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Abstract
Purpose To understand the influence of disease and treatment on the health-related quality of life (HRQOL) of children with brain tumors, compared to the HRQOL of children with other cancers, from the viewpoints of children and parents.
Methods A total of 133 children aged 5–18 years and 165 parents of children aged 2–18 completed questionnaires of the Pediatric Quality of Life Inventory Cancer Module (Pain and Hurt, Nausea, Procedural Anxiety, Treatment Anxiety, Worry, Cognitive Problems, Perceived Physical Appearance, and Communication scales); higher scores indicate a better HRQOL. The Cancer Module scores, weighted by age and treatment status, were compared to those obtained in a previous study of children with other cancers (mostly leukemia).
Results The weighted mean scores for Pain and Hurt (effect size $d = 0.26$) and Nausea ($d = 0.23$) from child reports and the scores for Nausea ($d = 0.28$) from parent reports were higher for children with brain tumors than scores for children with other cancers. The scores for Procedural Anxiety ($d = -0.22$) and Treatment Anxiety ($d = -0.32$) from parent reports were lower for parents of children with brain tumors than the scores for parents of children with other cancers. The child-reported Pain and Hurt score of the Cancer Module was higher ($d = 0.29$) and in less agreement (*intraclass correlation coefficient* = 0.43) with scores from the Brain Tumor Module, indicating that assessments completed with the Cancer Module misesteem pain and hurt problems in children with brain tumors.

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Conclusions The profiles of cancer-specific HRQOL in children with brain tumors differ from those of children with other cancers; we therefore suggest that these children receive specific psychological support.

Keywords Brain neoplasms · Child · Japan · Quality of life · Questionnaires

Introduction

While modern treatment methodologies have improved the outcome for pediatric cancer survival to approximately 70–80 % [1, 2], managing health-related quality of life (HRQOL) during and after treatment becomes a more important part of treatment. Brain tumors are the second most common (27 %) form of pediatric cancer after leukemia (33 %) [3]. Children with brain tumors often experience pain, nausea, lack of energy, and emotional distress [4, 5] and may also experience late effects, such as endocrinological problems, cognitive impairment, neurological (motor and sensory) disability, and posttraumatic stress symptoms [6–8]. Consequently, survivors of brain tumors who receive intensive treatment [9, 10] are at higher risk of physical, psychological, social, and developmental difficulties than survivors of other cancers [11–14]. By understanding the HRQOL profile of these children, medical practitioners can design targeted interventions to maintain and improve HRQOL in this population during and after treatment.

Global profiles of HRQOL (for example, physical, emotional, and social) in children with brain tumors are lower than those of children with other cancers or without cancer [15–18]. However, little information is available on disease-specific HRQOL profiles in children with brain tumors. Meeske et al. compared cancer-specific HRQOL between children with brain tumors and those with acute lymphoblastic leukemia (ALL) using the parent-reported Pediatric Quality of Life Inventory (PedsQL) Cancer Module [17], finding that parents of children with brain tumors and acute lymphoblastic leukemia report different experiences for their children during and after treatment. This highlights the need to understand how children with brain tumors perceive their own HRQOL.

The disease-specific HRQOL of patients with brain tumors can be measured with one of several cancer-specific tools [19–21], such as the PedsQL Cancer Module, or with a brain-tumor-specific tool [15, 22, 23], such as the PedsQL Brain Tumor Module. Different tools may provide different measures of HRQOL, as the questionnaire structure, number, and time of the questions differ among available tools. Here, we compared cancer-specific HRQOL in children with brain tumors with the HRQOL of children with other cancers, the reported views of children and their parents, and the HRQOL as measured by two PedsQL modules—the PedsQL Cancer and the PedsQL Brain Tumor Modules.

Methods

This study was conducted jointly with the development of the Japanese version of the PedsQL Brain Tumor Module [24].

Study population

Children with brain tumors and their parents were recruited from six hospitals across Japan and from the Children's Cancer Association of Japan (CCAJ) between September and December 2008. Inclusion criteria were as follows: age 5–18 years for children (the parent was included if their child was 2–18 years) and at least 1 month had passed since diagnosis. Children and parents were excluded if physicians at the hospital or social workers of the CCAJ determined that the family found the subject of the child's condition too uncomfortable to discuss.

Procedure

Researchers presented the study aims to 101 children and 122 parents at participating hospitals verbally and in writing, and the CCAJ sent a written notice to all families, inviting them to a meeting regarding brain tumors. Of 55 families from the CCAJ that provided informed consent or assent, 2 families were bereaved, 1 had an adult survivor, 6 children were aged 2–4 years, and 1 child old enough to provide his own consent opted out. A total of 98 children and 120 parents from the hospitals as well as 45 children and 52 parents contacted directly by the CCAJ agreed to participate. Questionnaires were distributed to 143 children and 172 parents.

Questionnaires for children were either self-administered or administered by an interviewer. When providing

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informed consent, parents determined whether or not their child was able to self-administer the questionnaire. In accordance with the PedsQL™ administration guidelines, children aged 5–7 years or who were otherwise determined incapable of self-administration were administered the questionnaire by either their parents or a researcher (children were allowed to decide). In both cases, the instructions and each item were read to the child. Parent report questionnaires were simultaneously self-administered.

The questionnaires were returned by 138 children and 167 parents. We excluded questionnaires from 5 children and 2 parents who did not answer any scales of the PedsQL Cancer Module, and we analyzed answers from 133 children and 165 parents. Next, we analyzed answers from 124 children and 143 parents after omitting questionnaires with missing data for any scale of the PedsQL Cancer Module. Given the lack of any significant differences between the results of the former and latter analyses, we report only the latter.

Ethical considerations

This study was approved by the review boards of all seven participating institutions. Children aged ≥12 years and the parents of all children provided written consent prior to participation. Children aged <12 years provided informed verbal assent.

Measurements

The cancer-specific HRQOL of the PedsQL Cancer Module [21, 25] has eight scales: Pain and Hurt (two items), Nausea (five items), Procedural Anxiety (three items), Treatment Anxiety (three items), Worry (three items), Cognitive Problems (five items), Perceived Physical Appearance (three items), and Communication (three items).

Respondents were asked to describe the extent to which each item troubled them over the past month. Although the PedsQL Cancer Module comprises the standard (covering the previous month) and acute versions (covering the previous 7 days), we used the standard version, because it served as a historical control (described in the next section). For the child reports for ages 8–18 and all parent reports, a 5-point Likert response scale was used (0 = never a problem; 1 = almost never; 2 = sometimes; 3 = often; 4 = almost always). For the child report for children ages 5–7, a 3-point face scale was used. Items were reverse scored and linearly transformed to a 0–100 scale, with higher scores indicating a better HRQOL. To account for missing data, scale scores were computed as the sum of the items divided by the number of items answered. If more than 50 % of the items were missing or incomplete, the scale score was not computed.

