

## Longitudinal study of quality of life in patients with localized prostate cancer undergoing radiotherapy

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**Abstract**—This study prospectively evaluated quality of life (QOL) in localized prostate cancer patients undergoing radiotherapy, and it examined the relationships between QOL, depression, fatigue, and sleep disturbance. Instruments that were used are Functional Assessment of Cancer Therapy for Prostate (FACT-P), Beck Depression Inventory (BDI), Piper Fatigue Scale (PFS), and Epworth Sleepiness Scale (ESS). We evaluated patients at preradiotherapy (PRT), midway radiotherapy (MRT), completion of radiotherapy (CRT), follow-up radiotherapy (4 to 8 wk) (FRT), and long-term follow-up radiotherapy (FRT2) (12 mo or more). Forty participants with a mean age of 67.8 yr were studied. Duration of radiotherapy was 7–8 wk. Mean long-term follow-up period post-CRT was 16.2 mo (range 12–24 mo). All patients had clinical T1c to T2b prostate cancer. Prostate Cancer Specific (PCS) and Physical Well-Being (PWB) subscales of FACT-P, scores at MRT and CRT were significantly lower than at PRT. At FRT2, PWB scores declined further, while PCS scores increased. PFS median scores were significantly higher at CRT and at FRT2 as compared with PRT. Patients scoring higher on PFS were more likely to report a poorer QOL and PWB as measured with FACT-P questionnaire. No significant changes were noted in the BDI and ESS scores during the study periods. The PWB declined during and at CRT and worsened at FRT2. Decline in PCS subscale scores during and at CRT reflects worsening of urinary symptoms and appearance of bowel problems. The scores improved at long-term follow-up. A relationship was found to exist between physical well-being and fatigue.

**Key words:** depression, fatigue, Functional Assessment of Cancer Therapy, outcomes, physical well-being, Piper Fatigue Scale, prostate cancer, quality of life, radiotherapy, sleep disturbance.

### INTRODUCTION

Cancer ranks second only to heart disease as the leading cause of death in North America. One in four deaths in the United States is due to cancer [1].

Prostate cancer is the most common cancer in men in the United States, accounting for almost 200,000 new cases and 40,000 deaths in 1998 [2]. Previous studies of prostate

**Abbreviations:** BDI = Beck Depression Inventory, CRT = completion of radiotherapy, ESS = Epworth Sleepiness Scale, EWB = Emotional Well-Being (subscale), FACT-G = Functional Assessment of Cancer Therapy—General, FACT-P = Functional Assessment of Cancer Therapy—Prostate, FRT = follow-up radiotherapy (4 to 8 weeks), FRT2 = long-term follow-up radiotherapy (12 months or more), FWB = Functional Well-Being (subscale), MRT = midway radiotherapy, PCS = Prostate Cancer Specific (subscale), PFS = Piper Fatigue Scale, PRT = preradiotherapy, PSA = prostate-specific antigen, PWB = Physical Well-Being (subscale), QOL = quality of life, RWD = relationship with doctor, SD = standard deviation, SWB = Social Well-Being (subscale).

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cancer have focused on survival as the primary outcome measure. Over the past few years, quality of life (QOL) issues in cancer patients have received increasing attention by researchers, clinicians, and patients [3–14]. Furthermore QOL is of great concern to patients considering treatment options for prostate cancer [15]. According to Cella, investigating the impact of cancer treatments on QOL is a two-tailed enterprise in which treatment toxicity is balanced not only against survival time but also against posttreatment function and well-being [16]. Furthermore, patients are increasingly interested in acquiring more information about their cancers and the impact of cancer treatments, because they would like to participate in decisions made about their treatment and overall care [17].

Several domains (physical well-being, psychological well-being, social well-being, and spiritual well-being) need to be considered when QOL of cancer patients is assessed. It is important that clinicians and/or researchers use instruments that capture the multidimensional aspects of QOL and yet remain user-friendly to a very diverse socioeconomic population. In a recent study on the health-related QOL and psychological factors in prostate cancer patients, van Andel and colleagues concluded that quantifying the impact of radical prostatectomy and external radiotherapy should be based mainly on longitudinal studies including baseline measures [18].

