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Comparison of Psychological Quality of Life Between Long-term Survivors of Childhood Cancer and Their Families

AU2 ► AU1 ►

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AU3 ► Purpose: Although treatment outcomes for childhood cancer have improved in recent years, some patients continue to experience physical symptoms and psychological stress several years after the end of treatment. This study aimed to examine the correlation between the quality-of-life (QOL) scores of childhood cancer survivors (CCSs) aged 18–39 and (1) their families and (2) the time since the end of treatment.

Methods: Measuring the QOL of CCSs attending the long-term follow-up (LTFU) and those of their families. The Short-Form Health Survey (SF-36) was used for CCSs and the Caregiver Quality of Life Index-Cancer (CQOLC) for their families. Spearman's rank correlation analyses were used to examine the relationship between the CCSs' and their families' QOL and the time since the end of treatment.

Results: Twenty-nine CCSs (mean age, 24.2 years; mean the time since the end of treatment, 13.9 years), each paired with one family member, were included. Time since the end of treatment was positively correlated with the CCSs' QOL on the physical component score ($\rho=0.42$, $p=0.03$) and negatively correlated with mental health (MH) ($\rho=-0.50$, $p=0.01$), a subscale of the mental component score (MCS). Furthermore, the CCSs' QOL on the MCS was positively correlated with their families' QOL scores ($\rho=0.58$, $p<0.01$).

Conclusion: Psychological stress may persist in CCSs long after treatment, even when physical symptoms improve. Therefore, it is necessary to establish a comprehensive support system for the LTFU of CCSs, including MH care and QOL monitoring for patients and their families.

Keywords: survivors of childhood cancer, follow-up care, psychosocial support systems, quality of life, family caregivers

Introduction

RECENTLY, REMARKABLE PROGRESS has been made in the treatment of childhood cancer, and the 5-year event-free survival rate is estimated to be 70%–80%.¹ In Japan, there are nearly 100,000 childhood cancer survivors (CCSs), and it is

estimated that approximately half of them are now in their 20s or older.² As CCSs become adolescents and young adults (AYAs), they may face several generation-specific challenges. They experience complex physical and psychosocial developments and a range of lifestyle changes, including higher education, employment, marriage, and childbirth. Transition

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after cancer treatment, CCSs face new challenges such as anxiety about relapse, returning to school or work, and living with late effects, they are more likely to experience psychological, social, and physical effects.^{3,4}

Clinical cancer research tends to focus on the patients themselves, but in the case of CCSs, the patient-family relationship is also important. Since AYAs are not completely socially or financially independent, their treatment is often family-based and parents are actively involved.⁵ It has been reported that >75% of AYAs attend follow-up with their parents.⁶ A study reported that parents of children with cancer have significantly lower quality-of-life (QOL) score than that of parents of healthy children, indicating the importance of mental health (MH) care for parents, spouses, caregivers, and patients.⁷

The importance of long-term follow-up (LTFU) for CCSs has been increasingly recognized. LTFU for CCSs consists of both medical aspects, such as providing surveillance of CCSs, and early detection and response to late effects, and supportive aspects, which address psychosocial issues.⁸ In Japan, the LTFU system has only been recognized for a few years.⁹ Pediatric endocrinologists primarily provide transitional care for CCS in Japan.¹⁰ In a survey of 183 members of the Pediatric Endocrine Society of Japan, 44% of respondents had facilities with LTFU. However, very few had transitional support programs or medical staff teams (7%–8%). Even when patients participate in LTFU, financial reasons, relocation, or lack of awareness of the patient's disease make long-term continuity of care difficult.¹⁰

QOL is an important measure of the physical and MH of CCSs, but few studies have examined how QOL changes over time after the end of treatment. It would be meaningful to examine the relationship between the QOL scores of CCSs who are adapting to changes in their environments and lifestyles and their close caregivers and of their family members in terms of the time since the end of treatment.

