



Relationship between quality of life before treatment and survival in patients with hematological malignancies: A meta-analysis

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Abstract

This meta-analysis aimed to investigate the impact of pretreatment quality of life (QoL) on overall survival (OS) in patients with hematological malignancies. The observational studies with relationship between QoL and OS in patients undergoing either hematopoietic stem cell transplantation (HSCT) or chemotherapy were collected. Stratification by treatment was performed to examine the association between QoL and OS. Six articles were included in the analysis. Overall, significant associations with OS were observed for global QoL (hazard ratio [HR] = 1.04, 95% confidence interval [CI] = 1.01–1.08), physical QoL (HR = 1.06, 95% CI : 1.02–1.10), and social QoL (HR = 1.02, 95% CI : 1.00–1.03). When stratified by treatment, HSCT showed significant associations between OS and both global QoL (HR = 1.05, 95% CI : 1.00–1.11) and physical QoL (HR = 1.03, 95% CI : 1.00–1.06). For chemotherapy, significant associations were also observed between OS and global QoL (HR = 1.04, 95% CI : 1.00–1.09), physical QoL (HR = 1.08, 95% CI : 1.00–1.17), role QoL (HR = 1.02, 95% CI : 1.00–1.04), and social QoL (HR = 1.02, 95% CI : 1.00–1.04). No significant associations were observed regarding emotional QoL, which was only analyzed in HSCT. The factors influencing OS may vary depending on the treatment, emphasizing the importance of recognizing QoL from the pretreatment stage.

Key words : hematopoietic stem cell transplantation, chemotherapy, quality of life, survival, meta-analysis

Trial registration

A systematic review with meta-analyses was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and was registered in the International Prospective Register of Systematic Reviews (registration number CRD42023398206)

Statements and Declarations

The authors have no conflicts of interest to declare.

Introduction

In recent years, advances in therapy and the development of supportive care have expanded the

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range of treatment options for cancer patients, resulting in improved survival rates. However, alongside therapeutic advancements, there is a growing challenge of treatment-related adverse events. Therapies for hematological malignancies continue to evolve with the development of new drugs, often involving long-term treatment courses. The complexity of the pathophysiology and treatment modalities of these diseases may profoundly impact the quality of life (QoL) and overall survival (OS) of patients.

Adverse events associated with cancer treatment, such as fatigue and anorexia, are common and contribute to a decline in physical function and activity levels, exacerbating the impact of treatment¹⁻⁴. There exists a close relationship between physical function, physical activity, and QoL, with reports across various cancer types indicating a decline in QoL associated with decreases in grip strength and lower limb function⁵⁻⁷. Moreover, low levels of physical activity have been linked to decreased QoL in cancer patients⁸⁻¹⁰. Additionally, factors affecting mental well-being, such as anxiety and depression, also influence QoL^{11,12}. Cancer patients often experience psychological stress related to treatment-related anxieties, fatigue, and other physical symptoms, further complicating QoL considerations. Therefore, addressing both physical and psychological aspects is essential in evaluating QoL in cancer patients. Furthermore, social factors such as personal economic situation and education have been reported to be associated with QoL in chemotherapy-treated cancer patients, emphasizing the importance of patient backgrounds¹³⁻¹⁵.

Recently, it has become clear that QoL also affects OS, further increasing the importance of QoL during cancer treatment. Zang *et al.*¹⁶ reported in a meta-analysis that baseline health-related QoL defined by physical function or the global QoL scale of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) predicts OS in digestive cancer patients. Moreover, their study also found that reduced global QoL, physical functioning, social functioning, and role functioning scales were significantly associated with decreased OS. Studies investigating QoL and OS in various cancer types and cancer survivors are ongoing, with QoL emerging as a significant predictor of OS¹⁷⁻²¹. However, there are conflicting reports, suggesting that the relationship between QoL and OS remains unclear in certain cancer stages²². Consequently, many aspects of the relationship between QoL and OS have yet to be

elucidated.

Notably, research on QoL and OS in the field of hematological malignancies is limited. Among the reviews reported to date that encompassed various cancer types, very few have included hematological malignancies^{23,24}. It is not clear which function parameters of QoL are involved in OS in patients with hematological malignancies, and there have been no studies stratified by treatment content. Factors related to QoL may vary among hematological malignancy patients, depending on the content and intensity of treatments such as hematopoietic stem cell transplantation (HSCT) and chemotherapy. Despite the possibility that there may be differences in the effect of each function parameter of QoL on OS, there are currently no reports on this point. Understanding the relationship between QoL and OS at the pretreatment stage would further emphasize the importance of intervention. Depending on the results, it may also support interventions by healthcare providers to maintain patients' QoL. Therefore, in this study, we aimed to investigate whether QoL affects OS, focusing specifically on hematological malignancy patients undergoing HSCT and chemotherapy, stratifying and analyzing them through meta-analysis.

Methods

A systematic review with meta-analyses was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and was registered in the International Prospective Register of Systematic Reviews (registration number CRD42023398206)^{25,26}.

Data searches and sources

Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed/MEDLINE, and Scopus databases from inception to December 2022 were searched based on QoL, EORTC QLQ-C30²⁷, Medical Outcomes Study Short-Form 36-Item Health Survey²⁸, Functional Assessment of Cancer Therapy-General (FACT-G)²⁹, as well as cancer, neoplasms, tumors, sarcomas, hematological malignancies, lymphomas, carcinosarcomas, leukemia, mortality, survival, relapses, and recurrences.

Study eligibility criteria and study selection

The study eligibility criteria were as follows : 1) observational studies ; 2) original human studies published in English ; 3) patients with hematologi-

cal malignancies in the pretreatment setting ; 4) patients treated with chemotherapy or HSCT ; and 5) studies on the relationship between QoL and mortality. Studies that examined the relationship between symptoms and mortality were excluded. After duplicates were removed, eight reviewers (TF, JN, SM, JI, TO, TT, KS, and KO) independently assessed study eligibility by reviewing the titles and abstracts of all potential citations according to the eligibility criteria. Full-text articles were retrieved for review if there was evidence of meeting the eligibility criteria or if there was insufficient information in the abstract or title. Final inclusion of eligible observational studies was determined in consensus meetings attended by all authors.