## OBJECTIVES

This study (1) prospectively evaluated QOL in localized prostate cancer patients undergoing external beam radiotherapy in an ambulatory clinic setting using validated multidimensional instruments and (2) examined the relationship among QOL, depression, sleep disturbance, and fatigue. The questions asked were—

1. What are the changes in QOL of patients with localized prostate cancer undergoing radiotherapy, at completion of radiotherapy (CRT) and at long-term follow-up radiotherapy (FRT2) (12 months or more)?
2. Is there a relationship between fatigue, depression, sleep disturbances, and QOL?

## METHODS

In our facility, patients diagnosed with localized prostate cancer receive information regarding various

available options such as surgery, radiotherapy, or wait and watch. Urologists provide this information. Patients who prefer radiotherapy or those who prefer but are not good candidates for surgery are referred for radiotherapy.

Inclusion and exclusion criteria have previously been described [19]. All participants underwent clinical screening that included a neurological examination. We completed assessments at preradiotherapy (PRT), midway radiotherapy (MRT), CRT, follow-up radiotherapy (FRT) 4 to 8 weeks after CRT, and FRT2. In addition, we monitored demographic data regarding patients' age, body weight, disease severity (TNM [tumor, lymph node, metastases] staging) [20], prostate-specific antigen (PSA), and hematocrit levels and also recorded radiation dosage.

## Instruments Used

To assess QOL, we used the Functional Assessment of Cancer Therapy—Prostate (FACT-P) (version 3) [21]. This self-report instrument consists of 34 items on Functional Assessment of Cancer Therapy—General (FACT-G) and a 12-item disease-specific subscale for prostate cancer called “Prostate Cancer Specific” (PCS) [21]. The FACT-G instrument has five subscales covering four domains of QOL: Physical Well-Being (PWB), Social Well-Being (SWB), Emotional Well-Being (EWB), and Functional Well-Being (FWB). It also includes two items to assess the patient's relationship with doctor (RWD) (fifth subscale, but not a domain). The last item of each of the five subscales asks respondents to rate how much that particular aspect of life affects their overall QOL. These five items (items 8, 16, 19, 26, and 34) are considered to be experimental and so are not used in either subscale scores or overall QOL score [21]. We scored the remaining items of FACT-G to provide a score for each domain and a composite score for the overall QOL. The FACT-G has well-established validity and reliability [5,21–22]. The PCS subscale has 12 items. It includes items related to sexuality, bowel/bladder function, and pain. Higher total scores for the FACT-P scale indicate a better overall QOL. Similarly, higher scores on the individual subscales suggest better functioning in these domains. Internal consistency estimates on the FACT-P total score were reported to be 0.87 and 0.89 on two samples used to validate the measure. Internal consistency estimates of the five general subscales and the PCS subscale ranged from 0.61 to 0.84 [5].

We used the Beck Depression Inventory (BDI) to screen for depression. This instrument includes 21 items

each comprising four self-descriptive statements, which the subject rates on a 4-point scale of severity [23]. Interpretation is based on a 0 to 63 total score. Scores from 0 to 9 are considered normal, 10 to 18 denote mild depression, and 19 to 27 moderate, and greater than 27 severe [23]. Test-retest reliability has been reported above 0.90 [24]. Spearman-Brown reliability is 0.93, and internal consistency for test items is 0.86 [25].

The Epworth Sleepiness Scale (ESS), a self-administered 8-item questionnaire, provides measurement of the subject's general level of daytime sleepiness [26]. Subjects rate their chances of dozing off or falling asleep in eight different situations commonly encountered in daily life, such as sitting and reading or watching TV. The eight items are scored 0 to 3 and total scores range from 0 to 24. A mean score of 5.9 for normal controls has been reported [26]. Higher scores suggest increased daytime sleepiness. Test-retest reliability is high. When 87 medical students were tested and retested 5 months later, their paired ESS scores did not change significantly and were highly correlated ( $r = 0.82$ ). Internal consistency has been reported to be high for patients with a variety of sleep disorders (0.88) and for students (0.73) [27].