Table 1 Characteristics of participants

	This study				Tsuji et al. [25] ($N = 245$)	
	All participants ($N = 165$)		Complete participants ($N = 143$)[a]			
	n	%	*n*	%	*n*	%
Gender						
Male	91	55.5	84	59.2	135	55.1
Female	73	44.5	58	40.8	110	44.9
Age (years)						
2–4	25	15.2	23	16.1	41	16.7
5–7	31	18.8	21	14.7	62	25.3
8–12	56	33.9	48	33.6	75	30.6
13–18	53	32.1	51	35.7	67	27.3
Tumor pathology						
Embryonal tumors	47	29.2	39	27.9	–	–
Germ cell tumors	36	22.4	34	24.3	–	–
High-grade glioma	24	14.9	19	13.6	–	–
Low-grade glioma	39	24.2	33	23.6	–	–
Other tumors	15	9.3	15	10.7	–	–
Treatment status						
On-treatment	63	39.4	56	39.2	88	35.9
Off-treatment ≤ 12 months	23	14.4	21	14.7	33	13.5
Off-treatment > 12 months	74	46.3	66	46.2	124	50.6
Age of guardian (years)						
21–28	7	4.3	4	2.8	5	2.1
29–34	23	14.0	18	12.7	40	16.9
35–39	47	28.7	41	28.9	72	30.4
40–60	86	52.4	78	54.9	120	50.6
≥61	1	0.6	1	0.7	0	0.0
Relationship to patient						
Mother	152	92.1	133	93.0	230	96.2
Father	10	6.1	8	5.6	9	3.8
Other guardian	3	1.8	2	1.4	0	0.0
Guardian's academic background						
Junior high school	3	1.9	2	1.4	4	1.7
High school	63	38.9	49	35.0	87	36.6
Vocational school	28	17.3	27	19.3	44	18.5
Junior college	29	17.9	28	20.0	48	20.2
University	36	22.2	32	22.9	52	21.8
Graduate school	3	1.9	2	1.4	1	0.4
Other	0	0.0	0	0.0	2	0.8

Missing data were excluded

[a] Sample without missing data for any scale of the PedsQL Cancer Module

The PedsQL Brain Tumor Module [15, 24] has six scales. Questions about Nausea, Procedural Anxiety, and Worry scales are identical to those in the PedsQL Cancer Module, whereas questions on the Pain and Hurt scale (three items) and Cognitive Problems scale (seven items)

differ from those in the PedsQL Cancer Module. The parent report for toddlers (ages 2–4) does not include the Cognitive Problems scale. The Movement and Balance scale is not reported here. Agreement between the parent and child reports (intraclass correlation coefficient [ICC]) was described previously as follows: 0.41 (Pain and Hurt), 0.65 (Nausea), 0.62 (Procedural Anxiety), 0.18 (Worry), and 0.49 (Cognitive Problems) [24].

Respondents were asked to describe the extent to which each item troubled them over the previous 7 days. Although the recall period of the questionnaire differed from that of the Cancer Module, no published studies using the Brain Tumor Module as the standard (1 month) version were available when the present study was planned and designed. Because the PedsQL Brain Tumor Module adopts the acute version (covering the previous 7 days) as a standard, we employed the acute version. The respondents, response scale, and scoring method were identical to the PedsQL Cancer Module. Parents were also asked to record their child's gender, date of birth, age, tumor pathology, date of diagnosis, and date of therapy completion.

Historical control

We used data reported by Tsuji et al. [25] as a control. This study reported scores from for Japanese children with cancer (67.8 % had leukemia, 9.0 % had malignant lymphoma, followed by neuroblastoma, Wilm's tumor, rhabdomyosarcoma, and hepatoblastoma) using the Japanese version of the PedsQL Cancer Module. Children with brain tumors were excluded in that study.

The average age of children with cancer was 10.5 years (standard deviation [SD] = 3.9 years), and 55.1 % of patients were boys (Table 1). Mothers answered 93.9 % of the questionnaires, and parents' ages ranged between 40 and 60 years.

Statistical analysis

Statistics were calculated using IBM SPSS software, version 19 (SPSS, Inc., Chicago, IL, USA), and the level of significance was defined as 0.05. We calculated the sample characteristics as follows: age distribution, disease, and treatment characteristics; and scale characteristics as follows: mean, SD, minimum and maximum scores. The internal consistency of each subscale was estimated using Cronbach's alpha coefficient [26] (good consistency > 0.70). The agreement between the child and parent reports was estimated using ICC in a two-way mixed effects model [27] (ICC value of 0.20 indicates fair agreement, 0.40 moderate, 0.60 good, and 0.80 high agreement).

The cancer-specific HRQOL of children with brain tumors was compared to the HRQOL of children with other cancers. We compensated for the effect of age (toddler, young child, school child, or adolescent) and treatment status (on-treatment, soon after treatment, or off-treatment) differences using the weighted means and SDs of the PedsQL Cancer Module scale scores, adjusted for age and treatment status. The age distribution of leukemia and brain-tumor onset differs [29, 30], and previous reports have found that treatment status affects the PedsQL Cancer Module score [21, 25]. We also found in this study that the treatment status affected the PedsQL Cancer Module score (see electronic Supplementary Table 1).

These values were calculated by dividing the total sample into different groups based on age and treatment status. The control study sample size (Nc_{total}) was 245, and the brain-tumor sample size (N_{total}) was 165 if all respondents completed the PedsQL Cancer Module scale. The control and study populations were divided into groups (Nc_{ij} and N_{ij}) separated by treatment status (on-treatment, off-treatment $\leq$12 months, or off-treatment >12 months; $i = 1$–3) and by age (2–4, 5–7, 8–12, or 13–18 years; $j = 1$–4). The weighted means [31] were calculated as follows:

$$\text{Weighted mean}(\bar{X}) = \sum_{k=1}^{N_{total}} W_k X_k / \sum_{k=1}^{N_{total}} W_k.$$

$$\left(\text{The common mean} = \sum_{k=1}^{N_{total}} X_k / N_{total}\right).$$

$$W_k = \left(\frac{Nc_{ij}}{Nc_{total}}\right) / \left(\frac{N_{ij}}{N_{total}}\right).$$

where X_k was the PedsQL Cancer Module scale score of each respondent that belonged to treatment status i and age j; the weights for each respondent (W_k) were calculated from the ratio of the age and treatment status of the standard population, divided by the proportion of the age and treatment status in this study.

The weighted SDs were calculated using the same weight (W_k) as follows:

$$\text{Weighted SD} = \sqrt{\sum_{k=1}^{N_{total}} W_k (X_k - \bar{X})^2 / \left(\sum_{k=1}^{N_{total}} W_k - 1\right)}.$$

$$\left(\text{The common SD} = \sqrt{\sum_{k=1}^{N_{total}} (X_k - \bar{X})^2 / (N_{total} - 1)}.\right)$$

We compared the cancer-specific HRQOL using Welch's t test and calculated the effect size d from the difference between the two means divided by the pooled SD of both samples.

Table 2 PedsQL Cancer Module scores of children with brain tumors ($N = 143$)

	Mean	SD	Min.	Max.	Alpha[a]	ICC[b]
Child report (n = 124)						
Pain and Hurt	90.4	17.6	0	100	0.62	0.20
Nausea	87.5	20.6	15.0	100	0.86	0.68
Procedural Anxiety	74.5	30.8	0	100	0.88	0.70
Treatment Anxiety	92.8	19.0	0	100	0.88	0.41
Worry	81.9	23.4	0	100	0.76	0.27
Cognitive Problems	73.6	22.4	0	100	0.78	0.44
Perceived Physical Appearance	73.8	26.3	0	100	0.71	0.28
Communication	68.5	29.9	0	100	0.77	0.45
Parent report (n = 143)						
Pain and Hurt	84.5	20.0	0	100	0.83	
Nausea	84.7	22.6	15.0	100	0.93	
Procedural Anxiety	59.8	35.4	0	100	0.96	
Treatment Anxiety	79.7	23.1	0	100	0.93	
Worry	78.3	22.3	0	100	0.86	
Cognitive Problems	66.0	23.8	0	100	0.89	
Perceived Physical Appearance	70.6	24.6	0	100	0.81	
Communication	59.5	29.6	0	100	0.89	

ICC intraclass correlation coefficient, *Max.* maximum, *Min.* minimum, *SD* standard deviation

[a] Cronbach's alpha coefficient

[b] ICC values for child and parent reports in the two-way mixed effects model ($n = 124$)

The agreement of the two modules was evaluated using paired t tests; the effect size d (the mean score difference divided by SD of the mean score difference) [28] designated as small (0.20), medium (0.50), and large (0.80) in magnitude and by the ICC calculated from a one-way random effects model [27].

