Annals of Hematology (2019) 98:2357–2366
https://doi.org/10.1007/s00277-019-03760-5

ORIGINAL ARTICLE

Comparison of quality of life and health behaviors in survivors of acute leukemia and the general population

Koung Jin Suh[1] · Dong-Yeop Shin[2] · Inho Kim[2,3] · Sung-Soo Yoon[2,3] · Jeong-Ok Lee[1] · Soo-Mee Bang[1] · Ja Min Byun[4] · Ki Hwan Kim[4] · Jin Hyun Park[4] · Sang Min Park[5] · Youngae Kim[6] · Young Ho Yun[5] · Youngil Koh[2,3,7]

Received: 13 February 2019 / Accepted: 12 July 2019 / Published online: 23 July 2019

Abstract

We aimed to compare the health-related quality of life and health behaviors of acute leukemia (AL) survivors with that of the general population from two cohorts. AL survivors ($n = 149$) completed a set of questionnaires to evaluate quality of life, mental status, and health behaviors. AL survivors had more physical and mental difficulties (problems with usual activities, 15% vs. 5%, $p < 0.001$; anxiety or depression, 24% vs. 9%, $p < 0.001$; pain, 35% vs. 20%, $p = 0.002$) and more financial difficulties ($p < 0.001$) than the general population. Survivors who received stem cell transplantation (SCT) had significantly worse problems with role functioning, fatigue, pain, dyspnea, and insomnia, and had higher depression scores than chemotherapy group ($p = 0.024$). In terms of health behaviors, AL survivors had lower rates of smoking and drinking and higher influenza vaccination rates than the general population. However, only 17% of survivors had been recommended to receive screening for other cancers from health-care providers, and 67% thought their risk for other cancers was equal or lower than that of the general population. Cancer screening rates were even lower in the SCT group than in the chemotherapy group ($p = 0.041$). Our study indicates that clinicians should establish more appropriate survivorship care plans.

Keywords Health-related quality of life · Acute leukemia · Hematopoietic stem cell transplantation

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00277-019-03760-5) contains supplementary material, which is available to authorized users.

✉ Youngil Koh
go01@snu.ac.kr

[1] Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Gyeonggi, South Korea

[2] Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, South Korea

[3] Cancer Research Institute, Seoul National University, Seoul, South Korea

[4] Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul National University College of Medicine, Seoul, South Korea

[5] Department of Family Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

[6] Division of Cancer Management Policy, National Cancer Control Institute, National Cancer Center, Goyang, Gyeonggi, South Korea

[7] Biomedical Research Institute, Seoul National University Hospital, Seoul, South Korea

Introduction

The long-term survival rate of adult acute leukemia (AL) has improved to 30–40% owing to high-dose chemotherapy and introduction of hematopoietic stem cell transplantation (SCT) in high-risk patients [1, 2]. As the survival rate of leukemia increased, interest in the health-related quality of life (HRQoL) after leukemia treatment gathered attention and led to many studies [3–20]. In studies of patients with various hematologic malignancies (36–47% of patients had AL) who had undergone SCT, patients reported poorer HRQoL than the healthy controls, especially in terms of physical health, physical functioning, social functioning, and financial problems [13, 15]. It has also been shown that the different post-remission treatments, consolidation chemotherapy, and SCT affected QoL significantly. Compared to conventional chemotherapy, almost all measures of QoL were inferior for patients who had received SCT [17].

Many of these studies were limited by several aspects. Some studies were not limited to AL, but also to various hematologic diseases such as lymphoma, multiple myeloma, aplastic anemia, and myelodysplastic syndrome, as well as

solid tumors. Even among studies focusing on acute leukemia, a small sample size, a different post-remission treatment, a different comparator group, and the inclusion of patients who did not achieve complete remission after induction chemotherapy in some cases are problematic. In addition, there is no information on health-care behavior, secondary cancer occurrence, and comorbidities that can affect the QoL.

Identifying differences in HRQoL among AL patients who received different treatment modalities is very important since it can help clinicians determine treatment strategies and communicate with the patients. In addition to HRQoL, differences in the health-care behaviors of survivors compared to the general population are also important. This study aimed to compare HRQoL and health behaviors of AL survivors with that of the general population and to compare HRQoL among AL survivors according to post-remission treatment modality.

Methods and materials

Study design and subjects

We enrolled 149 AL survivors from three Korean tertiary care centers from 1983 through 2014. The inclusion criteria were a diagnosis of AL (acute myeloid leukemia [AML], acute lymphoblastic leukemia [ALL], and acute biphenotypic leukemia [ABL]), being over 18 years of age at the time of diagnosis, treatment completion at least 1 year before inclusion in the study, and complete remission at the time of study inclusion.

General population control subjects were obtained from two cohorts. One cohort was from The Sixth Korean National Health and Nutrition Examination Survey (KNHANES VI), and control subjects from this cohort were 1:3 matched for age, sex, education status, marital status, and presence of any comorbidity ($n = 447$). The scores for the EuroQol five dimensions questionnaire (EQ-5D) and health behaviors regarding rate of smoking, drinking, health medical examination, cancer screening, and vaccination of AL survivors were compared with the subjects from this cohort. Another cohort is from a representative sample of the Korean adult population, consisting of 500 men and 500 women selected by a nationwide random route technique who completed the EORTC Quality of Life Core Questionnaire (QLQ-C30). Control subjects from this cohort were randomly sampled 1:2 by sex and age stratification ($n = 298$), and EORTC QLQ-C30 scores were compared with those of AL survivors.