Data extraction

Two reviewers (TF and JN) were responsible for data extraction. The following data were extracted from each included study : 1) last name of the first author ; 2) year of publication ; 3) study location ; 4) treatment (chemotherapy or HSCT) ; 5) number of patients ; 6) sex ; 7) age ; 8) QoL assessments ; 9) follow-up time ; 10) covariates adjusted for in multivariate analysis ; 11) number of deaths ; and 12) risk estimates for mortality (hazard ratio [HR] and 95% confidence interval [CI]). When multiple models of multivariate analyses were reported, we used the results from the model with the most complete adjustment for potential confounders.

Quality assessment

The Newcastle-Ottawa Scale was used to assess the quality of studies, including their risk of bias³⁰⁾. There are eight domains within this tool : representativeness of the exposed cohort ; selection of the non-exposed cohort ; ascertainment of exposure ; demonstration that the outcome of interest was not present at the beginning of the study ; comparability of cohorts based on design or analysis ; assessment of outcomes ; whether the follow-up period was sufficient for outcomes to occur ; and whether cohort follow-up was adequate. The items were scored by two trained reviewers in accordance with the criteria. Consensus meetings attended by all authors were used to resolve potential disagreements.

Data analysis

Risk estimates for total mortality associated with global QoL and its subscales (physical, emotional, role, social) were analyzed. In an additional

analysis, we examined the associations between global and subscales of QoL and total mortality by treatment (chemotherapy and HSCT). We used adjusted HRs and 95% CIs in the multivariate analysis as a measure of effect size for all studies. The univariate HR was used only if reported, but not the multivariate HR. For inverse variance-weighted means, the natural logarithmic HR was used, and the standard error was calculated using a random effects model. We also assessed heterogeneity using the I^2 statistic. All statistical analyses were performed with Review Manager version 5.1 (RevMan ; The Cochrane Collaboration, London, UK).

Results

The literature search yielded 119,061 articles, which was reduced to 2,483 articles after excluding duplicates and patients without hematological malignancies. Based on the screening of titles and abstracts, seven articles were deemed eligible and underwent full-text review. After review, one article was excluded because it was not a pretreatment setting. Finally, six articles were identified and determined to be suitable for meta-analysis (Fig. 1).

Study characteristics

The characteristics of the included studies are summarized in Table 1. This meta-analysis included a total of 2,202 patients from studies conducted in different countries. The mean age was 46–51 years, and 27–48% were female. There were two articles on HSCT^{31,32)} and four articles on chemotherapy^{33–36)}. QoL was assessed using the EORTC QLQ-C30^{33–36)}, FACT-G³¹⁾, and EuroQol 5 Dimensions³²⁾. Both of the HSCT studies that were employed involved patients with a variety of hematological malignancies. All four studies on chemotherapy included lymphoma patients only.

Risk of bias assessment

Risk of bias was assessed using the Newcastle-Ottawa Scale. Of the included studies, four were considered to be of high impact (8–9 points) and two were considered to be of moderate impact (6–7 points) (Table 2).

Association between global QoL and mortality risk

A random-effects meta-analysis included a total of six studies. A forest plot of inverse HR and 95% CI was used to estimate the association between global QoL and mortality risk. Overall, global QoL was significantly associated with mortality risk

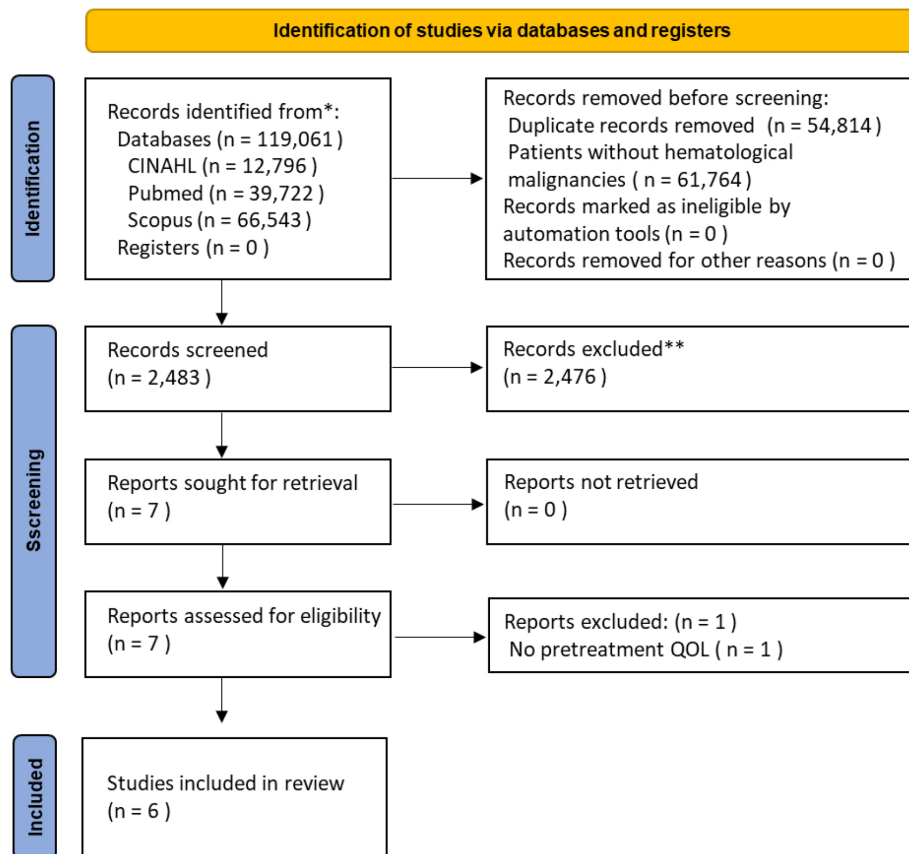


Fig. 1. Study flow diagram of the selection process

(HR : 1.04, 95% CI : 1.01–1.08, $p = 0.01$). A subgroup analysis by treatment showed borderline significance between global QoL and mortality risk in both HSCT (HR : 1.05, 95% CI : 1.00–1.11, $p = 0.05$, $I^2 = 0\%$) and chemotherapy (HR : 1.04, 95% CI : 1.00–1.09, $p = 0.05$, $I^2 = 74\%$). There were no significant differences between the subgroups ($p = 0.73$) (Fig. 2).