This study aimed to examine the correlation between CCSs and their families' QOL scores and the time since the end of treatment. We hope that this study will expand on the knowledge of the long-term impact of childhood cancer experiences on patients and their families and raise awareness of the importance of LTFU care.

Methods

This study is a secondary analysis of an original study that examined the patient-family perception gap in reports of QOL in young adult survivors of childhood cancer.¹¹ The original study (R2257-1) and this study (R3111) received ethical approval from the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine.

Participants and procedures

The original cross-sectional study used a self-reported questionnaire and included CCSs and their families (parents or cohabitating spouses). In the original study, patients were recruited at the LTFU outpatient clinic of the Department of Pediatrics, Kyoto University Hospital, between July and October 2020. The target population were CCSs aged 18–39 years who had completed treatment and were currently in remission or cured, and their families. Family members included parents and spouses who lived with patients in the same house.

Questionnaires were handed out or sent to 63 patients/families who met the criteria and agreed to participate. Participants from the original study were given the opportunity to decline inclusion in the secondary analysis by opting out.

The original study used different QOL scales for survivors and their families. For CCSs, the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36),¹² a health-related QOL questionnaire, was used. For families of CCSs, the Caregiver Quality of Life Index-Cancer (CQOLC)¹³ was used, which measures caregivers' QOL from a psychosocial perspective. We believe that the CQOLC is useful when measuring the QOL of CCSs' families. These questionnaires take ~5 minutes to complete. Demographic and clinical data of CCSs and their families were obtained from a self-administered questionnaire and health records.

Measures

The SF-36 is a generic scale that measures the physical and MH components of QOL.^{14,15} It contains 36 items that are clustered into the following eight domains: physical functioning, role-physical, bodily pain, general health, vitality (VT), social functioning (SF), role-emotional (RE), and MH. Two summary scores, the physical component score (PCS) and the mental component score (MCS), can be calculated from the SF-36 scale based on a standardized scoring method. VT, SF, RE, and MH have strong loadings on the MCS,¹⁶ with scores on each scale ranging from 0 to 100: a lower score indicates poorer health or functioning.

Families' QOL was measured using the CQOLC,¹³ which is used to measure caregivers' QOL and feelings of burden. The CQOLC has 21 items on a 6-point Likert scale. A higher total score is indicative of better QOL. The Japanese version of the scale was developed by Ando et al and he has shown good internal consistency/reliability and construct validity.¹⁷

Data analysis

Descriptive statistics (i.e., means and standard deviations) were used to characterize the demographic and clinical data. Correlations between variables were examined using Spearman's rank correlation coefficients. All statistical tests were two-sided and considered significant if $p < 0.05$. All analyses were conducted using JMP Pro 15.2 (SAS Institute, Cary, NC).

Results

Patient characteristics

Of the 63 patients/families to whom questionnaires were handed or sent, 29 pairs of 58 responded (completion rate: 92.1%). CCSs' and their families' demographic and clinical characteristics are shown in Table 1. Thirteen male (44.8%) and 16 female (55.1%) CCSs with a mean age of 24.2 ± 5.8 years participated. The mean age at cancer diagnosis was 7.9 ± 4.9 years, and the mean time since the end of treatment was 13.9 ± 6.3 years. The most common type of cancer was acute lymphocytic leukemia, which was diagnosed in 20 patients (69.0%). Nineteen patients (65.5%) received chemotherapy. The mean age of the CCSs' families was 48.7 ± 9.3 years. In terms of caregiver relationship with the CCSs, the highest number of respondents were mothers, 21 (72.4%), followed by fathers, 5 (17.2%), and spouses, 3 (10.3%). The mean values of the CCSs' QOL are shown in Table 2.

