

Fatigue in Young Survivors of Extracranial Childhood Cancer: A Finnish Nationwide Survey

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Although an increasing number of young patients with cancer are being successfully treated for their disease (Gatta et al., 2009), demanding treatment regimens may be having a negative impact on this population's health-related quality of life (HRQOL). The literature has focused on describing the HRQOL of young cancer survivors; however, fatigue usually is overlooked in favor of more obvious late effects of cancer and treatment (Hockenberry-Eaton et al., 1998). Previous reports have shown that fatigue can cause negative changes in HRQOL (Eddy & Cruz, 2007; Meeske, Katz, Palmer, Burnwinkle, & Varni, 2004; Meeske, Patel, Palmer, Nelson, & Parow, 2007; Varni, Burwinkle, Katz, Meeske, & Dickinson, 2002). Fatigue is a symptom that may affect a patient's life, both in the short and long term. Despite the fact that significantly less is known about cancer-related fatigue in children and adolescents than in adults (Whitsett, Gudmundsdottir, Davies, McCarthy, & Friedman, 2008), fatigue is recognized as a significant symptom experienced by children and adolescents with cancer (Gibson, Garnett, Richardson, Edwards, & Sepion, 2005; Meeske et al., 2004; Ruland, Hamilton, & Schjødt-Osmo, 2009; Whitsett et al., 2008). Minimal data are available concerning fatigue in these populations, but Varni et al. (2002) identified that young cancer survivors are more fatigued than their healthy control counterparts.

No shared understanding of the definition and meaning of fatigue exists for these young patients and survivors. As a whole, fatigue is a difficult concept to explain. The first study to evaluate fatigue in children with cancer (Hockenberry-Eaton et al., 1998) reported that the definition of fatigue varies depending on the developmental level of the participants. Another study (Hinds et al., 1999) reported that the patient, parents, and staff each defined fatigue differently. Children reporting fatigue noted increased levels of depressed

Purpose/Objectives: To evaluate self-reports of fatigue by young cancer survivors (aged 11–18 years), to compare young survivors' fatigue scores with the scores of a healthy control group and of the parent proxy evaluation, and to analyze whether demographic or disease-related factors are associated with young survivors' fatigue.

Design: Cross-sectional quantitative study.

Setting: An urban hospital in southwestern Finland.

Sample: 384 survivors diagnosed with an extracranial malignancy at age 16 or younger, who have survived four or more years postdiagnosis, and who are free of cancer. General matched population controls were randomly selected from the Finnish Population Registry.

Methods: Demographic data and a self-report written fatigue questionnaire.

Main Research Variables: Total fatigue (TF), general fatigue (GF), sleep or rest fatigue (SF), and cognitive fatigue.

Findings: The control populations reported significantly more issues with TF, GF, and SF than did the survivor population. In survivors, older age, the need for remedial education at school, and a sarcoma diagnosis were associated with increasing fatigue, whereas female gender, better school grades, and greater health-related quality-of-life (HRQOL) scores were associated with lower fatigue. The study variables explained 49%–65% of the variation in fatigue scores.

Conclusions: Although survivors and their matched controls seem to have similar fatigue, subgroups of survivors do experience excessive fatigue, which may have an impact on their HRQOL.

Implications for Nursing: This study increases the knowledge about fatigue levels of young survivors of extracranial malignancies and identifies the need for instruments specifically designed to assess fatigue in this population. The healthcare team should pay attention to the fatigue level of young survivors, particularly SF.

mood and different physical consequences; adolescents emphasized the dynamic sensation of physical or mental exhaustion. Parents defined fatigue as a state of

diminished or complete loss of energy and a decreased ability to participate in social, academic, physical, or self-care activities at the child's usual duration or intensity level. Healthcare professionals' definitions also included loss of will and spiritual distress.

Cancer-related fatigue is discussed in the pediatric oncology literature as a symptom unique to patients with cancer (McCabe, 2009). The preceding definitions may not, however, be directly adaptable to childhood cancer survivors. According to McCabe's (2009) evolutionary concept analysis on fatigue in children with long-term conditions, fatigue appears to be a subjective experience of tiredness or exhaustion that is multidimensional and includes physical, mental, and emotional aspects. Fatigue can be acute, episodic, or chronic (Hockenberry et al., 2003; Hockenberry-Eaton et al., 1999). Because fatigue is a subjective symptom, each patient's point of view has to be evaluated.

Few fatigue measures exist for children and adolescents. Some HRQOL instruments may contain questions about fatigue, but usually, when fatigue is considered, assessment is limited to a "yes" or "no" variable or a visual analog scale (Eddy & Cruz, 2007). Therefore, previous HRQOL reports regarding young cancer survivors often have omitted an in-depth look and the dimensions of fatigue. In addition, no instrument is specifically designed for assessing fatigue in pre-adulthood cancer survivors.

