

ORIGINAL ARTICLE

Impact of GvHD on quality of life in long-term survivors of haematopoietic transplantation

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Allogeneic haematopoietic stem cell transplantation (HCT) has become an effective therapy in patients with various haematological malignancies. GvHD is known to be a major complication in this patient group and is assumed to have a major impact on patients' quality of life (QOL). Patients after BMT or transplantation of mobilized PBSCs were considered for enrolment in the study 6 months after transplantation. QOL and symptom burden were assessed using the EORTC QLQ-C30 and the QLQ-HDC29. Data from age- and sex-matched healthy controls were collected for comparison. In all, 100 patients (55.0% women; mean age 46.3 years) after allogeneic HCT were included in the study. In this patient group, we found a clinically relevant impact of GvHD on role functioning, global QOL, fatigue, dyspnoea, gastrointestinal side effects, worries/anxiety and skin problems. In comparison to healthy controls, various aspects of QOL were severely impaired. Our study revealed severe impairments of QOL in survivors of HCT, in particular in those suffering from GvHD. Taking into account, that the prevalence of GvHD might be higher in patients after PBSCT compared with patients after BMT, PBSCT is expected to lead to more severe impairments of QOL than BMT.

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Introduction

Methodological and medical advancements have turned allogeneic haematopoietic stem cell transplantation (HCT)

into an established and effective therapy in patients with various haematological malignancies (acute and chronic leukaemias), but the clinical outcome in terms of treatment burden for patients in the long term is not yet clarified.¹

Survival rates and the length of relapse-free intervals have increased considerably. To date, BM as the original main source of stem cells has largely been replaced by the transplantation of mobilized PBSCT as the latter provides superiority in regard to faster recovery of neutrophil and platelet counts, fewer early infections and is less invasive for the donor. Nevertheless, overall and relapse-free survival is comparable regardless of stem cell source.^{2,3}

The impact of acute and late medical side effects on quality of life (QOL) is not well investigated and evidence regarding differences between BMT and PBSCT is lacking. Nevertheless, evidence on QOL in this patient group is of importance as long-term survival rates increase and QOL has proven to be a useful clinical outcome-measure and a major treatment goal in patients undergoing HCT.^{4,5}

Knowledge on QOL and its course over time may improve medical decision making and symptom management in this group of patients. This is especially true for long-term effects on QOL.

Although an improvement of QOL with time since PBCT seems to be a general conclusion of many studies, it has not been clarified at the moment to what degree PBCT and BMT long-time survivors remain impaired regarding QOL, in particular compared with the general population. Furthermore, prevalence of GHVD and its impact on physical performance and other various aspects of QOL in the long-term follow-up needs to be quantified and further investigation should provide more differentiated results on clinical outcome.

Patients and methods

Aims

In this study, we report on the long-term effect of HCT on patients' QOL focusing in particular on the impact of GvHD and the comparison of QOL outcome in PBSCT and BMT survivors to the general population. Thus, our study addressed the following aims:

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- (1) Investigation of the impact of GvHD on the QOL in survivors of BMT and PBSCT
- (2) Investigation of change of QOL over time
- (3) Comparison of QOL outcome in HCT survivors to healthy controls

Sample

Patients with haematological malignancies that underwent BMT or PBSCT at the Department of Internal Medicine at Innsbruck Medical University were considered for enrolment in the study. Inclusion criteria were:

- (1) time from transplantation at least 6 months
- (2) expected survival time at least 3 months
- (3) no overt cognitive impairments
- (4) fluency in German

Data assessment were done by a mail survey between June and July 2008. The letter explained that the return of the enclosed questionnaire indicates informed consent. A reminder call was made to those patients, who did not return the questionnaire within 4 weeks of receipt.

Sociodemographic data collection included gender, age, education, employment and marital status. Clinical data comprised diagnosis, type of transplantation, occurrence of GvHD, HLA mismatch, current immunosuppressants, relationship to donor and time since transplantation Table 1. Information on patients' medical characteristics was gathered from hospital records. As a measure of functioning, global QOL and symptoms, all patients completed the EORTC QLQ-C30 questionnaire and the QLQ-HDC29.⁶

In an earlier study on module development of the QLQ-HDC29,⁶ a number of 66 patients were included at our institution in 2002. Those patients alive were approached for this study to gain longitudinal data.