Association between physical QoL and mortality risk

Four studies were included in a random-effects meta-analysis. Overall, there was a significant association between physical QoL and mortality risk (HR : 1.06, 95% CI : 1.02–1.10, $p = 0.006$). In the subgroup analysis by treatment, there was a significant association between physical QoL and mortality risk in both HSCT (HR : 1.03, 95% CI : 1.00–1.06, $p = 0.02$) and chemotherapy (HR : 1.08, 95% CI : 1.00–1.17, $p = 0.04$, $I^2 = 66\%$), respectively. There were no significant differences between the subgroups ($p = 0.24$) (Fig. 3).

Association between emotional QoL and mortality risk

One study on HSCT was included in a random-

effects meta-analysis. There was no significant association between emotional QoL and mortality risk (HR : 1.00, 95% CI : 0.96–1.04, $p = 1.00$) (Fig. 4).

Association between role QoL and mortality risk

One study on chemotherapy was included in a random-effects meta-analysis. There was a significant association between role QoL and mortality risk (HR : 1.02, 95% CI : 1.00–1.04, $p = 0.009$) (Fig. 5).

Association between social QoL and mortality risk

Two studies were included in a random-effects meta-analysis. Overall, there was a significant association between social QoL and mortality risk (HR : 1.02, 95% CI : 1.00–1.03, $p = 0.04$). In the subgroup analysis by treatment, although there was no significant association between social QoL and mortality risk in HSCT (HR : 1.00, 95% CI : 0.97–1.04, $p = 1.00$), a significant association was observed in chemotherapy (HR : 1.02, 95% CI : 1.00–1.04, $p = 0.009$). There were no significant differences between the subgroups ($p = 0.30$) (Fig. 6).

Table 1. The characteristics of the included studies

Author, Year	Country	Patients (number, gender, age)	Treatment	QoL assessment	Follow-up period	Confounders	Number of deaths
Hamilton BK et al., 2015	USA	<i>n</i> = 409 Female, 48% Age:50 (18–70) years	HSCT	FACT-G	49 months (range, 1–128 months)	HCT-CI score, disease risk, HLA match, conditioning regimen intensity, graft source, year of transplant	Not reported
Huang H et al., 2022	Various (29) countries	<i>n</i> = 1239 Female, 47.4% Age:61.0 (18.0–86.0) years	Chemotherapy	EORTC-QLQ-C30	at least 3 years	International prognostic index, cell of origin, BCL2, total metabolic tumor volume	<i>n</i> = 258
Jerkeman M et al., 2001	Norway	<i>n</i> = 95 Female, 39% Age:46 (20–66) years	Chemotherapy	EORTC QLQ-C30	36 months (range: 12–77)	Serum LDH, PS, Ann Arbor Stage, age, extranodal sites	27%
Jung HA et al., 2012	Korea	<i>n</i> = 263 Female, 42.6% Age:55 (16–86) years	Chemotherapy	EORTC QLQ-C30	Until death	Age, PS, Ann Arbor stage, Serum LDH, extranodal involvement, functional scale, symptom/sign	Not reported
Kurosawa S et al., 2021	Japan	<i>n</i> = 145 Female, 36% Age:53 (18–71) years	HSCT	EQ-5D	3 months, 6 months, 1 year, and 2 years after HCT	Age, sex, disease, Disease Risk Index, donor type, HCT-CI	<i>n</i> = 53
Lindberg Å et al., 2022	Sweden, Norway, Denmark, Finland	<i>n</i> = 51 Female, 27% Age:71 (62–84) years	Chemotherapy	EORTC-QLQ-C30	52 months	TP53 mutation, CDKN2A deletion	Not reported

EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer QLQ-C30; EQ-5D, EuroQol 5 Dimensions; HCT-CI, Hematopoietic Cell Transplantation-specific Comorbidity Index; HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation; LDH, lactate dehydrogenase; PS, performance status; USA, United States of America.

Table 2. Quality assessment using the Newcastle-Ottawa Scale of cohort studies included in systematic review

Reference	Selection				Comparability		Outcome		Score
	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Hamilton, 2015	1	1	1	1	1	1	1	0	7
Huang, 2022	1	1	1	1	1	1	1	1	8
Jerkeman, 2001	1	1	1	1	2	1	1	0	8
Jung, 2012	1	1	1	1	2	1	1	0	8
Kurosawa S, 2021	1	1	1	1	2	1	1	0	8
Lindberg, 2022	1	1	1	1	1	1	1	0	7

Discussion

In this meta-analysis, we focused on whether QoL before treatment, including HSCT and chemotherapy, affects OS in patients with hematological

malignancy. The main findings of this systematic review and meta-analysis were as follows. Global QoL and physical QoL were associated with prognosis, and significant associations were also observed in the subgroup analyses of HSCT and chemotherapy.

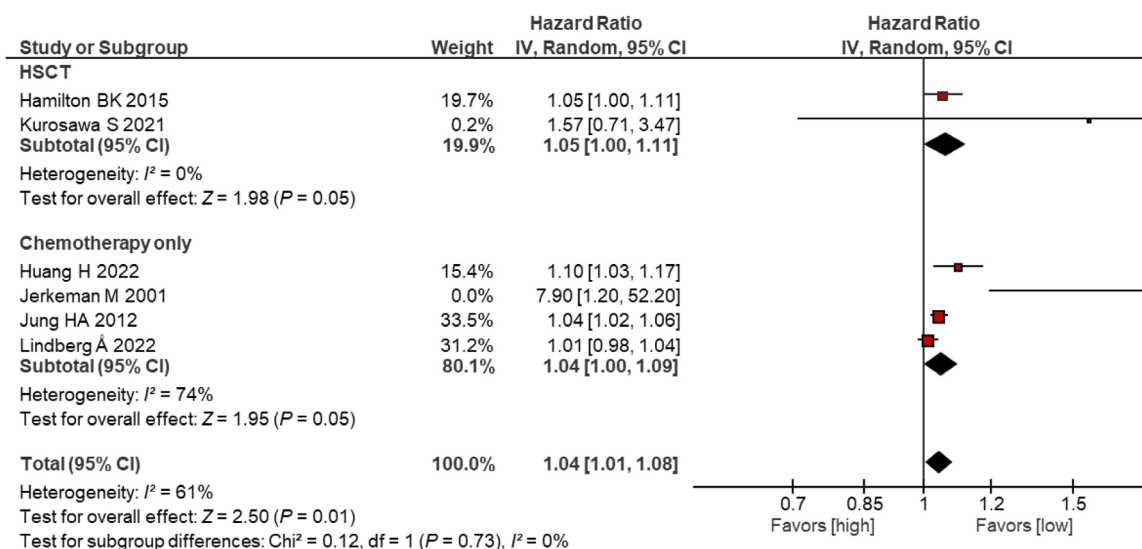


Fig. 2. Meta-analysis of the association between global QoL and mortality risk in patients with hematological malignancies