Fatigue in childhood and adolescent cancer survivors is underrecognized and underestimated, and, because of this, also may be undertreated (Gibson et al., 2005). Therefore, evaluating the amount of fatigue in young survivors can help the multidisciplinary follow-up team find better tools for handling this issue. The objectives of the current study were to (a) describe self-reported fatigue in childhood and adolescent cancer survivors with the Finnish version of the PedsQL™ Multidimensional Fatigue Scale (Varni et al., 2002), (b) compare survivors' fatigue scores with the scores of the healthy control group and of the parent proxy evaluation, and (c) analyze whether demographic or disease-related factors have associations with survivors' fatigue.

Methods

Sample and Data Collection

The total cohort of Finnish childhood and adolescent survivors with extracranial (excluding brain tumors) cancer was identified from the Finnish Cancer Registry (FCR). The following inclusion criteria were required: aged 11–18 years at the time of the study, an extracranial cancer diagnosis at age 16 or younger, alive at the end of 2006, survived at least four years postdiagnosis, and free of cancer at the time of the study. Five university hospitals provide pediatric cancer treatment in Finland

and inclusion criteria were verified and approved by the physicians responsible for cancer treatment at these hospitals. A total of 384 (204 male, 180 female) survivors met the criteria. The details of the cancer diagnosis (e.g., date of diagnosis, subtype, treating clinic) and limited data on the initial treatment were obtained from the FCR and reviewed by the treating clinicians.

This cross-sectional quantitative study data collection occurred in 2007. A questionnaire package sent to the survivors and their parents contained a cover letter about the study, instructions, consent forms, and the PedsQL Multidimensional Fatigue Scale, as well as a questionnaire for demographic details. Participants were asked to return the consent forms and coded questionnaires using the provided envelopes. One reminder was sent three weeks after the initial contact to survivors or parents who had not yet responded.

General population controls, three equally matched controls for each survivor, were randomly selected from the Finnish Population Registry. The controls, with no history of cancer, were matched for gender, age, and place of residence. The postal package was mailed first to the control subject and his or her parent and, if this person did not respond, additional control subjects were contacted. The authors' goal was to get one matched control and parent pair for each survivor and parent pair. The Finnish Ministry of Social Affairs and Health gave permission for the study, and the Ethical Committee of the South-West Finland Hospital District approved it. Informed consents were signed by all participants.

Questionnaires

The demographic questionnaires for children and their parents included variables such as gender, age at study, number of siblings, living situation, need for remedial education at a comprehensive school, and the overall average grade in the latest school report. In addition, the age, gender, and educational level of the parent were noted. The Finnish school grading system ranges from 4 (poorest) to 10 (best). Overall average grade is the mean calculated from the grades for each school subject (e.g., mathematics, languages, science). This mean is written in the school mark report together with the grades for each separate subject.

The demographic questionnaire for the children also posed questions such as, "Do you have any additional noncancer diagnosis?" and "Do you feel happy?" ("yes" or "no" responses). Cancer-related factors such as diagnosis, age at diagnosis, length of survival, cancer treatment modalities, and possible relapse were assessed to validate the FCR data. All diagnoses recorded from the FCR and reported from patients were compared and, if any discrepancies appeared, the diagnoses were confirmed by the treating clinicians from the five university hospitals.

Despite the lack of a specific fatigue instrument for young childhood cancer survivors, the authors found that the most suitable existing instrument for this population could be the PedsQL Multidimensional Fatigue Scale (Varni et al., 2002). The authors translated and validated this instrument into Finnish and used that version in the postal survey. One reason for choosing the PedsQL Multidimensional Fatigue Scale was that it captures total fatigue (TF), general fatigue (GF), sleep or rest fatigue (SF), and cognitive fatigue (CF), which offer an in-depth look into the different proposed dimensions of fatigue. It also covers the best theoretical definition of fatigue in children with long-term conditions. The instrument has separate versions for children aged 8–12 and 13–18, as well as separate versions for parent proxy reports (Varni et al., 2002). The instrument has shown good internal consistency reliability for all these groups (Varni et al., 2002), and it has been previously tested and used to evaluate fatigue among pediatric patients with cancer during treatments (Meeske et al., 2004; Varni et al., 2002), cancer survivors less than 12 months off therapy, and cancer survivors more than 12 months post-therapy (Varni et al., 2002). In addition, the PedsQL Multidimensional Fatigue Scale is brief and, therefore, suitable for a postal survey.