The Piper Fatigue Scale (PFS) consists of 22 numerically scaled items (0–10) that measure four dimensions of subjective fatigue [28–29]. The dimensions include Behavioral/severity (six items), Affective/meaning (five items), Sensory (five items), and Cognitive/mood (six items). Higher scores indicate more fatigue. According to Piper, patients scoring 6 or higher on the PFS could be considered as experiencing fatigue (personal communication). Internal reliability estimates for the PFS subscales ranged from 0.69 for the symptom dimension to 0.95 for the sensory dimension in a sample of radiotherapy patients.

In our study, with no help from the investigator, the patients completed all instruments independently. Upon receipt of the responses, the investigator made no attempt to verify completion of all items. For analysis of results, only those records were included in which all answers to all items across all the study periods had been completed.

### Radiotherapy

Patients underwent radiotherapy for 7 to 8 weeks by a Varian 2100 linear accelerator with 18 MV photons. We used the Closed-Box technique of del Regato [30] with 4-field prostate radiation at specific angles: anteroposterior (AP), posteroanterior (PA), right-lateral (RL), and left-lateral (LL) at 360°, 180°, 270°, and 90°, respectively.

Each subject received 68 to 70 Gy in 34 to 38 fractions at 1.80 to 2.00 Gy per fraction. Our intent for the treatment was to cure. During radiotherapy, no skin rash or loss of sensory-motor function was observed.

### Statistical Methods

Statistical assessments addressed changes in outcome variables between PRT and each of the four subsequent study periods (MRT, CRT, FRT, and FRT2). We used the SAS (Statistical Analysis System) Univariate procedure to perform routine calculations and the Shapiro-Wilk test to determine whether the change scores satisfied conditions for a normal distribution. Because most variables failed the normality test, comparisons between time periods were based on the Wilcoxon Signed-Rank test. Adjustments for multiple comparisons were based on the Bonferroni criteria. Spearman correlations were calculated between FACT-P and each of the other scales at each time period and with respect to changes across study periods.

### RESULTS

During the study period, the primary investigator (UM) treated 89 patients for localized prostate cancer. Twenty-seven patients were excluded from the study. Of these 27 patients, 7 were considered to have unstable medical problems such as diabetes mellitus and hypertension. Four patients did not understand the study protocol and two patients were visually impaired. Four patients were excluded because of history of psychiatric illness and five patients had clinical evidence of peripheral neuropathy. Five patients did not want to participate in the study. Complete information for all questionnaires across all study periods was available in 40 of the 62 remaining patients. No significant differences existed for various demographic and clinical variables between those patients with incomplete data and those with complete data. However, one patient in the incomplete database had a combined Gleason Score of 7, suggesting a relatively aggressive tumor. Data were analyzed and are presented on these 40 patients (**Table 1**). The mean age of the patients was 67.8 yr (range 55–78). At long-term follow-up, the mean age of the respondents was 69.2 yr (range 57–79 yr). The mean number of years of education was 12.4 (range 6–18). The number of patients married was 28, while the number of patients single, divorced, or separated was 12. All patients had disease localized to the prostate gland. The patients'

**Table 1.**

Demographics and clinical variables for patients with complete data and patients with incomplete data.

Variable	Complete Data (40 Patients)	Incomplete Data (22 Patients)
Average Age (yr)	67.8 (range 55–78)	66.3 (range 56–75)
Average Weight (lb)	185.1 (range 149–242.8)	183.5 (range 151.3–238.0)
Average Education (yr)	12.4 (range 6–18)	11.6 (range 7–16)
Marital Status		
Married	28 (70%)	17 (65.4%)
Single, Divorced, or Separated	12 (30%)	9 (34.6%)
Prostate-Specific Antigen Range	3.1–83.2	4.2–64.5
Combined Gleason Score	5.4 (range 3–6)	5.1 (range 3–7)
Hematocrit	42	43.5
Time Lapse Between Biopsy and Treatment (d)	27–320	20–275
Medical Problems		
Hypertension	11 (27.5%)	8 (30.7%)
Chronic Obstructive Pulmonary Disease	6 (15.0%)	5 (19.2%)
Diabetes Mellitus	7 (17.5%)	3 (11.5%)
Coronary Artery Disease	5 (12.5%)	4 (15.3%)
Follow-Up After Completion of Radiotherapy (mo)	16.1 (range 12–24)	14.7 (range 12–22)