For the purpose of comparison, we used EORTC QLQ-C30 data of age- and gender-matched healthy controls. These healthy subjects were randomly drawn from a larger sample representative of the Austrian general population. The sampling procedure of the general population sample is described in more detail elsewhere.⁷

Assessment instruments

EORTC QLQ-C30. The EORTC QLQ-C30,⁸ an internationally validated and widely used cancer-specific QOL instrument, assesses various facets of functioning, symptoms common in cancer patients as well as global QOL. All scales were scored according to the EORTC guidelines, resulting in a score range from 0 to 100 points.

To determine clinical relevance, we considered, with reference to Osoba *et al.*⁹ and Fayers and Machin,¹⁰ differences in QOL scores above 20 points as 'large', differences between 10 and 20 points as 'moderate' and differences of 5–10 points as 'small'.

EORTC QLQ-HDC29. The EORTC QLQ-HDC29⁶ is a supplement for the QLQ-C30 core questionnaire for the assessment of issues relevant for patients undergoing high-dose myeloablative treatment with haematological stem cell transplantation. It consists of six multi-item scales

Table 1 Descriptive statistics for sociodemographic and clinical variables ($n = 100$)

		Group comparisons for GvHD: never–previous–ongoing
<i>Age (years)</i>		
Mean (s.d.)	46.3 (14.7)	F = 0.42;
Range	16–76	P = 0.661
<i>Sex</i>		
Men	55.0%	$\chi^2 = 0.64$;
Women	45.0%	P = 0.728
<i>Education</i>		
Apprenticeship/ Professional school	53.0%	$\chi^2 = 1.21$;
Compulsory school or less	25.0%	P = 0.976
A-level	12.0%	
University	10.0%	
<i>Marital status</i>		
Married/with partner	66.0%	$\chi^2 = 5.38$;
Single	25.0%	P = 0.250
Widowed/divorced/ separated	9.0%	
<i>Employment status</i>		
Retired/pension	41.0%	$\chi^2 = 4.71$;
Full employment	29.0%	P = 0.788
Part-time employment	13.0%	
Homemaker	7.0%	
Other	10.0%	
<i>Diagnosis^a</i>		
AML	41.0%	$\chi^2 = 5.37$;
CML	22.0%	P = 0.497
ALL	12.0%	
Lymphoma	6.0%	
MDS	6.0%	
Myeloma	4.0%	
SAA	4.0%	
MPD	2.0%	
PNH	2.0%	
CLL	1.0%	
<i>Transplantation</i>		
PBSCT	56.0%	$\chi^2 = 15.17$;
BMT	44.0%	P = 0.001
<i>GvHD</i>		
Never	55.0%	—
Previous	31.0%	
Ongoing	14.0%	
<i>HLA-mismatch</i>		
No	89.0%	$\chi^2 = 0.33$;
Yes	11.0%	P = 0.849
<i>Current immunosuppressants</i>		
No	77.0%	$\chi^2 = 63.94$;
Yes	23.0%	P < 0.001
<i>Donor</i>		
Unrelated	67.0%	$\chi^2 = 4.86$;
Related	33.0%	P = 0.088
<i>Time since transplantation (months)</i>		
Mean (s.d.)	95.4 (75.5)	F = 7.62;
Range	6–296	P = 0.001

Abbreviations: MDS = myelodysplastic syndrome; SAA = severe aplastic anemia; MPD = myeloproliferative disorder; PNH = paroxysmal nocturnal hemoglobinuria.

^aFor group comparisons, we reduced diagnostic categories to AML, CML, ALL and other.

(Gastrointestinal Side Effects, Body Image, Impact on Family, Sexuality, Issues During Hospital Stay, and Worries/Anxiety) and eight single-items (Skin Problems, Fever, Aches in Bones, Urine Frequency, Ability to Finish Things, Taking Regular Drugs, Fear of Infertility, and Spirituality). Clinical relevance of differences was determined as described above. The QLQ-HDC29 was not used for data collection in general population due to inappropriateness.

Statistical analyses

Sample characteristics are presented as percentages, means, standard deviations and ranges.

The impact of sociodemographic and clinical variables on QOL was analysed with Pearson- χ^2 -tests and *t*-tests for independent samples and one-way analyses of variance. *Post hoc* group comparisons were done using least significant difference tests. Matched samples were compared using *t*-tests for dependent samples.

Cohen's *d* as measure of effect size is given for all mean differences [$d = (\text{mean}_1 - \text{mean}_2) / ((n_1 - 1) \times s_1^2 + (n_2 - 2) \times s_2^2)^{0.5}$].

A *P*-value below 0.05 was considered as statistically significant.

