Journal of Nursing and Care
ISSN: 2167-1168

Kirsch et al., J Nurs Care 2012, 1:5
DOI: 10.4172/2167-1168.1000116

Review Article Open Access

Self-Reported Symptoms and Concerns in Long-Term Survivors Attending Follow-Up Visits after Hematopoietic Stem Cell Transplantation: A Cross-Sectional Single Center Evaluation in Switzerland

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Abstract

Background: Health status self-reports are increasingly recognized as an important source of key follow-up data after hematopoietic stem cell transplantation (HSCT).

Purpose: The purpose of this study was to evaluate the occurrence of self-reported symptoms and concerns in long-term survivors and compare their prevalence's between allogeneic and autologous transplant recipients with various post-HSCT follow-up lengths.

Interventions/Methods: This cross-sectional survey included a convenience sample of 226 autologous and allogeneic HSCT recipients (54% male; 1 to 26 (median 6) years post-transplant) treated as outpatients by the multidisciplinary team of a Swiss stem cell transplant ambulatory. Symptoms and concerns were measured by a self-developed self-report questionnaire.

Results: The median number of self-reported physical symptoms per patient was 5(IQR 4-10), the most frequent being dry skin (47.8%), tiredness (42%), and dry eyes (42%). The most commonly cited concerns were difficulties managing stressful emotional situations (23.9%), anxiety regarding relapse (22.1%) and memory disturbance (21.2%). There were no notable differences in appraisal of performance and number of symptoms between different time groups.

Conclusion: The high frequency of self-reported symptoms and concerns in long-term survivors indicates a need for continuous monitoring by stem cell transplant follow up clinics, which would allow timely and effective interventions to prevent or alleviate late effects.

Implications for Practice: There seems to be good opportunity for health professionals to support long-term survivors by using self-report as clinical tool in follow-up care. Sharing information about problems and symptoms patients face post-treatment will benefit both professionals and patients.

Keywords: Stem cell transplantation; Survivorship; Late effects; Follow-up; Self report; Symptoms

Introduction

Hematopoietic Stem Cell Transplantation (HSCT) is a curative, intensive treatment for hematological and lymphoid cancers, and also for other autoimmune and genetic disorders [1]. Despite advances in procedure and supportive care, transplant related morbidity and mortality remains high. Many survivors have to adapt to physical complications and chronic health conditions - referred to here as 'late effects'- associated with high distress, poorer long-term adjustment and shorter survival [2,3]. Comprehensive follow-up of long-term survivors after HSCT is crucial, as the cure or control of the underlying disease may not be accompanied by a full restoration of health and a return to normality [4]. As many late effects are manifested in patient-perceptible symptoms, patient self-reporting, which captures issues assessable only or predominantly through patients' perceptions, is increasingly recognized as an important source of subjective information [5]. However, empirical evidence shows that many clinicians systematically downgrade or fail to note the severity of patient-reported symptoms, which may contribute to preventable late effects [6]. Therefore, a system of self-reporting allows healthcare professionals and patients to better communicate and understand each other, facilitates informed decisions regarding symptom management and treatment, and may even allow prevention of some late effects, it is recommended to treat self-reporting as a major element of follow-up care [7,8]. To provide effective symptom management for this population, nurses and physicians need an understanding of patients' specific problems and symptoms. Integrating self-reporting as a clinical patient management tool can help that patients prepare themselves for the consultation with the physician or nurse so that topics can be discussed in a structured format.

As suggested by psychosocial transition theory, [9] this study views patients' confrontations with serious illness, its treatment and consequences as major life experiences that require them 'to restructure their ways of looking at the world' and adapt their plans and actions accordingly. We developed the HSCT Assist Model to organize factors related to post-transplant life after the end of acute treatment. This study's framework is based on psychosocial transition theory, integrating evidence from the literature [10-22] with clinically known factors for the development of late effects (e.g., disease, treatment, transplant complications). The model summarizes nine domains of ongoing survivorship issues assessable via patient self-reporting. In

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Received May 10, 2012; **Accepted** June 25, 2012; **Published** June 27, 2012

Citation: Kirsch M, Halter J, Geest SD (2012) Self-Reported Symptoms and Concerns in Long-Term Survivors Attending Follow-Up Visits after Hematopoietic Stem Cell Transplantation: A Cross-Sectional Single Center Evaluation in Switzerland. J Nurs Care 1:116. doi:10.4172/2167-1168.1000116

addition to guidance for comprehensive assessment of survivorship issues, this provides a basis for later analysis (Figure 1).

Previous research using patient self-reporting focused mainly on the measurement of quality of life. However, it did not describe findings generated by measures employed in the clinical follow-up setting to assess common symptoms that might be linked to co-morbidities or late effects, i.e., conditions that would necessitate ongoing treatment by the multidisciplinary follow-up team. To our knowledge, there is no research describing results of routinely used self-report in HSCT long-term follow-up care. Another question that has recently been under discussion is whether autologous HSCT patients require the same follow-up care and surveillance as allogeneic HSCT recipients. Although it is commonly stated that autologous HSCT recipients need fewer follow-ups than allogenic recipients; some clinicians, however, put this in question considering the older age of auto HSCT recipients and the rising number of treatment indications.