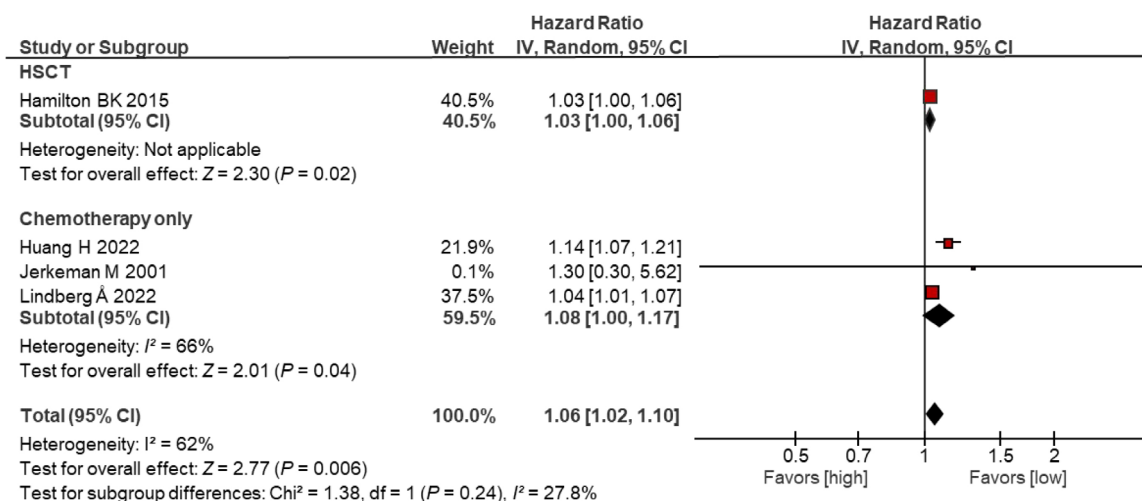


Fig. 3. Meta-analysis of the association between physical QoL and mortality risk in patients with hematological malignancies

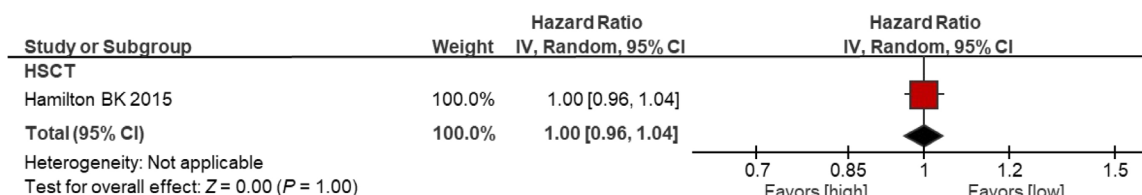


Fig. 4. Meta-analysis of the association between emotional QoL and mortality risk in patients with hematological malignancies

Role QoL showed an association with OS in the studies involving chemotherapy patients, although no such association was found among the HSC T patients. No relationship between social QoL and OS was observed in the HSC T studies, but one such

relationship was observed in the chemotherapy studies. Finally, emotional QoL did not exhibit a significant association with OS in any of the studies.

Traditionally, the survival rates of cancer patients have been attributed to factors related to the

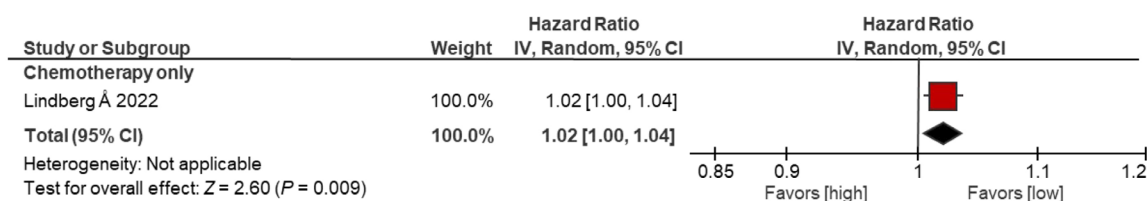


Fig. 5. Meta-analysis of the association between role QoL and mortality risk in patients with hematological malignancies

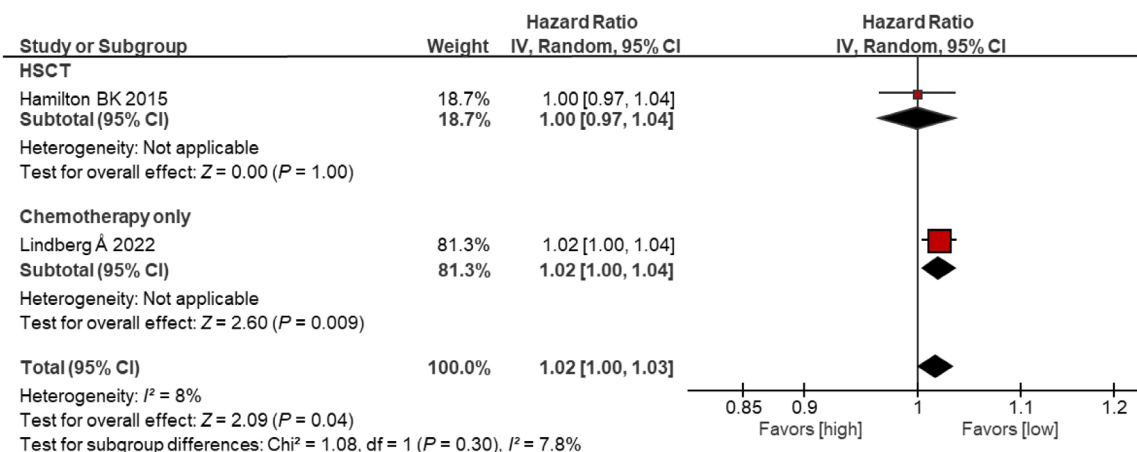


Fig. 6. Meta-analysis of the association between social QoL and mortality risk in patients with hematological malignancies