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TABLE 1. CHARACTERISTICS OF PARTICIPANT

	Mean ± SD	n	%		Mean ± SD	n	%
CCSs (n=29)				Families (n=29)			
Age	24.2 ± 5.8			Age	48.2 ± 9.5		
18–19		4	13.8	30–39		3	10.3
20–24		15	51.7	40–49		3	10.3
25–29		6	20.1	50–69		6	20.7
30–39		4	13.8	Unknown		17	58.6
Sex				Sex			
Male		13	44.8	Male		7	24.1
Female		16	55.1	Female		22	75.9
Employment status				Employment status			
Student		10	34.5	Company employee		7	24.1
Company employee		6	20.7	Self-employed		4	13.8
Part-time worker		4	13.8	Part-time worker		5	17.2
Other		6	20.7	Full-time housewife/husband		8	27.6
Unemployed		2	6.9	Other		5	17.2
Unknown		1	3.4	Relationship with the CCSs			
Age at diagnosis	7.9 ± 4.9			Father		5	17.2
0–9		20	69.0	Mother		21	72.4
10–16		8	27.6	Husband		1	3.4
Unknown		1	3.4	Wife		2	6.9
Time since diagnosis	15.8 ± 5.5						
Time since the end of treatment	13.9 ± 6.3						
Under 5 years		1	3.4				
5–9 years		5	17.2				
10–19 years		17	58.6				
Over 20 years		4	13.8				
Unknown		2	6.9				
Type of cancer							
Acute lymphocytic leukemia		20	69.0				
Acute myeloid leukemia		4	13.8				
Other		4	13.8				
Unknown		1	3.4				
Type of treatment							
Chemotherapy		19	65.5				
Transplant		5	17.2				
Chemotherapy and transplant		4	13.8				
Unknown		1	3.4				

CCS, childhood cancer survivors; SD, Standard deviation.

Correlation between the CCSs' and their families' QOL and the time since the end of treatment

The correlations between the CCSs' QOL and the time since the end of treatment are shown in Table 3. The QOL scores of the families are shown in Table 4. The longer the time since the end of treatment, the significantly higher the

TABLE 3. CORRELATION BETWEEN THE CHILDHOOD CANCER SURVIVORS' QUALITY OF LIFE AND THE TIME SINCE THE END OF TREATMENT

The CCSs' QOL (SF-36)	The time since the end of treatment	
	P	p
Summary score		
Physical component score	0.42	0.03*
Mental component score	-0.25	0.20
Subscale		
Physical functioning	0.14	0.49
Role-physical	0.26	0.20
Bodily pain	0.18	0.37
General health	-0.02	0.92
Vitality	-0.19	0.32
Social functioning	-0.05	0.80
Role-emotional	-0.15	0.44
Mental health	-0.50	0.01*

TABLE 2. THE MEAN VALUES OF THE CHILDHOOD CANCER SURVIVORS' QUALITY OF LIFE

The CCSs' QOL (SF-36)	Mean ± SD
Physical functioning	93.1 ± 9.0
Role-physical	94.4 ± 12.6
Bodily pain	87.4 ± 19.9
General health	68.6 ± 15.7
Vitality	65.3 ± 15.9
Social functioning	94.4 ± 10.2
Role-emotional	89.7 ± 11.5
Mental health	73.6 ± 14.4

QOL, quality of life; SF-36, Short-Form Health Survey.

* < 0.05.

TABLE 4. CORRELATION BETWEEN THE FAMILIES' QUALITY OF LIFE AND THE TIME SINCE THE END OF TREATMENT

The families' QOL (CQOLC)	The time since the end of treatment	
	ρ	p
Psychological burden	0.25	0.20
Affirmation of care	-0.13	0.51
Financial burden	-0.04	0.84
Disruption of life	-0.07	0.76
SUM	0.03	0.88

AU8 ► CQOLC, Caregiver Quality of Life Index-Cancer; SUM.

CCSs' QOL scores on the PCS ($\rho=0.42, p=0.03$). In contrast, MH were significantly lower ($\rho=-0.50, p=0.01$). Although no significant correlation was found between the CCSs' QOL on the MCS and the time since the end of treatment, the ρ values of the MCS and its component subscales (VT, SF, RE, MH) showed negative values. There was no significant correlation between families' QOL scores and the time since the end of treatment.

