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ORIGINAL ARTICLE

Fatigue scores in patients with brain metastases receiving whole brain radiotherapy

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Abstract
Purpose Whole brain radiotherapy (WBRT) is a treatment strategy used commonly to relieve burdensome symptoms and improve quality of life (QOL) in patients with multiple brain metastases. The purpose of this study is to determine changes in fatigue score following WBRT as it is a common symptom experienced in this population.
Methods Fatigue and overall QOL scores were collected prospectively in patients for up to 3 months post-WBRT by several questionnaires at different times including the following: Edmonton Symptom Assessment System (ESAS), Brain Symptom and Impact Questionnaire (BASIQ), Spitzer Questionnaire, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), EORTC brain module (EORTC QLQ-BN20+2), EORTC QLQ-C15-PAL, and Functional Assessment of Cancer Therapy—General (FACT-G). Questionnaires were grouped for analysis by Wilcoxon Signed Rank test according to the scale of ranking into 0–10, 1–4, and 0–4.
Results Thirty-six patients were interviewed with the ESAS or BASIQ. The median age was 65 years old, and median Karnofsky Performance Status (KPS) was 70. There was a significant increase in fatigue score from baseline to month 1 ($p=0.02$), and months 2 and 3 had no significant change. There was a significant correlation between fatigue and overall QOL score at baseline and month 1 ($p=0.01$, $p<0.0001$), respectively. Two hundred and twenty-eight patients were surveyed with Spitzer, C15-PAL, BN20+2, QLQ-C30, or FACT-G. Median age was 64 years old and median KPS was 80. Compared to baseline, fatigue score was significantly higher at month 1 ($p<0.0001$) and month 2 ($p=0.001$), with no significant change at month 3. Significant correlation was found between fatigue and overall QOL at baseline, months 1, 2 ($p<0.0001$), and 3 ($p=0.0009$). For all groups, there was no significant change in fatigue score between patients with or without dexamethasone (Dx), except for the fatigue changed score of the group with scale 0–4.
Conclusions Fatigue was significantly increased from baseline to month 1 in all patients, and most patients experienced no difference in fatigue if they were receiving Dx. Increased fatigue was significantly related with decreased overall QOL.

Keywords Whole brain radiotherapy · Fatigue · Quality of life · Brain metastases

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Introduction

Brain metastases are a source of significant morbidity, which develop in approximately 20–40 % of cancer patients. Brain metastases most frequently develop from lung and breast cancers [1]. Prevalence is increasing as cancer patients live longer due to more effective systemic treatments, as well as improved screening and detection [2, 3]. Symptoms resulting from brain metastases may include headaches, focal weakness, seizures, and ataxia [1, 2]. It is estimated that 65 % of brain metastases patients may experience some cognitive impairment. The primary purpose of treatment is to improve quality of life (QOL) by relieving burdensome symptoms, without solely focusing on survival [3]. Without any treatment, the average survival for this patient group is guarded at 1 month. Past studies regarding this patient population have emphasized the importance of treatment strategies to balance improvement in QOL with the relative burden of treatment

[1]. Symptom outcomes are also imperative in maintaining QOL and performance status as several symptoms are predictive of overall well-being [4–7].

Whole brain radiotherapy (WBRT) in combination with corticosteroids is one of the most common treatments in patients with multiple brain metastases [8, 9]. Select patients with better prognosis, solitary brain metastasis, good performance status, and limited extracranial disease may be eligible for more aggressive strategies such as stereotactic radiosurgery (SRS), or surgical resection followed by radiation [8].

Fatigue is a common patient-rated symptom that is experienced in brain metastases patients. Past patient-rated symptom questionnaires have determined that fatigue may be a symptom that deteriorates after WBRT. Other treatment strategies such as conservative treatment with corticosteroids alone to reduce cerebral edema, or more aggressive SRS may result in less residual symptoms and morbidity [8]. There are several questionnaires used to assess overall QOL that include items assessing patient-rated fatigue. Past studies completed in the Rapid Response Radiotherapy Program (RRRP) have administered a variety of QOL questionnaires to brain metastases patients. Therefore, we have analyzed these questionnaires by extracting the fatigue and overall QOL scores at baseline and monthly follow-ups extending up to 3 months post-WBRT.

