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ORIGINAL ARTICLE

EORTC QLQ-C15-PAL quality of life scores in patients with advanced cancer referred for palliative radiotherapy

Amanda Caissie · Shaelyn Culleton · Janet Nguyen · Liying Zhang · Liang Zeng · Lori Holden · Kristopher Dennis · Esther Chan · Florencia Jon · May Tsao · Cyril Danjoux · Arjun Sahgal · Elizabeth Barnes · Kaitlin Koo · Edward Chow

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Abstract
Purpose Symptom control and improved quality of life (QOL) are primary goals of treatment in palliative oncology. The present study assessed and compared patient demographics, baseline Karnofsky Performance Status (KPS) and QOL using the QLQ-C15-PAL questionnaire prior to palliative radiotherapy (RT) for bone, brain, or lung disease. Few studies have used this questionnaire, an abbreviated version that was developed by the European Organization for Research and Treatment of Cancer specifically for patients with advanced cancer to decrease the burden of completing the longer, more time-consuming QLQ-C30.
Methods Patients referred to an outpatient palliative RT clinic completed QLQ-C15-PAL questionnaires prior to palliative RT for bone, brain, or lung cancer sites. The associations between baseline QLQ-C15-PAL functional/symptom scales, patient demographics, and clinical variables including KPS were explored.
Results When data from all 369 patients were analyzed, higher KPS scores correlated significantly with better overall QOL and higher physical and emotional functioning. The QLQ-C15-PAL provided more detailed information regarding how symptom burden varied depending on disease site. Patients with bone metastases had worse QLQ-C15-PAL scores for pain, while those with brain and lung disease had worse scores for fatigue. Other health-related QOL scores measured by the QLQ-C15-PAL varied as a function of age and gender.
Conclusion As the QLQ-C15-PAL provides detailed and often critical information regarding symptom burden, it may eventually be recognized as a universal core questionnaire to assess QOL in this patient population with advanced cancer while relieving the survey burden.

Keywords QLQ-C15-PAL · Quality of life · Bone metastases · Brain metastases · Lung cancer · Radiotherapy

A. Caissie · S. Culleton · J. Nguyen · L. Zhang · L. Zeng · L. Holden · K. Dennis · E. Chan · F. Jon · M. Tsao · C. Danjoux · A. Sahgal · E. Barnes · K. Koo · E. Chow
Rapid Response Radiotherapy Program, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada

E. Chow (✉)
Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre,
2075 Bayview Avenue,
Toronto, ON, Canada M4N 3M5
e-mail: edward.chow@sunnybrook.ca

Introduction

Symptom control and quality of life (QOL) preservation are important goals in oncology regardless of disease site or stage. Symptom burden may arise from the disease itself and/or systemic or localized treatments patients receive. As cure and other traditional oncologic endpoints, such as prolonged survival, are not possible in most palliative oncology settings, significant treatment-induced side effects are not acceptable. The most important endpoints in the palliative setting are symptom palliation and improvement or maintenance of QOL [1]. Accurate baseline or pre-treatment assessments of health-related QOL are crucially important if these endpoints are to be met.

QOL is a subjective multidimensional construct that takes psychosocial issues into consideration along with the physical symptoms patients experience such as pain [2, 3]. Standardized assessment of QOL is crucial [4] and to address this need in patients with cancer, various QOL

questionnaires have been developed including the now well-established European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire [5, 6]. The QLQ-C30 has been used not only to monitor treatment response [7–10] but also to investigate the relationship between QOL and various other factors such as prognosis [11]. The use of QLQ-C30 has become so widespread that it has even been utilized to identify baseline QOL as a predictor of treatment response in women with advanced breast cancer [12].

The burden on the patient should, however, also be taken into consideration for certain study populations. The length of the QLQ-C30 may be onerous for patients with advanced cancer, as these patients often have a significant symptom burden and poor performance status that makes longer, more rigorous questionnaires difficult to use. Progress has been made in the field of QOL research for these patients with the development of an abbreviated version of the QLQ-C30, known as the QLQ-C15-PAL [13]. This shortened QOL questionnaire aimed to decrease the burden on patients with advanced cancer, while still reliably capturing important aspects of patient's QOL. Yet, despite the availability of this new tool, few studies have used the QLQ-C15-PAL in this patient population [14, 15]. Accordingly, the present study used the QLQ-C15-PAL to assess QOL in patients with advanced cancer prior to palliative radiotherapy (RT) to bone, brain, or lung sites.