The PedsQL Multidimensional Fatigue Scale consists of 18 five-point Likert-type scales ranging from 0 (never a problem) to 4 (almost always a problem), which, together with questions about how much trouble children have been experiencing in the past month, form a TF score as well as three subscales: a six-item GF (e.g., "I feel too tired to do things that I like to do."), a six-item SF (e.g., "I feel tired when I wake up in the morning."), and a six-item CF (e.g., "It is hard for me to keep my attention on things.") score. The authors performed the scoring. After transformation, higher scores on the 0–100 scale indicate less fatigue. In this study, TF score reliability coefficients (Cronbach alpha) were 0.91 for survivors and 0.89 for their controls. The parent proxy TF score reliability coefficients were 0.93 for survivors' parents and 0.9 for controls' parents.

The authors have previously analyzed HRQOL scores for this same population using generic score scales from PedsQL, version 4.0 (Varni et al., 2002; Varni, Seid, & Rode, 1999). Associations of the previously gained HRQOL scores with the fatigue scores also were analyzed.

Statistical Analysis

The outcome variables in this study were the multidimensional TF score, which includes the GF, SF, and CF. The authors calculated descriptive statistics for all variables. The Wilcoxon signed ranks test was used for comparing different fatigue dimensions within survivors and controls. Differences in the demographic char-

acteristics were analyzed with chi-square tests, Mann-Whitney U test, and Spearman's correlation coefficients.

The Mann-Whitney U test was used to compare survivors' fatigue scores to the scores of the control group, and to compare survivors' parent proxy scores to the controls' parent proxy scores. Survivor fatigue scores were compared to parent proxy scores by using the Wilcoxon signed ranks test. After that, parent and survivor intercorrelations were analyzed with Spearman's correlation coefficients. To analyze demographic and disease-related factors that may have association with survivors' fatigue, the authors used chi-square tests, the Mann-Whitney U test, or the Kruskal Wallis test. The authors made comparisons between continuous variables by using Spearman's correlation coefficients.

A multiple regression model was developed for the outcome variables. First, the authors analyzed demographic factors as predictors of fatigue scores within the control group and survivor group separately. Thereafter, to investigate which variables might explain the variation in survivors' fatigue, the authors added into the model the statistically significant demographic factors (age, gender, possible additional diagnosis, need for remedial education at school, the overall average grade in the latest school report, and the HRQOL score) from the univariate analysis, as well as cancer diagnosis, cancer treatment modalities, length of survival, and self-rated happiness to create a hierarchical regression model. Clinical judgment also was used to create order of the regression model. For example, the authors wanted to evaluate the effects of cancer before the treatment and treatment before the length of survival, as well as the possible consequences of the treatment (other diagnoses, school achievements) just after the length of survival. At first (step 1), the authors used age at the time of the study and gender as independent variables. In the second phase (step 2), the authors added cancer diagnosis and then (step 3) treatment modalities, followed by length of survival (step 4) to the equation. Next, the possible additional diagnosis, need for remedial education at school, and the overall average grade in the latest school mark report were added into the model (step 5). The self-rated happiness and HRQOL total score were added at the last step (step 6) because the authors wanted to evaluate the effects of other variables without the confounding effect of the strongest predictors of the outcome revealed in the univariate analyzes. For each step, the change in coefficient of determination (R^2 change) gained by variables at that step and the coefficient of determination (total R^2), which describes the total explained variation, was calculated. Leukemia, non-Hodgkin lymphoma, and neuroblastoma were entered as separate diagnoses, but to get larger sample sizes, the authors combined sarcoma diagnoses (osteosarcoma and soft tissue sarcoma) for one group and all the other diagnoses (Hodgkin lymphoma, Wilms tumor,

gonadal tumor, retinoblastoma) to a group labeled "other cancer diagnosis."

Internal consistency estimates on reliability using Cronbach alpha were computed in the TF for both survivor and parent proxy versions. All data analyses were conducted using SPSS®, version 13.0. Statistical significance was set at $p < 0.05$.

Results

The response rate was 53% ($n = 199$) for survivors and 55% ($n = 209$) for parents of the survivors. The authors received responses from 252 controls and parents of the controls. A total of 192 survivor-parent pairs (from the same family) and 251 control-parent pairs replied. Table 1 shows the demographic characteristics of responding survivors and their controls. No significant differences were noted between the demographic characteristics of responding survivors and the controls. The survivors' mean age at diagnosis was 3.6 years (range = 0–12 years, $SD = 2.98$). The mean length of survival was 10 years (range = 4–17 years, $SD = 3.25$). The mean age of the parents was 44.1 years for survivors and 44.4 years for

controls. Most of the responding parents were mothers ($n = 196$, 93% for survivors; $n = 240$, 95% for controls).