Other survey results, including EORTC QLQ-C30, were analyzed among the leukemia survivors to evaluate the impact on QoL of post-remission treatment strategy (SCT or chemotherapy). The institutional review boards of the participating institutions approved the study, and informed consent was obtained from all subjects.

Study instruments

Survivors completed a set of questionnaires that included demographic characteristics, self-reported comorbidities, and standardized instruments that evaluate HRQoL, fatigue, and anxiety and depression. The EORTC QLQ-C30 is a 30-item cancer-specific questionnaire for assessing the general HRQoL of cancer patients [21]. The EQ-5D is one of the most commonly used standardized instruments to measure general health status [22]. The Korean version of EQ-5D and EORTC QLQ-C30 questionnaires has been validated [23, 24]. Depression and anxiety were assessed using the hospital anxiety and depression scale (HADS) [25]. Fatigue was assessed by the Brief Fatigue Inventory (BFI), which was developed to measure fatigue in cancer populations and to determine how much disease and treatment influence fatigue [26]. The Brief Encounter Psychosocial Instrument (BEPSI) is a six-item instrument developed to measure stress in a busy clinical setting [27]. The Korean versions of HADS (HADS-K) and BFI have been validated [28, 29]. Survivors with a current partner completed the Abbreviated Dyadic Adjustment Scale (ADAS). The Dyadic Adjustment Scale (DAS) consists of 32 items and is a widely used measure of satisfaction and adjustment in marital or committed couple relationships [30], and the Korean version of abbreviated DAS (ADAS), which consists of 10 items, has been validated [31]. Family APGAR, which is a validated instrument to measure a subject's satisfaction with five components of family function, was also included in the questionnaire [32].

Statistical analysis

We used descriptive statistics for clinical, socioeconomic, and therapeutic variables and t tests and chi-square tests. We scored the QLQ-C30 items according to the EORTC scoring manual, and handled incomplete questionnaires according to the developers' recommendations. We linearly transformed the QLQ-C30 data to yield scores from 0 to 100; a higher score represented a better level of functioning or a higher level of symptoms. We compared AL survivors with the general population controls on the basis of mean HRQoL score. We defined a "clinically significant" difference in HRQoL as a 10-point difference in the mean score. p values of < 0.05 were considered significant. All statistical tests were two-sided. All analyses were performed by SPSS software version 21 (Chicago, IL).

Results

Subjects and demographics

We identified 338 potentially eligible AL survivors from the three participating institutions. Of these, 316 patients were

invited by the institutions to participate in the study, and 237 patients were successfully contacted. Among the contacted AL survivors, 149 patients (63%) consented to participate, and all subjects with consent completed the questionnaire (Fig. 1).

Median age of the study participants was 44 years (range, 16–78), and there were 75 men (50%) and 74 women (50%). A majority of the patients had AML (n = 121); others had ALL (n = 24) and ABL (n = 4). Among the survivors, 93 received chemotherapy and 56 received SCT as post-remission treatment. Patients who received SCT were more likely to be younger and have ALL. Median duration of time between treatment completion and the study survey was 59 months. The clinical and demographic characteristics of study participants are described in Table 1.

Comparison of HRQoL between AL survivors and the general population

Examination of each of the five dimensions of the EQ-5D showed that the AL survivor group was having more difficulties or problems than the general population (Table 2). More than twice as many respondents with AL survivors reported having problems with usual activities (15% vs. 5%, $p < 0.001$), and anxiety or depression (24% vs. 9%, $p < 0.001$). Furthermore, a significant proportion of patients reported pain compared with their matched population (35% vs. 20%, $p < 0.001$). Mean EQ-5D index was 0.90 (standard deviation [SD], 0.11; range, 0.66–1.00) for the chemotherapy group, 0.86 (SD, 0.14; range, 0.58–1.00) for the SCT group, and 0.94 (SD, 0.11; range, 0.57–1.00) for the control group (chemotherapy group vs. SCT group, $p = 0.125$; chemotherapy group vs. control group, $p = 0.025$; SCT group vs. control group, $p < 0.001$; p values were compared using ANOVA).

Most of the EORTC QLQ-C30 subscale scores were similar for AL survivors and control subjects (Table 3). Social functioning and financial difficulty scores showed a statistically significant difference between the groups; however, financial difficulty was the only subscale that showed clinically significant differences between AL survivors and control subjects. In general, most QLQ-C30 subscale scores were similar for the chemotherapy group and the general population group. Although the chemotherapy group had similar scores in cognitive functioning, nausea/vomiting, and financial difficulty subscales compared to the control group, none of these showed clinically meaningful differences. In contrast, the SCT group reported more problems than the control group; social functioning, insomnia, and financial difficulty subscale scores showed clinically meaningful, significant differences compared with those of the control group.