body weight ranged from 149.0 lb to 242.8 lb, with a mean body weight of 185.1 lb before starting radiotherapy. At completion of radiotherapy the body weight ranged from 144.8 lb to 244 lb with a mean body weight of 184.1. The range of PSA levels was 3.1 to 83.2. The tumor stages ranged from T1c to T2b. Time lapse between prostate biopsy and radiation treatment ranged from 27 to 320 days. Average duration of follow-up was 16.1 months (range 12–24 months). Duration of follow-up after completion of treatment was 12 months in 10 patients, 13 to 18 months in 18 patients, and 19 to 24 months in the remaining 12 patients. Radiotherapy was the primary treatment for all patients. Not one of the patients was treated surgically. No clinical evidence of tumor recurrence occurred, and PSA levels remained low at FRT2.

Associated medical problems included 11 patients with hypertension, 6 with chronic obstructive pulmonary disease, 7 with controlled diabetes mellitus, and 5 with a history of coronary artery disease. All patients were medically stable at the time of entry into the study.

Eighteen patients (45%) developed mild to moderate symptoms of proctitis during radiotherapy. Ten of these patients had a history of hemorrhoids before starting radiotherapy. Patients with symptoms of proctitis were treated with 10 percent hydrocortisone rectal foam. Ten patients developed diarrhea that was controlled with Imodium. One patient complained of some blood-stained mucus and no diarrhea at FRT.

Fourteen patients (35%) had a history of frequency of urination and nine patients (22%) complained of nocturia before radiotherapy was started. Another nine patients (22%) developed frequency during treatment. At FRT, only six patients were left with increased frequency of urination.

We found no significant change in the mean scores of hematocrit (42.0 at PRT and 41.6 at CRT) or body weight during the study period. PSA decreased for all patients at follow-up. We found no relationship between mean scores of body weight, PSA level, stage of the disease, and scores on FACT-P across all study points. Mean, standard deviation (SD), and median scores on FACT-P, SWB, EWB, FWB, and RWD scores over study periods are provided in **Table 2**. No significant changes were found on FACT-P, SWB, FWB, and RWD scores across all study periods. Mean, SD, and median scores of PWB and PCS subscales of FACT-P and PFS are provided in **Table 3**.

Compared to PRT, a significant decline in PWB subscale scores of FACT-P (**Table 3**) was found at MRT, CRT, and FRT2 (corrected for multiple comparisons;  $p < 0.0008$ , 0.002, and 0.004, respectively). PWB scores increased at FRT but did not reach baseline levels. Compared to PRT scores, a significant decline in PCS subscale scores was found at MRT and CRT ( $p < 0.001$  and 0.02 respectively, adjusted for multiple comparisons). These scores increased at FRT but did not return to baseline scores. At FRT2, the

**Table 2.**

Mean, standard deviation (SD), and median scores of Functional Assessment of Cancer Therapy—Prostate (FACT-P) scale and Social Well-Being (SWB), Emotional Well-Being (EWB), Functional Well-Being (FWB), and Relationship with Doctor (RWD) subscales of FACT-P at preradiotherapy (PRT), midway radiotherapy (MRT), completion of radiotherapy (CRT), 4–8 weeks follow-up radiotherapy (FRT), and long-term (12 months or more) follow-up radiotherapy (FRT2).

Subscale	PRT (Mean ± SD)	MRT (Mean ± SD)	CRT (Mean ± SD)	FRT (Mean ± SD)	FRT2 (Mean ± SD)
FACT-P	122.7 ± 20.4	116.9 ± 19.6	119.4 ± 16.5	121.7 ± 19.5	119.4 ± 18.4
Median	122	122	120.5	122	118
SWB	20.7 ± 6.7	21.0 ± 5.9	22.4 ± 5.8	21.5 ± 6.0	20.6 ± 6.1
Median	23	22	24	22	23
EWB	18.0 ± 2.3	18.0 ± 2.6	18.1 ± 2.4	18.1 ± 2.1	17.4 ± 3.3
Median	18	19	19	19	19
FWB	20.9 ± 5.7	20.4 ± 6.1	19.4 ± 5.7	19.5 ± 6.0	18.9 ± 7.0
Median	21	21	20	20	22
RWD	7.3 ± 1.6	7.8 ± 0.7	7.8 ± 0.6	7.8 ± 0.6	7.8 ± 0.8
Median	8	8	8	8	8

**Table 3.**

Mean, standard deviation (SD), and median scores of Physical Well-Being (PWB) and Prostate Cancer Specific (PCS) subscales of Functional Assessment of Cancer Therapy—Prostate (FACT-P) and Piper Fatigue Scale (PFS) at preradiotherapy (PRT), midway radiotherapy (MRT), completion of radiotherapy (CRT), 4–8 weeks follow-up radiotherapy (FRT), and long-term (12 months or more) follow-up radiotherapy (FRT2).