Results

Sample characteristics

The median age of the children with brain tumors was 10.0 years (range: 2–18) (Table 1), and the sample was heterogeneous for tumor pathology. Most children presented with embryonal tumors, low-grade gliomas, and germ cell tumors. Median age at diagnosis was 6.0 years; 63 children (39.4 %) were still receiving treatment, while 97 (60.6 %) had completed treatment, and the interval from completion of treatment to the survey ranged from 0.1 to 13.3 years. Most children on treatment were younger than the children who had completed treatment.

With the exceptions noted below, no significant differences were observed between the characteristics of the children and their parents and those of the historical control (Table 1). The differences were as follows: The present study enrolled fewer children between the ages of 5 and 7 years and more between the ages of 13 and 18 years ($P = 0.069$, Chi-square test).

Scale descriptions

The child-reported scores were higher than parent-reported scores on all scales of the PedsQL Cancer Module and were internally consistent for all scales except for the Pain and Hurt scale (Cronbach's alpha coefficient = 0.62); parent-reported scores were internally consistent for all scales (Table 2). Agreement between the child and parent reports was good for the Nausea and Procedural Anxiety scales, moderate for the Treatment Anxiety, Cognitive Problems, and Communication scales, and fair for the Pain and Hurt, and Perceived Physical Appearance scales.

Cancer-specific HRQOL in children with brain tumors compared with the HRQOL of children with other cancers

We noted small but significant differences between the children's reports for Pain and Hurt ($d = 0.26$) and Nausea ($d = 0.23$) and the parents' reports for Nausea ($d = 0.28$), Procedural Anxiety ($d = -0.22$), and Treatment Anxiety ($d = -0.32$) (Table 3). The scores for Pain and Hurt and Nausea were higher for children with brain tumors than for children with other cancers, indicating better HRQOL. However, the scores for Procedural Anxiety and Treatment Anxiety were lower for children with brain tumors than for children with other cancers, indicating worse HRQOL. The direction of the effects was the same for the scales reported by parents and children.

Table 3 Comparison of cancer-specific HRQOL in children with brain tumors and those with other cancers

	This study[a]		Tsuji et al. [25][b]			P[c]	Effect size d[d]
	Mean	SD	n	Mean	SD		
$N = 143$							
Child report ($n = 124$)							
Pain and Hurt	89.8	19.3	202	84.7	19.7	0.024	0.26
Nausea	88.0	20.0	199	83.0	24.0	0.044	0.23
Procedural Anxiety	72.5	32.8	203	72.9	31.0	0.910	−0.01
Treatment Anxiety	90.7	22.8	203	93.1	17.0	0.302	−0.12
Worry	81.0	25.8	202	76.6	25.9	0.140	0.17
Cognitive Problems	72.3	23.8	200	71.5	22.1	0.775	0.03
Perceived Physical Appearance	71.9	28.7	204	70.3	28.6	0.639	0.05
Communication	65.5	32.6	204	67.0	27.0	0.656	−0.05
Parent report ($n = 143$)							
Pain and Hurt	84.9	20.9	242	82.9	22.0	0.367	0.09
Nausea	87.0	20.8	233	80.5	25.7	0.008	0.28
Procedural Anxiety	55.7	36.6	242	63.2	31.8	0.043	−0.22
Treatment Anxiety	77.9	24.4	241	84.9	19.0	0.004	−0.32
Worry	79.0	23.6	242	81.4	21.9	0.334	−0.10
Cognitive Problems	65.8	24.9	243	69.4	21.6	0.151	−0.15
Perceived Physical Appearance	71.7	25.3	243	73.8	24.9	0.437	−0.08
Communication	60.1	31.1	241	62.2	25.4	0.496	−0.07

HRQOL health-related quality of life, *SD* standard deviation

[a] Means and SDs of the PedsQL Cancer Module score in children with brain tumors adjusted for age and treatment status to subjects reported by Tsuji et al. [25]

[b] Previously reported data in children with the other cancers

[c] P value from the Welch t test

[d] Effect size d defined by Cohen [28] is the difference between two means divided by a pooled SD with two samples. A positive value indicates that children with brain tumors have higher HRQOL scores compared with children with other cancers

Agreement between the PedsQL cancer and the PedsQL Brain Tumor Modules of the PedsQL

Children and parents reported higher Pain and Hurt scores ($d = 0.29$, $P = 0.001$ and $d = 0.22$, $P = 0.010$, respectively) on the Cancer than on the Brain Tumor Module (Table 4). Children reported higher Procedural Anxiety ($d = 0.31$, $P = 0.001$) and Cognitive Problems scores ($d = 0.28$, $P = 0.003$) on the Cancer Module. The agreement between the PedsQL Cancer and the PedsQL Brain Tumor Modules was very high (ICC > 0.80) except for the Pain and Hurt scale for the child report where the agreement was moderate (ICC = 0.43). The agreement according to treatment status is shown in Supplementary Table 2.

Discussion

We report here that children with brain tumors perceive their HRQOL differently from children with other cancers. Several aspects of HRQOL were more difficult (for example, procedural and treatment anxiety) for patients with brain tumors, while other aspects (nausea, pain and hurt) were less difficult, and a number of factors may be responsible for these differences. In particular, the brain is the center of multiple functions. The brain integrates the information received from, and coordinates the physical and mental activity of, the whole body. Thus, the unique HRQOL of children with brain tumors likely reflects the vast complexity of brain function. Knowledge of these differences should help medical practitioners design-specific support and care strategies for these children.

A total of 29 % of children in this study suffered from embryonal tumors (mainly medulloblastomas), and treatment for these tumors requires surgery, radiation, and chemotherapy [32, 33]. The main treatments for children with germ cell tumors (mainly germinomas) include surgery, radiation, and chemotherapy [34], with chemotherapy representing the main treatment for children with leukemia (controls). Each treatment method will affect a child's HRQOL differently.