Results

Sample characteristics

A number of 147 patients was found eligible for the study and was contacted via mail. In all, 100 patients sent back the completed questionnaires (response rate 68.0%). Non-responder analysis showed that there were no significant differences between patients who sent back questionnaires and patients who did not with regard to sex ($P = 0.602$), age ($P = 0.702$), age at transplantation ($P = 0.659$), diagnosis ($P = 0.823$), type of transplantation ($P = 0.625$) or time since transplantation ($P = 0.866$).

Mean patient age was 46.3 years (s.d. 14.7) and 45 patients were female. At HCT, mean patient age was 37.7 years (s.d. 15.8).

Time since transplantation correlated significantly only with the scale Taking regular Drugs ($r = -0.24$). Fear of Infertility was the only scale on which men and women scored differently (46.9 vs 23.7 points; $t = 2.04$, $P = 0.046$).

Of 66 patients included in an earlier study in 2002,¹¹ 33 patients (24 patients after BMT and 9 patients after PBSCT) could be included in this study. In all, 21 patients died since then and 12 did not respond to the mail survey. These data allowed longitudinal analyses for the QLQ-C30 (Table 2).

In the age- and sex-matched healthy controls ($n = 100$) from the Austrian general population, mean age was 46.3 years (s.d. 14.6) and 45.0% were female.

Internal consistency of the QLQ-HDC29 scales

For the QLQ-HDC29, we performed psychometric analyses based on the provisional subscale structure proposed by its authors.⁶ In our sample, we found good internal consistency for the scales Gastrointestinal Side Effects (Cronbach's $\alpha = 0.80$), Body Image (0.73) and Sexuality (0.82). Internal consistency for Worries/Anxiety (0.63) was moderate and poor for the Impact on Family scale (0.52).

Impact of GvHD on QOL

Group comparisons between patients with ongoing GvHD, patients without occurrence of GvHD and patients with previous occurrence of GvHD proved a severe impact of GvHD on various aspects of QOL, whereas scores for patients without and patients with previous GvHD were rather similar.

Significant impairments of patients with GvHD were found for role functioning, and global QOL. With regard to symptoms, these patients indicated more fatigue, dyspnoea, gastrointestinal side effects, worries/anxiety and skin problems. Furthermore, these patients naturally reported more taking of regular drugs. For further details see Tables 3 and 4.

Course of QOL over time

The course of QOL over time was analysed by comparing scores of those patients ($n = 33$) that were already assessed

Table 2 Longitudinal statistics for QOL scores—EORTC QLQ-C30 ($n = 33$)

QLQ-C30 mean (s.d.)	Assessment 2002	Assessment 2008	Effect size	<i>t</i> -value	<i>P</i> -value	Correlation
Physical functioning	80.6 (22.9)	79.8 (19.6)	0.04	0.28	0.781	0.70*
Social functioning	68.8 (32.2)	72.4 (33.2)	0.11	-0.84	0.406	0.51*
Role functioning	68.2 (38.5)	73.2 (29.1)	0.15	0.75	0.460	0.48*
Emotional functioning	65.2 (32.5)	61.1 (28.0)	0.14	-0.51	0.612	0.60*
Cognitive functioning	63.0 (35.9)	65.6 (23.9)	0.09	-0.59	0.558	0.43**
Global QOL	67.7 (27.6)	66.1 (23.9)	0.06	0.30	0.763	0.37**
Fatigue	35.4 (34.8)	37.8 (31.8)	0.07	-0.43	0.672	0.54*
Nausea/vomiting	9.4 (22.8)	2.6 (6.1)	0.41	1.85	0.074	0.46*
Pain	21.2 (34.4)	29.8 (36.7)	0.24	-1.32	0.195	0.45*
Dyspnoea	24.2 (32.6)	25.3 (31.2)	0.03	-0.18	0.856	0.51*
Sleeping disturbances	28.3 (37.4)	24.2 (33.6)	0.12	0.56	0.580	0.32
Appetite loss	11.5 (26.2)	8.3 (22.4)	0.13	0.53	0.598	0.08
Constipation	6.3 (13.2)	7.3 (18.4)	0.06	-0.44	0.662	0.69*
Diarrhea	16.7 (31.7)	9.4 (19.4)	0.28	1.16	0.256	0.09
Financial impact	35.4 (38.1)	38.4 (40.9)	0.08	-0.49	0.629	0.59*

Abbreviation: QOL = quality of life.