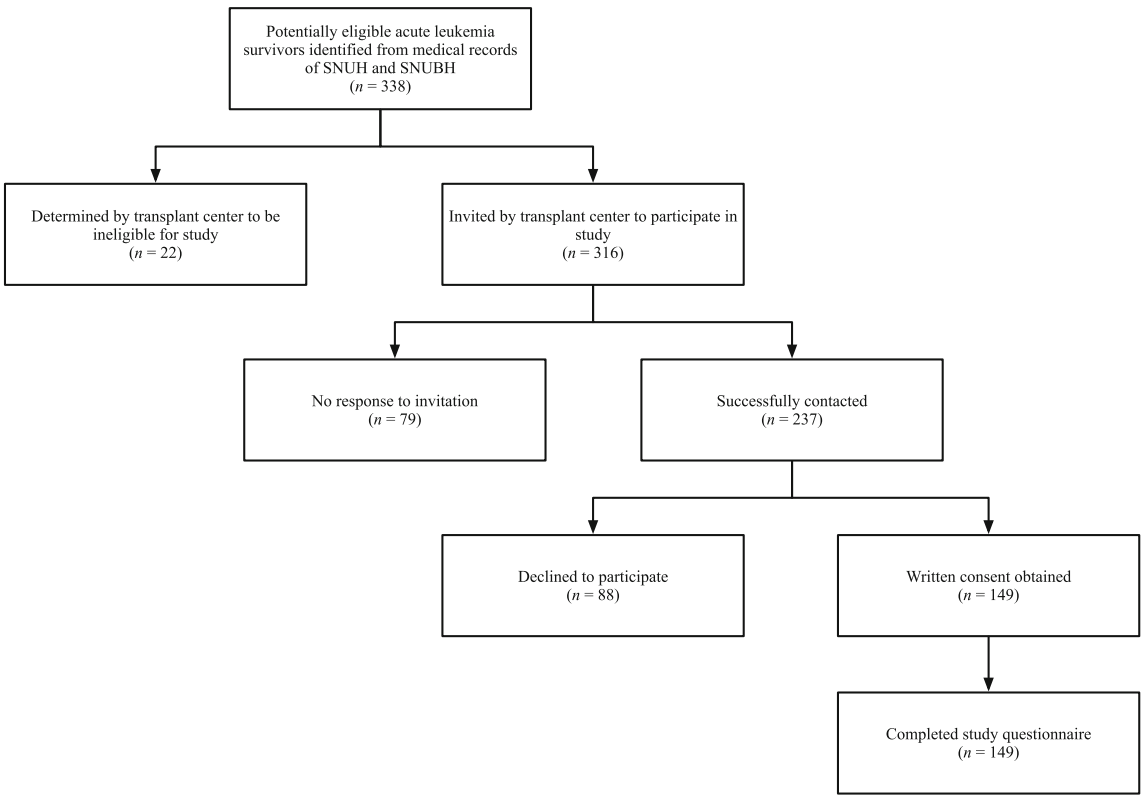

Fig. 1 Flow chart summarizing the recruitment of acute leukemia survivors

Table 1 Clinical and demographic characteristics of study participants ($n = 149$)

	Chemotherapy ($n = 93$)	SCT ($n = 56$)	p value
Median age, years (range)	55 (19–82)	48 (23–65)	0.021
Sex			
Men	47 (50)	28 (50)	
Women	46 (50)	28 (50)	
BMI, kg/m^2	23.7 (16.0–32.7)	22.3 (16.2–30.8)	0.002
Diagnosis			
AML	84 (90)	37 (66)	0.001
ALL	8 (9)	16 (29)	
ABL	1 (1)	3 (5)	
Time to survey from treatment completion, median (range)	60 (14–316)	53 (9–236)	0.495
Marital status			
Married	61 (66)	37 (66)	0.834
Single	32 (34)	18 (32)	
Education			
< high school graduate	26 (28)	7 (13)	0.080
High school graduate	30 (32)	24 (43)	
College degree	37 (40)	25 (45)	
Religion			
Nonreligious	32 (34)	26 (46)	0.414
Christian	26 (28)	13 (23)	
Catholic	12 (13)	9 (16)	
Buddhist	18 (19)	7 (13)	
Others	5 (5)	1 (2)	
Employment status			
Working or student	41 (44)	23 (41)	0.605
Not working	4 (4)	1 (2)	
Retired or homemaker	44 (47)	30 (54)	
Monthly household income[a]			
< $1725	21 (23)	11 (20)	0.934
$1725–$3450	33 (36)	21 (38)	
> $3450	27 (29)	18 (32)	
Not answered	12 (13)	6 (11)	
Comorbidities			
None	30 (32)	23 (41)	0.276
Any	63 (68)	33 (59)	
HTN/CAD	17 (18)	9 (16)	
Diabetes	11 (12)	4 (7)	
Dyslipidemia	9 (10)	1 (2)	
Chronic hepatitis B	8 (9)	6 (11)	
Depression	5 (5)	2 (4)	
Thyroid disease	7 (8)	2 (4)	
Asthma/COPD/pulmonary TB	2 (2)	3 (5)	
Others	10 (11)	10 (18)	

Abbreviations: *SCT*, stem cell transplantation; *BMI*, body mass index; *AML*, acute myeloid leukemia; *ALL*, acute lymphoblastic leukemia; *ABL*, acute biphenotypic leukemia; *HTN*, hypertension; *CAD*, coronary artery disease; *COPD*, chronic obstructive pulmonary disease; *TB*, tuberculosis

[a] All costs are represented using an exchange rate of Korean won at 1160 to US dollar at 1, which was the annual exchange rate in 2016