Correlation between the CCSs' and their families' QOL

T5 ► The correlations between the CCSs' and their families' QOL scores are shown in Table 5. The higher the CCSs' QOL score on the PCS, the lower their families' QOL scores ($\rho=-0.52, p=0.01$). In particular, financial burden ($\rho=-0.52, p<0.01$) and disruption of life due to care ($\rho=-0.42, p=0.02$) were significantly negatively correlated with the CCSs' QOL scores on the PCS. A scatter plot of the correlation analysis between the CCSs' QOL scores on the PCS and their families' QOL scores is shown in Figure 1. Although there was a correlation between the two, there was a large variation in the data, and the R^2 values were very low ($R^2=0.15$).

F1 ► In contrast, as the CCSs' QOL scores on the MCS declined, as did those of their families ($\rho=0.58, p<0.01$). In particular, psychological burden ($\rho=0.53, p<0.01$) and financial burden ($\rho=0.50, p<0.01$) were significantly positively correlated with the CCSs' QOL scores on the MCS. A scatter plot of the cor-

relation analysis between the CCSs' QOL scores on the MCS and their families' QOL scores is shown in Figure 2. This shows a clear positive correlation with little variation in the data. ◀F2

Discussion

This study examined the correlation between CCSs' and their families' QOL scores and the time since the end of treatment. We found that the time since the end of treatment was positively correlated with the CCSs' QOL scores on the PCS and negatively correlated with MH, a subscale of the MCS. Furthermore, the CCSs' QOL scores on the MCS were positively correlated with their families' QOL scores.

Previous studies of pediatric patients with cancer have shown that the longer the time since diagnosis, the greater the improvement in physical functioning.¹⁸ Similar results were obtained in this study, suggesting that the perception of the biological effects of the disease improved over time after the treatment completion and the CCSs' physical aspect of QOL improved. However, the results of the CCSs' mental aspects of QOL differ from those of previous studies. A Korean study examining the QOL scores of CCSs attending LTFU care found that patients at >3 years posttreatment had higher QOL scores in physical and mental aspects than those at <3 years.¹⁹ This difference in mental status may be partly because many of the CCSs in this study were off therapy for at least 10 years or longer.

The original study found that families overestimated CCSs' role-social aspect of QOL,¹¹ possibly because the family may feel more comfortable as the CCSs gradually adjusted to normal life over a longer period and may overlook invisible psychological stress.¹¹ In addition, a previous study on psychological QOL in adolescents diagnosed with cancer over 10 years after diagnosis found that the SF-36 subscales of MH, and VT improved up to 4 years after diagnosis, but then began to decline at 6 years.²⁰ Therefore, the psychological risks for patients diagnosed with cancer at a young age can emerge many years after treatment. Problems can be serious; previous study has shown that 20.5% of CCSs in AYAs experienced posttraumatic stress.²¹

This study also found that as the CCSs' QOL scores on the MCS declined, the QOL scores of their family members also

TABLE 5. CORRELATION BETWEEN THE CHILDHOOD CANCER SURVIVORS' AND FAMILIES' QUALITY OF LIFE

The CCSs' QOL (SF-36)	Families' QOL (CQOLC)									
	Psychological burden		Affirmation of care		Financial burden		Disruption of life due to care		SUM	
	ρ	p	ρ	p	ρ	p	ρ	p	ρ	p
Summary score										
Physical component score	-0.21	0.27	0.04	0.84	-0.52	<0.01*	-0.42	0.02*	-0.52	<0.01*
Mental component score	0.53	<0.01*	-0.07	0.72	0.50	<0.01*	0.33	0.08	0.58	<0.01*
Subscale										
Physical functioning	0.22	0.24	-0.28	0.15	0.02	0.92	0.06	0.74	-0.06	0.76
Role-physical	0.12	0.54	-0.02	0.93	-0.28	0.14	-0.04	0.85	-0.07	0.72
Bodily pain	0.21	0.27	0.04	0.83	0.18	0.37	-0.15	0.44	0.16	0.41
General health	0.32	0.09	-0.11	0.54	0.32	0.09	0.18	0.35	0.25	0.18
Vitality	0.56	<0.01*	-0.17	0.38	0.41	0.03*	0.29	0.12	0.51	<0.01*
Social functioning	0.12	0.54	-0.16	0.42	0.11	0.56	0.00	0.99	0.01	0.97
Role-emotional	0.24	0.22	-0.16	0.42	0.03	0.88	0.10	0.61	0.03	0.88
Mental health	0.32	0.09	-0.18	0.35	0.52	<0.01*	0.37	0.05*	0.40	0.03*