Self-Reported Fatigue and Comparisons Between the Survivors and Their Controls

Table 2 shows the scale descriptives for the PedsQL Multidimensional Fatigue Scale self-report for survivors and their controls and comparisons between the groups. The survivors scored their GF (median = 87.5) as significantly less ($p < 0.001$) than their SF (median = 70.83). The controls reported significantly more fatigue in TF ($p < 0.01$, median = 80.56 versus 83.33), CF ($p < 0.05$, median = 87.5 versus 91.67), and SF ($p < 0.01$, median = 66.67 versus 70.83) than did survivors.

Parent Proxy Reported Fatigue

Table 2 also shows the scale descriptives for the PedsQL Multidimensional Fatigue Scale by survivors' parent proxy, their controls' parent proxy, and comparisons between the proxy groups. No significant differences were noted in any fatigue score comparisons between the proxy responses. Both proxy respondent groups estimated a high score (least problematic) for their child's CF ranking (median = 91.67) and a low score (most problematic) for their child's SF ranking (median = 75).

Parent and Child Concordance

The survivors scored statistically significantly more fatigue (median = 70.83) in SF ($p < 0.001$) when compared with their parent proxy scores (median = 75). The controls scored statistically significantly more fatigue in SF ($p < 0.001$), CF ($p < 0.01$) and TF scores ($p < 0.001$) compared with their parent proxy scores. As expected, children's self-rated fatigue scores correlated significantly positively with their parent scores (all p values < 0.01 ; Spearman's rho 0.5–0.53 for survivors, 0.43–0.54 for controls).

Associations Between the Demographic and Disease-Related Factors and Fatigue

Male survivors appeared significantly more fatigued in SF score ($p = 0.02$, median = 66.67 versus 75) and CF ($p = 0.05$, median = 87.5 versus 91.67) than female survivors did. In TF (median = 80.56 for males and 84.72 for females) and GF (median = 87.5 for both genders) scores, significant differences were noted. For controls, gender did not have any significant effect on fatigue scores.

Age increase associated with more fatigue in TF ($p = 0.01$, Spearman's rho -0.18) and SF ($p < 0.001$, Spearman's rho -0.13), but not with other fatigue scores. Survivors with additional non-cancer diagnoses scored as significantly more fatigued ($p = 0.03$) in CF (median = 87.5) than those who had no additional diagnoses (median = 91.67). Survivors who needed remedial education

Table 1. Demographic Characteristics of Childhood Cancer Survivors and Their Controls

Characteristic	Survivors (N = 199)		Controls (N = 252)	
	\bar{X}	Range	\bar{X}	Range
Age at study (years)	14.4	11–18	14.5	11–18
Overall average at latest school report ^a	8.08	6–9.7	8.2	6.1–9.9
Characteristic	n	%	n	%
Gender				
Male	101	51	119	47
Female	98	49	133	53
Population in the area of residence				
Less than 10,000	63	32	69	27
10,000–50,000	77	39	102	41
50,001–100,000	21	11	22	9
More than 100,000	38	19	59	23
Need for remedial education at school				
Yes	54	27	71	28
No or not stated	145	73	181	72
Additional noncancer diagnosis				
Yes	51	26	60	24
No or not stated	148	74	192	76
Happiness				
Happy	192	96	241	96
Not happy or not stated	7	4	11	4

^a Higher scores (on a 4–10 scale) indicate better school success. Note. Because of rounding, percentages may not total 100.

at school scored more fatigue in TF ($p = 0.02$, median = 79.86 versus 83.33) and CF ($p < 0.001$, median = 79.17 versus 91.67) compared to those who did not. The overall average grade in the latest school report associated significantly positively (i.e., grade increase associated with less fatigue) with TF ($p = 0.002$, Spearman's rho 0.23), SF ($p = 0.01$, Spearman's rho 0.19), and CF ($p < 0.001$, Spearman's rho 0.25). Survivors' area of residence or self-rated happiness did not have significant effect on fatigue scores.

For controls, age increase was associated with significantly more fatigue in all fatigue scores. Gender and area of the residence did not have a significant effect on controls' fatigue scores. The higher overall average grade in the latest school report and higher HRQOL total score indicated significantly less fatigue in all fatigue scores of the controls. Controls who had needed remedial education reported significantly more fatigue in TF, GF, and CF, and controls who had any noncancer diagnosis scored significantly more fatigue in all fatigue scores. Self-rated unhappiness indicated significantly more fatigue in all fatigue scores for controls.

Table 3 shows the descriptive statistics of cancer-related factors and fatigue of survivors. The survival time increase associated with more fatigue in TF ($p = 0.01$, Spearman's rho -0.18) and SF ($p = 0.01$, Spearman's rho -0.19), but not in other fatigue scores. Such disease-related factors as diagnostic group, treatment modality, relapse status, or age at diagnosis did not have a significant effect on any fatigue scores in the univariate analysis.