Table 2 Numbers and proportions reporting levels with EQ-5D dimensions

EQ-5D-3L dimension	Level[a]	AL survivors			Control	*p* value[b]
		Chemotherapy	SCT	All survivors		
Mobility	1	81 (90)	49 (90)	130 (90)	402 (90)	0.850
	2	9 (10)	5 (10)	14 (10)	45 (10)	
	3	0	0	0	1 (0)	
	No. of reporting problem	9 (10.0)	5 (10)	14 (10)	46 (10)	
Self-care	1	88 (98)	52 (96)	140 (97)	441 (98)	0.883
	2	2 (2)	2 (4)	4 (3)	7 (2)	
	3	0	0	0	0	
	No. of reporting problem	2 (2)	2 (4)	4 (3)	7 (2)	
Usual activities	1	82 (91)	41 (76)	123 (85)	427 (95)	< 0.001
	2	8 (9)	13 (24)	21 (15)	19 (4)	
	3	0	0	0	2 (1)	
	No. of reporting problem	8 (9)	13 (24)	21 (15)	21 (5)	
Pain/discomfort	1	65 (72)	29 (54)	94 (65)	357 (78)	< 0.001
	2	25 (28)	23 (43)	48 (33)	86 (19)	
	3	0	2 (3)	2 (1)	5 (1)	
	No. of reporting problem	25 (28)	25 (46)	50 (35)	91 (20)	
Anxiety/depression	1	72 (80)	38 (70)	110 (76)	407 (91)	< 0.001
	2	17 (19)	16 (30)	33 (23)	40 (9)	
	3	1 (1)	0	1 (1)	1 (0)	
	No. of reporting problem	18 (20)	16 (30)	34 (24)	41 (9)	

Data are presented as number (%)

SCT, stem cell transplantation

[a] 1, no problem; 2, moderate problems; 3, extreme problems

[b] *p* values were calculated comparing the AL survivors and the control group using chi-square test

Comparison of HRQoL between SCT group and chemotherapy group

Among the survivors, the SCT group had significantly worse problems with role functioning, fatigue, dyspnea, and insomnia than the chemotherapy group with clinical significance (score difference > 10) (Table 3). BFI-K short form results show that the proportion of patients reporting moderate to severe usual fatigue and worst fatigue was higher in the SCT group than that in the chemotherapy group (usual fatigue, 43% vs. 53%; worst fatigue, 56% vs. 74%) (Fig. 2) (Table S1). The SCT group also had statistically significantly worse problems with physical and emotional functioning, pain, and appetite loss, but the differences were not clinically significant. Depression was higher in SCT patients than in chemotherapy patients (mean HADS-depression score 4.99 vs. 6.56, $p = 0.024$) (Table 4). There was no difference in the HADS-anxiety score and BEPSI score between the subgroups (Table 4). Dyadic adjustment and family function were similar between the subgroups (Table S2).

Comparison of health behaviors between AL survivors and the general population

In terms of health behaviors, the acute leukemia survivor group had a lower rate of smoking (6% vs. 25%, $p < 0.001$) and drinking in the past 1 year (42% vs. 77%, $p < 0.001$), and a higher rate of influenza vaccination (64% vs. 35%, $p < 0.001$) (Table 5). Only 17% of the leukemia survivors reported that they had been recommended to receive screening for other cancers from health-care providers, and 27% and 40% reported that they thought their risk for other cancers was equal or lower than that of the general population. However, this lack of recommendation for second cancer screening and the misperception of second cancer risk did not have a negative impact on cancer screening behaviors (cancer screening in recent 2 years, 46% for survivor group vs. 52% general population, $p = 0.175$; health examination, 61% vs. 63%, $p = 0.632$). Among AL survivors, the rate of cancer screening was lower in the SCT group than that in the chemotherapy group ($p = 0.041$). In terms of employment status, the proportion of patients working decreased from the

Table 3 EORTC QLQ-C30 subscales in acute leukemia survivors and general population (control subject)

	AL survivors		Control		*p* value			
	CT ($n = 93$)	SCT ($n = 56$)	All ($n = 149$)	($n = 298$)	AL vs. control	CT vs. control	SCT vs. control	CT vs. SCT
Global health status/QoL	70.32 (17.90)	63.99 (18.33)	67.96 (18.25)	67.7 (17.88)	0.886	0.447	0.351	0.106
Functioning								
Physical functioning	86.28 (14.32)	77.61 (16.69)	83.00 (15.77)	83.79 (19.06)	0.671	0.490	0.056	0.016
Role functioning	90.72 (18.54)	80.19 (23.58)	86.76 (21.13)	87.47 (18.20)	0.718	0.336	0.028	0.004
Emotional functioning	86.69 (15.95)	79.09 (17.11)	83.81 (16.75)	82.14 (19.27)	0.378	0.107	0.508	0.048
Cognitive functioning	89.58 (16.44)	84.59 (17.24)	87.70 (16.86)	85.31 (17.87)	0.053	0.034	0.987	0.240
Social functioning	86.59 (20.46)	79.25 (28.66)	83.81 (24.06)	91.56 (16.96)	0.001	0.101	< 0.001	0.078
Symptom scales								
Fatigue	22.21 (17.77)	33.32 (20.80)	26.41 (19.66)	23.84 (21.11)	0.225	0.790	0.006	0.006
Nausea and vomiting	2.67 (7.10)	5.35 (9.12)	3.67 (8.00)	6.84 (14.55)	0.003	0.020	0.716	0.447
Pain	8.72 (13.83)	17.61 (18.24)	12.06 (16.68)	11.56 (18.24)	0.893	0.378	0.056	0.011
Single items								
Dyspnea	9.08 (15.75)	20.12 (27.99)	11.81 (18.31)	13.46 (20.95)	0.917	0.201	0.086	0.008
Insomnia	13.63 (22.39)	25.15 (29.89)	17.96 (25.98)	13.47 (21.49)	0.076	0.998	0.002	0.011
Appetite loss	6.06 (12.92)	15.09 (20.21)	9.45 (16.57)	11.92 (21.22)	0.186	0.039	0.528	0.024
Constipation	12.12 (23.26)	16.97 (24.99)	13.94 (23.95)	14.03 (21.23)	0.970	0.757	0.645	0.417
Diarrhea	11.36 (18.14)	12.57 (18.74)	11.81 (18.31)	9.36 (19.55)	0.211	0.667	0.500	0.930
Financial difficulties	13.79 (24.14)	21.79 (35.48)	16.78 (29.04)	7.01 (16.11)	< 0.001	0.023	< 0.001	0.077

Abbreviations: *EORTC QLQ-C30*, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; *AL*, acute leukemia; *CT*, chemotherapy; *SCT*, stem cell transplantation; *QoL*, quality of life

time of diagnosis and the time of survey (Fig. 3). In the SCT group, 80% of patients were employed or were students at the time of diagnosis, but the proportion decreased to 43% at the time of survey. In the chemotherapy group, the proportion of patients decreased from 73% at the time of diagnosis to 45% at the time of survey.