* $P < 0.01$; ** $P < 0.05$.

Table 3 GvHD and QOL scores—EORTC QLQ-C30 (*n* = 100)

QLQ-C30 mean (s.d.)	No GvHD ¹ (<i>n</i> = 55)	Previous GvHD ² (<i>n</i> = 31)	Ongoing GvHD ³ (<i>n</i> = 14)	Effect size (1 vs 3)	F-value	P-value
Physical functioning	78.5 (21.3) ³	78.9 (20.3) ³	64.8 (19.5) ^{1,2}	0.65	2.69	0.073
Social functioning	74.2 (29.7)	69.4 (27.9)	58.3 (35.1)	0.52	1.61	0.206
Role functioning	69.7 (31.1) ³	75.3 (27.2) ³	36.9 (34.1) ^{1,2}	1.03	8.23	<0.001
Emotional functioning	67.6 (27.4)	68.5 (26.4)	58.9 (23.2)	0.33	0.70	0.497
Cognitive functioning	70.9 (29.6)	77.2 (27.2)	58.3 (25.1)	0.44	2.13	0.125
Global QOL	73.2 (21.7) ³	70.0 (24.6) ³	50.6 (18.9) ^{1,2}	1.07	5.78	0.004
Fatigue	37.0 (29.1) ³	33.0 (29.2) ³	61.1 (30.4) ^{1,2}	0.82	4.75	0.011
Nausea/vomiting	8.0 (22.1)	5.0 (13.9)	13.1 (28.6)	0.22	0.71	0.495
Pain	26.1 (33.9)	18.3 (27.7)	38.1 (34.2)	0.35	1.87	0.160
Dyspnoea	23.0 (30.7) ³	25.8 (30.7) ³	59.5 (43.7) ^{1,2}	1.09	7.15	0.001
Sleeping disturbances	24.8 (34.1)	26.9 (33.8)	35.7 (38.0)	0.31	0.55	0.577
Appetite loss	16.4 (29.3)	8.9 (24.7)	21.4 (31.0)	0.17	1.13	0.328
Constipation	10.5 (23.2)	8.9 (23.0)	11.9 (28.1)	0.06	0.09	0.919
Diarrhea	8.0 (20.4)	11.1 (23.7)	19.0 (33.9)	0.47	1.22	0.301
Financial impact	25.3 (34.2)	32.3 (38.0)	42.9 (38.0)	0.50	1.42	0.248

Abbreviation: QOL = quality of life.

Superscript numbers indicate significance (*P* < 0.05) of *post hoc* group comparisons (least significant difference test).

Table 4 GvHD and QOL scores—EORTC QLQ-HDC29 (*n* = 100)

QLQ-HDC29 mean (s.d.)	No GvHD ¹ (<i>n</i> = 55)	Previous GvHD ² (<i>n</i> = 31)	Ongoing GvHD ³ (<i>n</i> = 14)	Effect size (1 vs 3)	F-value	P-value
Gastrointestinal side effects	11.8 (17.2) ³	12.7 (15.0) ³	36.2 (30.4) ^{1,2}	1.19	9.73	<0.001
Body image	30.6 (31.4)	28.5 (34.7)	48.8 (35.5)	0.56	2.03	0.137
Impact on family	26.7 (23.2)	21.9 (19.1)	36.3 (18.9)	0.43	2.13	0.124
Sexuality	39.5 (38.6)	41.4 (35.6)	59.5 (41.2)	0.51	1.55	0.218
In-patient issues ^a	—	—	—	—	—	—
Worries/anxiety	34.7 (23.3) ³	29.0 (19.9) ³	58.3 (19.6) ^{1,2}	1.04	8.95	<0.001
Skin problems	28.4 (32.6) ³	20.4 (31.8) ³	52.4 (28.4) ^{1,2}	0.75	4.90	0.009
Fever/chills	23.5 (52.9)	16.7 (34.7)	14.3 (25.2)	0.19	0.36	0.701
Aches in bones	23.9 (32.9)	14.4 (25.8)	19.0 (21.5)	0.16	1.00	0.372
Urinary frequency	21.6 (27.3)	23.3 (31.7)	27.8 (31.2)	0.22	0.22	0.801
Ability to finish things	19.8 (27.9)	15.6 (24.3)	26.2 (26.7)	0.23	0.77	0.466
Taking regular drugs	25.9 (30.8) ³	22.6 (35.2) ³	66.7 (32.0) ^{1,2}	1.31	10.13	<0.001
Fear of infertility	44.4 (44.6)	16.7 (40.8)	27.3 (44.3)	0.38	2.17	0.124
Spirituality	73.5 (35.1)	67.8 (40.6)	81.0 (31.3)	0.22	0.65	0.526

Abbreviation: QOL = quality of life.

