on average? (0=No fatigue, 10=Fatigue as bad as you can imagine)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

10. Your level of support from friends and family? (0=No support, 10=Highest level of support)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

11. Your financial concerns? (0=Constant concerns, 10=No concerns)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

12. Your legal concerns (will, advanced directives, etc.)? (0=Constant concerns, 10=No concerns)

● N/A ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

View Survey Response   **Clear Survey**

Figure 1.
Electronic Collection of LASA Data. LASA indicates linear analog self-assessment.

Patient XYZ01 : LASA Scores by Week Since Treatment Started   Return to Main Menu | Click here to log out

Please click on the QOL domain links for Disease Management Pathways.

Items in **BLUE** represent complaints that are worse than average (5 points or below for QOL OR 5 points or above for Pain/Fatigue) and may warrant attention.
Items in **RED** represent a drop of 2 points or more
Items in **GREEN** represent a 2 points or more improvement on the measure since the last visit.

Factor Measured (0=Worst QOL and 10=Best QOL) or **(0=No Pain/Fatigue and 10=Constant Pain/Tiredness)	Baseline	Week 1	Week 3	Week 5	Last Week of Tx	Last Week of Tx Minus Week 5
Quality of Life	9	4	6	7	6	-1
Mental (intellectual) WB	9	4	6	8	7	-1
Physical WB	8	4	7	5	6	1
Emotional WB	7	4	7	7	7	0
Social Activity Level	9	6	8	7	6	-1
Spiritual WB	8	8	9	9	8	-1
Pain Frequency**	1	6	5	4	3	1
Pain Severity**	1	3	3	2	2	0
Fatigue Level**	2	5	7	5	7	-2
Level of Support	10	8	10	9	9	0
Financial Concerns	8	3	3	3	8	5
Legal Concerns	1	2	10	0	10	10

Figure 2.
Data Display Provided to Clinicians. LASA indicates linear analog self-assessment; QOL, quality of life; WB, well-being.

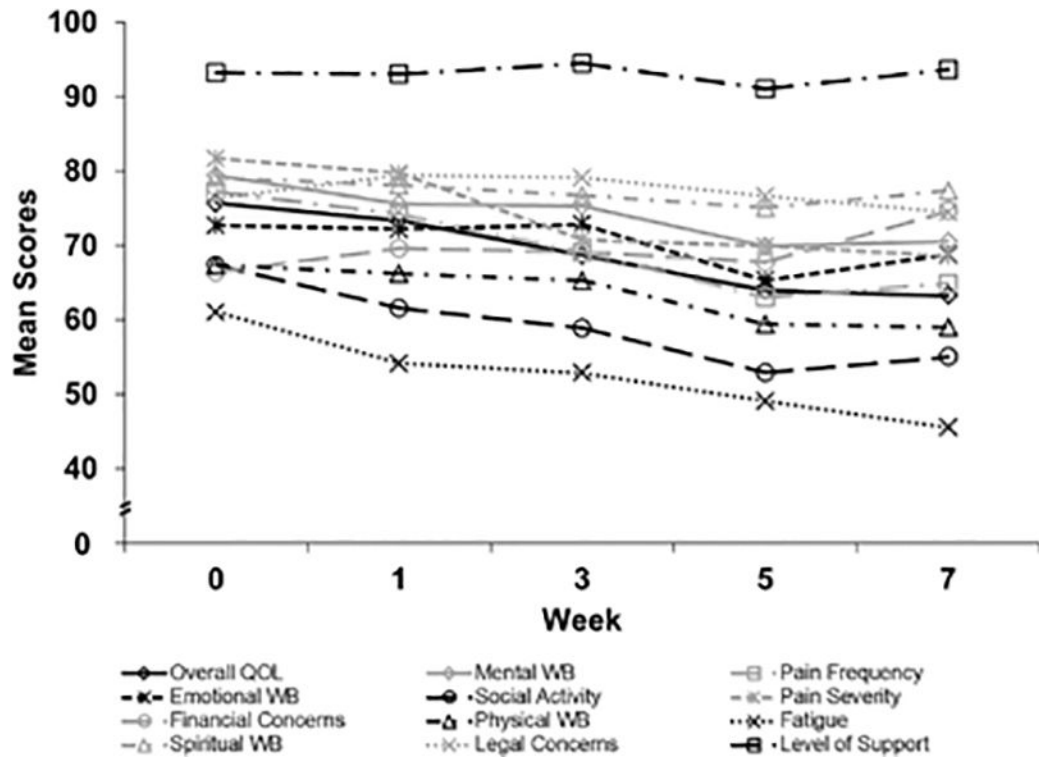**Figure 3.**
Overall LASA Scores (0 = Low QOL; 100 = High QOL). LASA indicates linear analog self-assessment; QOL, quality of life; WB, well-being.
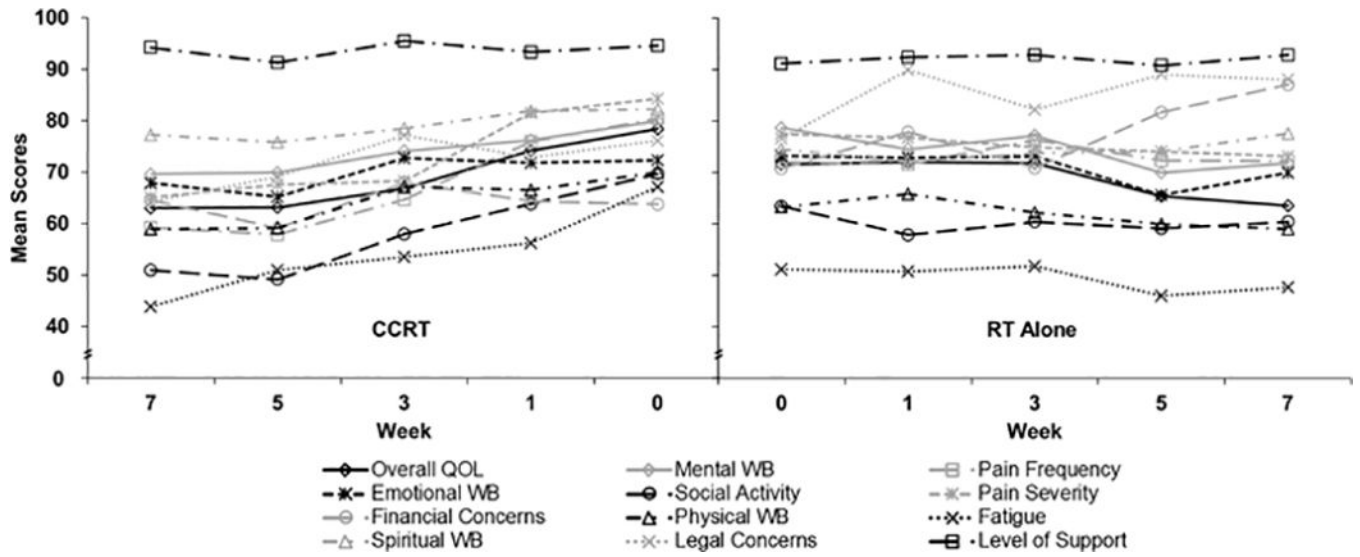
Figure 4.
Butterfly Plot of LASA Scores by Treatment Status (0 = Low QOL; 100 = High QOL).
CCRT indicates concurrent chemoradiotherapy; LASA, linear analog self-assessment; QOL,
quality of life; RT, radiotherapy; WB, well-being.