Subscale	PRT (Mean ± SD)	MRT (Mean ± SD)	CRT (Mean ± SD)	FRT (Mean ± SD)	FRT2 (Mean ± SD)
PWB	23.9 ± 3.9	21.4 ± 4.4*	21.7 ± 4.2 <sup>†</sup>	22.6 ± 4.4	20.7 ± 5.5 <sup>‡</sup>
Median	25	22	22	24	22
PCS	33.0 ± 8.6	29.6 ± 7.6 <sup>§</sup>	29.8 ± 7.2 <sup>¶</sup>	32.1 ± 7.8	33.8 ± 7.4 <sup>§</sup>
Median	35	31	30	32	35
PFS	2.7 ± 2.0	3.7 ± 2.3 <sup>**</sup>	4.1 ± 2.5 <sup>††</sup>	3.6 ± 2.4 <sup>‡‡</sup>	4.3 ± 2.5 <sup>§§</sup>
Median	2.4	3.1	4.2	3.9	5.0

\* $p < 0.0008$  (all  $p$ -values adjusted for multiple comparisons)

<sup>†</sup> $p < 0.0016$ , <sup>‡</sup> $p < 0.0036$ , <sup>§</sup> $p < 0.001$ , <sup>¶</sup> $p < 0.02$ , <sup>\*\*</sup> $p < 0.004$ , <sup>††</sup> $p < 0.001$ , <sup>‡‡</sup> $p < 0.03$ , <sup>§§</sup> $p < 0.003$

scores returned to PRT level and were significantly higher ( $p < 0.001$ , corrected for multiple comparison) than post-CRT scores, suggesting improvement in bladder/bowel related symptoms as compared with the scores at CRT.

Mean, SD, and median scores for each time period for PFS are provided in **Table 3**. PFS scores increased significantly at MRT, CRT, FRT, and FRT2 as compared with PRT ( $p = 0.004$ ,  $p < 0.001$ ,  $p < 0.03$ ,  $p < 0.003$ , respectively; corrected for multiple comparisons). Compared to MRT and CRT, scores were lower at FRT, though they did not return to the PRT level. After we excluded patients with depressive symptomatology (scores of 10 or higher on BDI), the scores on PFS remained significantly higher at MRT, CRT, and FRT2 as compared with PRT

scores ( $p = 0.03$ ,  $0.02$ , and  $0.01$ , respectively) (not shown). Four patients scored 6 or higher on PFS at PRT evaluation. PFS scores remained high in two of these four patients at CRT (scoring 6 or higher could be considered as experiencing fatigue). Thirteen patients (including two patients who scored higher than 6 at PRT) scored 6 or higher on PFS at CRT. At FRT2, 16 patients scored 6 or higher on PFS. Thus 10 percent of patients experienced fatigue at PRT, versus 33 percent at CRT and 40 percent at FRT2.

A significant relationship was found between PWB subscale scores of FACT-P and PFS scores at PRT, during radiotherapy, and CRT, as well as at FRT and FRT2. The relationship between the PWB subscale and the PFS

scores was such that those patients scoring higher on PFS were more likely to report a poor quality of physical well-being.

Mean, SD, and median scores of BDI and ESS at PRT, MRT, CRT, FRT, and FRT2 are provided in **Table 4**. No significant changes were noted in BDI scores at different evaluation periods (**Table 4**). However, a significant relationship existed between depression and overall QOL (as measured by FACT-P) across study periods. Ten patients (25%) scored 10 or more on BDI before starting radiotherapy, suggesting depressive symptomatology. Of these, 7 patients (18%) still scored 10 or more at CRT. Among the remaining patients, none reported depressive symptoms during or at CRT. At FRT2, 12 patients (30%)—5 previously identified and 7 newly identified—scored 10 or higher on BDI. No significant changes were found on ESS scores.