Patients and methods

Patients

The Rapid Response Radiotherapy Program (RRRP) is a rapid-access outpatient palliative RT clinic running daily in the Odette Cancer Centre at the Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada. All research was therefore conducted following approval from the Sunnybrook Health Science Centre research ethics board. This study included patients seen in RRRP consultation between October 2007 and July 2010 who were ≥18 years of age, had histologically or cytologically proven malignancy, had radiological evidence of either non-curative primary lung cancer or metastases to the lung, brain, or bone, and were able to provide informed and written consent. Patients who refused palliative RT, were non-English speaking, declined participation, or were cognitively unable to complete the assessment were not accrued.

Patients completed QLQ-C15-PAL questionnaires prior to palliative RT for bone metastases, brain metastases, or advanced lung cancer. The term advanced lung cancer will be used throughout the manuscript referring to patients who were seen in consultation for palliative RT of non-curative primary lung cancer or lung metastases. Baseline patient data collected included age, Karnofsky performance status (KPS), gender, primary cancer site and presence of other metastases, including visceral or bone metastases outside of the RT site. Opioid data was collected for patients with bone metastases and converted to daily oral morphine equivalent dose (OMED). A trained research assistant who attended the daily radiotherapy clinics scored and recorded the patient's KPS at initial consultation.

The reason for referral among patients with bone metastases was classified as either “bone pain” or “others”. Recorded RT-related factors for bone metastases included the number of treatment sites planned (single versus multiple) and the main target site to be treated. For patients with multiple RT sites planned, the most painful area identified by the patient at the time of initial assessment was considered the main target site. The reason for referral among patients with brain metastases was classified as either “post-operative RT”, “single metastasis”, or “multiple metastases”. The reason for referral among patients with advanced lung cancer was classified as either “dyspnea”, “pain”, “hemoptysis”, “coughing” or “others”.

The QLQ-C15-PAL

Prior to RT, QOL was assessed using the QLQ-C15-PAL. This QOL measurement tool consists of 15 questions: 2 multi-item functional scales (physical and emotional functioning), 2 multi-item symptom scales (fatigue and pain) along with 5 single-item symptom scales (nausea/vomiting, dyspnea, insomnia, appetite loss, constipation), and 1 final question referring to overall QOL. Patients rated each question/item on a numeric scale from 1 (not at all) to 4 (very much), with the exception of global QOL which was rated from 1 (very poor) to 7 (excellent). The EORTC QLQ-C30 scoring manual [16] was used to generate the QLQ-C15-PAL scores (0–100) for the unchanged pain scale and the four single items unchanged from the QLQ-C30 (dyspnea, insomnia, appetite loss, constipation). Scores (0–100) for the remaining scales were generated using the QLQ-C15-PAL scoring addendum available from the EORTC Quality of Life Unit [6]. On the scale of 0–100, higher scores for each symptom scale reflect greater symptom burden. However, a higher score is favorable for both functional scales, as well as the final question of the QLQ-C15-PAL, which refers to the patient's perceived global QOL.

Statistical analysis

For continuous demographics, results were expressed as means, standard deviations (SD), inter-quartiles, medians, and ranges, while categorical demographics were expressed