Methods

This retrospective study incorporated prospective data from previous studies conducted in the RRRP from 2005 to 2012. Studies included in the analysis must have collected data in brain metastases patients at baseline and at least one follow-up time point of 1 month after receiving WBRT. Follow-up time points collected ranged from 1 month up to 3 months following treatment. Select studies included data for alternative treatments, such as SRS or post-operative WBRT. For the purpose of this study, only patients who received WBRT alone were included in the analysis. Baseline demographic information collected included age, Karnofsky Performance Status (KPS), gender, primary cancer, number of brain metastases, systemic treatment, and if receiving dexamethasone. Primary objective was to determine changes in fatigue after 1 month post-treatment. Secondary objectives included effects of dexamethasone on fatigue and fatigue changes at 2 and 3 months.

Questionnaires

Fatigue scores were obtained through the following seven QOL and symptom questionnaires. The Edmonton Symptom Assessment System (ESAS) was among the questionnaires employed and is a validated nine-item symptom questionnaire [6]. Fatigue is among one of the nine symptoms assessed, scored on a scale of 0=not tired to 10=worst possible tiredness. The Brain Symptom and Impact Questionnaire (BASIQ) is an assessment which has recently undergone testing of validity in our center. It is a brief 18-item questionnaire designed specifically for the brain metastases population. Patients were asked to rank how tired they felt on a scale of 0=not at all to 10=extremely. Spitzer Quality of Life Index, composed of five domains, assessed fatigue (defined as tiredness or lack of energy), from none, mild, moderate, to severe [5]. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Core 15 Palliative (EORTC QLQ-C15-PAL) is a 15-item shortened questionnaire, with the fatigue item scored 1=not at all, 2=a little bit, 3=quite a bit, and 4=very much. The C15-PAL has been used in conjunction with the 22 item European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Brain Neoplasm (EORTC QLQ-BN20+2) [3]. Fatigue was measured by the BN20+2 regarding the amount of weakness in the legs. The EORTC Core 30 (EORTC QLQ-C30) questionnaire appropriately measures fatigue as how "tired" the patient felt on the same scale as the C15-PAL, 1=not at all, 2=a little bit, 3=quite a bit, and 4=very much [7]. The Functional Assessment of Cancer Therapy—General (FACT-G) scale assesses cancer in five domains and, specifically, fatigue as a lack of energy over the past 7 days and 24 h using the scale 0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much [1].

All patients received WBRT, with the same radiation dose and technique, as treatment for brain metastases. Various, but not all, patients were given differing dexamethasone prescriptions and tapering dosages. Questionnaires were grouped for analysis depending on their respective scoring scales. Group 1 had a scale of 0–10 and encompassed the ESAS and BASIQ data. Group 2, scale 1–4, includes the Spitzer, C15-PAL, BN20+2, QLQ-C30, and FACT-G. FACT-G data for this group was derived from a scoring of 0–4 by combining a score of 2 (somewhat), and 3 (quite a bit). Group 3 included all of the questionnaires from Group 2, but analyzed the FACT-G as original scoring of 0–4.

Statistical analysis

In each group, fatigue scales 0–10, 1–4, and 0–4 were separately analyzed. Wilcoxon Signed Rank test was conducted for all groups to detect for significant fatigue changes from baseline to each follow-up time point. To determine if there were significant fatigue changes for patients with and without dexamethasone, the Wilcoxon Rank-sum test was employed at month 1 only. The relationship between fatigue score and overall QOL score was examined using Spearman correlation coefficient r and general linear regression analysis. Natural log-transformation was applied for fatigue and overall QOL scores to normalize the distribution. Fatigue score changes over time were tested for association with time-dependent

overall QOL, using the general linear mixed model (GLMM). The outcome of GLMM was fatigue (log scale), and the fixed effects were time (0 to 3 denotes for baseline to month 3) and time-dependent variable of overall QOL (time×QOL). Subjects were considered as the random effect. The relationship between fatigue score and baseline KPS was also examined using the above methods. Group 2 (1–4 scale) and Group 3 (0–4 scale) were analyzed for categorical fatigue score changes using McNemar's test applied to four categories as the scale ranges from 1 to 4. To detect for differences in Groups 2 and 3 of the proportions of those with or without dexamethasone that had decreased, increased or no change in fatigue score, Fisher exact test was conducted. All analyses were conducted using Statistical Analysis Software (SAS version 9.3), and p value<0.05 was considered as statistically significant.