cancer itself, such as stage and site, as well as patient-related factors like age, health status, and treatment resistance³⁷⁻³⁹. Performance status (PS) has been particularly recognized as a convenient assessment scale for understanding a patient's overall condition, often guiding treatment decisions due to its association with treatment-related adverse events⁴⁰. Furthermore, PS has been reported to be associated with survival rates in various types of cancer⁴¹⁻⁴⁴, and has also been identified as a factor influencing survival in patients with hematological malignancies⁴⁵⁻⁴⁸. The present study revealed that pretreatment global QoL significantly influenced survival rates. Jerkeman *et al.*³⁴ reported that, among aggressive lymphoma patients undergoing chemotherapy, pretreatment global QoL emerged as a significant prognostic factor for survival, surpassing PS. However, given the limited number of patients with PS > 1 in their study, it was suggested that evaluating global QoL rather than PS could be useful in predicting survival, especially among younger patients or patients with good overall health status. Similarly, Jung *et al.*³⁵ suggested that diffuse large B-cell lymphoma patients with low pretreatment global QoL exhibited poor resistance to chemotherapy, leading to decreased OS, regardless of age or PS. Moreover, patients who died due to

treatment-related complications had lower pretreatment global QoL scores, indicating increased treatment-associated mortality. Thus, the results of the present review indicate that pretreatment global QoL affects OS in patients undergoing either HSCT or chemotherapy alone, underscoring its recognition as a valuable factor for improving OS. Furthermore, healthcare providers should acknowledge that pretreatment global QoL may offer superior prognostic capabilities compared to factors previously reported to influence survival rates. However, whether this applies universally across hematological malignancies or only to specific patient groups remains uncertain due to insufficient evidence, highlighting the need for further research in this area.

Among the QoL parameters, both global QoL and physical QoL were associated with favorable OS in patients undergoing HSCT or chemotherapy. The impact of pre-treatment QoL on OS has also been observed in other cancer types⁴⁹⁻⁵¹. While pretreatment global QoL may be crucial in predicting survival rates, detailed evaluation of physical function is also deemed necessary. Global QoL encompasses various factors, including age, cancer stage, nutrition, and activity level, which may act as surrogate markers for OS. Moreover, patients with hematologic malignancies are more likely to be

younger at the time of diagnosis compared to those with other cancers, and those undergoing HSCT are often also younger. The decision-making process in cancer treatment varies by age, with young adult patients more likely to undergo aggressive treatments aimed at prolonging life⁵²⁾. Given the younger demographic often seen in patients with hematologic malignancies, it is expected that they would likely be able to maintain relatively good general QoL and physical well-being prior to treatment. Physical function has also been associated with post-HSCT prognosis⁵³⁾, suggesting that patients with better physical function before treatment may have higher physical QoL, enabling them to undergo more aggressive treatments that could, in turn, improve OS. Hamilton *et al.*³¹⁾ reported, that among HSCT patients, physical function, particularly physical well-being, correlated with OS, although no association with non-relapse mortality was observed. The underlying reasons for the differing associations between QoL and both survival rates and non-relapse mortality remain unclear, but physical function may be influenced not only by cancer-specific symptoms and physical characteristics, but also by comorbidities, as noted in reports by Kurosawa *et al.*³²⁾. However, despite the influence of comorbidities, if the evaluation of physical QoL as a QoL parameter enables the prediction of OS, it should be assessed at the pre-transplantation stage. Similarly, in chemotherapy patients, physical QoL among QoL parameters influenced OS. Huang *et al.*³³⁾ and Lindberg *et al.*³⁶⁾ reported that, among QoL parameters, physical QoL was associated not only with OS but also with progression-free survival (PFS). Hematological malignancy patients exhibit decreased muscle strength, overall endurance, and skeletal muscle mass even before transplantation or chemotherapy, with differences in physical function observed based on hemoglobin levels, an indicator of anemia^{24,54-56)}. Moreover, treatment-related declines in physical function have been observed^{2,57-59)}. Thus, cancer itself and its treatment may precipitate decreases in physical function, emphasizing the need for healthcare providers to focus not only on the global QoL but also on physical QoL before treatment initiation. Chemotherapy alone had a higher HR for OS compared to HSCT. It is possible that the HSCT patients may have had a decline in physical function due to prior experience with various treatments and associated adverse events, possibly leading to a lower HR for OS compared to chemotherapy-only patients. Assessing physical QoL as a QoL parameter is straightforward and feasible for healthcare

providers, and combining actual physical function evaluations, such as comorbidities, muscle strength, and overall endurance, may not only enhance the predictive accuracy of individual patient OS and PFS, but also contribute to comprehensive treatment strategies.

Moreover, role QoL and social QoL among the QoL parameters did not show a significant association with OS in the HSCT studies, whereas they exhibited a significant association in the chemotherapy studies. In HSCT, patients undergo several rounds of treatment in the stages leading up to transplantation. In addition, the aggressive treatment of transplantation often results in hospitalization and aseptic management due to marked immune compromise. On the other hand, chemotherapy-only treatment often follows an outpatient course. In addition, since most patients tend to live at home during the pretreatment phase of chemotherapy, it is likely that most of them have a normal social life. In outpatient treatment, patients are expected to undergo treatment while fulfilling: their social roles, such as performing household chores like cooking and laundry; their employment responsibilities; and their community engagements. Therefore, in patients undergoing HSCT, the opportunities to fulfill the above roles and social aspects decrease with hospitalization, and there is a potentially significant association with OS observed in studies focusing on the use of chemotherapy in patients who are predominantly home-based. Additionally, patients with strong psychosocial support systems tend to have better health outcomes, as these factors are known to enhance resilience and treatment adherence⁶⁰⁾. When role and social aspects of QoL are high before treatment, it is likely that a robust psychosocial support system is already in place, which could contribute to a favorable treatment course and potentially extend OS. Conversely, when physical, role, and social QoL are low prior to treatment, greater support may be needed during the treatment process. In some cases, the lack of sufficient support may hinder the continuation of aggressive treatment, potentially leading to a decrease in OS. Lindberg *et al.*³⁶⁾ reported that according to their multivariate analysis, decreases in physical QoL and role QoL before treatment were associated with decreased OS. From the univariate analysis results, associations with OS were also found for social QoL, with correlations observed between role QoL and PFS as well as between role QoL and PS. While fewer studies have reported associations with OS compared to global QoL and physical QoL, it is