as proportions. Normality tests including skewness, kurtosis, and Shapiro–WilK W test were conducted for each QLQ-C15-PAL scale. Skewness near 0, kurtosis close to 3, and non-significant p values from Shapiro–Wilk W test were considered as normality [17]. Natural log transformation was used to normalize the distribution if non-normal distribution was encountered. General linear regression analysis was used to explore the association between traditional oncologic patient demographics, clinical variables such as KPS and the QLQ-C15-PAL scales at baseline, prior to palliative RT for the above-mentioned cohort (bone, brain, and lung). For each QLQ-C15-PAL scale (the outcome variable), five univariate linear regression models were conducted. The independent demographic factors were age, gender, KPS, other metastases, and primary cancer site. Linear regression analysis was also performed for age/gender with the QLQ-C15-PAL scales after adjusting for KPS and the reason for referral. The above analyses were performed in the three different cohorts. The coefficient, standard error (SE) of the coefficient, p value, and mean square error (MSE) of the model were estimated for each model. A p value<0.05 was considered statistically significant. All analysis was conducted by Statistical Analysis Software (SAS version 9.2 for Windows), and PROC GLM procedure was used for linear regression analysis.

Results

A total of 369 patients with advanced cancer completed the QLQ-C15-PAL questionnaires prior to RT for bone (n=190), brain (n=150), or lung (n=29). Baseline patient characteristics are presented in Table 1. The normality tests for the symptom, functioning, and overall QOL scales on the QLQ-C15-PAL in each patient group revealed that the distribution was far from normal for all QOL scales. Therefore, a natural log transformation was applied to normalize the distribution. The linear regression and p values of each QOL scale with demographic variables following normalization were examined.

For patients receiving RT for bone metastases (n=190), bone pain was the most common reason for referral (n=154, 81%). Pain (item 5) had the highest percentage scoring "very much" in Fig. 1. The majority of patients with bone metastases (75%) had only one site treated. The main target RT sites included thoracic/lumbar spine (35%), leg/hip (28%), pelvis/sacrum (21%), arm/shoulder (8%), chest wall/rib (7%), or others (2%). Fifty-seven patients (30%) were on an OMED of zero, while the median OMED for the remaining patients was 18 mg (range 0.5–880 mg). Of the 190 patients receiving RT to bone metastases, 24 (13%) were inpatients, 136 (72%) were

Table 1 Patient characteristics

RT treatment site	Bone (n=190)	Brain (n=150)	Lung (n=29)
Age (years)			
n	190	150	29
Mean±SD	67±13	63±11	68±12
Inter-quartiles	59–77	56–71	58–78
Median (range)	68 (26–89)	64 (22–86)	70 (38–85)
KPS			
n	184	149	29
Mean±SD	67±14	74±15	67±16
Inter-quartiles	60–80	60–90	60–80
Median (range)	70 (30–100)	80 (30–100)	70 (30–90)
Gender			
Male	116 (61%)	65 (43%)	18 (62%)
Female	74 (39%)	85 (57%)	11 (38%)
Primary cancer site			
Lung	41 (22%)	80 (53%)	24 (83%)
Breast	42 (22%)	30 (20%)	1 (3%)
Prostate	63 (33%)	1 (1%)	0 (0%)
Renal Cell	18 (9%)	9 (6%)	1 (3%)
Colorectal	6 (3%)	9 (6%)	3 (10%)
Unknown	4 (2%)	4 (3%)	0 (0%)
Others	16 (8%)	17 (11%)	0 (0%)
Other metastases			
No	146 (77%)	79 (53%)	9 (31%)
Yes	44 (23%)	71 (47%)	20 (69%)