Table 4 Comparison of cancer-specific HRQOL using the PedsQL cancer and PedsQL Brain Tumor Modules

	n	Dif.[a]	95 % CI of the Dif.		*P*[b]	Effect size *d*[c]	ICC (5–18 years)[d]	ICC (2–18 years)[e]
			Lower	Upper				
$N = 143$								
Child report ($n = 124$)								
Pain and Hurt	124	5.41	2.12	8.70	0.001	0.29	0.43	–
Nausea	124	0.91	−0.91	2.72	0.325	0.09	0.88	–
Procedural Anxiety	123[f]	4.34	1.80	6.87	0.001	0.31	0.89	–
Worry	124	1.95	−0.39	4.30	0.102	0.15	0.84	–
Cognitive Problems	124	3.64	1.29	5.99	0.003	0.28	0.81	–
Parent report ($n = 143$)								
Pain and Hurt	143	2.50	0.60	4.40	0.010	0.22	0.82	0.91
Nausea	143	0.59	−1.20	2.39	0.515	0.05	0.91	0.89
Procedural Anxiety	142[f]	2.14	−0.77	5.05	0.148	0.12	0.88	0.87
Worry	143	1.46	−0.20	3.11	0.084	0.15	0.90	0.90
Cognitive Problems	124[g]	−0.99	−2.89	0.91	0.304	−0.09	0.89	–

CI confidence interval, *Dif.* difference, *HRQOL* health-related quality of life, *ICC* intraclass correlation coefficients, *PedsQL* pediatric quality of life inventory, *SD* standard deviation

[a] Mean score differences (PedsQL Cancer Module—PedsQL Brain Tumor Module). A positive value indicates that participants (children with brain tumors or parents of children with brain tumors) have higher scores in the PedsQL Cancer Module (fewer problems) than in the PedsQL Brain Tumor Module

[b] *P* value from the paired *t* test

[c] Effect size *d* defined by Cohen [28] is the mean score difference divided by SD of the mean score difference. A positive value indicates that participants (children with brain tumors or parents of children with brain tumors) scored higher in the PedsQL Cancer Module (fewer problems) than the PedsQL Brain Tumor Module

[d] ICC values for the PedsQL Cancer Module and the PedsQL Brain Tumor Module in the one-way random effects model among children aged 5–18 years

[e] ICC values for the PedsQL Cancer Module and the PedsQL Brain Tumor Module in the one-way random effects model among children aged 2–18 years

[f] Missing data for the Brain Tumor Module ($n = 1$) were excluded

[g] The PedsQL Brain Tumor Module parent report for toddlers (ages 2–4) does not include the Cognitive Problems scale

Children with brain tumors reported less difficulty with pain and hurt than children with other cancers; however, we believe it unlikely that these children actually experienced less pain, as here and in a previous study [17], parents reported similar difficulty with pain and hurt irrespective of cancer type. Children with brain tumors reported pain and hurt more frequently than children with lymphoma at a similar frequency to children with leukemia and less frequently than children with solid tumors [4]. These inconsistencies may arise due to scale characteristics. The agreement between Pain and Hurt scores in the Cancer and Brain Tumor Modules was moderate, while the agreement on other scales was high. These findings suggest that the Pain and Hurt scale of the PedsQL Cancer Module may not consider problems for children with brain tumors compared with the Brain Tumor Module.

The Pain and Hurt scale of the Cancer Module asks about generalized body pain but does not localize the pain. For example, "I ache or hurt in my joints and/or muscles," versus "I hurt a lot." Further, the Brain Tumor Module measures two items present in the Cancer Module and, uniquely, "I get headaches." Thus, the Brain Tumor Module includes a question about headaches, which are frequent in patients and survivors of brain tumors [35]. Headache is the most frequently reported initial symptom of pediatric brain tumors in children aged ≥2 years and may be interpreted with particular meaning for these children [36]. Headache would remind the children and parents of the first brain tumor and induce worry about a relapse. Such headaches cause physical distress and psychosocial concern. Therefore, we prefer to use the Brain Tumor to the Cancer Module to measure disease-specific HRQOL for these children.

Children with brain tumors and their parents reported less difficulty with nausea than children with other cancers. Causes of nausea may include side effects of chemotherapy, radiation sickness, postoperative reactions, tumors close to the area postrema, intracranial hypertension, gastrointestinal pathology, and anxiety [37, 38]. Here, at least 1 month had passed since diagnosis, and factors such as

postoperative reaction, brain-tumor activity, and intracranial hypertension would have been controlled, resulting in less difficulty with nausea [39, 40].

Patients may experience strong nausea and vomiting at the onset of brain tumors as well as in the perioperative period; therefore, pediatric patients may evaluate their experience with treatment-induced nausea and vomiting as less trying than that experienced perioperatively. In contrast, children with ALL (control group majority) are treated at the first remission-induction phase using moderately emetogenic chemotherapy (i.e., vincristine, daunorubicin, L-asparaginase) [41], and severe emetogenic chemotherapy (i.e., cyclophosphamide, ifosfamide) is added during the intensification phase. Treatment type and course will affect a child's experience, so a longitudinal study will be required to assess how the experience of children with brain tumors changes after diagnosis and treatment.

Parents of children with brain tumors reported more procedural and treatment anxiety for their children than did the parents of children with other cancers. The PedsQL Cancer Module evaluates children's and parents' perception of a child's anxiety about needle sticks, blood tests, seeing a doctor, and hospitalization, which relate to trauma and stressor-related symptoms that are classified as anxiety disorders. Perceived life threat and treatment intensity are directly associated with posttraumatic stress disorder [42]. We assume that intensive symptoms and the treatment of pediatric brain tumors increase anxiety.

Our findings here of increased anxiety in children with brain tumors differ from those of a previous study conducted in the United States [17]. Although we cannot explain the reason for this discrepancy, pediatric oncology practice differs between the United States and Japan [43], and patients in Japan may not be fully informed of the diagnosis, which affects posttraumatic stress disorder [44]. Cognitive problems of children with brain tumors might also limit their understanding of disease and treatment course. Each child's psychological readiness for each stage of the diagnosis and treatment may be affected by the information provided and by the child's cognitive ability.

Several limitations of the present study warrant mention. First, the study and controls were heterogeneous and included various pathologies. All children in this study suffered central nervous system damage from invasion, compression, or hydrocephalus as well as from therapy. Further investigations of tumor types and treatment should reveal how HRQOL differs between children with brain tumors and those with other cancers.

Second, data obtained from children and parents were not completely equivalent; the ages of self-reporting children ranged between 5 and 18 years, whereas parental-reporting included children 2–18 years of age. Further, the varying degrees of patients' impairments prevented optimum accuracy of reporting [17]. However, the number of children participating in the present study (133) was similar to that of participating parents of children aged 5–18 years (140) because of assisted administration. Further, HRQOL reporting by children is not significantly influenced by the administration technique [24, 45].

Third, the PedsQL Cancer and Brain Tumor Modules employ different recall periods, as described above [15, 25]. This difference must be taken into account when interpreting data. Although the items on the Procedural Anxiety subscale are identical in both modules, children with brain tumors studied here reported less difficulty with procedural anxiety using the Cancer than with the Brain Tumor Module. The recall period may alter a child's perception of procedural anxiety. Further research is required to determine why children reported less anxiety over the past month than over the previous 7 days.

Fourth, our ability to generalize the data is limited. For example, at the CCAJ, several hundred families, including those not eligible to participate, were notified of this study; therefore, the true response rate is unknown. Families were excluded if doctors or social workers determined that the family found the child's condition too uncomfortable to discuss. Although the number of such excluded families was not recorded, this exclusion may have limited data collection.

Fifth, when comparing children with brain tumors to those with other cancers, certain parental characteristics could not be taken into account, as Tsuji et al. [25] did not report them. Parental reports might have been influenced by factors such as parental mental health, which may limit comparability. However, all child and parent characteristics reported here, except for age and tumor pathology, were similar.

Conclusion

Here, we found that children with brain tumors reported less difficulty with the categories of pain and hurt and nausea than children with other cancers that included mostly leukemia. Parents of the children with brain tumors reported more procedural and treatment anxiety. The information will help medical professionals and researchers to understand the influence of the disease and treatment on the HRQOL of children with brain tumors regardless of age and treatment status.