crucial to recognize role QoL and social QoL as important prognostic factors. These QoL reflect roles and sociability in daily life activities and social interactions. Reports have indicated that role and social QoL are lower in hematological malignancy patients compared to healthy individuals^{61,62}. Patients with hematological malignancies develop the condition at a younger age compared to other types of cancer, and it has been reported that the lack of social support negatively affects QoL⁶³. Treatment-related declines in physical function restrict subsequent social life. Roles and social QoL are not only issues related to daily life and social activities, but may also be factors involved in OS. Ueno *et al.*⁶⁴ suggested that interdisciplinary care in cancer treatment should be provided by teams with roles such as active care staff who provide medical care to patients, base support care staff who support patient needs, and community support staff, who need to cooperate with each other to provide patient-centered care. From the pretreatment stage, it may be necessary to evaluate the QoL from various perspectives, including not only global QoL, but also physical, role, and social QoL, in order to improve patient prognosis while considering the involvement of healthcare professionals and regional resources. Emotional QoL was not associated with either HSCT or chemotherapy. Patients with hematologic malignancies often experience psychological stress because they are treated in private rooms for aseptic management and are required to take strict infection control measures. Therefore, emotional QoL is considered one of the important aspects of QoL for HSCT patients; however, only one paper on HSCT was included in the present study, which may not have led to the conclusion of an association with OS.

This review has several limitations. Firstly, although this review utilized relatively large databases such as CINAHL, PubMed/MEDLINE, and Scopus, there may be other databases with relevant articles. Secondly, only six studies were selected for this review, with varied QoL assessment tools including EORTC-QLQ-C30, EQ-5D, and FACT-G, contributing to heterogeneity due to differences in evaluation items and the limited number of articles. Therefore, the need for further research must be emphasized to provide clearer evidence for the present results. Thirdly, this review included hematological malignancy patients with various disease states who had been treated with different methods such as HSCT and chemotherapy, potentially overlooking differences in QoL due to these

variations. Finally, based on the results of the present study, it would be a more clinically relevant assessment if the level of QoL could be quantified and consistently assessed by specialists in multiple professions. However, that was not within the scope of the present study, and quantification and scoring of QoL evaluations should be investigated in the future.

Conclusion

In the present review, it was revealed that pretreatment global QoL and physical QoL were associated with OS in patients with hematological malignancy treated with HSCT or chemotherapy. In addition, role QoL and social QoL were found to be associated with OS in chemotherapy patients, with different factors associated with OS depending on treatment. Evaluating QoL overall and by parameter from the pretreatment stage enables the prediction of OS, thereby suggesting the potential of supportive therapy during and after treatment. However, many mechanisms regarding how pretreatment QoL influences OS remain unclear, emphasizing the need for further research.

Author contributions

All authors contributed to the study conception and design. Material preparation and data collection and analysis were performed by KO, SM, JN, JL, TO, KS, TT, and TF. The first draft of the manuscript was written by KO, and all authors commented on intermediate versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethical approval

Not applicable

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References

1. Buffart LM, De Backer IC, Schep G, Vreugdenhil A, Brug J, Chinapaw MJM. Fatigue mediates the relationship between physical fitness and quality of life in cancer survivors. *J Sci Med Sport*, **16** : 99-104, 2013.
2. Duan L, Cui H, Zhang W, Wu S. Symptoms and experiences of frailty in lung cancer patients with chemotherapy : A mixed-method approach. *Front Oncol*, **12** : 1019006, 2022.
3. Morishita S, Kaida K, Yamauchi S, *et al.* Relationship between corticosteroid dose and declines in physical function among allogeneic hematopoietic stem cell transplantation patients. *Support Care Cancer*, **21** : 2161-2169, 2013.
4. Polat K, Karadibak D, Güç ZGS, Yavuzşen T, Öztıp İ. The Relationship between Exercise Capacity and Muscle Strength, Physical Activity, Fatigue and Quality of Life in Patients with Cancer Cachexia. *Nutr Cancer*, **76** : 55-62, 2024.
5. Morishita S, Hirabayashi R, Tsubaki A, *et al.* Relationship between balance function and QOL in cancer survivors and healthy subjects. *Medicine (Baltimore)*, **100** : e27822, 2021.
6. Osaki K, Morishita S, Takami S, *et al.* Quality of life of patients with hematological malignancies and factors affecting health state utility values. *Support Care Cancer*, **30** : 5319-5327, 2022.
7. Su M, Yao N, Shang M, *et al.* Frailty and its association with health-related quality of life among older cancer patients : an evidence-based study from China. *Health Qual Life Outcomes*, **20** : 124, 2022.
8. Aguiñaga S, Ehlers DK, Cosman J, Severson J, Kramer AF, McAuley E. Effects of physical activity on psychological well-being outcomes in breast cancer survivors from prediagnosis to posttreatment survivorship. *Psychooncology*, **27** : 1987-1994, 2018.
9. Lin YY, Wu YC, Rau KM, Lin CC. Effects of physical activity on the quality of life in taiwanese lung cancer patients receiving active treatment or off treatment. *Cancer Nurs*, **36** : E35-41, 2013.
10. Manneville F, Rotonda C, Conroy T, Bonnetain F, Guillemin F, Omorou AY. The impact of physical activity on fatigue and quality of life during and after adjuvant treatment for breast cancer. *Cancer*, **124** : 797-806, 2018.
11. Bellali T, Manomenidis G, Meramveliotaki E, Minasidou E, Galanis P. The impact of anxiety and depression in the quality of life and psychological well-being of Greek hematological cancer patients on chemotherapy. *Psychol Health Med*, **25** : 201-213, 2020.
12. Poort H, Jacobs JM, Pirl WF, Temel JS, Greer JA. Fatigue in patients on oral targeted or chemotherapy for cancer and associations with anxiety, depression, and quality of life. *Palliat Support Care*, **18** : 141-147, 2020.
13. Li Q, Lin Y, Qiu Y, Gao B, Xu Y. The assessment of health-related quality of life and related factors in Chinese elderly patients undergoing chemotherapy for advanced cancer : a cross-sectional study. *Eur J Oncol Nurs*, **18** : 425-435, 2014.
14. Ramasubbu SK, Pasricha RK, Nath UK, Rawat VS, Das B. Quality of life and factors affecting it in adult cancer patients undergoing cancer chemotherapy in a tertiary care hospital. *Cancer Rep (Hoboken)*, **4** : e1312, 2021.
15. Schwartz RM, Bevilacqua KG, Alpert N, *et al.* Educational Attainment and Quality of Life among Older Adults before a Lung Cancer Diagnosis. *J Palliat Med*, **23** : 498-505, 2020.
16. Zang Y, Qiu Y, Sun Y, Fan Y. Baseline functioning scales of EORTC QLQ-C30 predict overall survival in patients with gastrointestinal cancer : a meta-analysis. *Qual Life Res*, **33** : 1455-1468, 2024.
17. De Aguiar SS, Bergmann A, Mattos IE. Quality of life as a predictor of overall survival after breast cancer treatment. *Qual Life Res*, **23** : 627-637, 2014.
18. Hiratsuka Y, Kim YJ, Suh SY, *et al.* The association between changes in symptoms or quality of life and overall survival in outpatients with advanced cancer. *Ann Palliat Med*, **11** : 2338-2348, 2022.
19. Kypriotakis G, Vidrine DJ, Francis LE, Rose JH. The longitudinal relationship between quality of life and survival in advanced stage cancer. *Psychooncology*, **25** : 225-231, 2016.
20. Mackay TM, Latenstein AEJ, Sprangers MAG, *et al.* Relationship Between Quality of Life and Survival in Patients With Pancreatic and Periapillary Cancer : A Multicenter Cohort Analysis. *J Natl Compr Canc Netw*, **18** : 1354-1363, 2020.
21. McGarrah P, Hubbard J, Novotny PJ, *et al.* Baseline Quality of Life is a Strong and Independent Prognostic Factor for Overall Survival in Metastatic Colorectal Cancer. *Cancer Control*, **30** : 10732748231185047, 2023.
22. Monteiro MR, Nunes NCC, Crespo J, *et al.* Patient-centered Outcomes in Breast Cancer : Description of EQ-5D-5L and EORTC-QLQ-BR23 Measurements in Real-world Data and Their Association With Survival. *Clin Oncol (R Coll Radiol)*, **34** : 608-616, 2022.
23. Ediebah DE, Quinten C, Coens C, *et al.* Quality of life as a prognostic indicator of survival : A pooled analysis of individual patient data from canadian cancer trials group clinical trials. *Cancer*, **124** : 3409-3416, 2018.

