Growth, endocrine function and quality of life after haematopoietic stem cell transplantation

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QUALITY OF LIFE IN ADULTS FOLLOWING BONE MARROW TRANSPLANTATION DURING CHILDHOOD

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Abstract

To Quality of life (QOL) was assessed in 22 young adults, 14 years -on average- after having received bone marrow transplantation (BMT) during childhood at the Leiden University Medical Centre. All were disease-free and >16 years when interviewed. The sickness impact profile and the Medical Outcome Study 36-item Short Form Health Survey were used as generic questionnaires in the assessment of QOL. The Functional Assessment of Cancer Therapy-Bone Marrow Transplant Scale (FACT-BMT) was used as a disease-specific measure of QOL. Coping was assessed by means of the Utrecht coping list. BMT-related variables were obtained from medical files. Of the generic QOL measures, most results fell within the normal range of functioning, although some illness-related impairment was reported on subscales for general and work-related functioning. Compared to a reference sample of patients who had received BMT as adults, patients involved in this study scored significantly higher on the ‘emotional well-being’ subscale of the FACT-BMT, indicating significantly better emotional functioning. The age at BMT and total body irradiation (TBI) were not related to patients’ QOL. We can conclude that at long term, having received BMT during childhood does not negatively affect the QOL of patients.

Introduction

Bone marrow transplantation (BMT) has become a standard treatment option for many children with congenital or malignant disorders of the haematological system [1]. It is an intensive procedure associated with lengthy hospitalisation (for some time in protective isolation), and risk of severe pre-treatment and treatment-related morbidity [2;3]. As the number of survivors of BMT increases, the long-term effects of this treatment procedure on the quality of life (QOL) of patients and their family members are becoming more important.

QOL has been defined as 'the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient'. [4] QOL research has long been plagued by a lack of consensus on the definition of the core concepts and by a lack of standardisation of assessment tools [5;6]. QOL measures include generic and disease-specific ones. While generic measures of QOL can be used across different patient populations, the disease-specific ones include aspects of health (symptoms, impairments, and disabilities) that are relevant to patients with a particular disease. The choice of measure to use in an investigation into QOL is a difficult one to make [7]. Inherent to the assessment of QOL are also a number of methodological considerations, including the phenomenon of 'response shift' (a change in the meaning of an individual's self-reported QOL), that can affect the validity of the measures used [8-11]. However, despite the ongoing debate on the meaning of QOL, its assessment, and its usefulness in health care [5-16], most would argue that assessing the QOL when investigating the impact of a clinical intervention provides valuable information on patient outcome [17].

Studies conducted on the QOL of *adult* BMT recipients have yielded contradictory results. While some studies indicate that the QOL of adult recipients is relatively unaffected, at long term, others report a wide variety of problems, including low energy levels and sleep difficulties, low self-esteem, sexual difficulties, psychological distress, and impaired social relationships [18-25]. Two recent reviews highlight these contrasting findings and attribute them, in part, to differences in methodology [26;27].

Notwithstanding the differences in methodology, the reviews point to some interesting research findings. Firstly, age at BMT seems to play an important role in the QOL of adult BMT recipients, younger BMT recipients doing better following BMT [26]. Secondly, TBI dose seems to be related to poorer sexual, cognitive, and physical functioning [26]. Thirdly, the time post BMT has been found to be unrelated to psychosocial status, functional QOL, and affective status [26]. Fourthly, fatigue, psychological distress, and sexual dysfunction are frequently reported following BMT [27].

The long-term effects of having received BMT during *childhood* or *adolescence* have hardly been studied. A recent prospective longitudinal study on children who received haematopoietic stem cell transplantation (HSCT) indicated that both at 1 year and 2 years post HSCT, there was a low prevalence of behavioural and social problems in children [28]. These findings support the results of a recent cross-sectional retrospective study on paediatric patients who received a BMT 1–13 years earlier. Most patients (75%) reported no physical or psychological impairment [29]. Another cross-sectional study revealed that young adults who underwent BMT during childhood reported fewer problems when compared with their healthy peers with respect to interpersonal relationships, sleep, depression, and leisure possibilities, 3-9 years after BMT [30]. On the other hand, they reported more problems with regard to their physical appearance, and their studies and work possibilities [30]. A fourth cross-sectional retrospective study revealed that patients who underwent stem cell transplantation (SCT) between the ages of 5 and 18 years were at a risk of developing long-term emotional or social problems, 2-13 years later [31]. In turn, a fifth study assessing the behavioural adjustment, QOL, and adaptive functioning of children and adolescents, pre- and 6 months post BMT, revealed an improvement in overall QOL at 6 months post BMT, and no symptoms of serious psychological maladjustment at either pre- or 6 months post BMT (as rated by their mothers) [32].