This study is the only comparison, to our knowledge, of the PedsQL Cancer and Brain Tumor Modules. The PedsQL Cancer Module compares cancer-specific HRQOL of children with brain tumors and those with other cancers. However, the PedsQL Brain Tumor Module is more

sensitive for brain-tumor-specific aspects of the HRQOL and should be used to assess HRQOL in children with brain tumors.

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ORIGINAL ARTICLE

Recent employment trend of childhood cancer survivors in Japan: a cross-sectional survey

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Abstract
Background Previous research has shown that some adult childhood cancer survivors (CCSs) have experienced employment difficulties. However, the actual employment status of CCSs in Japan has not been studied.
Participants and methods The participants were selected from the membership directory of Heart Link mutual-aid health insurance and recruited by the Childhood Cancer Patients' Network. We conducted a cross-sectional survey (a self-rated questionnaire on employment) via postal mail or an email communication with a link to an Internet website. We explored the association between the characteristics of CCSs who require disability qualification and having experienced unemployment. The adjusted odds ratios (ORs) for the factors with an outcome of interest were estimated with logistic regression analysis.
Results In total, 44 CCSs indicated that they had a disability qualification. The significant independent factors related to needing a disability qualification were late effects [OR 12.3; 95 % confidence interval (CI) 3.37–45.2], brain tumors (OR 9.55; 95 % CI 1.90–48.0), and being a high school graduate (OR 9.86; CI 2.67–36.4). The unemployment rate was 15.9 % among CCSs, excluding homemakers and students. Approximately 70 % of unemployed CCSs had some late effects; independent factors related to unemployment were late effects (OR 6.22; 95 % CI 1.80–21.40), dropping out of school (OR 8.46; 95 % CI 1.66–43.10), and brain tumors (OR 2.73; 95 % CI 0.83–8.96). Most unemployed CCSs were likely to seek work, despite their health problems.
Conclusions The unemployment rate is not high in Japan, but some CCSs need extended disability qualification. The independent factors related to unemployment were late effects and dropping out of school.

Keywords Childhood cancer survivors · Employment · Unemployment · Occupation · Social outcome · Disability

Abbreviations

CCS	Childhood cancer survivors
CCSS	The Childhood Cancer Survivor Study
OR	Odds ratio
CI	Confidence interval

Introduction

Because of advances in treatment, 70–80 % of children diagnosed with cancer become long-term survivors. In Japan, the estimated number of childhood cancer survivors (CCSs) is greater than 50,000, and we expect that at least 30,000 survivors have already reached adulthood (20 years of age or older). Although there is an increased number of CCSs, many survivors experience various health problems

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later in life because of the cancer and its treatment [1, 2]. In addition, these various physical problems (termed "late effects") also seem to affect CCSs' social outcomes (e.g., marriage, education, and employment, etc.), both directly and indirectly [3].

Previous research has suggested that adult CCSs experience employment difficulties [4–7]. In the previous Childhood Cancer Survivor Study (CCSS), a greater percentage of survivors reported a lack of any employment in the past 12 months (9.3 %) than their siblings did (6.7 %) [8]. Elevated risk for never having been employed was associated with failing to complete high school, young age (<4 years) at diagnosis, cranial radiation therapy of 30 Gy, and being female [9]. CCSs from all diagnostic categories were less likely to have been employed during the past 12 months than members of the sibling group; the age- and sex-adjusted likelihood of being employed was lowest among brain and bone tumor survivors [9].

Despite these findings, the actual employment status of CCSs in Japan has not been studied. In the current study, we conducted a cross-sectional survey of CCSs in Japan in order to identify their employment outcomes.

Participants and methods

Study design

We performed a cross-sectional survey (a self-rated employment questionnaire) via postal mail or email with a link to an Internet website (see Supplemental Appendix 1). The study was conducted from July until September 2012.

Participants

The first sample group was selected from 631 applications to or the membership directory of Heart Link mutual-aid health insurance in Niigata [10]. The second sample group was recruited from the Childhood Cancer Patients' Network, including the Pediatric Brain Tumor Association in Japan [11].

Survey method

The first group was sent a brochure explaining the purpose and methods of the study, and asking them to return the questionnaire directly to the Heart Link mutual-aid health insurance office by postal mail anonymously within 1 month. The second group was sent an email explaining the purpose and methods of the study, and asking them to respond to the questionnaire via an Internet website link. Informed consent was assumed if the participant returned the questionnaire.

The questionnaire consisted of 32 items, with 9 items (questions Q1–8 and Q15) that asked about the participant's basic characteristics. Through the questionnaire, we evaluated regular, routine checkups (Q9), health status and the presence of late effects (Q10–Q11), disability qualification (Q12 and 14), employment (Q13), marriage (Q16–17), and present issues found worrisome (Q18). Through Q21–Q23, we assessed job satisfaction, influence of childhood cancer experience, and sharing about the cancer diagnosis with one's employer. Q24 through Q30 assessed unemployment-related issues: reasons for unemployment, employment difficulties, worries about unemployment, major living costs, and whether participants' and/or their parents want them to work. Q31 assessed worries of student CCSs about future employment.

Ethical issues

The study was performed in accordance with the Declaration of Helsinki and approved by the ethics committee of St. Luke's International Hospital, no. 12-R046.

Statistical analyses

We performed χ^2 tests (or Fisher's exact tests for cells with expected counts of more than five) within categorical predictors. A trend test was used to rank trends of health and economic status over CCSs with late effects. We explored the association between characteristics of the CCSs who required a disability qualification (limited to the CCSs who were 18 years or older to evaluate educational achievement) and those who had experienced unemployment (excluding housewives and students). The adjusted odds ratios (ORs) for factors with an outcome of interest were estimated with logistic regression analysis. Data were analyzed with SPSS software, v. 20.0 (IBM Japan, Tokyo, Japan).

Results

A total of 240 questionnaires (217 from the first sample group and 23 from the second sample group) were collected by November 2012. The response rate was 34.4 % (217 out of 631) for the first sample group. The response rate for the second sample group could not be calculated because we only informed the web-site homepage of this research to the Childhood Cancer Patients' Network and we couldn't know the number of the CCSs who have watched the homepage. One questionnaire was excluded because the CCS did not answer the questionnaire him/herself. There were 123 male and 116 female respondents.

Demographic data

The participants' demographic characteristics are listed in Table 1. The mean age was 24.3 years (median 24; range