Superscript numbers indicate significance (*P* < 0.05) of *post hoc* group comparisons (least significant difference tests).

^aNot applicable in outpatient sample.

with the QLQ-C30 in 2002. No significant differences between these assessment time points were found for the QLQ-C30 scales (observed differences below 5 points for 11 of the 15 scales and below 10 points for the other scales). Correlations were above 0.5 for 7 of the 14 scales and below 0.1 for Appetite Loss and Diarrhea.

Comparison with healthy controls

The comparison of the BMT/PBSCT sample with age- and sex-matched healthy controls (drawn from a representative sample of Austrian general population) revealed large differences (> 20 points) for role functioning, dyspnoea and financial impact (see Table 5). Moderate differences (10–20 points) were found for physical functioning, social functioning, cognitive functioning, fatigue and pain. Small differences (5–10 points) were found for global QOL, sleeping disturbances and appetite loss. Differences for emotional functioning and nausea/vomiting just failed

significance (*P* = 0.06) and constipation and diarrhea were very similar in both groups. All differences were in favour of the healthy controls. Exclusion of patients up to 12 months after transplantation revealed very similar results (not shown).

Discussion

Patient-reported outcomes have gained considerable importance in the evaluation of the treatment process of various haematological malignancies. Especially, QOL including functioning and symptom burden is of high relevance to HCT survivors. The occurrence of chronic GvHD as a major complication in this patient group is expected to have a significant impact on patients' QOL.

In our study, we investigated which aspects of QOL are affected by chronic GvHD and to what degree they are impaired. Furthermore, we compared QOL in long-time

Table 5 QOL scores (EORTC QLQ-C30) in patients with BMT/PBSCT ($n = 100$) and in healthy controls ($n = 100$)

QLQ-C30 mean (s.d.)	Healthy controls	Patients	Effect size	t-value	P-value
Physical functioning	92.6 (15.0)	76.3 (21.1)	0.89	-7.19	<0.001
Social functioning	89.4 (22.6)	70.2 (30.1)	0.72	-5.33	<0.001
Role functioning	89.2 (21.5)	66.5 (32.5)	0.82	-6.66	<0.001
Emotional functioning	73.5 (23.6)	66.8 (26.6)	0.27	-1.89	0.062
Cognitive functioning	85.7 (19.4)	71.3 (28.7)	0.59	-4.45	<0.001
Global QOL	78.1 (20.4)	69.2 (23.4)	0.41	-3.06	0.003
Fatigue	20.2 (20.9)	39.6 (30.5)	0.74	6.34	<0.001
Nausea/vomiting	3.5 (10.2)	8.0 (21.2)	0.27	1.87	0.064
Pain	13.9 (24.3)	25.7 (32.6)	0.41	2.90	0.005
Dyspnoea	8.6 (20.0)	29.9 (34.9)	0.75	5.58	<0.001
Sleeping disturbances	17.7 (25.4)	27.2 (34.6)	0.31	2.26	0.026
Appetite loss	5.5 (16.4)	15.1 (28.5)	0.41	2.97	0.004
Constipation	8.7 (21.2)	10.4 (23.8)	0.08	0.61	0.544
Diarrhea	8.7 (20.7)	10.8 (23.9)	0.09	0.63	0.530
Financial impact	6.5 (18.3)	29.6 (36.1)	0.81	5.62	<0.001

Abbreviation: QOL = quality of life.

survivors to healthy controls and analysed changes of QOL over time in this patient group.

We found that patients suffering from chronic GvHD showed deteriorated role functioning and global QOL, increased fatigue, dyspnoea, gastrointestinal side effects, worries/anxiety and skin problems and consequently those patients were taking more drugs. Compared with patients without GvHD, these differences were considered to be large with regard to clinical relevance. However, patients with previous chronic GvHD showed no relevant impairments when compared with those that never experienced chronic GvHD.

Analysing the course of QOL in long-term survivors, we found that QLQ-C30 scores did not change significantly over a 6-year period between the two assessments (observed differences below clinical relevance for most scales), indicating stable, though reduced QOL. In comparison with age- and sex-matched healthy controls HCT patients showed considerably poorer social functioning, role functioning, fatigue, dyspnoea and financial impact. Moderate differences were found for physical functioning, cognitive functioning, pain, sleeping disturbances and appetite loss. Rather high correlations between the two assessment time points for most of the scales, indicating that a patient's QOL is rather stable also relative to other HCT patients.