Results

Group 1 (scale 0–10) had a total of 36 patients with one follow-up, the median age of 65 years old, 61 % were females, and median KPS was 70 (range 40–90) (Table 1). The most common primary cancer site was the lung 67 % (n=24) and breast 19 % (n=7). Number of brain metastases ranged from 1 (n=3), 2–3 (n=4), to >3 (n=6). The remainder of the patients (n=23) had an unknown number of brain metastases as this was not assessed in their respective studies. Fourteen patients had information if they were on dexamethasone, 11 patients were not on dexamethasone at baseline, and three were on dexamethasone at baseline and month 1. Sample sizes were small for complete data at month 2 and month 3 as the study involving the BASIQ only collected data for a 1 month follow-up. Completion rates at 1 month, 2 months, and 3 months were 92 %, 29 %, and 20 % respectively. A higher score from 0 to 10 of fatigue is indicative of worsened fatigue, and an increase of score for QOL on a scale of 0–10 indicates an improvement in QOL. The Wilcoxon Signed Rank test determined that there was a significant fatigue score increase from baseline median fatigue score of 5.0 to a score of 7.0 at 1 month (p=0.02) (Table 2). The other 2 months had no significant change, likely due to small sample sizes. A high attrition rate also likely contributed to the small sample size; therefore it is also probable these patients experienced increased fatigue as they deteriorated. Fatigue scores were also compared between patients receiving dexamethasone and those without, and the Wilcoxon Rank-sum test determined no significant fatigue score change from baseline to 1 month (p=0.05). All patients with fatigue score data had a corresponding overall QOL score at each follow-up. Significant correlation was detected at baseline (r=−0.42; p=0.01) and month 1 (r=−0.69; p<0.0001) between fatigue and overall QOL scores. Therefore, negative r determined that patients with higher fatigue scores have lower overall QOL. Linear regression analysis also detected a significant association between fatigue and overall QOL score at baseline (p=0.03) and month 1 (p=0.001). Overall QOL score decreased from a median score of 6.0 at baseline to 5.0 at month 1, on a scale of 0–10 (Table 2). As determined by the general linear mixed model, fatigue scores significantly increased over time from baseline to month 3 (p=0.006). Table 2 illustrates the increasing time trends on fatigue and associated QOL score from baseline to month 3, such as median fatigue score increases from 5 at baseline to 7 at month 1, 6 at month 2, and 9 at month 3; median overall QOL increases from 6 at baseline to 7 at months 2 and 3.

Group 2 (scale 1–4) had 228 patients with at least one follow-up. Demographic information included median age 64 years old, 66 % were male, and median KPS was 80 (range 30–100) (Table 3). Lung 56 % (n=128) and breast 23 % (n=53) were again the most common primary cancer types.

Table 1 Group 1 demographics

Age (years)	
n	36
Mean±SD	64.1±11.3
Inter-quartiles	55–73
Median (range)	65 (39–84)
KPS	
n	35
Mean±SD	70.3±12.2
Inter-quartiles	60–80
Median (range)	70 (40–90)
Gender	
Male	14 (38.89 %)
Female	22 (61.11 %)
Primary cancer site	
Lung	24 (66.67 %)
Breast	7 (19.44 %)
Gastrointestinal	1 (2.78 %)
Others	2 (5.56 %)
Unknown	2 (5.56 %)
Number of brain metastases	
1	3 (23.08 %)
2–3	4 (30.77 %)
>3	6 (46.15 %)
With dexamethasone (DEX) treatment	
No	11 (78.57 %)
Yes	3 (21.43 %)
DEX dose only in those with treatment (mg)	
n	3
Mean±SD	10.7±6.1
Inter-quartiles	4–16
Median (range)	12 (4–16)

Table 2 Group 1 fatigue and overall QOL

In all patients		Visit			
		Baseline	Month 1	Month 2	Month 3
Fatigue (0–10)	N	35	33	10	7
	Mean	4.71	5.91	5.30	8.14
	Std	2.83	3.12	3.53	1.95
	Median	5.0	7.0	6.0	9.0
	Min	0.0	0.0	0.0	4.0
	Max	9.0	10.0	10.0	10.0
Overall QOL (0–10)	N	35	33	10	7
	Mean	6.11	5.33	6.90	6.00
	Std	2.47	3.28	2.96	3.27
	Median	6.0	5.0	7.0	7.0
	Min	1.0	0.0	2.0	1.0
	Max	10.0	10.0	10.0	9.0