The aim of this study is to assess the long-term effects of having undergone BMT in childhood on QOL in young adulthood. In addition to assessing the health-related QOL of young BMT recipients, we included demographic and BMT-related variables (e.g. age, gender, age at BMT, intelligence quotient (IQ)) into our investigations. Recent studies have indicated that these variables may be associated with the QOL of BMT recipients [26;33;34]. For example, younger BMT recipients have been found to overcome BMT-related toxicities more readily than adult BMT recipients, females have been found to be at a greater risk of developing sexual problems post BMT, TBI dose has been reported to be associated with BMT patients’ cognitive functioning, and higher intellectual ability has been linked to better coping with childhood cancer and its treatment [26;33;34]. Furthermore, research has indicated that patients' QOL is not determined exclusively by disease-related factors. Psychological concomitants of an illness, such as the way in which patients cope with it, have been found to play a crucial role [35-39]. Thus, in addition to demographic and BMT-related variables, we aimed at investigating the role of coping in the QOL of young adults who underwent BMT during childhood.

Patients and methods

Patients and procedure

The assessment of QOL was part of a larger investigation into the long-term consequences of BMT during childhood. The study was approved by the Medical Ethics Committee of the Leiden University Medical Centre (LUMC). Individuals who were invited to participate in these investigations were recruited from the total number of patients who had received allogeneic BMT at the department of Paediatrics of the LUMC between 1968 and January 1993. They were selected on the basis of five criteria: 1. having received a (first) BMT at least 5 years prior to the study; 2. having been below the age of 18 years when receiving BMT; 3. having received BMT on the basis of the indication of haematological malignancy or severe aplastic anaemia; 4. being 16 years or older when participating in the current study; and 5. the disease being in complete remission when participating.

A total of 61 patients met the selection criteria. In all, 12 patients could not be contacted, because they had moved house without leaving a forwarding address, or because they had moved to another country. Thus, a total of 49 patients were invited to participate, of whom 22 participated. Signed informed consent was obtained from all participants. The characteristics of both participants and non-participants are summarised in table 1.

The health status of participants was compared to non-participants' by chart review. Health status did not differ between the two groups: 7/22 participants suffered from severe transplant-related morbidity (e.g. severe chronic graft-versus-host disease or secondary neoplasms) compared to 5/27 non-participants. The reasons for not participating were: the time-consuming nature of the study (n=8, 30%), patients attending another hospital for their regular check-ups (n=7, 26%), reasons not given (n=5, 19%), patients not considering themselves as being ill (n=4, 15%), and the study being regarded as too physically and emotionally taxing (n=3, 11%).

Table 1 Sample characteristics

	Participants		Non-participants	
	N (%)	Mean (s.d.; median; range)	N (%)	Mean (s.d.; median; range)
Sex				
- Female	12 (54.5%)		12 (44.4%)	
- Male	10 (45.5%)		15 (55.6%)	
Age (years)		25 (5; 24; 18–32)		22 (5; 21; 18–36)
Age at BMT (years)		11 (4; 11; 1–16)		11 (3; 12; 5–17)
Time since BMT (years)		14 (4; 14; 6–21)		11 (4; 11; 6–26)
Indication of BMT				
- Severe aplastic anaemia	4 (18.2%)		6 (22.2%)	
- Acute myeloid leukaemia	9 (40.9%)		11 (40.7%)	
- Acute lymphoblastic leukaemia	5 (22.7%)		7 (25.9%)	
- Chronic myeloid leukaemia	1 (4.5%)		0 (0%)	
- Myelodysplastic syndrome	2 (9.1%)		2 (7.4%)	
- Non-Hodgkin's lymphoma	1 (4.5%)		1 (3.7%)	
TBI dose				
- No TBI	3 (13.6%)		2 (7.4%)	
- 4–5 Gy	2 (9.1%)		4 (14.8%)	
- 7–8 Gy	13 (59.1%)		13 (48.1%)	
- 2 x 6Gy	4 (18.2%)		8 (29.6%)	
IQ		110 (16; 81–131)		

Patients who agreed to participate were invited to attend the LUMC to undergo a series of tests and complete a number of questionnaires. Pulmonary function, endocrinological variables, ophthalmological variables, and QOL were assessed. In this paper, we will report the findings on the patients' QOL.