## DISCUSSION

The results of our prospective study of QOL in patients with localized prostate cancer treated with conventional external beam radiation cannot be directly compared with those of other studies. This is because we are unaware of any other prospective studies of QOL using the FACT-P instrument in a population of localized prostate cancer patients treated with conventional external beam radiation.

No significant change (neither decline nor improvement) in overall QOL across study periods was observed. This is in contrast to the findings by Lee et al., who reported statistically significant differences for the composite scores at 1- and 3-month follow-ups in localized prostate cancer patients treated with brachytherapy [9]. In their study, the composite FACT-P score decreased by 14 points 1 month following patients' completion of brachy-

therapy and the FACT-G score decreased by more than 6 points. Although the PRT composite FACT-P score was lower in our study than in Lee's study, the decline in composite FACT-P score was less marked, the score declining only by 2 points at 1-month follow-up. Similarly, our study noted lesser score changes at 4 to 8 weeks follow-up in PWB and PCS subscales of FACT-P than in Lee's study (1.5 vs. 3.0 for PWB and 0.6 vs. 7.5 for PCS), again suggesting that the patients in the current study experienced less morbidity during radiotherapy, at CRT, and at follow-up. The PCS scores increased at FRT2, suggesting improvement in urinary and bowel symptoms.

Our patients did not show a significant decline in FWB across the study periods, in contrast to the significant decline noted by Lee and associates [9]. These outcome differences cannot be explained by age and pretreatment PSA levels. Lee et al. did not investigate fatigue, depression, and sleep disturbances, and information regarding hematocrit and weight is not available in their study [9]. The observed outcome differences may reflect the difference in modes of treatment, suggesting a better QOL outcome with conventional radiotherapy versus interstitial brachytherapy. This finding is congruent with the most recent report by Lee et al. [31].

In their comprehensive comparison of health-related QOL outcomes after contemporary therapies for localized prostate cancer, Wei and colleagues reported that several domains of health-related QOL after brachytherapy were significantly less favorable than after either radical prostatectomy or external radiation [32]. Apparently, morbidity as measured by the FACT-P instrument is relatively less severe in patients treated with conventional radiotherapy than with brachytherapy.

We are unaware of any study that has investigated the relationship between QOL, fatigue, depression, and

**Table 4.**

Mean, standard deviation (SD), and median scores of Beck Depression Inventory (BDI) and Epworth Sleepiness Scale (ESS) at preradiotherapy (PRT), midway radiotherapy (MRT), completion of radiotherapy (CRT), 4–8 weeks follow-up radiotherapy (FRT), and long-term (12 months or more) follow-up radiotherapy (FRT2).

Scale	PRT (Mean ± SD)	MRT (Mean ± SD)	CRT (Mean ± SD)	FRT (Mean ± SD)	FRT2 (Mean ± SD)
BDI	5.6 ± 5.1	6.4 ± 5.0	6.0 ± 4.7	5.6 ± 4.6	6.3 ± 5.2
Median	4.5	5.0	5.0	4.5	4.5
ESS	7.2 ± 5.7	8.1 ± 5.8	7.5 ± 5.7	7.3 ± 4.9	6.7 ± 4.9
Median	6.0	7.0	7.0	8.0	7.0

sleep disturbances. In our study, we found a parallel change in PFS and PWB scores, meaning patients who experienced fatigue reported a poorer physical well-being across the study periods. Our study was not designed to investigate the causal relationship between these two variables. The decline in PWB and increase in PFS scores during radiotherapy and at CRT appears to be transient, because the scores improved at FRT, although they did not return to baseline scores. PWB scores declined again and PFS scores increased further at FRT2, indicating worsening of physical well-being and increased fatigue. These findings suggest that increasing fatigue and decline in physical well-being are caused by different mechanisms. We previously have proposed that subjective expression of fatigue during and at CRT is due to a transient decline in neuromuscular efficiency [33]. Fatigue at FRT2 may be the result of an inactive lifestyle following the diagnosis and treatment of cancer.