*<0.05.

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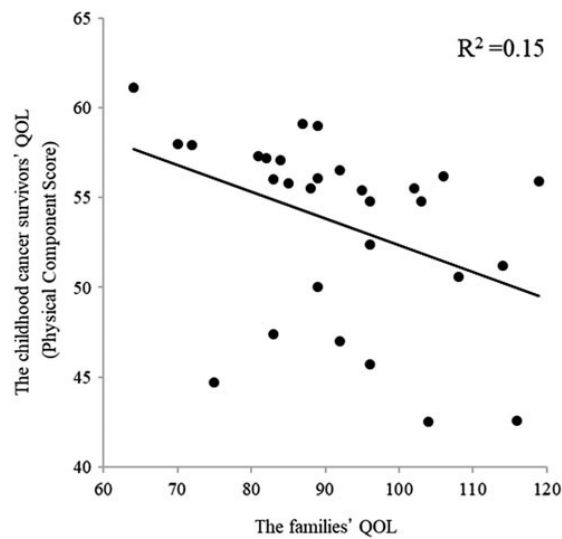


FIG. 1. Correlation scatter plot between the CCSs' QOL on the physical component score and families' QOL. CCSs', childhood cancer survivors; QOL, quality of life.

declined, and higher CCSs' QOL scores on the MCS correlated with higher QOL scores of their families. In a review study, 10%–44% of the parents of children with cancer reported severe posttraumatic stress symptoms during and/or after their child's cancer treatment.²² A study comparing the QOL of spouses of patients after one year of cancer treatment with that of the general population found that the physical aspect of QOL was comparable, but the mental aspect of QOL was lower.²³ The results of these studies suggest that the QOL of parents and spouses of CCSs declines during and after treatment.

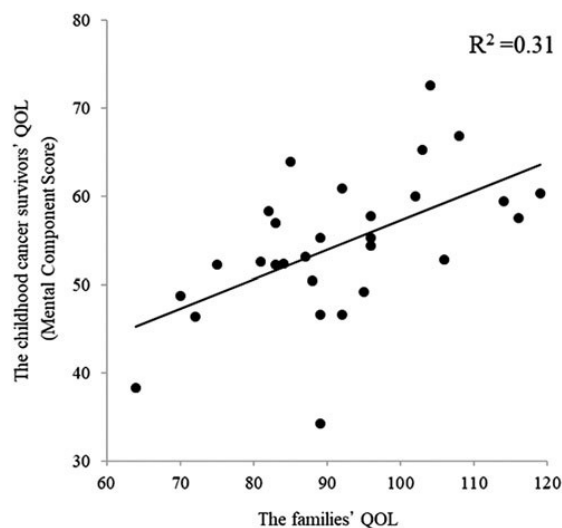


FIG. 2. Correlation scatter plot between the CCSs' QOL on the mental component score and families' QOL.

This study suggests that the QOL of CCSs' families also declines as the CCSs' mental aspect of QOL declines, even long after the end of treatment. Comprehensive care that includes CCSs' families in the follow-up is crucial.