24. Gotay CC, Kawamoto CT, Bottomley A, Efficace F. The prognostic significance of patient-reported outcomes in cancer clinical trials. *J Clin Oncol*, **26** : 1355-1363, 2008.
25. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses : the PRISMA Statement. *Open Med*, **3** : e123-130, 2009.
26. Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement : an updated guideline for reporting systematic reviews. *Syst Rev*, **10** : 89, 2021.
27. Aaronson NK, Ahmedzai S, Bergman B, *et al.* The European Organization for Research and Treatment of Cancer QLQ-C30 : a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*, **85** : 365-376, 1993.
28. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*, **30** : 473-483, 1992.
29. Cella DF, Tulsky DS, Gray G, *et al.* The Functional Assessment of Cancer Therapy scale : development and validation of the general measure. *J Clin Oncol*, **11** : 570-579, 1993.
30. Ottawa Hospital Research Institute. Accessed May 30, 2024. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
31. Hamilton BK, Law AD, Rybicki L, *et al.* Prognostic significance of pre-transplant quality of life in allogeneic hematopoietic cell transplantation recipients. *Bone Marrow Transplant*, **50** : 1235-1240, 2015. doi : 10.1038/bmt.2015.122
32. Kurosawa S, Yamaguchi T, Mori A, *et al.* Prognostic Impact of Pretransplantation Quality of Life and Its Post-Transplantation Longitudinal Change after Allogeneic Hematopoietic Cell Transplantation : A Prospective Study That Administered the Short-Form Health Survey (SF-12) and EuroQol 5. *Transplant Cell Ther*, **27** : 935.e1-935.e9, 2021.
33. Huang H, Datye A, Fan M, *et al.* Patient-reported outcomes provide prognostic information for survival in patients with diffuse large B-cell lymphoma : Analysis of 1239 patients from the GOYA study. *Cancer Med*, **11** : 3312-3322, 2022.
34. Jerkeman M, Kaasa S, Hjermstad M, Kvaløy S, Cavallin-Stahl E. Health-related quality of life and its potential prognostic implications in patients with aggressive lymphoma : a Nordic Lymphoma Group Trial. *Med Oncol*, **18** : 85-94, 2001.
35. Jung HA, Park S, Cho JH, *et al.* Prognostic relevance of pretreatment quality of life in diffuse large B-cell lymphoma patients treated with rituximab-CHOP : results from a prospective cohort study. *Ann Hematol*, **91** : 1747-1756, 2012.
36. Lindberg Å, Eskelund CW, Albertsson-Lindblad A, *et al.* Pre-treatment health-related quality of life parameters have prognostic impact in patients >65 years with newly diagnosed mantle cell lymphoma : The Nordic Lymphoma Group MCL4 (LENA-BERIT) experience. *Hematol Oncol*, **40** : 22-30, 2022.
37. Hui D. Prognostication of Survival in Patients With Advanced Cancer : Predicting the Unpredictable? *Cancer Control*, **22** : 489-497, 2015.
38. Mahesh PA, Archana S, Jayaraj BS, *et al.* Factors affecting 30-month survival in lung cancer patients. *Indian J Med Res*, **136** : 614-621, 2012.
39. Mariotto AB, Noone AM, Howlader N, *et al.* Cancer survival : an overview of measures, uses, and interpretation. *J Natl Cancer Inst Monogr*, **2014** : 145-186, 2014.
40. Ahmed T, Lycan T, Dothard A, *et al.* Performance Status and Age as Predictors of Immunotherapy Outcomes in Advanced Non-Small-Cell Lung Cancer. *Clin Lung Cancer*, **21** : e286-e293, 2020.
41. Bowden JCS, Williams LJ, Simms A, *et al.* Prediction of 90 Day and Overall Survival after Chemoradiotherapy for Lung Cancer : Role of Performance Status and Body Composition. *Clin Oncol (R Coll Radiol)*, **29** : 576-584, 2017.
42. Dziggel L, Gebauer N, Bartscht T, Schild SE, Rades D. Performance Status and Number of Metastatic Extra-cerebral Sites Predict Survival After Radiotherapy of Brain Metastases from Thyroid Cancer. *Anticancer Res*, **38** : 2391-2394, 2018.
43. Keane N, Fragkos KC, Patel PS, *et al.* Performance Status, Prognostic Scoring, and Parenteral Nutrition Requirements Predict Survival in Patients with Advanced Cancer Receiving Home Parenteral Nutrition. *Nutr Cancer*, **70** : 73-82, 2018.
44. Nguyen T, Bartscht T, Schild SE, Rades D. Performance Status Is Associated With Survival in Elderly Patients Irradiated for Cerebral Metastases from Prostate Cancer. *Anticancer Res*, **40** : 1665-1668, 2020.
45. Afram G, Gran C, Borg Bruchfeld J, *et al.* Impact of performance status on overall survival in patients with relapsed and/or refractory multiple myeloma : Real-life outcomes of daratumumab treatment. *Eur J Haematol*, **105** : 196-202, 2020.
46. Arboe B, Halgren Olsen M, Duun-Henriksen AK, *et al.* Prolonged hospitalization, primary refractory disease, performance status and age are prognostic factors for survival in patients with diffuse large B-cell lymphoma and transformed indolent lymphoma undergoing autologous stem cell transplantation. *Leuk Lymphoma*, **59** : 1153-1162, 2018.
47. Corry J, Smith JG, Wirth A, Quong G, Liew KH. Primary central nervous system lymphoma : age