Discussion

In our study of 149 AL survivors from Korean tertiary care centers and matched general population subjects from two respective cohorts, we found that survivors of acute leukemia have significantly worse long-term effects on QoL compared to the general population. Moreover, patients who received SCT for post-remission treatment had poorer QoL than those treated with chemotherapy. Health behaviors were comparable between the survivors and the general population. However, misperception on second cancer risk and lack of recommendations on second cancer screening by health-care providers were noticed. To the best of our knowledge, no studies have previously reported these findings.

In general, AL survivors reported poor QoL compared to the general population. Compared to the general population

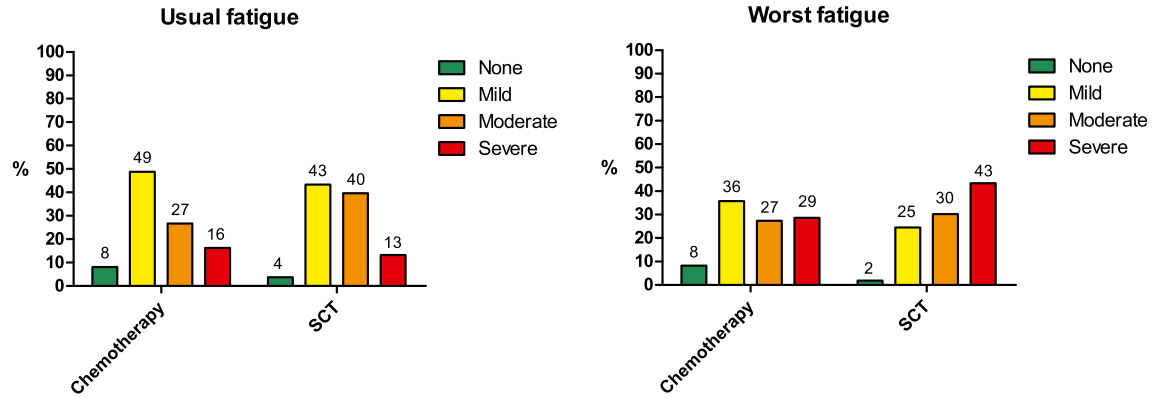

Fig. 2 Distribution of fatigue severity in acute leukemia survivors

Table 4 Comparison of anxiety, depression, and stress between chemotherapy group and SCT group

	Chemotherapy ($n = 93$)	SCT ($n = 56$)	p value
HADS-K score			
HADS-anxiety, mean (SE)[a]	4.21 (0.33)	5.28 (0.44)	0.057
HADS-depression, mean (SE)[a]	4.99 (0.41)	6.57 (0.54)	0.024
Sadness or despair lasting over 2 weeks			
Yes	10 (11)	9 (16)	0.346
No	83 (89)	47 (84)	
Suicidal idea during the past year			
Yes	12 (13)	11 (19)	0.224
No	81 (87)	44 (79)	
Not answered	0	1 (2)	
Suicidal attempt during the past year			
Yes	0	0	0.292
No	91 (98)	53 (95)	
Not answered	2 (2)	2 9 (5)	
Counseling due to psychological problems during the past year			
Yes	2 (2)	2 (4)	0.631
No	91 (98)	54 (96)	
BEPSI score, mean (SE)[a]	1.49 (0.06)	1.64 (0.09)	0.160

p values are from analysis of covariance with a generalized linear model

Abbreviations: *SCT*, hematopoietic stem cell transplantation; *HADS-K*, hospital anxiety and depression scale for Korean; *BEPSI*, Brief Encounter Psychosocial Instrument

[a] Adjusted for age, sex, disease subtype, education, religion, marital status, household income, and any comorbidity

from KNHANES VI using EQ-5D, AL survivors had more problems with usual activity, pain, and anxiety or depression. However, these differences of QoL were mainly derived from the SCT group. Only 5% of the general population and 10% of the chemotherapy group reported problems in usual activities, but 14.6% of SCT survivors reported problems. Similarly, pain was more frequently reported in the SCT group (46%) than in the control (20%) and the chemotherapy groups (28%). Comparisons with other cohorts using the EORTC QLQ-C30 also demonstrated consistent results. Compared to the control group, AL survivors reported more difficulties in social functioning, nausea and vomiting, and financial difficulties; however, none of the differences were in a clinically significant range. On the other hand, SCT survivors had significantly more problems associated with social functioning, insomnia, and financial difficulties than the general population, and more problems with role functioning, fatigue, dyspnea, and insomnia than the chemotherapy group. These findings are in line with those of previous studies. Andrykowski et al. [13] reported that SCT survivors ($n = 662$; 36% of study participants had AML and ALL) had poorer physical health, physical functioning, and psychological adjustment than the age- and sex-matched healthy controls. Kopp et al. [15] also reported that SCT recipients ($n = 34$; 47% of study participants had acute leukemia) reported problems with social functioning and financial difficulties. However, these previous studies included autologous stem cell transplantation and patients with hematologic disease other than acute leukemia, such as chronic leukemia, multiple myeloma, and lymphoma. In a study on the impact of post-remission treatment on QoL in AML survivors, SCT had worse long-term effects in QoL than conventional chemotherapy [17]. Compared to these previous studies, our study was done on a relatively homogenous disease group (acute leukemia) with comparisons to the general population and treatment modalities, providing more integrated information on QoL of AL survivors.