In addition, this study showed a negative correlation between the CCSs' QOL scores on the PCS and their families' QOL. This was especially true for QOL regarding the financial burden and disruption of life due to care. In terms of financial burden, 74% of parents of CCSs report severe or moderate financial hardship following their child's cancer diagnosis.²⁴ In addition to treatment and other expenses, at least one parent often quits their job to focus on their child's treatment. One study reported that most fathers of CCSs work full-time, while 87% of mothers worked part-time or were unemployed,²⁵ suggesting that mothers may play the role of caregiver in many cases. This result is supported by the fact that the average age of family members participating in this study was 48.2 years, an age at which individuals are generally engaged in work; 75.9% were female, and about half were part-time or unemployed.

Furthermore, it is conceivable that the burden will increase as the CCSs' QOL scores on the PCS improve, as people return to society or as hospital visits become the main focus of treatment. It is also possible that the increased financial burden and disruption of life due to care may have improved the CCSs' QOL scores on the PCS. However, this is not certain because the causal relationship is unclear. As the R^2 values of the scatter plots were small, further study is needed on the observed negative correlation between the CCSs' physical aspects of QOL and their families' QOL.

This study has several limitations. The first is the selection bias of the participants, which was conducted on CCSs in the LTFU outpatient clinic. Therefore, whether the results are similar for CCSs, in general, requires further research. Second, this is a cross-sectional study; because CCSs in AYAs undergo complex physical and psychosocial development and experience a variety of lifestyle changes, it is important to examine changes in psychological problems and QOL over time, and longitudinal studies are needed. Further examination of possible confounding factors is also required. Third, the small sample size limits conclusions, and differences between groups in some demographic characteristics may have influenced findings. Future research should investigate these associations using a larger sample.

Conclusion

This study showed that the psychological impact of childhood cancer might persist long after the end of treatment, even if physical symptoms had improved. Furthermore, families' QOL was related to the CCSs' mental aspect of QOL, suggesting a comprehensive support system for LTFU care of CCSs, including MH care and QOL monitoring for the patients and their families, is needed.

Authors' Contributions

Y.S. designed the study, analyzed and interpreted the data, and wrote the article. T.M. was the first author of the original study, designed the study, and collected the data. K.S., N.Q., K.M., C.C., N.M., H.S., A.T., A.H., M.N.-T., M.O., T.K., H.T., and T.T. interpreted the data and reviewed the article. M.M. collected and interpreted the data and reviewed the

article. S.A. and J.T. collected the data and reviewed the article. T.A. reviewed the article and supervised the entire research process. All authors read and approved the final article.

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Disclaimer

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Author Disclosure Statement

No competing financial interests exist.