Number of brain metastases were 1 (n=9), 2–3 (n=14), >3 (n=8), and the remainder (n=197) had an unknown number of metastases or this data was not collected for the study. There were 157 patients with dexamethasone information at baseline, 128 and 46 of which were on dexamethasone at baseline and month 3, respectively. As in the 0–10 scale, a higher score on the fatigue item is indicative of a worsened symptom and an increased score on the QOL question indicates a better overall QOL. Wilcoxon Signed Rank test detected significant fatigue score increases from a median score of 2.0 at baseline compared to a score of 3.0 at months 1 (p<0.0001) and 2 (p=0.001) (Table 4). As in Group 1, there were no significant fatigue score changes when comparing patients with and without dexamethasone. Spearman correlation and linear regression analysis detected a significant negative correlation between fatigue and overall QOL at baseline and months 1 (p<0.0001), 2 (p<0.0001), and 3 (p=0.0009), which implies that QOL decreases (decreased score) as fatigue worsens (increased score). Fatigue scores were highly significantly increasing over time from baseline to month 3 (p<0.0001).

Group 3, scale of 0–4, encompasses the same set of patients as Group 2 (Table 3). Table 5 illustrates the fatigue and overall QOL scores for this patient group from baseline to month 3. Similar to the results from other questionnaires, fatigue score significantly increased at month 1 (p<0.0001) and month 2 (p=0.001) from baseline. Numerical fatigue scores were as follows, baseline median score of 2.0, compared to a score of 3.0 at both months 1 and 2. Again, no significant difference on fatigue changed score between patients with and without dexamethasone was detected. However, there was a significant difference on fatigue changing categories between patients with or without dexamethasone at month 1 (p=0.01). Therefore, patients with fatigue scores that did not increase or decrease from baseline to month 1 were more likely to be receiving dexamethasone.

Analysis was performed to detect for a relationship between baseline KPS and fatigue. Group 1 (0–10) had no significant relationship between fatigue and baseline KPS at each visit. All groups had no significant correlation between fatigue changed score and baseline KPS at any visit. In Group 2 (1–4) and Group 3 (0–4), Spearman correlation detected a significant negative correlation between baseline KPS and fatigue scores at baseline (p<0.0001), month 1 (p<0.0001), and month 2 (p=0.046). The negative correlation indicates that patients with high fatigue score (more severe fatigue) have low baseline KPS values. At baseline (p<0.0001) and month 1 (p<0.0001), there was a highly significant association between fatigue and baseline KPS using linear regression analysis. The general linear mixed model indicated that patients with severe fatigue symptoms (higher score) are more likely to have lower baseline KPS over time (p<0.0001). In all groups, there was no significant correlation between fatigue changed scores and baseline KPS at any follow-up visit.

Discussion

There was a significant relationship determined between baseline and increased fatigue following WBRT. The primary endpoint of WBRT is to improve QOL by providing symptom relief [8], yet there is emerging evidence that WBRT causes decreased symptom control of fatigue and is directly related to a decrease of QOL. Kondziolka et al. [10] conducted a prospective study which assessed symptoms in 200 patients that received gamma knife radiosurgery. A 10-item brain metastasis patient survey was sent to all patients, and 104 patients completed the questionnaire. There were 72 (69 %) respondents who also received WBRT following radiosurgery. Excess fatigue was a major side effect reported by 85 % of the patients who received WBRT [10]. Because the performance

Table 3 Group 2 demographics

Age (years)	
n	228
Mean±SD	63.6±10.9
Inter-quartiles	57–71
Median (range)	64 (22–88)
KPS	
n	227
Mean±SD	74.0±15.6
Inter-quartiles	60–90
Median (range)	80 (30–100)
Gender	
Male	151 (66.23 %)
Female	77 (33.77 %)
Primary cancer site	
Lung	128 (56.14 %)
Breast	53 (23.25 %)
Kidney/renal cell	14 (6.14 %)
Colon	8 (3.51 %)
Gastrointestinal	2 (0.88 %)
Melanoma	1 (0.44 %)
Others	16 (7.02 %)
Unknown	6 (2.63 %)
Number of brain metastases	
1	9 (29.03 %)
2–3	14 (45.16 %)
>3	8 (25.81 %)
Previous systemic treatment	
No	102 (82.26 %)
Yes	22 (17.74 %)
With dexamethasone (DEX) treatment	
No	29 (18.47 %)
Yes	128 (81.53 %)
DEX dose only in those with treatment	
n	128
Mean±SD	12.4±5.2
Inter-quartiles	8–16
Median (range)	16 (0.5–24)