- and performance status are more important than treatment modality. *Int J Radiat Oncol Biol Phys*, **41** : 615-620, 1998.
48. Saraceni F, Labopin M, Forcade E, *et al.* Allogeneic stem cell transplant in patients with acute myeloid leukemia and karnofsky performance status score less than or equal to 80% : A study from the acute leukemia working party of the European Society for Blood and Marrow Transplantation (EBMT). *Cancer Med*, **10** : 23-33, 2021.
 49. Inoue J, Morishita S, Okayama T, *et al.* Impact of quality of life on mortality risk in patients with esophageal cancer : a systematic review and meta-analysis. *Esophagus*, **21** : 270-282, 2024.
 50. Okayama T, Suzuki K, Morishita S, *et al.* Pre-treatment quality of life and survival in patients with lung cancer : a systematic review and meta-analysis [published correction appears in *BMC Cancer*. 2024 Apr 25 ; 24 : 529.]. *BMC Cancer*, **24** : 495, 2024.
 51. Ishiyama H, Kawakami S, Sekiguchi A, *et al.* Quality of life score as a prognosticator for pharyngeal cancer patients treated with radiotherapy. *Sci Rep*, **12** : 2387, 2022.
 52. Shrestha A, Martin C, Burton M, Walters S, Collins K, Wyld L. Quality of life versus length of life considerations in cancer patients : A systematic literature review. *Psychooncology*, **28** : 1367-1380, 2019.
 53. Mishra A, Pidala J, Thapa R, *et al.* Objective and subjective physical function in allogeneic hematopoietic stem cell transplant recipients. *Bone Marrow Transplant*, **56** : 2897-2903, 2021.
 54. Fukushima T, Nakano J, Ishii S, *et al.* Influence of Hemoglobin Level on Muscle and Physical Functions, Activities of Daily Living, and Quality of Life in Patients With Hematological Malignancies. *Integr Cancer Ther*, **18** : 1534735419842196, 2019.
 55. Morishita S, Kaida K, Tanaka T, *et al.* Prevalence of sarcopenia and relevance of body composition, physiological function, fatigue, and health-related quality of life in patients before allogeneic hematopoietic stem cell transplantation. *Support Care Cancer*, **20** : 3161-3168, 2012.
 56. Xiao DY, Luo S, O'Brian K, *et al.* Impact of sarcopenia on treatment tolerance in United States veterans with diffuse large B-cell lymphoma treated with CHOP-based chemotherapy. *Am J Hematol*, **91** : 1002-1007, 2016.
 57. Klepin HD, Tooze JA, Pardee TS, *et al.* Effect of Intensive Chemotherapy on Physical, Cognitive, and Emotional Health of Older Adults with Acute Myeloid Leukemia. *J Am Geriatr Soc*, **64** : 1988-1995, 2016.
 58. Liu MA, DuMontier C, Murillo A, *et al.* Gait speed, grip strength, and clinical outcomes in older patients with hematologic malignancies. *Blood*, **134** : 374-382, 2019.
 59. Morishita S, Kaida K, Yamauchi S, *et al.* Relationship of physical activity with physical function and health-related quality of life in patients having undergone allogeneic haematopoietic stem-cell transplantation. *Eur J Cancer Care (Engl)*, **26**, 2017.
 60. Eiser C. Beyond survival : quality of life and follow-up after childhood cancer. *J Pediatr Psychol*, **32** : 1140-1150, 2007.
 61. Else M, Smith AG, Cocks K, *et al.* Patients' experience of chronic lymphocytic leukaemia : baseline health-related quality of life results from the LRF CLL4 trial. *Br J Haematol*, **143** : 690-697, 2008.
 62. Holzner B, Kemmler G, Kopp M, Nguyen-Van-Tam D, Sperner-Unterweger B, Greil R. Quality of life of patients with chronic lymphocytic leukemia : results of a longitudinal investigation over 1 yr. *Eur J Haematol*, **72** : 381-389, 2004.
 63. Braamse AMJ, Gerrits MMJG, van Meijel B, *et al.* Predictors of health-related quality of life in patients treated with auto- and allo-SCT for hematological malignancies. *Bone Marrow Transplant*, **47** : 757-769, 2012.
 64. Ueno NT, Ito TD, Grigsby RK, Black MV, Apted J. ABC conceptual model of effective multidisciplinary cancer care. *Nat Rev Clin Oncol*, **7** : 544-547, 2010.