Another aspect that is noticeable in this study is the financial difficulty reported by AL survivors. Although there is no data on the financial impact of AL patients receiving chemotherapy, we have previously reported that total medical costs within 1 year of SCT in an acute leukemia patient are $88,967 for myeloablative conditioning regimen and $68,938 for reduced intensity conditioning regimen, constituting 357% and 273% of the per capita income in Korea [33]. If you exclude the proportion reimbursed by the National Health Insurance Service, thus paid by the patients themselves, one patient needs approximately $29,000 to $30,000 for 1 year after SCT, which is above the per capita income in Korea. Economic well-being is an important part of the quality of life, but little has been known about the socioeconomic activities

Table 5 Health behaviors in acute leukemia survivors compared with the general population

	Chemotherapy ($n = 93$)	SCT ($n = 56$)	KNHANES ($n = 447$)	p value[a]	p value[b]
Smoking					
Never smoker	54 (70)	39 (80)	223 (50)	0.417	< 0.001
Ex-smoker	29 (17)	14 (14)	108 (24)		
Current smoker	7 (9)	1 (2)	112 (25)		
Not answered	3 (4)	2 (4)			
Drinking					
Never drinker	45 (48)	35 (63)	42 (10)	0.107	< 0.001
Ever drinker	44 (47)	21 (38)	401 (90)		
Not answered	4 (4)	0			
Influenza vaccination during the past year					
Yes	56 (60)	35 (63)	158 (35)	0.734	< 0.001
No	34 (37)	18 (32)	288 (65)		
Not answered	3 (3)	3 (5)			
Medical examination during the past 2 years					
Yes	62 (67)	27 (48)	283 (63)	0.067	0.632
No	30 (32)	27 (48)	165 (37)		
Not answered	1 (1)	2 (4)			
Cancer screening during the past 2 years					
Yes	46 (50)	21 (38)	234 (52)	0.041	0.175
No	47 (50)	32 (57)	213 (48)		
Not answered	0	3 (5)			
Sleeping hours	7 (2–12)	7 (3–10)	7 (3–12)	0.762	0.024
Stress					
Very much	1 (1)	0	11 (3)	0.237	0.223
Much	11 (12)	13 (23)	90 (20)		
Little	62 (67)	35 (63)	252 (57)		
Very little	19 (20)	8 (14)	90 (20)		

Abbreviations: *SCT*, hematopoietic stem cell transplantation; *KNHANES*, The Korea National Health and Nutrition Examination Survey

[a] p values comparing chemotherapy and SCT

[b] p values comparing acute leukemia survivors (chemotherapy and SCT group combined) and general population (KNHANES)

of transplant recipients. In relation to this, our study also showed that a significant proportion of AL survivors failed to return to work. Eighty percent of patients in the SCT group and 73% in the chemotherapy group were workers or students at time of diagnosis, but only 43% and 45% of patients remained at work or study at time of survey. Further studies are needed from this perspective to clarify the economic burden on the patient as well as to guide the development of

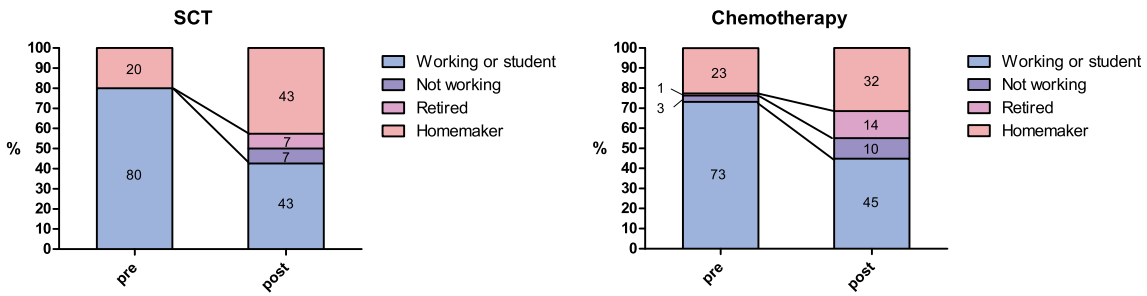

Fig. 3 Employment status of acute leukemia survivors before and after treatment

possible approaches to help the patients. The situation may vary from country to country due to different monetary values and health-care systems; however, given that Korea's health-related indicators are relatively good among the countries of the Organization for Economic Cooperation and Development (OECD), the results of our study will be applicable to other OECD countries as well.

AL survivors are at increased risk for developing cancers at other sites. One recent US population-based study revealed that the risk of all-site cancer, cancer of gastrointestinal system, and oral and pharyngeal cancer was significantly higher among patients with AML than that among the general US population [34]. Despite this, little is known about the current status of second cancer screening practices and related factors in AL survivors. The data from our study showed that most survivors (83%) had not received a recommendation for cancer screening from health-care providers, and more than half of the study participants had a misconception that their risk of second cancer was lower than or similar with that of the general population. Although this lack of knowledge did not lead to lack of cancer screening or negative health behavior in AL survivors, our study highlights that health-care providers should be aware of the risk of second cancer and should include screening recommendations in the AL survivorship care plan. Importantly, although rate of cancer screening was similar in the AL survivor group and the general population, among AL survivors, the SCT group received fewer cancer screenings than the chemotherapy group. SCT patients visit the hospital more frequently in general; hence, patients in the SCT group might think that all tests are being done and may not be aware of the need for second cancer screening.