status of our study population is generally poor as the RRRP treats only palliative cancer patients, increasing burden of disease may result in more severe fatigue regardless of treatment received. However, in the study by Kondziolka et al., KPS was >90 in 90 % of the patients and fatigue was still reported as a severe side effect. As both studies reported an increased fatigue score regardless of patient population, it is likely that a component of the excess fatigue can be contributed to an effect of WBRT. Our group [8] conducted a prospective study in the RRRP administering the ESAS before WBRT and at 1, 2, 4, 8, and 12 weeks post-treatment. After receiving radiation, there was a statistically significant deterioration in the mean difference of fatigue from baseline. Wong et al. [9] also reported fatigue being among the most commonly experienced symptoms, as determined by the Spitzer Questionnaire, following WBRT.

Table 4 Group 2 fatigue and overall QOL scores

In all patients		Visit			
		Baseline	Month 1	Month 2	Month 3
Fatigue (1–4)	N	225	217	89	55
	Mean	2.06	2.59	2.58	2.55
	Std	0.99	1.05	0.94	0.88
	Median	2.0	3.0	3.0	3.0
	Q1	1.0	2.0	2.0	2.0
	Q3	3.0	3.0	3.0	3.0
	Min	1.0	1.0	1.0	1.0
	Max	4.0	4.0	4.0	4.0
Overall QOL (1–7)	N	180	172	87	55
	Mean	4.64	3.95	4.09	3.82
	Std	1.81	1.92	2.03	2.20
	Median	4.0	4.0	4.0	4.0
	Q1	4.0	3.0	3.0	1.0
	Q3	6.5	5.0	6.0	5.0
	Min	1.0	1.0	1.0	1.0
	Max	7.0	7.0	7.0	7.0

In all patient groups of this study, fatigue was significantly correlated with the overall QOL score at baseline and at least one follow-up. In the study conducted by Caissie et al. [3], there was a negative correlation at baseline between KPS and

Table 5 Group 3 fatigue and overall QOL scores

In all patients		Visit			
		Baseline	Month 1	Month 2	Month 3
Fatigue (0–4)	N	225	217	89	55
	Mean	2.02	2.58	2.58	2.55
	Std	1.01	1.05	0.94	0.88
	Median	2.0	3.0	3.0	3.0
	Q1	1.0	2.0	2.0	2.0
	Q3	3.0	3.0	3.0	3.0
	Min	0.0	1.0	1.0	1.0
	Max	4.0	4.0	4.0	4.0
Overall QOL (1–7)	N	180	172	87	55
	Mean	4.64	3.95	4.09	3.82
	Std	1.81	1.92	2.03	2.20
	Median	4.0	4.0	4.0	4.0
	Q1	4.0	3.0	3.0	1.0
	Q3	6.5	5.0	6.0	5.0
	Min	1.0	1.0	1.0	1.0
	Max	7.0	7.0	7.0	7.0

the C15-PAL fatigue scale in the 108 patients receiving WBRT. These results show that fatigue is an important symptom for advanced cancer patients with brain metastases as it affects overall QOL and, therefore, performance status, two primary endpoints of treatment for brain metastases. As increased fatigue is correlated with decreased QOL and KPS, other symptom outcomes and benefits must be examined to determine the effectiveness of WBRT. Lien et al. [11] conducted an analysis of 1439 ESAS assessments and fatigue was found to be a significant predictor for worse well-being in palliative cancer patients. Not only in brain metastases patients, but also in the general cancer population increased fatigue is related to lower QOL [7, 11]. It is important to note that overall QOL was one point higher at months 2 and 3 (7.0) compared to baseline (6.0) for the 0–10 scale group. This is possibly due to the control of other physical symptoms directly related to the brain metastases that improved following treatment. As these physical symptoms are debilitating and concerning for the patient, it may not be overly surprising that the QOL score slightly increased following treatment. In Groups 1 and 2, there was a significant relationship detected between baseline KPS and fatigue scores. Severe fatigue scores were highly correlated with lower baseline KPS. However, as patients were not required to return to clinic for assessment, KPS at each follow-up visit was unknown and we can only conclude that poorer performance status at baseline is significantly associated with worse feelings of fatigue.