In patients experiencing chronic GvHD after PBSCT or BMT, various aspects of QOL were severely deteriorated, and even up to 25 years after transplantation, patients do not recover to a normal level, not only with regard to symptoms but also with regard to social and financial issues. Moreover, further improvement is not to be expected as QOL scores did not change much over a time period of 6 years.

A limitation of our study is the rather small sample size that restricted the possibility for detailed subgroup analyses. But especially for this patient group, large survivor samples are difficult to recruit because of the low prevalence rates of haematological malignancies and the rather low survival rates for these patients. Nevertheless, looking at the literature, our sample size is comparable to various other studies with a single centre design,¹² investigating the differences of clinical outcome between

PBSCT and BMT. In addition, the age- and sex-matched healthy controls were drawn from a larger sample from general population that was already assessed in 2002. Thus, there might be an effect of calendar year affecting comparability of patients and controls.

A further comparison of QOL in survivors of BMT and PBSCT would have been desirable. But this proves difficult, as transplantation methods have changed during the last decade, in a way that since the introduction of PBSCT, this transplantation method is preferred widely over BMT. This results in a confounding of transplantation method and time since transplantation as found in our sample.

This is the first study to report results for the recently developed QLQ-HDC29, a module specifically developed to assess issues relevant to patients treated for haematological malignancies. Although, originally developed for the assessment in patients up to 6 months after transplantation, the applicability of this questionnaire may be broader, as already stated by its authors.⁶ Our results show that even in the long-term survivors, up to 25 years after transplantation, the covered symptoms are still of relevance, as indicated by rather high mean scores for these scales. This is especially true for patients suffering from chronic GvHD. Nevertheless, the scales Worries/Anxiety and Impact on Family showed poor internal consistency in our study.

Our main findings, showing the strong impairments caused by GvHD are in line with other longitudinal QOL studies on this issue. In a study by Kiss *et al.*¹³ with CLM patients all HCT survivors who had developed any kind of GvHD experienced worse QOL than the healthy control group 10 years and more after transplantation. This was true for patients who had a previous acute GvHD as well as for patients with a history of or ongoing chronic GvHD. A history of chronic GvHD was associated with worse physical functioning, role functioning and social functioning, and the incidence of an ongoing chronic GvHD with mental health indicating mainly to problems with physical performance. Patients with previous acute GvHD had reduced general health. These results are almost in accordance with our findings that patients with an ongoing chronic GvHD have a reduced QOL in the long term and that they differ significantly from the general population.

In contrast to our findings, that previous GvHD (acute or chronic) did not affect present QOL, Kiss *et al.* found also strong impairments for this patients' group.

Lee *et al.*¹⁴ proved GvHD to emerge in 30–70% of HCT patients, and there is evidence that GvHD varies in incidence over both therapy regimes and seems to be a more relevant long-term complication in PBSCT survivors. In a large meta-analysis of the Stem Cell Trialists' Collaborative Group,¹² 47 and 68% of PBSCT patients developed an extensive or any-stage chronic GvHD at 3 years whereas 31 vs 52% of BMT patients did at the same time. No group difference related to acute GvHD was found. Also Arai and Klingemann² claimed GvHD to be a more relevant long-term complication in PBSCT survivors than in BMT survivors which may lead to lower QOL in this patient group.

Further, the stem cell source may have an impact on symptom burden and QOL. Cutler *et al.*¹⁵ claimed the stem cell source to have a significant effect on the prevalence of GvHD. In their meta-analysis of 20 studies with 2.144 patients, they concluded that the risk for acute GvHD is slightly and for chronic GvHD largely increased after PBSCT in comparison to BMT.

Thus, taking our findings regarding the impact of chronic GvHD on QOL into account, it may be assumed that PBSCT might result in lower QOL compared with BMT.

Overall, the results from our study highlight the importance of adequate symptom monitoring and management in long-term survivors of BMT and PBSCT. Adequate symptom assessment should not only cover physical but also psychosocial issues. Furthermore, knowledge on the detrimental impact of GvHD on QOL could enhance patient information on treatment consequences and contribute to medical decision making. This is especially true for evaluation of the long-term sequelae of PBSCT and BMT.

Conflict of interest

The authors declare no conflict of interest.

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