Results of other investigations (e.g. lung function and renal function) will be reported elsewhere.

Measures Demographic and BMT-related variables

Patients were asked to report their age and sex and, as a part of the larger study, patients' IQ was assessed by means of the Wechsler adult intelligence scale-revised (WAIS-R) [40]. Information on patients' disease characteristics (e.g. indication for BMT, age at BMT, use of TBI) was obtained from their medical files.

QOL measures

As mentioned earlier, choosing the appropriate measure to investigate the QOL of a given patient sample is difficult [7]. For the purpose of the study described here, we chose to assess BMT patients' QOL by means of two widely known generic measures of QOL, with proven reliability and validity, in addition to using a recently developed disease-specific measure of QOL, which has not yet been used in a paediatric sample. By this means, we intended to benefit from advantages offered by both generic measures (e.g. availability of data for comparison across different patient populations and from large community samples) and disease-specific ones (greater sensitivity to changes in QOL caused by factors associated with a specific health problem) [41].

Thus, we used two generic QOL measures: the sickness impact profile (SIP) and the Medical Outcome Study 36- item Short Form Health Survey (MOS SF-36) [42;43]. The SIP and the SF-36 have proven to be reliable and valid instruments, and have been used in a wide variety of patient populations, including patients with cancer [44-48]. The SIP focuses on the impact of an illness as reported by the patient, and contains 136 items in 12 categories, from which three additional aggregate scores can be calculated ('physical dimension', 'psychosocial dimension', and 'total score'). SIP scores are presented as percentages of maximal dysfunction ranging from 0 to 100, higher scores indicating higher level of dysfunction [42]. SIP scores lower than 6 indicate no impairment, scores between 6 and 10 are indicative of mild impairment, scores between 15 and 20 indicate moderate to severe impairment, and scores above 20 are indicative of severe illness-related impairment [49]. The MOS SF-36 comprises 36 items in eight functional dimensions: 'physical functioning', 'role functioning - physical', 'bodily pain', 'general health', 'vitality', 'social functioning', 'role functioning - emotional', and 'mental health'. The raw scores are transformed in order to obtain a 0–100 scale, higher scores indicating better functioning [43].

To assess the disease-specific QOL of BMT patients, we used the 4th version of the Functional Assessment of Cancer Therapy-Bone Marrow Transplant Scale (FACTBMT) [50]. It is a valid and reliable measure of QOL in BMT patients [50;51]. The FACT-BMT consists of the 35-item Functional Assessment of Cancer Therapy (FACT-G) and a 12-item Bone Marrow Transplantation Subscale (BMTS). The latter assesses specific BMT-related issues. The FACT-BMT assesses the effects of cancer therapy on patients in four areas: physical well-being, social/family well-being, emotional well-being, and functional well-being. A higher score indicates better QOL.

In addition, we assessed the strategies patients used to cope with problems in daily life by means of the Utrecht Coping List (UCL) [52;53]. The UCL is a reliable and valid Dutch questionnaire consisting of 49 items that are categorised into seven scales: 'seeking distraction', 'expressing emotions', 'seeking social support', 'avoiding', 'fostering reassuring thoughts', 'passive coping', and 'active coping'. Patients were asked to rate how often they adopted certain coping behaviours on a four-point scale, ranging from 'seldom/never' to 'very often'. Higher scores indicate a more frequent use of a given coping strategy.

Statistical analyses

Firstly, to investigate the impact of having received BMT in the past on patients' QOL, we compared patients' scores on the SIP, MOS SF-36, FACTBMT, and UCL, to the scores of reference samples, by means of t-tests. Secondly, we conducted simple Pearson correlation analyses between patients' demographic and BMT-related variables, and patients' scores on the SIP, MOS SF-36, FACT-BMT, and UCL.