Table 1.

Baseline Demographic and Clinical Characteristics[a]

Characteristic	CCRT (n=40)	RT Alone (n=25)	Total (N=65)	P Value
Age				0.002[b]
Mean (SD)	61.4 (11.2)	71.5 (12.4)	65.3 (12.6)	
Range	(32.0–83.0)	(43.0–89.0)	(32.0–89.0)	
Sex, No. (%)				0.20[c]
Female	6 (15.0)	7 (28.0)	13 (20.0)	
Male	34 (85.0)	18 (72.0)	52 (80.0)	
Race (self-identified), No. (%)				>0.99[d]
American Indian/Alaska Native	1 (2.5)	0 (0.0)	1 (1.5)	
Asian	1 (2.5)	0 (0.0)	1 (1.5)	
Black	1 (2.5)	1 (4.0)	2 (3.1)	
Pacific Islander	1 (2.5)	0 (0.0)	1 (1.5)	
White	36 (90.0)	24 (96.0)	60 (92.3)	
Radiotherapy, No. (%)				0.03[c]
Adjuvant	21 (52.5)	20 (80.0)	41 (63.1)	
Definitive	19 (47.5)	5 (20.0)	24 (36.9)	
Dose of radiation				0.05[b]
Median	60.0	60.0	60.0	
Range	(50.0–70.0)	(50.0–70.0)	(50.0–70.0)	
Staging, No. (%)				NA
Stage I	0 (0.0)	6 (24.0)	6 (9.2)	
Stage II	4 (10.0)	5 (20.0)	9 (13.8)	
Stage III	7 (17.5)	3 (12.0)	10 (15.4)	
Stage IV	29 (72.5)	10 (40.0)	39 (60.0)	
Recurrent	5 (12.5)	7 (28.0)	12 (18.5)	
Primary Site, No. (%)				NA
Oral cavity/oropharynx	23 (57.5)	6 (24.0)	29 (44.6)	
Larynx	4 (10.0)	4 (16.0)	8 (12.3)	
Skin	2 (5.0)	6 (24.0)	8 (12.3)	
Nasopharynx	5 (12.5)	0 (0.0)	5 (7.7)	
Nasal cavity/paranasal sinus	0 (0.0)	4 (16.0)	4 (6.2)	
Salivary	1 (2.5)	3 (12.0)	4 (6.2)	
Other	4 (10.0)	3 (12.0)	7 (10.8)	
Histologic diagnosis, No. (%)				NA
Squamous cell carcinoma	36 (90.0)	15 (60.0)	51 (78.5)	
Spindle cell carcinoma	0 (0.0)	2 (8.0)	2 (3.1)	
Papillary thyroid	0 (0.0)	2 (8.0)	2 (3.1)	
Melanoma	0 (0.0)	2 (8.0)	2 (3.1)	