Our study differs from others in several ways. First, we matched AL survivors and control subjects from two cohorts. Control subjects from KNHANES VI were matched 1:3 for age, sex, education status, marital status, and presence of any comorbidity, and those from the representative sample of Korean adult population were 1:2 matched for age and sex. Using these two different cohorts with a number of variables matched, we reduced the risk of a selection bias and could provide more consistent results. Secondly, in addition to the QoL, health behaviors and second cancer screening were also described in detail.

Our study has some limitations. First, the response rate was only 44% (149 out of 338 potential subjects); thus, we might have underestimated or overestimated HRQoL problems because nonresponders could have a lower or higher HRQoL. Second, the study was limited by the cross-sectional design. Also, our study participants were accrued from three tertiary hospitals in Korea, which might have led to selection bias and lack of generalizability. Finally, our finding cannot be used as a tool for guiding treatment between stem cell transplantation and chemotherapy, since the worse HRQOL in SCT group can stem from the confounding factors such as the patients' inherent disease-specific risk factors.

In conclusion, our study showed that AL survivors, especially those who received SCT as post-remission treatment, had poor HRQoL compared to the general population. Difficulties in social functioning and finances were noteworthy, and the proportion of patients who were employed was reduced by approximately 30% at time of survey. Misperception on second cancer risk and lack of recommendation on second cancer screening by health-care providers were also demonstrated. This information will be useful in making appropriate survivorship care plans both at the physician level and at the government level.

Funding This study was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI14C1277).

Compliance with ethical standards

The institutional review boards of the participating institutions approved the study, and informed consent was obtained from all subjects.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Bassan R, Hoelzer D (2011) Modern therapy of acute lymphoblastic leukemia. J Clin Oncol 29:532–543. https://doi.org/10.1200/JCO.2010.30.1382
2. Estey E, Döhner H (2006) Acute myeloid leukaemia. Lancet 368:1894–1907. https://doi.org/10.1016/S0140-6736(06)69780-8
3. Zittoun R, Suciu S, Watson M, Solbu G, Muus P, Mandelli F, Stryckmans P, Peetermans M, Thaler J, Resegotti L, Dardenne M, Willemze R (1997) Quality of life in patients with acute myelogenous leukemia in prolonged first complete remission after bone marrow transplantation (allogeneic or autologous) or chemotherapy: a cross-sectional study of the EORTC-GIMEMA AML 8A trial. Bone Marrow Transplant 20:307–315. https://doi.org/10.1038/sj.bmt.1700888
4. Schumacher A, Kessler T, Büchner T, Wewers D, van de Loo J (1998) Quality of life in adult patients with acute myeloid leukemia receiving intensive and prolonged chemotherapy—a longitudinal study. Leukemia 12:586–592
5. Hjermstad M, Holte H, Evensen S, Fayers PM, Kaasa S (1999) Do patients who are treated with stem cell transplantation have a health-related quality of life comparable to the general population after 1 year? Bone Marrow Transplant 24:911–918. https://doi.org/10.1038/sj.bmt.1701998
6. Hjermstad MJ, Evensen SA, Kvaløy SO, Fayers PM, Kaasa S (1999) Health-related quality of life 1 year after allogeneic or autologous stem-cell transplantation: a prospective study. J Clin Oncol 17:706–718. https://doi.org/10.1200/JCO.1999.17.2.706
7. Broers S, Kaptein AA, Le Cessie S et al (2000) Psychological functioning and quality of life following bone marrow transplantation: a 3-year follow-up study. J Psychosom Res 48:11–21
8. Lee SJ, Fairclough D, Parsons SK, Soiffer RJ, Fisher DC, Schlossman RL, Antin JH, Weeks JC (2001) Recovery after stem-cell transplantation for hematologic diseases. J Clin Oncol 19:242–252. https://doi.org/10.1200/JCO.2001.19.1.242