Results

Sample characteristics

Table 1 describes the characteristics of the sample involved in the current study. The sample consisted of 12 females (54.5%) and 10 males (45.5%) with a mean age of 25 years (s.d.=5; range=18–31 years) and a mean IQ score at the time of assessment of QOL of 110 (s.d.=16). The mean age at which the patients had received BMT was 11 years (s.d.=4). All patients received allogeneic transplants. Conditioning for BMT consisted of cyclophosphamide (60 mg/kg once daily for 2 consecutive days), in most patients combined with TBI. TBI was delivered by a linear accelerator with energies of either 5.0 or 6.0MV, and at a midline instantaneous dose rate of approximately 23 cGy/min. Patients receiving BMT for SAA received either no TBI or 4 Gy single-fraction TBI. One patient, receiving BMT for MDS in the first year of life, received 5 Gy single-fraction TBI. The remaining patients received either a single fraction of 7.5-8.0 or 12 Gy in two fractions.

Generic QOL

Compared to reference data from randomly selected Dutch individuals (n=192), between the ages of 18 and 30 years, who were interviewed as part of a validation study (n=594) of the Dutch version of the SIP [54], the scores of BMT patients did not differ significantly from those of reference individuals, except on the aggregate 'total score' of the SIP, with BMT patients functioning worse than reference individuals. Furthermore, the scores of BMT patients on the 'work' subscale of the SIP fell into the 'severe illness-related impairment' range of SIP scores (7/22 BMT patients scored 30 or higher on the 'work' subscale; table 2). Of the BMT patients involved in this study, three were unemployed, of whom one was unable to work because of a physical handicap. The remaining participants were either employed or were fulltime students.

When compared to healthy reference Dutch individuals, ages 25-34 years (n=221), who were involved in a study on the validation of the Dutch version of the MOS SF-36 [55], the scores of BMT patients again did not differ significantly from those of reference individuals, except where general health was concerned. BMT patients scored significantly lower on the 'general health' subscale (18/22 BMT patients scored 75 or lower on this subscale), indicating significantly worse functioning (table 3).

Table 2. Mean scores (and standard deviations) of BMT patients (n=22) compared to the scores of a reference sample of randomly selected Dutch individuals (n=192) [54] on the sickness impact profile.

SIP	BMT patients Mean (s.d.)	Reference individuals Mean (s.d.)	t
Sleep and rest	4.4(7.2)	2.8 (5.5)	1.0
Eating	0.9(2.1)	0.9 (2.8)	—
Work	20.4(29.7)	6.7 (19.4)	2.1
Home management	5.6(10.3)	1.2 (5.5)	2.0
Recreation and pastimes	5.4(8.9)	4.2 (9.7)	0.6
Ambulation	2.3(5.9)	0.5 (2.8)	1.4
Mobility	1.2(3.3)	0.5 (2.8)	1.0
Body care and movement	1.7(2.5)	0.5 (1.4)	2.2
Social interaction	4.2(5.1)	2.1 (5.5)	1.8
Alertness behaviour	4.8(10)	2.7 (6.9)	1.0
Emotional behaviour	5.6(7.9)	3.0 (6.9)	1.5
Communication	0.4(1.9)	0.6 (2.8)	-0.4
Physical dimension	1.6(2.6)	0.5 (1.4)	2.0
Psychosocial dimension	3.8(4.4)	2.1 (4.2)	1.7
Total score	3.9(3.9)	1.7 (2.8)	2.6**

** P<0.01.

Table 3 Mean scores of BMT patients (n=21) and of a reference sample of randomly selected Dutch individuals (n=221) [55] on the Medical Outcome Study Short Form Health Survey

MOS SF-36	BMT patients Mean (s.d.)	Reference individuals Mean (s.d.)	t
Physical functioning	80.4(24.4)	89.5 (17.8)	-1.7
Role functioning-physical	73.8(33.0)	82.5 (32.4)	-1.2
Bodily pain	83.4(19.0)	84.1 (23.9)	-0.2
General health	62.9(16.1)	77.5 (19.7)	-3.9***
Vitality	61.4(17.4)	69.1 (19.0)	-1.9
Social functioning	79.2(22.5)	90.7 (16.5)	-2.3
Role functioning-emotional	90.0(21.9)	86.8 (29.6)	0.6
Mental health	75.6(13.3)	78.8 (17.5)	-1.0

*** P<0.001.

Disease-specific QOL

Compared to a sample of 56 adults who received a BMT in adulthood participating in a prior study by Kopp et al. (mean age=34.01, s.d.=9.73; mean time from BMT until study (in months)=44.82, s.d.=38.56) [51], patients involved in the current study scored significantly higher on the 'emotional well-being' subscale, indicating significantly better emotional functioning (table 4).