Table 1 Background of the participating childhood cancer survivors

	Male ($n = 123$)	Female ($n = 116$)	χ^2 (p value)
Age at survey (years)			
20 years or younger	39 (32 %)	33 (28 %)	0.226
21–24 years	26 (21 %)	30 (26 %)	
25–29 years	35 (29 %)	23 (20 %)	
30 years or older	22 (18 %)	30 (26 %)	
Diagnosis of cancer			
Leukemia	60 (50%)	66 (57 %)	0.681
Lymphoma	15 (13 %)	8 (7 %)	
Other solid cancers	18 (15 %)	19 (16 %)	
Bone/soft tissue sarcoma	7 (6 %)	6 (5 %)	
Brain tumor	20 (17 %)	17 (15 %)	
Age at diagnosis (years)			
3 years or younger	36 (29 %)	33 (28 %)	0.341
4–7 years	32 (26 %)	25 (22 %)	
8–12 years	27 (22 %)	37 (32 %)	
13 years or older	28 (23 %)	21 (18 %)	
Treatment			
Chemotherapy	108 (88 %)	106 (91 %)	0.367
Radiation	63 (51 %)	59 (51 %)	0.956
Surgery	47 (38 %)	42 (36 %)	0.749
Stem cell transplantation	29 (24 %)	19 (16 %)	0.165
Immunotherapy	6 (4 %)	3 (3 %)	0.501[a]
Others	11 (9 %)	6 (5 %)	0.257
Regular checkup (per year)			
None	37 (30 %)	30 (26 %)	0.327
Once per several years	2 (2 %)	7 (6 %)	
Once	40 (33 %)	43 (37 %)	
Twice	20 (16 %)	12 (10 %)	
Three times	7 (6 %)	9 (8 %)	
More than four times	17 (14 %)	15 (13 %)	
Living district			
Hokkaido/Tohoku	5 (4 %)	9 (8 %)	0.516
Kanto (excepting Niigata)	48 (39 %)	38 (33 %)	
Niigata	31 (25 %)	25 (22 %)	
Tokai/Hokuriku	13 (11 %)	10 (9 %)	
Kinki	13 (11 %)	14 (12 %)	
Chu-shikoku/Kyusyu	13 (11 %)	19 (17 %)	
Education			
Junior high school	10 (8 %)	8 (7 %)	0.263[a]
High school	35 (29 %)	26 (22 %)	
College or vocational school	16 (13 %)	25 (22 %)	
University or graduate school	53 (43 %)	53 (46 %)	
Dropout	9 (7 %)	4 (3 %)	

[a] Fisher's exact test

16–42 years). While female CCSs tended to be somewhat older, this difference was not significant. More than half of the CCSs (both male and female) had suffered from hematological cancers, and approximately 15 % had suffered from brain tumors and solid cancers, respectively. The mean age at cancer diagnosis was 7.5 years (median 7; range 0–19 years). The mean age at treatment completion was 10.4 years (median 10; range 0–27 years), and this survey was conducted approximately 14 years after treatment completion. Regarding primary cancer treatment, 90 % of CCSs received multiagent chemotherapy, 51 % received radiation, 37 % underwent surgery, and 20 % received hematopoietic stem cell transplantation. There were no statistical differences between males and females for all basic characteristics. Approximately 28 % of CCSs had not had a regular checkup at the time of this survey, but 33 % had regular checkups once per year, and another 33 % had two or more regular checkups per year. There was no statistical difference between the geographic locations of males and females; a majority of the participants lived in the Kanto area, including the Niigata prefecture.

CCS characteristics

Table 2 lists the current status of different CCS characteristics according to gender. Nearly half of the CCSs reported the presence of various late effects. The most predominant late effects were endocrinological problems and short stature, which was found in both males and females. The marriage rate of females was significantly higher than that of males in the 30 years or older group. There were 17 male and 16 female unemployed CCSs; 8 of the females were housewives. The unemployment rate was 15.9 % (25 of 157), excluding homemakers and students. More than half of CCSs were in good health, and approximately 10 % were in poor or bad health. Approximately 50 % reported good or fair economic status, but male CCSs reported poor or bad economic status significantly more often than females did.

Association between CCS characteristics and late effects

The prevalence of late effects was significantly associated with multiple CCS characteristics (see Table 3). The specific cancer diagnosis was associated with different proportions of reported late effects: CCSs who had been diagnosed with a brain tumor or bone/soft tissue sarcoma reported significantly more prevalence of late effects than those with other diagnoses (76 and 67 %, respectively). With respect to cancer treatment, radiation, surgery, and stem cell transplantation were associated with a higher prevalence of late effects than other treatments (66, 61, and 77 %, respectively). Approximately 70 % of unemployed CCSs experienced some late effects compared with 44 % of employed CCSs. Finally, CCSs who had better subjective health and economic status were significantly less likely to report late effects.

Table 2 Present status of the total childhood cancer survivors

	Male (n = 123)	Female (n = 115)	χ^2 (p value)
Late effects			
Yes	60 (49 %)	52 (45 %)	0.582
Endocrinological problems	22 (18 %)	26 (22 %)	0.383
Short stature	20 (16 %)	13 (11 %)	0.258
Neurocognitive problems	10 (8 %)	7 (6 %)	0.529
Skin/hair loss	9 (7 %)	6 (5 %)	0.494
Eye problems	5 (4 %)	6 (5 %)	0.683
Hearing imparement	5 (4 %)	4 (3 %)	0.999[a]
Bone/muscle problems	4 (3 %)	2 (2 %)	0.684[a]
Psychological problems	3 (2 %)	2 (2 %)	0.999[a]
Surgery-related problems	3 (2 %)	2 (2 %)	0.999[a]
Secondary cancer	0	2 (2 %)	0.235[a]
Marriage			
20 years or younger	0/39 (0 %)	0/33 (0 %)	N/A
21–24 years	1/25 (4 %)	1/30 (3 %)	0.718[a]
25–29 years	3/35 (9 %)	5/23 (22 %)	0.259[a]
30 years or older	7/22 (32 %)	15/30 (50 %)	0.040
Employment			
Yes	66 (54 %)	66 (57 %)	0.733
No at present	16 (13 %)	16[b] (14 %)	
Never	1 (1 %)	0	
Student	40 (33 %)	34 (29 %)	
Health status at present			
Good	61 (50 %)	67 (58 %)	0.418
Fair	23 (19 %)	19 (16 %)	
Moderate	28 (23 %)	17 (15 %)	
Poor	9 (8 %)	12 (10 %)	
Bad	2 (2 %)	1 (1 %)	
Economic status			
Good	12 (10 %)	23 (20 %)	0.043
Fair	42 (35 %)	48 (42 %)	
Poor	33 (28 %)	21 (18 %)	
Bad	14 (12 %)	6 (5 %)	
Unknown	19 (16 %)	16 (14 %)	

N/A not applicable

[a] Fisher's exact test

[b] Eight out of 16 female CCSs were housewives

Table 3 Association factors or status with late effects

Late effects	Yes (n = 112)	No (n = 123)	χ^2 (p value)
Age at survey (years)			
20 years or younger	32 (44 %)	40 (56 %)	0.914
21–24 years	26 (46 %)	30 (54 %)	
25–29 years	27 (47 %)	31 (53 %)	
30 years or older	26 (51 %)	25 (49 %)	
Diagnosis of cancer			
Leukemia	52 (41 %)	74 (59 %)	0.002
Lymphoma	9 (39 %)	14 (61 %)	
Other solid cancers	15 (41 %)	22 (59 %)	
Bone/soft tissue sarcoma	8 (67 %)	4 (33 %)	
Brain tumor	28 (76 %)	9 (24 %)	
Age at diagnosis (years)			
3 years or younger	32 (46 %)	37 (54 %)	0.854
4–7 years	27 (47 %)	30 (53 %)	
8–12 years	28 (44 %)	36 (56 %)	
13 years or older	25 (52 %)	23 (48 %)	
Treatment			
Chemotherapy	104 (49 %)	109 (51 %)	0.111
Radiation	80 (66 %)	42 (34 %)	<0.001
Surgery	54 (61 %)	35 (39 %)	0.001
Stem cell transplantation	37 (77 %)	11 (23 %)	<0.001
Immunotherapy	4 (44 %)	5 (56 %)	0.999[a]
Marriage			
Yes	14 (44 %)	19 (56 %)	0.687
Employment			
Yes	57 (44 %)	74 (56 %)	0.041
No at present	22 (69 %)	10 (31 %)	
Never	1 (100 %)	0	
Student	32 (43 %)	42 (57 %)	
Health status at present			
Good	35 (27 %)	93 (73 %)	<0.001
Fair	25 (60 %)	17 (40 %)	<0.001[b]
Moderate	30 (68 %)	14 (32 %)	
Poor	20 (95 %)	1 (5 %)	
Bad	2 (67 %)	1 (33 %)	
Economic status			
Good	11 (31 %)	24 (69 %)	0.04
Fair	40 (45 %)	49 (55 %)	0.005[b]
Poor	28 (52 %)	26 (48 %)	
Bad	14 (70 %)	5 (30 %)	