In all groups analyzed, there was no significant association between fatigue scores and patients receiving dexamethasone, except for Group 3 in fatigue changing categories. This conclusion may not be applicable to the entire study population, as many studies used in the analysis did not collect any data regarding dexamethasone dose or treatment. It is also important to note that in Group 1, fatigue changed score from baseline to month 1 between patients with or without dexamethasone was approaching significance (p=0.0501), however this group had a very small sample size of patients with dexamethasone information (n=14). Of the 128 patients on dexamethasone at baseline in Group 2, 119 still remained on steroid after 1 month though there was no significance detected in this group. Similar distributions were determined in Group 3, as 118 of the 127 patients from baseline on dexamethasone were still taking it after 1 month. As both relationships in Groups 1 and 3 regarding dexamethasone use were detected even after 1 month from baseline, it is important to consider the role of dexamethasone toxicity due to the long term steroid use. The Dexamethasone Symptom Questionnaire (DSQ) developed by Vardy et al. [12], was used in brain metastases patients receiving WBRT by Nguyen et al. [13] to examine the side effects related to extended dexamethasone use. Related side effects include gastritis, myopathy, peripheral edema, insomnia, or depression, some of which may contribute to worsened fatigue independent of treatment effects. Nguyen et al. found that patients on a higher dose of dexamethasone 2 weeks post-WBRT scored higher on the item assessing fatigue severity (p=0.0414). Review of the literature by Nguyen et al. reported that increased toxicity and less symptom relief were associated with patients who were not tapered off of dexamethasone after treatment and used dexamethasone for a long duration [13]. Potential steroid toxicity could contribute to the lack of significance of fatigue differences, especially at longer follow-up periods.

As WBRT likely results in increased fatigue, other treatment options may be more applicable for patients to minimize burden and maximize benefits. In the study by Kondziolka et al. [10], fatigue was only prevalent in 28 % of patients who received gamma knife radiosurgery alone, compared to 85 % of patients with the addition of WBRT. Bezjak et al. [14] also determined that conservative treatment with corticosteroids for poor prognosis patients may be equal in effectiveness to WBRT, but without debilitating side effects and symptom burden. Tsao et al. [15] conducted a meta-analysis comparing WBRT alone versus WBRT plus SRS boost. The primary endpoint was to compare overall survival, local control, and distal brain control; however, the authors also commented on the comparison of relative side effects and changes in performance status. The recommendation was to suggest use of SRS alone as it has a lower risk of delayed side effects due to more targeted treatment and typically does not negatively alter performance status [15]. Emerging treatment options such as SRS, when investigating endpoints related to QOL especially, offer an alternate treatment strategy which may spare burden by sparing side effects and increased fatigue.

A limitation of this retrospective study was the lack of information regarding other treatments such as surgery, chemotherapy, hormone therapy, and additional radiation, which may impact feelings of fatigue. In the future, it may be useful to examine the effects of other treatments closely to more definitively determine the cause of more fatigue. Further investigations may be strengthened with use of the same definition of fatigue through the use of one questionnaire only. Our study required the use of several different fatigue items and, therefore, resulted in more variable interpretations of the assessment of fatigue. Another limitation is in the consideration of clinical versus statistical significance. Even though there were statistically significant fatigue increases, this is difficult to clinically correlate, as well as separate from normal disease progression and burden resulting in patients feeling generally unwell. This also contributes to the difficulty in assessing changes in overall QOL. The patients who continued on the study were likely those with better performance status, less disease burden, and, therefore, better QOL. It is reasonable to conclude this as a contributing factor too, despite the initial decrease in QOL for Group 1, QOL stayed generally stable. Unfortunately, the effects of dexamethasone on fatigue were mainly inconclusive to the general study population as

specific doses were unknown. Future studies may benefit from more closely examining the relationship between steroid use and fatigue in brain metastases patients.

As determined by this retrospective analysis, fatigue is worsened in most patients after WBRT and shares a negative correlation with overall QOL. The questionnaires used to assess fatigue and QOL score were from previous studies and may be more appropriately assessed in future prospective trials with more optimal data collection and information recorded such as concurrent systemic or corticosteroid treatment. As fatigue causing symptom burden significantly increased following WBRT, further studies should focus on differentiating between fatigue increases from radiation treatment rather than normal progression of disease, steroid toxicity, or due to a synergistic effect of both treatment and increasing burden of disease.

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Conflict of interest None.

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