The relationship between PWB and fatigue was such that those who scored higher on PFS were more likely to report poor physical well-being. Whether fatigue induces decline in physical well-being or conversely is not clear. In the presence of increasing PFS scores and declining PWB, one would expect a decline in PWB scores. However, no such changes were noted in our study. Possibly, a marked decline in physical well-being or severe fatigue must occur before changes in functional well-being can be detected or experienced.

We noted no significant changes in the EWB domain. This finding mirrors scores on the BDI that also did not change significantly between study periods. Many of our patients were depressed even before starting treatment. The number of depressed patients increased at FRT2, although no significant change in mean BDI scores was found.

Many authors have reported the possible influence of psychological factors on QOL and fatigue [34–38]. Depression in particular is considered a contributor to fatigue in cancer [39]. However, depression may be not only a cause but also a result of persistent feelings of tiredness and poor QOL. Furthermore, depression and fatigue both may result from the same biological factors [38].

In relation to fatigue, our findings and the one reported by King et al. are similar [40], in that the number of patients experiencing fatigue at CRT increased. However, the incidence of fatigue at CRT was lower in our study than in that of King et al. (25% vs 65%) [40]. These differences may be due to study design, patient

population, and assessment tool variations and could not be explained by age or total radiation dose variations. Mean age and range in both of these studies were similar (67.50 and range 54–77 yr in King's study vs. 66 and range 55–75 yr in our study). Range of radiation dose and range of mean total dose are somewhat higher in our study as compared with the study by King et al. (68–70 Gy vs. 60.0–66.2 Gy) [40].

In this study, higher scores on the PFS at CRT, along with no change in BDI scores or ESS scores, suggest that fatigue most likely was not the result of depression and/or sleep disturbance. At PRT assessment, the prevalence of depression in this study did not appear to be different from that experienced by the elderly living in the community. Fry suggested that, based on prevalence studies, 15 to 20 percent of all persons over the age of 65 yr and living in the community show significant depressive symptoms [41]. However, the prevalence of depression increased at FRT2. This may relate to uncertainty regarding prognosis, decline in physical well-being, increased fatigue, and change in vocational status.

Other correlates that have been proposed to influence QOL include malnutrition, weight loss [42], anemia, electrolyte and fluid disturbance, medications [37], and sleep disturbance [43]. However, no consistent relationships among these variables and QOL have been found in prostate cancer patients. An increase in the number of patients experiencing fatigue and decline in physical well-being at CRT and at FRT2, as found in this study when compared with PRT, cannot be explained by anemia, sleep disturbances, excessive weight gain, or weight loss, because no significant changes were found in these variables during the study period.

Limitations of the study include lack of a control group and a select patient population. Notwithstanding, the primary objective of the study was to prospectively describe overall QOL, as well as its various domains, in a clinical setting, during radiotherapy, and at CRT and FRT2.

## CONCLUSIONS

In this study of patients with localized prostate cancer undergoing external beam radiotherapy, no significant change in overall QOL across study periods was noted. However, a statistically significant decline of the PWB and PCS subscale scores of FACT-P was noted at

FRT and at CRT. Statistically, PFS scores increased significantly at the CRT as compared with PRT scores. However, these changes appeared to be transient, because scores tended to move toward baseline scores at FRT. At FRT2, again a decrease in physical well-being and an increase in PFS scores occurred, which appeared to be even more pronounced than at CRT. On the other hand, PCS subscale scores increased, suggesting improvement in urinary and bowel symptoms. A statistically significant relationship was found between PFS scores and those on the PWB subscale of FACT-P, meaning that patients scoring higher on the PFS were more likely to report poor quality of physical well-being. No statistically significant changes were noted on the BDI and ESS scores. This study was not designed to look at a causal relationship between depression, physical well-being, and fatigue. A statistically significant increase in PFS scores with no change in BDI and ESS scores suggests that fatigue was not the result of depression or sleep disturbances. Based on previous experience, we propose that fatigue may have different mechanisms at different times during the course of the disease [33].

It is important for both the clinician and the patient with cancer to know the QOL before starting any treatment and for the clinician to study the impact of treatment intervention on various aspects of QOL following CRT. This will help to identify and understand the domains that are most frequently affected and will lead to the development of rehabilitation interventions to prevent decline in these domains.

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