[a] Fisher's exact test

[b] Trend test

Disability qualification

Among the 239 participants, 29 CCSs (12 %) already had the disability qualification, and an additional 15 reported that they needed it (Fig. 1). The total number of CCSs who need the disability qualification is 44. Table 4 shows associations between CCS characteristics and the need for the disability qualification limited to survivors 18 years or older. Univariate analysis showed that the significantly

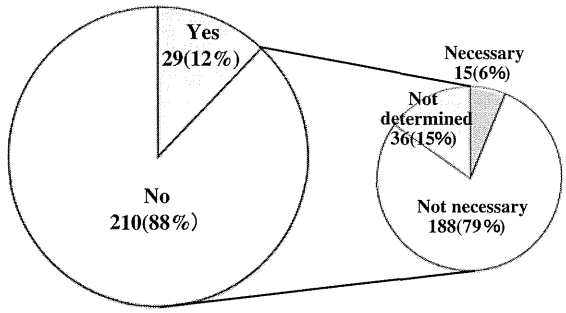

Fig. 1 Do you have or need the disability qualification?

related factors were education, primary cancer diagnosis, radiation, surgery, and late effects. Logistic regression analysis revealed that the significant independent related factors were late effects (OR 12.3; 95 % CI 3.37–45.2), brain tumors (OR 9.55; 95 % CI 1.90–48.0), lymphoma (OR 5.92; 95 % CI 1.07–32.7), and being a high school graduate (OR 9.86; CI 2.67–36.4). Gender and treatment contents were not associated with reporting a need for the disability qualification after adjustment of other factors.

Employment status

We classified the CCSs into three groups according to employment status: employed, unemployed, and students (see Table 5). More than half of the employed CCSs reported being satisfied with their current job, but approximately 40 % also reported that their work had been influenced by their childhood cancer experience. In addition, 61 % had told their employer and/or colleagues about their cancer diagnosis. There were no significant differences between males and females.

In contrast to employed CCSs, 60–80 % of unemployed CCSs reported having experienced some job

Table 4 Related factors of childhood cancer survivors who need the disability qualification (limited to survivors 18 years or older)

	Necessary (n = 37)	Not necessary (n = 164)	χ^2 (p value)	Logistic regression analysis	
				Odds ratio (95 % CI)	p value
Age at survey (years)					
20 years or younger	10 (25 %)	30 (75 %)	0.582	N/A	
21–24 years	8 (15 %)	45 (85 %)		N/A	
25–29 years	9 (15 %)	49 (85 %)		N/A	
30 years or older	10 (20 %)	40 (80 %)		N/A	
Gender					
Male	23 (22 %)	81 (78 %)	0.16	1.58 (0.57–4.36)	0.376
Education					
Dropout	2 (15 %)	11 (85 %)	0.005	0.79 (0.10–6.38)	0.826
Junior high school	4 (22 %)	14 (78 %)		2.28 (0.04–141)	0.695
High school	21 (35 %)	39 (65 %)		9.86 (2.67–36.4)	0.001
College or vocational school	5 (13 %)	34 (87 %)		1.26 (0.28–5.79)	0.766
University	2 (12 %)	90 (88 %)		Ref.	
Diagnosis of cancer					
Leukemia	8 (8 %)	97 (92 %)	<0.001	Ref.	
Lymphoma	7 (32 %)	15 (68 %)		5.92 (1.07–32.7)	0.002
Other solid cancers	2 (7 %)	28 (93 %)		0.67 (0.07–6.09)	0.720
Bone/soft tissue sarcoma	3 (25 %)	9 (75 %)		4.11 (0.52–32.3)	0.179
Brain tumor	17 (57 %)	13 (43 %)		9.55 (1.90–48.0)	0.006
Treatment					
Chemotherapy	33 (18 %)	148 (82 %)	0.846	1.11 (0.16–7.66)	0.917
Radiation	27 (25 %)	80 (75 %)	0.008	1.81 (0.52–6.32)	0.353
Surgery	25 (32 %)	53 (68 %)	<0.001	1.91 (0.52–6.99)	0.326
Stem cell transplantation	7 (17 %)	34 (83 %)	0.805	0.37 (0.10–1.39)	0.141
Late effects					
Yes	40 (37 %)	67 (63 %)	<0.001	12.3 (3.37–45.2)	<0.001

Hosmer–Lemeshow: $\chi^2 = 3.37$ ($p = 0.909$)

N/A not applicable

Table 5 Employed, unemployed and student childhood cancer survivors

Employed childhood cancer survivors ($n = 131$)	Male ($n = 65$)	Female ($n = 66$)	χ^2 (p value)
Job satisfaction			
Good	11 (18 %)	12 (18 %)	0.690
Fair	19 (31 %)	26 (39 %)	
Moderate	21 (34 %)	16 (24 %)	
Poor	8 (13 %)	7 (11 %)	
Bad (want to quit)	3 (5 %)	5 (8 %)	
Influence by childhood cancer experience			
Much	12 (19 %)	13 (20 %)	0.626
Fair	15 (23 %)	14 (21 %)	
Moderate	9 (14 %)	10 (15 %)	
Little	17 (26 %)	11 (17 %)	
Not at all	12 (26 %)	18 (27 %)	
Telling the cancer diagnosis to the company and/or colleagues			
Yes	40 (61 %)	34 (52 %)	0.288
No	25 (39 %)	31 (48 %)	
Un-employed childhood cancer survivors ($n = 31$)	$n = 16$	$n = 15$	χ^2 (p value)
Some difficulties in employment by childhood cancer experience			
Yes	13 (81 %)	9 (60 %)	0.193
No	3 (19 %)	6 (40 %)	
Please specify the reasons of unemployment			
Failure despite of job seeking	5 (31 %)	4 (27 %)	0.921
No job seeking	2 (12 %)	1 (7 %)	
Unable to get a job because of late effects	3 (19 %)	3 (20 %)	
Others	6 (38 %)	7 (47 %)	
Worry about un-employment			
Not at all	0	1 (6 %)	0.020
Little	2 (13 %)	1 (6 %)	
Moderate	0	3 (19 %)	
Some	0	5 (31 %)	
Much	12 (75 %)	4 (25 %)	
Others	2 (13 %)	1 (6 %)	
Your parent's wish			
Prefer you to work	13 (81 %)	8 (53 %)	0.271
Either will do	0	3 (20 %)	
Prefer not you to work	1 (6 %)	1 (7 %)	
Unknown	2 (12 %)	3 (20 %)	
Major living costs covered by			
Yourself	3 (19 %)	0	0.012
Parents	11 (69 %)	7 (44 %)	
Spouse	0	8 (50 %)	
Public help	1 (6 %)	1 (6 %)	
Do you want to work if they understand CCSs?			
Yes, much to work	7 (41 %)	7 (47 %)	0.755
Yes, if possible	5 (27 %)	4 (27 %)	
It depend on the job	2 (12 %)	3 (20 %)	
Others	2 (12 %)	1 (7 %)	