Characteristic	CCRT (n=40)	RT Alone (n=25)	Total (N=65)	P Value
Merkel cell	2 (5.0)	0 (0.0)	2 (3.1)	
Adenocarcinoma	1 (2.5)	1 (4.0)	2 (3.1)	
Other	1 (2.5)	3 (12.0)	4 (6.2)	
Concurrent chemotherapy, No. (%)				NA
Cisplatin	22 (55.0)	0 (0.0)	22 (33.8)	
Cetuximab	7 (17.5)	0 (0.0)	7 (10.8)	
Carboplatin	5 (12.5)	0 (0.0)	5 (7.7)	
Cisplatin after induction	3 (7.5)	0 (0.0)	3 (4.6)	
Cetuximab after induction	1 (2.5)	0 (0.0)	1 (1.5)	
Cetuximab, carboplatin, paclitaxel	1 (2.5)	0 (0.0)	1 (1.5)	
Induction only	1 (2.5)	0 (0.0)	1 (1.5)	
None	0 (0.0)	25 (100.0)	25 (38.5)	

Abbreviations: CCRT, concurrent chemoradiotherapy; RT, radiotherapy.

[a] Percentages do not add to 100 because of rounding.

[b] Wilcoxon rank sum test.

[c] χ^2 text.

[d] Fisher exact test.

Table 2

Summary of Maximum-Grade Adverse Events per Patient (Start to Completion of Radiotherapy)

Adverse Event	CCRT (n=40)		RT Alone (n=25)		Wilcoxon *P* Value
	Grade	No. (%)	Grade	No. (%)	
Aspiration	1	0	1	0	.07
	2	3 (7.5)	2	0	
	3	2 (5.0)	3	0	
	4	0	4	0	
Constipation	1	14 (35.0)	1	2 (8.0)	.005
	2	4 (10.0)	2	0	
	3	1 (2.5)	3	1 (4.0)	
	4	0	4	0	
Cough	1	4 (10.0)	1	3 (12.0)	.96
	2	3 (7.5)	2	2 (8.0)	
	3	1 (2.5)	3	0	
	4	0	4	0	
Dermatitis	1	2 (5.0)	1	2 (8.0)	.11
	2	35 (87.5)	2	22 (88.0)	
	3	3 (7.5)	3	0	
	4	0	4	0	
Diarrhea	1	9 (22.5)	1	4 (16.0)	.26
	2	0	2	0	
	3	2 (5)	3	0	
	4	0	4	0	
Dysphagia	1	3 (7.5)	1	1 (4.0)	.92
	2	5 (12.5)	2	5 (20.0)	
	3	2 (5.0)	3	0	
	4	0	4	0	
Lung infection	1	0	1	0	.07
	2	1 (2.5)	2	0	
	3	4 (10.0)	3	0	

Adverse Event	CCRT (n=40)		RT Alone (n=25)		Wilcoxon P Value
	Grade	No. (%)	Grade	No. (%)	
	4	0	4	0	
Mucositis	1	9 (22.5)	1	8 (32.0)	<.001
	2	24 (60.0)	2	8 (32.0)	
	3	6 (15.0)	3	0	
	4	0	4	0	
Nausea	1	12 (30.0)	1	4 (16.0)	<.001
	2	13 (32.5)	2	2 (8.0)	
	3	8 (20.0)	3	1 (4.0)	
	4	0	4	0	
Odynophagia	1	5 (12.5)	1	6 (24.0)	<.001
	2	29 (72.5)	2	9 (36.0)	
	3	5 (12.5)	3	0	
	4	0	4	0	
Oral pain	1	1 (2.5)	1	6 (24.0)	.30
	2	13 (32.5)	2	3 (12.0)	
	3	2 (5.0)	3	0	
	4	0	4	0	
Rash acneiform	1	3 (7.5)	1	0	.02
	2	4 (10.0)	2	0	
	3	0	3	0	
	4	1 (2.5)	4	0	
Sinus crusting	1	0	1	0	.03
	2	0	2	3 (12.0)	
	3	0	3	0	
	4	0	4	0	
Somnolence	1	0	1	0	.27
	2	1 (2.5)	2	0	
	3	1 (2.5)	3	0	
	4	0	4	0	
Thromboembolic event	1	0	1	0	.08

Adverse Event	CCRT (n=40)		RT Alone (n=25)		Wilcoxon *P* Value
	Grade	No. (%)	Grade	No. (%)	
	2	0	2	0	
	3	0	3	2 (8.0)	
	4	0	4	0	
Xerostomia	1	13 (32.5)	1	6 (24.0)	.01
	2	19 (47.5)	2	6 (24.0)	
	3	0	3	0	
	4	0	4	0	
Overall maximum grade adverse event	1	0	1	0	.002
	2	20 (50.0)	2	22 (88.0)	
	3	18 (45.0)	3	3 (12.0)	
	4	2 (5.0)	4	0	

Abbreviations: CCRT, concurrent chemoradiotherapy; RT, radiotherapy.