We were unable to compare our results on the FACT Total (Fact-G) and the BMTS to the findings of Kopp et al. [51], because we used the fourth version of the FACT-BMT, as opposed to Kopp and colleagues who used the third version of this assessment scale. The fourth version of the FACT-BMT includes an additional subscale (relation with doctor), and incorporates 12 items in the calculation of the BMTS, whereas in the third version only 10 items are scored.

Table 4 Scores of BMT patients (n=21) on the Functional Assessment of Cancer Therapy-Bone Marrow Transplant Scale (FACT-BMT) compared to those of a reference sample of adult BMT recipients (n=56) [51] by means of t-tests.

FACT-BMT	BMT patients[a] Mean (s.d.)	Reference individuals[b] Mean (s.d.)	t
Physical well-being (0–28)	23.9 (3.8)	21.1(7.0)	2.2
Social/family well-being (0–28)	22.4 (3.6)	20.1(5.3)	2.2
Emotional well-being (0–24)	22.0 (3.5)	15.6(4.3)	6.7***
Functional well-being (0–28)	21.1 (2.6)	20.5(5.7)	0.6
FACT total (FACT-G) (0–108)	89.4 (10.7)	—	—
BMTS (0–40)	31.3 (6.0)	—	—

*** P<0.001.

[a] One patient did not complete the FACT-BMT.

[b] Kopp et al. [51] used the third version of the FACT-BMT, which included an additional subscale ('relationship with doctor'), relative to the fourth version that we used in the study described here. Furthermore, in the third version of the FACT-BMT, 12 items are scored in the calculation of the BMTS, whereas in the fourth version, only 10 items are scored. Therefore, it was not possible to compare our results on the FACT-G and the BMTS with those of Kopp et al. [51]

Coping

We compared the scores of BMT patients on the UCL to healthy Dutch students (n=55, ages 20–30 years) involved in a validation study of this questionnaire [53], and found that BMT patients scored significantly lower on the 'passive coping' and 'fostering reassuring thoughts' subscales of the UCL, indicating a less frequent use of these coping strategies compared to reference individuals (table 5).

Table 5. The scores of BMT patients (n=21) [a] on the Utrecht Coping List (UCL) compared to those of healthy reference individuals (n=55) [53] by means of t-tests

UCL subscales	BMT patients Mean (s.d.)	Reference individuals Mean (s.d.)	t
Active coping	17.5(3.3)	19.2 (3.7)	-1.9
Seeking distraction	16.0(3.7)	18.3 (3.1)	-2.5
Avoiding	15.3(2.1)	15.8 (3.5)	-0.8
Seeking social support	12.7(3.2)	14.9 (4.2)	-2.4
Passive coping	9.2(2.4)	12.5 (2.7)	-5.2***
Expressing emotions	6.1(1.7)	7.0 (1.8)	-2.0
Fostering reassuring thoughts	10.7(1.9)	13.2 (2.7)	-4.5***

*** P<0.001.

a One patient did not fill in the UCL.

Correlations

Patients' scores on the QOL measures (FACT-BMT, SIP, and MOS-36) were significantly correlated with each other in a comprehensible and predictable manner (table 6).

Demographic and BMT-related variables (age, sex, age at BMT, time since BMT, indication BMT, TBI dose, IQ) were not significantly correlated with patients' QOL or with their coping behaviour as assessed by the UCL, except where age at BMT was concerned. The younger the patients were at receiving

BMT, the more they are inclined at expressing their emotions as a coping strategy (r= -0.63, P<0.01). Finally, seeking social support as a means of coping with stress was significantly positively related to the emotional component of BMT patients' role functioning (r=0.63, P<0.01), whereas passive coping was significantly negatively related to patients' mental health (r= -0.67, P<0.01).

Table 6. Correlations between the measures of BMT patients' quality of life[a]

	1	2	3	4	5	6	7	8	9	10	11
SIP											
1. total score	-										
MOS SF-36											
2. Physical functioning	-0.75***	-									
3. Role functioning-physical	-0.59**	0.72***	-								
4. Bodily pain		0.69***		-							
5. General health	-0.68**	0.59**			-						
6. Vitality	-0.78***	0.68**	0.57**		0.64**-	-					
7. Social functioning	-0.75***	0.60**			0.61**	0.55**-	-				
8. Role functioning-emotional	-0.59**	0.63**	0.58**			0.59**	-				
9. Mental health					0.69***		0.69**	-			
FACT											
10. FACT total (FACT-G)	-0.70***	0.66**	0.70***		0.66**	0.64**	0.64**	0.73***	0.66**		
11. BMTS	-0.88***	0.65**	0.58**		0.64**	0.80**				0.75***	-

*** P<0.001, ** P<0.01,

[a] Only significant correlations are depicted in this table.