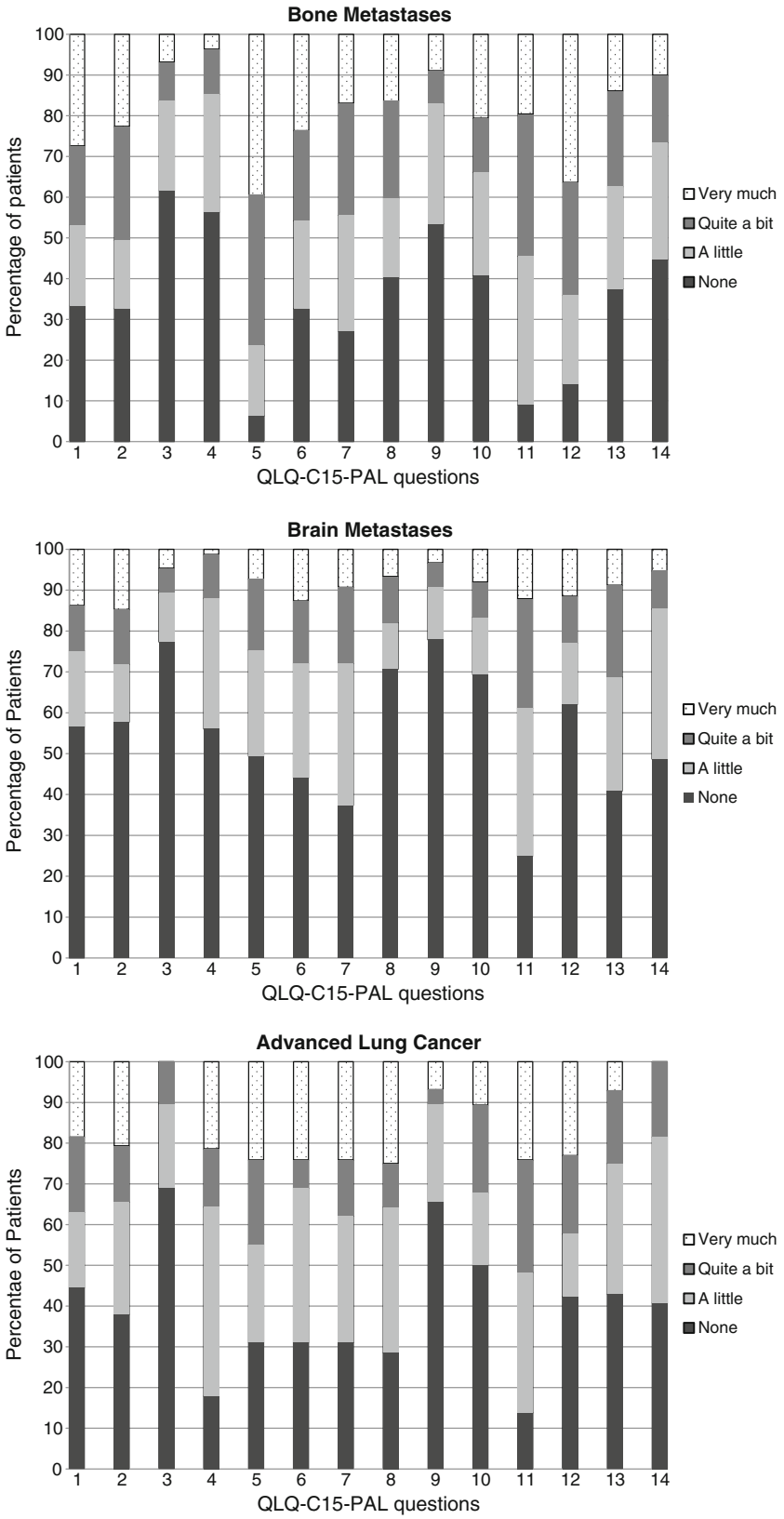

Fig. 1 Baseline patient responses to the QLQ-C15-PAL questions 1 to 14 are presented graphically (on a scale of 1–100) according to disease site and broken down by severity of symptom or functional impairment. QLQ-C15-PAL questions 1 through 14: (1) Do you have any trouble taking a short walk outside the house? (2) Do you need to stay in bed or a chair during the day? (3) Do you need help with eating, dressing, washing yourself, or using the toilet? During the past week: (4) Were you short of breath? (5) Have you had pain? (6) Have you had trouble sleeping? (7) Have you felt weak? (8) Have you lacked appetite? (9) Have you felt nauseated? (10) Have you been constipated? (11) Were you tired? (12) Did pain interfere with your daily activities? (13) Did you feel tense? (14) Did you feel depressed?

outpatients, while the remaining patients have missing data regarding hospital admission status.

Mean baseline QLQ-C15-PAL symptom scoring ranged from 17.90 (nausea/vomiting) to 65.44 (pain), with higher

scores reflecting greater symptom burden. The mean scores for physical functioning, emotional functioning, and overall QOL were 48.17, 66.53, and 48.02, respectively. Higher scores are favorable for these scales (Table 2).