Table 4 shows the results of variables that explained the variation in the fatigue of the survivors at each step of the multivariate regression analysis. Age and gender, entered into the regression model at first, explained 6%–14% of the total variation of the scores. Age increase indicated more fatigue. Males were significantly more fatigued in SF than females. Diagnosis, entered into the regression model at the second step, explained an additional 4%–5% of the total variation of the scores. Sarcoma diagnosis indicated statistically significantly more fatigue than a leukemia diagnosis. Treatment modalities, entered at the third step, explained an additional 1%–4% of the total variation of the scores. In step 4, more than 10 years of survival indicated

statistically ($p < 0.001$) more problems with SF. In step 5, additional noncancer diagnosis, need for remedial education at school, and overall average grade at the latest school report explained an additional 2%–4% of the variation of scores. Controlling for overall average grade and other variables in the model, those survivors who did not get remedial education indicated statistically significantly more problems with SF than those survivors who received remedial education at school. The last entered variables, self-rated happiness and HRQOL scores, together with all other variables of the regression model, explained 49%–65% of the variation of the fatigue scores ($p < 0.001$). A better HRQOL score indicated statistically significantly ($p < 0.001$) less problem with fatigue in all dimensions.

Discussion

In this Finnish total population cohort study, fatigue in young survivors of extracranial malignancies was evaluated with self-reports and parent proxy reports. Matched population controls were used. The controls reported significantly more fatigue than the survivors. Both the survivors and their controls suffered most with SF and least with GF. Previous studies have mainly reported fatigue in adult survivors of childhood cancer.

Table 2. PedsQL Multidimensional Fatigue Scale for Survivors and Controls as Well as Proxy Reports

Group	General Fatigue	Sleep or Rest Fatigue	Cognitive Fatigue	Total Fatigue
Child Self-Reports				
Survivors (N=192)				
Median	87.5	70.83	91.67	83.33
Range	12.5–100	8.33–100	12.5–100	18.06–100
Controls (N=251)				
Median	87.5	66.67	87.5	80.56
Range	20.83–100	33.33–100	8.33–100	29.17–100
Difference ^a	0	4.16**	4.17*	2.77**
Parent Proxy Reports				
Parents of survivors (N=192)				
Median	87.5	75	91.67	84.03
Range	30.33–100	20.83–100	25–100	29.17–100
Difference ^b	0	-4.17^{***}	0	-0.7
Parents of controls (N=251)				
Median	83.33	75	91.67	83.33
Range	29.17–100	37.5–100	33.33–100	40.28–100
Difference ^c	4.17	-8.33^{***}	-4.17^{**}	-2.77^{***}

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

^a Represents the difference between the median scores of the survivors and their controls

^b Represents the difference between the median scores of the survivors and of the parents of survivors (calculated for 192 child-parent pairs)

^c Represents the difference between the median scores of the controls and of the parents of controls (calculated for 251 child-parent pairs)

Note. A higher score equals less fatigue.

Table 3. Descriptive Statistics of Cancer-Related Factors and Fatigue of Survivors

Factor	n	%	GF Median	SF Median	CF Median	TF Median
Cancer diagnosis						
Leukemia	110	55	89.58	72.92	91.67	83.33
Non-Hodgkin lymphoma	13	7	83.33	62.5	91.67	79.17
Hodgkin lymphoma	5	3	95.83	79.12	95.83	91.67
Neuroblastoma	15	8	87.5	70.83	75	76.89
Wilms tumor	16	8	87.5	70.83	93.75	81.94
Gonadal tumor	7	4	91.67	79.17	87.5	84.72
Osteosarcoma	6	3	79.17	64.58	77.08	75.69
Retinoblastoma	6	3	97.92	68.75	100	88.89
Soft tissue sarcoma	13	7	81.5	66.67	79.17	79.17
Other	8	4	93.75	81.25	91.67	86.81
Age at diagnosis (years)						
0–4	145	73	87.5	70.83	91.67	81.94
5–9	41	21	87.5	70.83	87.5	83.33
10–12	13	7	91.67	62.5	95.83	84.72
Length of survival (years)^a						
4–10	104	52	91.67	75	91.67	84.72
11–17	95	48	87.5	66.67**	91.67	80.56*
Treatment modality						
Surgery only	7	4	95.83	75	75	81.94
Chemotherapy (alone or with surgery)	115	58	87.5	70.83	91.67	83.33
Radiation (alone or with chemotherapy or surgery)	32	16	87.5	66.67	91.67	80.56
Stem cell transplantation	26	13	89.58	70.83	89.58	83.33
Not known or not stated	19	10	87.5	66.67	83.33	79.17
Relapse						
Yes	16	8	89.58	75	89.58	86.81
No	183	92	87.5	70.83	91.67	81.94

N = 191

* $p < 0.05$; ** $p < 0.01$ ^a Represents the difference between the median scores of the 10 years or less and more than 10 years length of survival time

CF—cognitive fatigue; GF—general fatigue; SF—sleep or rest fatigue; TF—total fatigue

Note. Higher scores equal less fatigue.