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References

1. Gatta G, Botta L, Rossi S, et al. Childhood cancer survival in Europe 1999–2007: Results of EUROCARE-5-a population-based study. *Lancet Oncol* 2014;15(1):35–47.
2. Ishida Y. “*Syounigankeikennsyu no coukiforôappu nikansuru momdai*” [Issues related to the long-term follow-up of childhood cancer survivors]. *J Pediatr Hematol Oncol* 2018; 55(2):141–147. (In Japanese)
3. Geenen MM, Cardous-Ubbink MC, Leontien M, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. *JAMA* 2007;297(24): 2705–2715.
4. Kim MA, Yi J. Psychological distress in adolescent and young adult survivors of childhood cancer in Korea. *J Pediatr Oncol Nurs* 2013;30(2):99–108.
5. Doshi K, Kazak AE, Hocking MC, et al. Why mothers accompany adolescent and young adult childhood cancer survivors to follow-up clinic visits. *J Pediatr Oncol Nurs* 2014;31(1):51–57.
6. Signorelli C, Wakefield C, McLoone JK, et al. Childhood cancer survivorship: Barriers and preferences. *BMJ Support Palliat Care* 2019;0:1–9.
7. Witt WP, Litzelman K, Wisk LE, et al. Stress-mediated quality of life outcomes in parents of childhood cancer and brain tumor survivors: A case-control study. *Qual Life Res* 2010;19(7):995–1005.
8. Future Pediatric Cancer Control Measures. “Reference material for the report of the Expert Committee on Pediatric Cancer Control to the Council for Promotion of Cancer Control, Council for Promotion of Cancer Control.” 2011. Available from: <https://www.mhlw.go.jp/stf/shingi/2r985200001n1eo-att/2r985200001n1mm.pdf> [Last accessed: September 17, 2021].
9. JPLSG Long-Term Follow-up Committee Working Group for Long-Term Follow-up Guidelines. “Guidelines for long-term follow-up after treatment of childhood cancer.” Available from: http://jccg.jp/wp-content/uploads/FU_guide_line.pdf [Last accessed: July 11, 2021].
10. Miyoshi Y, Yorifuji T, Shimizu C, et al. A nationwide questionnaire survey targeting Japanese pediatric endocrinologists regarding transitional care in childhood, adolescent, and young adult cancer survivors. *Clin Pediatr Endocrinol* 2020;29(2):55–62.
11. Morino T, Shinohara Y, Niu Q, et al. Perception gap in health-related quality of life between young adult survivors of childhood cancer and their family. *J Adolesc Young Adult Oncol* 2021; doi: 10.1089/jayao.2020.0232.
12. Ware JE, Snow KK, Kosinski M, et al. *SF-36 Health Survey Manual and Interpretation Guide*; 1993. Available from: https://czresearch.com/info/SF36_healthsurvey_ch6.pdf [Last accessed: July 11, 2021].
13. Weitzner MA, Jacobsen PB, Wagner H, et al. The Caregiver Quality of Life Index-Cancer (CQOLC) scale: Development and validation of an instrument to measure quality of life of the family caregiver of patients with cancer. *Qual Life Res* 1999;8(1–2):55–63.
14. Fukuhara S, Bito S, Green J, et al. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol* 1998;51(11):1037–1044.
15. Fukuhara S, Ware JE, Kosinski M, et al. Psychometric and clinical tests of validity of the Japanese SF-36 Health Survey. *J Clin Epidemiol* 1998;51(11):1045–1053.
16. Fukuhara S, Suzugamo Y, Oto S, et al. *SF-36 Japanese Manual* (Ver. 1.2). Public Health Research Center: Tokyo; 2001.
17. Ando S, Harada M, Weitzer MA, et al. Caregiver Quality of Life Index-Cancer (CQOLC) Verification of the reliability and validity of the Japanese version [Japanese]. *Palliat Care* 2013;8(2):286–292.
18. Hamner T, Latzman RD, Latzman NE, et al. Quality of life among pediatric patients with cancer: Contributions of time since diagnosis and parental chronic stress. *Pediatr Blood Cancer* 2015;62(7):1232–1236.
19. Rhee MA, Chung KM, Lee Y, et al. Impact of psychological and cancer-related factors on HRQoL for Korean childhood cancer survivors. *Qual Life Res* 2014;23(9):2603–2612.
20. Ander M, Grönqvist H, Cernvall M, et al. Development of health-related quality of life and symptoms of anxiety and depression among persons diagnosed with cancer during adolescence: A 10-year follow-up study. *Psychooncology* 2016;25(5):582–589.
21. Hobbie WL, Stuber M, Meeske K, et al. Symptoms of posttraumatic stress in young adult survivors of childhood cancer. *J Clin Oncol* 2000;18(24):4060–4066.
22. Cordova MJ, Riba MB, Spiegel D. Post-traumatic stress disorder and cancer. *Lancet Psychiatry* 2017;4(4):330–338.
23. Gotze H, Ernst J, Braehler E, et al. Predictors of quality of life of cancer patients, their children, and partners. [Abstract] *Psychooncology* 2015;24(7):787–795.
24. Health JA, Lintuuran RM, Ringguto G, et al. Childhood cancer: Its impact and financial costs for Australian families. *Pediatr Hematol Oncol* 2006;23(5):439–448.
25. Svavarsdottir EK. Caring for a child with cancer: A longitudinal perspective. *J Adv Nurs* 2005;50(2):153–161.

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