Linear regression showed that a higher KPS was significantly related to the better overall QOL ($p=0.0047$), physical functioning ($p<0.0001$), emotional functioning ($p=0.0056$). A lower KPS indicated greater fatigue ($p=0.0019$), nausea/vomiting ($p=0.0002$), pain ($p=0.0213$), appetite loss ($p<0.0001$), and constipation ($p=0.0049$). Better physical functioning was significantly more likely in those scheduled for RT to a single site or RT sites other than a leg or hip. RT to the chest wall or ribs was associated with higher dyspnea scores. The linear regression model with age after adjusting for KPS and the reason for referral still showed significant relationships with KPS and overall QOL ($p=0.0007$), physical functioning ($p<0.001$), emotional functioning ($p=0.0014$), fatigue ($p=0.0015$), nausea/vomiting ($p<0.0001$), pain ($p=0.0010$), appetite loss ($p<0.0001$), and constipation ($p=0.0032$). Similarly, the model with gender after adjusting for KPS and reason for referral showed the same significant relationships between KPS and all of the scales, except for insomnia and dyspnea.

For patients receiving RT for brain metastases, reasons for referral included multiple metastases ($n=117$, 78%), a solitary metastasis ($n=27$, 18%), or post-operative RT ($n=6$, 4%). The majority of patients received whole brain RT ($n=115$, 77%), while 22% ($n=33$) received stereotactic RT and 1% ($n=2$) received intensity-modulated RT. As seen in Fig. 1, a large percentage of patients scored high on fatigue and shortness of breath. Dexamethasone data was collected for patients with brain metastases, of which only 12 patients were not

Table 2 Descriptive QLQ-C15-PAL functioning/symptom scales and overall QOL scale in patients treated with RT to the bone, brain, or lung

	N	Mean	Std	Median	Q1	Q3	Min	Max
Bone metastases								
Overall QOL	185	48.02	26.62	50.00	33.33	66.67	0.00	100.00
Physical functioning	186	48.17	29.70	46.67	26.67	73.33	0.00	93.33
Emotional functioning	187	66.53	30.91	66.67	50.00	100.00	0.00	100.00
Fatigue	189	51.68	28.71	55.56	33.33	66.67	0.00	100.00
Nausea/vomiting	189	17.90	29.40	0.00	0.00	16.67	0.00	100.00
Pain	190	65.44	30.11	66.67	50.00	83.33	0.00	100.00
Dyspnea	190	20.70	27.51	0.00	0.00	33.33	0.00	100.00
Insomnia	190	45.61	38.96	33.33	0.00	66.67	0.00	100.00
Appetite loss	189	38.80	37.66	33.33	0.00	66.67	0.00	100.00
Constipation	189	37.92	38.78	33.33	0.00	66.67	0.00	100.00
Brain metastases								
Overall QOL	149	61.19	28.24	66.67	50.00	83.33	0.00	100.00
Physical functioning	145	65.61	29.20	73.33	46.67	93.33	0.00	93.33
Emotional functioning	147	72.22	24.62	66.67	50.00	100.00	0.00	100.00
Fatigue	149	39.30	27.75	33.33	22.22	66.67	0.00	100.00
Nausea/vomiting	149	8.50	21.28	0.00	0.00	0.00	0.00	100.00
Pain	150	23.22	30.09	16.67	0.00	33.33	0.00	100.00
Dyspnea	150	19.11	24.53	0.00	0.00	33.33	0.00	100.00
Insomnia	150	32.22	35.06	33.33	0.00	66.67	0.00	100.00
Appetite loss	150	18.00	31.29	0.00	0.00	33.33	0.00	100.00
Constipation	150	18.44	31.74	0.00	0.00	33.33	0.00	100.00
Lung cancer/metastases								
Overall QOL	28	47.62	31.33	50.00	25.00	75.00	0.00	100.00
Physical functioning	27	57.28	31.06	60.00	26.67	93.33	6.67	93.33
Emotional functioning	27	72.53	23.89	66.67	50.00	100.00	16.67	100.00
Fatigue	29	50.57	32.61	44.44	22.22	66.67	0.00	100.00
Nausea/vomiting	29	12.64	26.60	0.00	0.00	16.67	0.00	100.00
Pain	29	41.38	35.53	33.33	16.67	83.33	0.00	100.00
Dyspnea	28	46.43	34.35	33.33	33.33	66.67	0.00	100.00
Insomnia	29	41.38	38.48	33.33	0.00	66.67	0.00	100.00
Appetite loss	28	44.05	38.55	33.33	0.00	83.33	0.00	100.00
Constipation	28	30.95	36.21	16.67	0.00	66.67	0.00	100.00