Discussion

The aim of this study was to assess the long-term effects on QOL of young adults who had undergone BMT in childhood. When compared to healthy reference individuals, the scores of BMT patients on generic measures of QOL were not significantly different from those of healthy individuals. BMT patients reported functioning as well as healthy individuals on different aspects of health-related QOL, except where general health and overall functioning were concerned, where patients reported worse functioning. These results are in line with previous studies on the long-term effects of having undergone BMT during childhood [28;29;32].

Where work-related functioning was concerned, our patients reported suffering from some illness-related impairment (e.g. working fewer hours per week because of illness-related complaints; only being able to do easy/light chores due to illness-related impairment; only being able to work continuously for a short period of time or having to take regular breaks). In total, three participants were unemployed, of whom one was unable to work because of a physical handicap. The remaining participants were employed or fulltime students, and reported some problems in their work-related functioning, which they considered to be related to their having undergone BMT during childhood. These findings are in line with Barrera and colleagues [32], who reported that young adults, who underwent BMT during childhood, experienced more problems, compared to their peers, with regard to their studies and work possibilities.

When compared to adults who underwent BMT during adulthood, BMT patients involved in the current study, scored significantly better on a disease-specific measure of emotional well-being, indicating better emotional functioning. Despite the problems involved in comparing adult BMT recipients to childhood BMT recipients, this finding could illustrate the role of age at receiving BMT on patients' QOL. As previously reported by Schmidt and colleagues, and later by Andrykowski in the review paper, younger patients may overcome BMT-related difficulties more readily than older BMT recipients [26;56]. However, when we investigated whether demographic and BMT-related variables (e.g. age, gender, age at BMT, TBI dose) were related to patients' QOL, we found no relationships between these variables and measures of patients' QOL. Further research on QOL following undergoing BMT in childhood could shed more light on this topic.

We also investigated which strategies BMT patients adopted to cope with problems they encounter in everyday life. Patients reported coping with their problems in quite the same manner as their peers, with the exception that they reported adopting less passive coping strategies (e.g. isolating themselves from others) and fostering less reassuring thoughts (e.g. telling oneself everything will be all right). These findings could be interpreted as reflecting a more positive and mature coping style in childhood BMT survivors relative to their peers. Similar findings have been reported in previous studies on survivors of childhood cancer [57;58]. Furthermore, seeking social support as a means of coping with stress was related to better role functioning (emotional part), whereas passive coping was related to poorer mental health. These results are in line with coping literature [59;60].

When interpreting the results, a number of limitations of this study should be kept in mind. Firstly, the cross-sectional nature of the study described here makes it impossible to draw conclusions about causality. Longitudinal studies on the long-term effects of receiving BMT are needed. Secondly, the reference groups we used in this study merit attention. We compared the scores of our BMT patient sample on the FACT-BMT to those of adult BMT recipients. This was the best reference published. Thirdly, the low response rate is another limitation of this study. As mentioned before, the main reasons for not participating were: patients attending another hospital for their regular check-ups, the time-consuming nature of the study, and the study being regarded as too physically and emotionally taxing. We did not attempt to include patients in the QOL study, described here, without them participating in the physiological measures needed for the larger study. Participating in only one section of the large study on long-term consequences of undergoing BMT during childhood was not an option. Since information gathered on non-participants via chart review showed that they did not differ from participants on demographic and BMT-related variables (e.g. sex, age at BMT, time since BMT, TBI dose; table 1), we believe that the low response rate did not affect the validity of our findings. However, participants and non-participants could have differed on other important variables such as on their way of coping with BMT. Finally, the relatively small number of participants, and the relatively large number of variables we investigated could be considered another limitation.

Notwithstanding these limitations, an important finding of this study pertains to the apparently adequate adaptation of the patients to such an intensive medical procedure as receiving BMT. Future research should focus on identifying patients at risk for developing a maladaptive response to BMT. This would help refining psychosocial support offered to BMT recipients. Studies already conducted on adult BMT recipients could be used as a model for developing studies on children receiving BMT [21;61].

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