9. Heinonen H, Volin L, Uutela A, Zevon M, Barrick C, Ruutu T (2001) Quality of life and factors related to perceived satisfaction with quality of life after allogeneic bone marrow transplantation. Ann Hematol 80:137–143
10. Edman L, Larsen J, Hägglund H, Gardulf A (2001) Health-related quality of life, symptom distress and sense of coherence in adult survivors of allogeneic stem-cell transplantation. Eur J Cancer Care (Engl) 10:124–130
11. Syrjala KL, Langer SL, Abrams JR, Storer B, Sanders JE, Flowers ME, Martin PJ (2004) Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. JAMA 291:2335–2343. https://doi.org/10.1001/jama.291.19.2335
12. Hjermstad MJ, Knobel H, Brinch L, Fayers PM, Loge JH, Holte H, Kaasa S (2004) A prospective study of health-related quality of life, fatigue, anxiety and depression 3-5 years after stem cell transplantation. Bone Marrow Transplant 34:257–266. https://doi.org/10.1038/sj.bmt.1704561
13. Andrykowski MA, Bishop MM, Hahn EA, Cella DF, Beaumont JL, Brady MJ, Horowitz MM, Sobocinski KA, Rizzo JD, Wingard JR (2005) Long-term health-related quality of life, growth, and spiritual well-being after hematopoietic stem-cell transplantation. J Clin Oncol 23:599–608. https://doi.org/10.1200/JCO.2005.03.189
14. Syrjala KL, Langer SL, Abrams JR, Storer BE, Martin PJ (2005) Late effects of hematopoietic cell transplantation among 10-year adult survivors compared with case-matched controls. J Clin Oncol 23:6596–6606. https://doi.org/10.1200/JCO.2005.12.674
15. Kopp M, Holzner B, Meraner V, Sperner-Unterweger B, Kemmler G, Nguyen-van-Tam DP, Nachbaur D (2005) Quality of life in adult hematopoietic cell transplant patients at least 5 yr after treatment: a comparison with healthy controls. Eur J Haematol 74:304–308. https://doi.org/10.1111/j.1600-0609.2004.00402.x
16. Bevans MF, Marden S, Leidy NK, Soeken K, Cusack G, Rivera P, Mayberry H, Bishop MR, Childs R, Barrett AJ (2006) Health-related quality of life in patients receiving reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant 38:101–109. https://doi.org/10.1038/sj.bmt.1705406
17. Messerer D, Engel J, Hasford J, Schaich M, Ehninger G, Sauerland C, Buchner T, Schumacher A, Krahl R, Niederwieser D, Krauter J, Ganser A, Creutzig U, Dohner H, Schlenk RF, for the German AML Intergroup (2008) Impact of different post-remission strategies on quality of life in patients with acute myeloid leukemia. Haematologica 93:826–833. https://doi.org/10.3324/haematol.11987
18. Pidala J, Anasetti C, Jim H (2009) Quality of life after allogeneic hematopoietic cell transplantation. Blood 114:7–19. https://doi.org/10.1182/blood-2008-10-182592
19. Andersson I, Ahlberg K, Stockelberg D, Brune M, Persson LO (2009) Health-related quality of life in patients undergoing allogeneic stem cell transplantation after reduced intensity conditioning versus myeloablative conditioning. Cancer Nurs 32:325–334. https://doi.org/10.1097/NCC.0b013e31819b5c81
20. Gupta V, Panzarella T, Li L, Khan J, Sharma A, Lipton JH, Kuruvilla J, Messner H, Alibhai SMH (2012) A prospective study comparing the outcomes and health-related quality of life in adult patients with myeloid malignancies undergoing allogeneic transplantation using myeloablative or reduced-intensity conditioning. Biol Blood Marrow Transplant 18:113–124. https://doi.org/10.1016/j.bbmt.2011.05.022
21. Fayers P, Aaronson N, Bjordal K (2001) The EORTC QLQ-C30 scoring manual, ed 3. European Organization for Research and Treatment of Cancer, Brussels
22. Brooks R (1996) EuroQol: the current state of play. Health Policy Amst Neth 37:53–72
23. Kim M-H, Cho Y-S, Uhm W-S, Kim S, Bae SC (2005) Cross-cultural adaptation and validation of the Korean version of the EQ-5D in patients with rheumatic diseases. Qual Life Res 14:1401–1406
24. Yun YH, Park YS, Lee ES, Bang SM, Heo DS, Park SY, You CH, West K (2004) Validation of the Korean version of the EORTC QLQ-C30. Qual Life Res 13:863–868. https://doi.org/10.1023/B:QURE.0000021692.81214.70
25. Snaith RP (2003) The hospital anxiety and depression scale. Health Qual Life Outcomes 1:29. https://doi.org/10.1186/1477-7525-1-29
26. Mendoza TR, Wang XS, Cleeland CS, Morrissey M, Johnson BA, Wendt JK, Huber SL (1999) The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. Cancer 85:1186–1196
27. Frank SH, Zyzanski SJ (1988) Stress in the clinical setting: the Brief Encounter Psychosocial Instrument. J Fam Pract 26:533–539
28. Oh SM, Min KJ, Park DB (1999) A study on the standardization of the hospital anxiety and depression scale for Koreans: a comparison of normal, depressed and anxious groups. J Korean Neuropsychiatr Assoc 38:289–296
29. Yun YH, Wang XS, Lee JS, Roh JW, Lee CG, Lee WS, Lee KS, Bang SM, Mendoza TR, Cleeland CS (2005) Validation study of the Korean version of the brief fatigue inventory. J Pain Symptom Manag 29:165–172. https://doi.org/10.1016/j.jpainsymman.2004.04.013
30. Busby DM, Christensen C, Crane DR, Larson JH (1995) A revision of the dyadic adjustment scale for use with distressed and nondistressed couples: construct hierarchy and multidimensional scales. J Marital Fam Ther 21:289–308. https://doi.org/10.1111/j.1752-0606.1995.tb00163.x
31. Cho H, Choi SM, Oh HJ, Kwon JH (2011) Validity of the short forms of the Korean dyadic adjustment scale. Korean J Couns Psychother 23:655–670
32. Smilkstein G, Ashworth C, Montano D (1982) Validity and reliability of the family APGAR as a test of family function. J Fam Pract 15:303–311
33. Suh KJ, Kim I, Lim J, Ha H, Park S, Koh Y, Yoon SS, Park S (2015) Total costs and clinical outcome of hematopoietic stem cell transplantation in adults with leukemia: comparison between reduced-intensity and myeloablative conditioning. Clin Transpl 29:124–133. https://doi.org/10.1111/ctr.12492
34. Ghimire KB, Shah BK (2014) Second primary malignancies in adult acute myeloid leukemia—a US population-based study. Anticancer Res 34:3855–3859