prescribed dexamethasone prior to RT (10%). The remaining patients were on a median dexamethasone dose of 16 mg/day (range 0.5–16 mg/day) prior to RT. Nineteen patients (13%) were inpatients and 89 (59%) were outpatients, while patient status was missing for the remaining 28%. Mean baseline QLQ-C15-PAL symptom scoring ranged from 8.5 (nausea/vomiting) to 39.30 (fatigue). The mean scores for physical functioning, emotional functioning, and overall QOL were 65.61, 72.22, and 61.19, respectively (Table 2).

Linear regression showed that KPS was significantly related to the overall QOL variable ($p=0.0047$) and the physical functioning ($p=0.0189$), fatigue ($p<0.0001$), nausea/vomiting ($p=0.0078$), and pain ($p=0.0046$) scales. The linear regression model with age after adjusting for KPS and the reason for referral again showed significant relationships with KPS and overall QOL ($p=0.0033$), physical functioning ($p<0.0001$), fatigue ($p<0.0001$), nausea/vomiting ($p=0.0005$), and pain ($p=0.0020$). When the model with gender was adjusted for by KPS and reason for referral, KPS was again significantly related to the above five scales.

For patients receiving RT for advanced lung cancer, the most common reasons for referral included dyspnea and pain in 52% ($n=15$) and 28% ($n=8$) of patients, respectively. Figure 1 confirms that a fairly high percentage of patients referred for RT to the lung scored shortness of breath (item 4), tiredness (item 11), and pain (item 5) as a problem. Out of 29 patients, only 2 (7%) were inpatients. Mean baseline QLQ-C15-PAL symptom scoring ranged from 12.64 (nausea/vomiting) to 50.57 (fatigue). The mean scores for physical functioning, emotional functioning, and overall QOL were 57.28, 72.53, and 47.62, respectively (Table 2).

Linear regression showed that KPS was significantly related to the overall QOL variable ($p=0.0018$), all functional scales (physical functioning $p<0.0001$, emotional functioning, $p=0.0151$), and one symptom scale (appetite loss $p=0.0088$). The linear regression model with age after adjusting for KPS and the reason for referral showed significant relationships with KPS and overall QOL ($p=0.0024$), physical functioning ($p=0.0002$), emotional functioning ($p=0.0143$), and appetite loss ($p=0.0157$). When the model with gender was adjusted for by KPS and reason for referral, KPS was again significantly related to the above four scales.

Discussion

While the QLQ-C15-PAL has been discussed in editorials [18, 19] and papers discussing its planned use in upcoming studies [20–22], only two other studies to date have assessed QOL using the QLQ-C15-PAL [14, 15]. Of those two studies, only one had used the QLQ-C15-PAL prior to RT [14]. In their pilot study of patients with brain metastases, Steinmann et al. found better compliance and practicality with the abbreviated QLQ-C15-PAL as compared to the QLQ-C30, and the group reported use of the QLQ-C15-PAL in their currently ongoing, larger scale study. Moreover, in the pilot study, the QLQ-C15-PAL identified prominent fatigue and insomnia but very little nausea pre-RT [14]. In the present study, similar results regarding the above three symptoms were seen in our subpopulation of patients with brain metastases.