Note. Because of rounding, percentages may not total 100.

ment, have greater fatigue than the healthy population control group evaluated by parent proxy. For child self-report in the same study, however, no significant differences were noted between the more than 12 months off treatment group and the healthy population (Varni et al., 2002).

Some explanations for encouraging results in the survivor group may be given. The survivors may have a unique way to deal with fatigue compared to their matched controls. Davies, Whitsett, Bruce, and McCarthy (2002) reported that children with cancer have developed unique strategies, such as conserving, replenishing, and preserving strategies (e.g., resting the mind by trying not to think, creating a quiet environment, taking naps) aimed at resupplying resources and minimizing additional energy loss. In all likelihood, these learning strategies help the survivor move beyond cancer. In addition, these conserving, replenishing, and preserving strategies could be useful in dealing with possible fatigue later in life. On the other hand, the survivors may experience fatigue, in general, differently from healthy children who have not encountered cancer-related fatigue. The survivors may underestimate their fatigue after cancer and its treatment and they also may have

Zelter et al. (1997) reported similar fatigue levels between the adult acute lymphoblastic leukemia survivors and sibling controls. Langeveld, Grootenhuis, Voûte, de Haan, and van den Bos (2003) found less fatigue in adult childhood cancer long-term survivors than in the general population. Mulrooney et al. (2008), on the other hand, reported that adult survivors of childhood cancer reported more fatigue compared to sibling controls. Some reports of young adult childhood cancer survivors have found that fatigue remained the salient aspect of their HRQOL (Langeveld, Ubbink, & Smets, 2000; Sundberg, Lampic, Björk, Arvidson, & Wettergren, 2009; Zebrack & Chesler, 2002). Reports focusing on young survivors of childhood cancer found that long-term survivors of acute lymphoblastic leukemia experienced no more fatigue than their healthy peers when evaluated by parent proxy (Meeske et al., 2004). Varni et al. (2002) found that survivors, more than 12 months off treat-

a more positive view of life and themselves (Sundberg et al., 2009). In addition, survivors may have adapted to their fatigue level (Langeveld et al., 2000) and have become tolerant to the feelings of fatigue, decreasing their inclination to report fatigue (Perdikaris et al., 2008). Therefore, the positive results of self-report with a generic fatigue instrument do not necessarily mean that a survivor is not fatigued. Although generalized instruments are useful for comparing survivors to the general population, the significance and value of experiences of fatigue may be markedly different (Parsons & Brown, 1998). In Woodgate's (2008) qualitative study, children and adolescents with cancer pointed out that their own feelings were hard to put in the scale, and their unique feelings may not exist as described in the instrument. Therefore, in the future, researchers need instruments that are specifically designed for assessing fatigue in young childhood cancer survivors.

Table 4. Summary of the Results of the Multivariate Regression Analysis

Variable	Total Fatigue		General Fatigue		Sleep or Rest Fatigue		Cognitive Fatigue	
	R ²	B	R ²	B	R ²	B	R ²	B
Step 1								
Age at study	–	–1.87***	–	–1.31*	–	–2.74***	–	–1.55**
Gender	–	–	–	–	–	–	–	–
Male	–	–	–	–	–	–	–	–
Female	–	2.99	–	0.3	–	5.36*	–	3.31
R ² change	0.1***	–	0.04	–	0.14***	–	0.06*	–
Total R ²	0.1***	–	0.04	–	0.14***	–	0.06*	–
Step 2								
Diagnosis (leukemia)								
NHL	–	–2.49	–	–3.14	–	–4.07	–	–0.26
Sarcoma	–	–14.28**	–	–13.52*	–	–14.81*	–	–14.52*
NBL	–	–2.3	–	–1.15	–	1.43	–	–7.17
Other	–	–0.85	–	–0.78	–	–2.07	–	0.3
R ² change	0.05	–	0.04	–	0.04	–	0.05	–
Total R ²	0.15***	–	0.08	–	0.18***	–	0.11**	–
Step 3								
Treatment modality								
Surgery alone	–	–	–	–	–	–	–	–
Chemotherapy	–	–4.2	–	–5.57	–	–8.54	–	1.52
Radiation	–	–8.73	–	–11.17	–	–13.42	–	–1.6
SCT	–	–3.17	–	–3.9	–	–5.73	–	0.12
Other treatment	–	–5.09	–	–5.3	–	–11.96	–	1.72
R ² change	0.03	–	0.04	–	0.03	–	0.01	–
Total R ²	0.18**	–	0.12*	–	0.21***	–	0.12*	–
Step 4								
Length of survival								
10 years or less	–	–	–	–	–	–	–	–
More than 10 years	–	–3.6	–	–2.55	–	–6.04*	–	–2.21
R ² change	0.02	–	0	–	0.04*	–	0	–
Total R ²	0.2**	–	0.12	–	0.25***	–	0.12	–
Step 5								
Additional diagnosis								
Yes	–	–	–	–	–	–	–	–
No	–	2.2	–	1.92	–	0.76	–	3.34
Remedial education								
Yes	–	–	–	–	–	–	–	–
No	–	–1.43	–	–1.02	–	–6.54*	–	3.26
Overall average grade	–	2.47	–	2.22	–	3.35	–	1.84
R ² change	0.02	–	0.02	–	0.03	–	0.04	–
Total R ²	0.22**	–	0.14	–	0.28***	–	0.16*	–
Step 6								
Self-rated happiness								
Yes	–	–	–	–	–	–	–	–
No	–	–1.13	–	–0.9	–	0.55	–	–3.05
HRQOL score	–	0.87***	–	0.93***	–	0.81***	–	0.86***
R ² change	0.43***	–	0.43***	–	0.22***	–	0.33***	–
Total R ²	0.65***	–	0.57***	–	0.5***	–	0.49***	–