Table 5 continued

Un-employed childhood cancer survivors ($n = 31$)	$n = 16$	$n = 15$	χ^2 (p value)
Do you want the job-training place like the heart link working project?			
Yes	15 (94 %)	15 (100 %)	0.999[a]
No	1 (6 %)	0	
Students ($n = 69$)	**$n = 39$**	**$n = 30$**	**χ^2 (p value)**
Do you have some worries about your future employment?			
Yes	19 (49 %)	18 (60 %)	0.352
No	20 (51 %)	12 (40 %)	

[a] Fisher's exact test

Table 6 Related unemployment factors (excluding housewives and students)

	Unemployed ($n = 25$)	Employed ($n = 131$)	χ^2 (p value)	Logistic regression analysis	
				Odds ratio (95 % CI)	p value
Age at survey (years)					
20 years or younger	4 (29 %)	10 (71 %)	0.608	N/A	
21–24 years	6 (14 %)	37 (86 %)		N/A	
25–29 years	8 (15 %)	45 (85 %)		N/A	
30 years or older	7 (15 %)	39 (85 %)		N/A	
Gender					
Male	17 (21 %)		0.098	2.05 (0.71–5.90)	0.183
Education					
Dropout	5 (39 %)	8 (62 %)	0.110	8.46 (1.66–43.1)	0.010
Junior high school	1 (17 %)	5 (83 %)		1.66 (0.11–24.8)	0.713
High school	8 (21 %)	30 (79 %)		1.78 (0.52–6.12)	0.359
College or vocational school	4 (12%)	29 (88 %)		1.26 (0.29–5.54)	0.757
University	7 (10 %)	60 (90 %)		Ref.	
Diagnosis of cancer					
Leukemia	10 (12 %)	74 (88 %)	0.016	Ref.	
Lymphoma	4 (25 %)	12 (75 %)		1.55 (0.34–7.19)	0.575
Other solid cancers	1 (4 %)	23 (96 %)		0.22 (0.02–2.32)	0.210
Bone/soft tissue sarcoma	2 (18 %)	9 (82 %)		1.05 (0.14–7.92)	0.964
Brain tumor	8 (38 %)	13 (62 %)		2.73 (0.83–8.96)	0.098
Treatment					
Chemotherapy	24 (17 %)	118 (83 %)	0.303	N/A	
Radiation	16 (19 %)	70 (81 %)	0.312	N/A	
Surgery	12 (19 %)	50 (81 %)	0.426	N/A	
Stem cell transplantation	8 (23 %)	26 (77 %)	0.564	N/A	
Late effects					
Yes	21 (27 %)	57 (73 %)	<0.001	6.22 (1.80–21.4)	0.004

Hosmer–Lemeshow: $\chi^2 = 4.99$ ($p = 0.759$)

N/A not applicable

difficulties because of the childhood cancer experience. While only 10 % reported not having tried to find work, 30 % reported failure in job seeking, and 20 % reported the inability to obtain employment because of their late effects. A majority of the CCSs reported worry concerning their unemployment status, especially the males

(75 %). Both males (81 %) and females (51 %) reported that their parents preferred they find employment. For the majority of the sample, living costs were being covered by parents or spouses (females only). Most unemployed CCSs reported wanting to work if their employers understood CCSs better.

Table 6 shows associations between CCS characteristics and employment status. Univariate analysis revealed significant associations between primary cancer diagnosis and late effects. Logistic regression analysis revealed the independent related factors for unemployment were late effects (OR 6.22; 95 % CI 1.80–21.40) and dropping out (OR 8.46; 95 % CI 1.66–43.1). Finally, brain tumors tended to be associated with a high unemployment rate (OR 2.73; 95 % CI 0.83–8.96).

Discussion

We found that the unemployment rate was 15.9 % among the CCSs, excluding homemakers and students, and that 40 % of all employed CCSs reported that their work had been influenced by their childhood cancer experience. Approximately 70 % of unemployed CCSs reported having some late effects. The independent related factors for unemployment were late effects (OR 6.22), dropping out of school (OR 8.46), and brain tumors (OR 2.73). Most unemployed CCSs were likely to seek work despite their health problems and the presence of late effects.

The prevalence of late effects in this study was similar to that in previous studies [12], including other Japanese populations [2]. Frequently reported late effects included endocrine dysfunction, short stature, and neurocognitive problems (that latter is frequently observed in brain tumor survivors). The high prevalence of neurocognitive problems can be explained by the high percentage of brain tumor survivors (15 %) in this study. The finding that the presence of late effects is inversely associated with employment, health, and economic status (see Table 3) is consistent with previous research [13].

A total of 44 CCSs reported that the disability qualification is necessary. The most significant related independent factors were late effects (OR 20.1), brain tumors (OR 9.29), and lower academic achievement (OR 6.3 for junior high school). The Japanese government proposed the new Cancer Control Act in 2012, which explores the employment needs and work-related problems of cancer survivors, promotes employer understanding and an employer-sponsored consultation system, and establishes a society in which cancer survivors can work and live in trust. In the US, the Americans with Disabilities Act of 1990 states that a covered entity shall not discriminate against a qualified individual with a disability, including cancer patients. This applies to job application procedures, hiring, advancement and discharge of employees, workers' compensation, job training, and other terms, conditions, and privileges of employment. In Japan, cancer survivors are not included in the disability qualification. They discussed which types of cancer survivors could be included in the current disability qualification.

In this study, the unemployment rate was 15.9 % among the CCSs, excluding homemakers and students. This rate was similar to the rate of 11 % in the CCSS study [6] and the rate of 16 % in Sweden [14], but relatively lower than the rate of 37 % in Turkey [15]. Independent factors related to unemployment were late effects (OR 6.22), dropping out of school (OR 8.46), and brain tumors (OR 2.73). de Boer et al. [16] reported a meta-analysis on adult CCSs and unemployment. CCSs were nearly twice as likely to be unemployed as healthy controls (OR 1.85, 95 % CI 1.27–2.69). Brain tumor survivors were nearly five times more likely to be unemployed (OR 4.74; 95 % CI 1.21–18.65), whereas the risks for blood or bone cancer survivors were elevated but not statistically significant (OR 1.42; 95 % CI 0.79–2.55; OR 1.97; 95 % CI 0.88–4.40, respectively). Apart from type of diagnosis, predictors of unemployment were a younger age, lower education, being female, late effects, and radiotherapy. Our results are primarily consistent with these findings [14, 16–18].

We have the unpublished data that most CCSs are highly motivated to become helpful to others (a survey by the Children's Cancer Association of Japan). In this study, many unemployed CCSs were likely to seek work despite their health problems and late effects [19]. They require social understanding regarding their specific difficulties including late effects, and we as a society need to make advocacy on their behalf a priority [20].

Our study has two key strengths. First, this is the first nationwide survey in Japan that has focused on CCSs' employment problems. Second, we included a large enough sample to conduct a multivariate analysis on the factors with two outcomes of interest. There are, however, some limitations to the study. First, this is a cross-sectional study, so it cannot determine causal relationships. Second, we did not include a comparison group (such as siblings of CCSs). Finally, the response rate was fairly low (34.4 %) for the first sample group and unknown for the second sample group. The results may be subject to response bias (i.e., those with a stronger interest in the topic may have been more likely to respond to the survey). These disadvantages must be considered given the logistic difficulty of obtaining information from some isolated CCSs. Our ongoing research focuses on seeking out these isolated, unemployed CCSs and individually interviewing them.

In conclusion, our study suggests that the unemployment rate of CCS in Japan is not high, but that some CCSs need