A recent study has investigated both age and gender differences in terms of symptom intensity and symptom clustering in patients with advanced cancer [23]. However, the study did not distinguish between patients receiving palliative treatments affecting different anatomic sites. This is common to many QOL studies in patients with advanced cancer where patients undergoing the same treatment are grouped together, when in fact their symptoms, functioning, and overall QOL are likely to differ based on the site that requires treatment. The present study did distinguish between patients with advanced cancer based on RT treatment site, as there were different QOL profiles as shown in Fig. 1. While pain was the most severe symptom in patients prior to RT of bone, fatigue was the highest scored symptom scale for those patients requiring RT to brain or lung. Shortness of breath was also scored very high in patients referred for RT to the lung. While it is intuitive that patients referred for RT to advanced lung cancer would have high scores of dyspnea and those referred for bone metastases would have high scores of pain, the results of the present study show that QLQ-C15-PAL scores are fairly accurate in reflecting the patients' most distressing symptoms due to bone, brain, or lung disease.

There was a significant association of KPS with physical functioning, emotional functioning, and overall QOL in patients prior to RT of bone, brain, or lung. Other results of this study were not surprising, such as the finding of better physical functioning in patients scheduled for RT to a single bone metastasis site or RT sites other than a leg or hip. KPS was not, however, associated with all symptom scales of the QLQ-15-PAL and as noted above, the symptom profile was not the same for all patient groups.

The study is not without limitations. It is difficult to determine the etiology of patients' reported symptoms, as it could be from disease, treatment(s), or both. Symptoms from the disease may be mediated by medications such as opioids, steroids, or anti-cancer treatments such as chemotherapy. A period of several weeks is, however, often required between interventions such as surgery or chemotherapy and palliative RT, suggesting many of the QLQ-C15-PAL scores may be related to the disease itself.

Another limitation to this study is that the patients have been grouped according to RT site, although many of the patients have multiple sites of disease or metastases that

may contribute to their QLQ-C15-PAL profile. This is reflected in the fact that the majority of referrals to the RRRP are to treat bone and brain metastases, even in patients with primary lung cancer. In this study, there were, therefore, a very low number of patients treated with RT to the lung when compared to those receiving treatment to the bone or brain. Reducing the numbers down further, not all patients who require RT consented to participate, particularly if they are very ill. The baseline QOL in these patients may then not be representative of the entire population of patients receiving palliative RT.

The QLQ-C15-PAL was originally validated in patients with advanced cancer under palliative care services, showing feasibility of use in a population of poor prognosis [13]. Patients seen in the RRRP have a very limited survival. They include inpatients and outpatients, and while some of these inpatients may actually be under palliative care facilities, these patients can still be referred for palliative radiotherapy. As the shortened palliative general QOL questionnaire QLQ-C15-PAL is available, it was considered appropriate for the QOL assessment in this palliative patient population to reduce the survey burden as much as possible while maximizing patient participation. This is also in accordance with the findings by Steinmann et al. [14].

The QLQ-C15-PAL may be useful in the context of clinical research to assess the effectiveness of interventions in palliative cancer patients. As the current study only reports the QOL scores prior to palliative RT, further studies are ongoing to assess how patients' symptoms, functioning and QOL change over time following palliative RT. The use of the QLQ-C15-PAL may also increase the chance of maintaining follow-up, not only to assess treatment response but also to monitor for treatment side effects or disease progression, and thereby identify patients in need of additional support. The present study does show feasibility and logical clinical correlations (i.e., KPS and physical functioning); therefore, although the aims of this study were not to validate the QLQ-C15-PAL, this does support the external validity of the tool.

The present study is only the second report describing assessments of QOL with the QLQ-C15-PAL in patients with advanced cancer prior to RT. The present study highlighted the various symptom profiles and baseline QOL scores in patients initially referred for palliative RT to various sites. Such QOL assessments are of use in the context of clinical practice, as an aid for patient assessment which may then guide both the physician and the patient in making treatment decisions. The abbreviated QLQ-C15-PAL is useful and may allow for better accrual among patients with advanced cancer as compared to lengthier questionnaires. It is hoped that the QLQ-C15-PAL will eventually be recognized as a universal core questionnaire used to assess QOL in this patient population while relieving the survey burden.

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Conflict of interest statement None.

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