* p < 0.05; ** p < 0.01; *** p < 0.001

HRQOL—health-related quality of life; NBL—neuroblastoma; NHL—non-Hodgkin lymphoma; SCT—stem cell transplantation

Note. R² is the coefficient of determination, which shows the proportion of effect in the scores, and B is the unstandardized regression coefficient, which shows the direction and amount of the effect of each variable when compared to the reference.

In parent proxy evaluations, the results were mostly in line with their children's self-reports. The literature has produced discussions as to whether the ratings of children and parents have agreement or not. The parent reports may be subject to inflation because of personal stress (Meeske et al., 2004), and parents tend to rate the HRQOL of their children poorer than what the children themselves report (Johnston, Steele, Herrera, & Phipps, 2003). In addition, children or adolescents may want to hide their symptoms from those close to them and, if the child or adolescent feels (or rates) their symptoms as normal, they may not seek help (Woodgate, 2008). Also, parents may be influenced by their children's previous cancer-related fatigue, as discussed earlier. Although fatigue is a subjective symptom and has to be evaluated, whenever possible, from an individual's point of view, situations may arise where children are not capable of answering for themselves. In the current study, parents of survivors were seemingly able to estimate their children's fatigue broadly, similar to the children themselves. This finding is in keeping with the results of a study on chemotherapy-related fatigue by Whitsett et al. (2008). However, Varni et al. (2002) found that concordance intercorrelations between child self-report and parent report were only moderate (effect size = 0.3–0.4), and this supports the need to measure both the child's and his parents' perspectives when evaluating fatigue with the PedsQL Multidimensional Fatigue Scale. In the current study, the survivors scored more fatigue in SF compared to their parent proxy scores. On the other hand, the controls and their parents had agreement only in GF. Despite statistically significant differences, these differences were quite small and are probably not clinically meaningful.

Based on the authors' findings about the effects of the survivors' demographic factors, male survivors had more problems with fatigue than females. This outcome was not in line with other cancer-related fatigue studies. Perdikaris et al. (2008) reported that young girls (ages 7–12 years) with cancer were more fatigued than boys of the same age range. In a study of survivors aged 16–49 years, Langeveld et al. (2003) also reported that females experienced more fatigue than males. Interestingly, in the current study, gender did not have any significant effect on the fatigue scores of the controls.

In the univariate analysis, the age increase and the longer survival time were associated with more severe fatigue. The age and the length of survival also correlated with each other. However, multivariate analyses of more than 10 years of survival indicated significantly more problems only with SF. Therefore, it seems that age is more important, similar to controls where age increase was associated with more fatigue.

The authors' findings on better HRQOL scores indicate that less fatigue is consistent with other studies (Eddy & Cruz, 2007; Meeske et al., 2004, 2007; Varni et

al., 2002). Interestingly, among survivors, the self-rated happiness did not correlate significantly with fatigue, although it did among controls. Of note, however, is that only a few survivors self-reported that they were unhappy. Survivors who needed remedial education at school scored more fatigue in TF and CF compared to those who did not need it. The overall average grade in the latest school report associated positively with TF, CF, and SF scores. This may mean that poorer success at comprehensive school correlates with more fatigue or that excess fatigue leads to poorer school performance. These results are in line with a meta-analysis by Dewald, Meijer, Oort, Kerkhof, and Bogels (2010) in which poor sleep quality and insufficient sleep were significantly associated with poor school performance.

When survivors' fatigue was analysed by disease-related factors, a sarcoma diagnosis was associated with increasing fatigue in multivariable analysis. This finding is consistent with the finding of another study (Aksnes, Hall, Jepsen, Fosså, & Dahl, 2007) where young (age 27–35) survivors of malignant bone tumors (osteosarcoma and Ewing sarcoma) were reported to be more fatigued than the normative sample controls. This result might be caused by physical limitations and impairments for patients with sarcomas after cancer treatment. Another study reported that the adult survivors of childhood leukemia or non-Hodgkin lymphoma without cranial radiation therapy were more likely fatigued than survivors with other cancer diagnoses. The researchers could not find explanation for these findings (Langeveld et al., 2003). In the current study, such disease-related factors as treatment modality, relapse status, or age at diagnosis did not have a significant effect on any fatigue scores. Similar findings have been reported with adult cancer survivors (Servaes, Verhagen, & Bleijenbergh, 2002).

The authors' results suggest that the PedsQL Multidimensional Fatigue Scale is a reliable instrument for self-assessment and parent proxy assessment of fatigue in children and adolescents with regard to the internal consistency of the used instrument. Multidimensional fatigue assessment is more informative than a measure of severity alone (Whitehead, 2009), and the used instrument gives an opportunity to evaluate different dimensions of fatigue. However, this instrument was not originally designed to measure child and parent perceptions of fatigue in the special group of childhood cancer survivors. For example, the PedsQL Multidimensional Fatigue Scale does not separate acute and chronic fatigue, which could be an important aspect for childhood cancer survivors. In previous reports, survivors who have been diagnosed before adolescence have identified fatigue as one part of their entire life and have told that fatigue still negatively impacts their daily lives (Langeveld et al., 2000). In all likelihood, their fatigue is chronic. The other problem of few available fatigue instruments for children and adolescent is that

the cutoff score is unknown, and that information is clinically relevant and meaningful for evaluating children's everyday lives. The problems of the fatigue instruments and adults are similar. A literature review (Whitehead, 2009) on the measurement of fatigue in chronic illness for adults pointed out that only 3 of 22 fatigue measurements have a suggested cutoff score for a clinically relevant level of fatigue. Some studies have used cutoff scores taken from the control population results. However, this is not an ideal solution as normal populations also can be fatigued. Mears, Taylor, Jordan, and Binns (2004) and ter Wolbeek, van Doornen, Kavelaars, and Heijnen (2006) found that fatigue prevalence among healthy adolescents is quite high. This also was seen in the current study, and the fact that many Finnish children and adolescents seem to suffer, particularly from SF, is alarming. The large number of research studies evaluating sleep in adolescents have found that sleep regulation, behavior, and timing substantially change during adolescence, with many not getting sufficient sleep. Sleep deprivation is associated with increased risk for accidents and injuries and has negative effects on control of behavior, emotion, and attention (Carskadon, Acebo, & Jenni, 2004; Dahl & Lewin, 2002; Wolfson & Carskadon, 1998). Therefore, the research for children's fatigue and different dimensions of it are needed as well as more attention paid to the sleep regulation, behavior, and habits of children and adolescents to secure normal development and growth for children and adolescents.

Certain limitations must be considered when interpreting the results of the current study. First, the authors cannot totally exclude the possibility that the most fatigued children and adolescents did not have energy to fill in the questionnaire. However, this did not appear on parent proxy scores. It seems likely that parents whose children are fatigued would have been the most willing to reply. Secondly, leukemia was the most common diagnosis in the study group; leukemia comprises almost 50% of the extracranial childhood malignancies and the prognosis of leukemia is very good.

The strengths of the current study were that the authors were able to use child-parent pairs for statistical

analyses, and that the controls were matched by age, gender, and place of residence.

Conclusion

A limited number of long-term follow-up reports document fatigue as a symptom experienced by survivors of childhood cancer and, to the authors' knowledge, only a few concentrate on young survivors. The authors were unable to identify any studies that used both survivor's self-assessment and parent proxy assessment along with gender, age, and place of residence matched controls. This study has increased the knowledge about the fatigue level of young cancer survivors.

Implications for Nursing Practice

Although survivors seemingly do not experience any more fatigue than their matched controls, subgroups of survivors (e.g., sarcoma survivors) experience excessive fatigue that may have an impact on their HRQOL. The healthcare team should identify these survivors as soon as possible after treatment to prevent fatigue from becoming chronic and to ensure that they have energy for the developmental work of childhood. Interventions to prevent fatigue in young cancer survivors also should be developed in the future.

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