The purpose of the current study was threefold: (1) to describe allogeneic and autologous HSCT recipients' self-reported symptoms and concerns during routine follow-up; (2) to determine differences in the prevalence of physical or psychological symptoms between allogeneic and autologous transplanted patients; and (3) to explore differences among groups in different post-HSCT follow-up periods.

Methods

Design

We used a cross-sectional study design analyzing data of a routine follow-up survey implemented during daily clinical practice at each yearly follow-up visit in a single HSCT center in Switzerland.

Sample and setting

All patients attending 2008 yearly follow-up consultations in the Haematology Department of the University Hospital Basel (USB) were invited to fill out a self-developed survey. Patient inclusion criteria for the present study were: ≥ one year after autologous or allogeneic HSCT; ≥ 18 years of age at the time of follow-up; and completion of the questionnaire. Patients who did not return their questionnaires were considered non-responders.

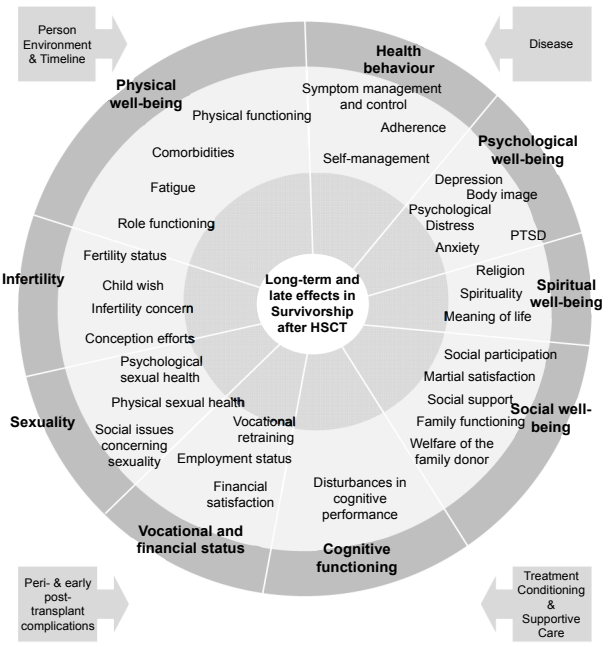


Figure 1: The Hematopoietic Stem Cell Transplantation-Assist Model illustrates the nine overall domains in which long-term survivors might experience alterations and show a need for assistance from the health care provider. Within each domain, the concepts give more specific information about the patient's condition. Concepts are measured via indicators/symptoms. A wide range of indicators exist: however, none are displayed in this overview. The four arrow boxes depict factors which influence alterations decisively.

The USB is located in the German-speaking part of Switzerland, but the hematology clinic's patients come from all over the country, and therefore, may also be mother-tongue speakers of French, Italian, Romansch or any of a broad range of foreign languages. As health insurance is mandatory, all are insured and eligible for regular life-long follow-up care. After their first year of survival, all patients are requested to return to the center for yearly check-ups. The outpatient care team included one senior physician, two junior physicians and 12 registered nurses sharing 7.5 full time positions.

Variables and measurement

Demographic and clinical variables: Patients' demographic and clinical data were retrieved from medical files and an electronic transplant database. Variables included gender, age, native language, marital status and current working status, coverage of disability insurance and years of post-HSCT follow-up. Patients' follow-up times were categorized in 4 groups: 1-2 years; 3-5 years; 6-9 years; and ≥ 10 years. Clinical variables included hematological diagnosis, type and source of transplant, donor relationship, whether total body irradiation was used or not, Karnofsky Performance Status (KPS) [23] and presence of chronic GvHD, scored according to the National Institute of Health grading system [24].

Symptoms and concerns

The clinical survey (Table 1) used to assess symptoms and concerns possibly associated with late effects were developed in 2002 by the USB's multidisciplinary HSCT follow-up healthcare team. It was designed to gather subjective information to inform clinicians about the patient's perspective encountered during yearly check-up visits. Thus far, validation of the survey has been limited to face validity. In order to further assess its content validity we reviewed its content using the nine domains of the HSCT Assist model as a framework (Figure 1). In the survey, only seven of the nine domains were partly captured via 70 items for women and 66 items for men. 'Spiritual well-being' and 'health behaviour' were not addressed. Except for one open question (Kind of changes experienced in spousal relationship after HSCT), items were scored as "yes" or "no". The time frame for responses was the previous year. The survey exists in French and German (Table 1).

Data collection

This study was approved by the local ethics committee. As part of a standard clinical follow-up, survey forms were mailed to patient's homes prior to their annual follow-up appointments. Responders then brought their completed forms to their check-ups and gave them to their treating physicians, who referred to the survey as a source of information during the clinical visit. Patients were asked for consent and informed that their responses would be used for research purposes. Confidentiality was also assured. Completed surveys were added to the patients' medical files. For data entry, questionnaires were retrieved from medical files by the first author and one research assistant. Data were entered manually to an anonymized database and checked for consistency and accuracy.

Data analysis

Descriptive analysis involved frequencies and calculations of central tendencies and distributions as appropriate. Characteristics of responders and non-responders were compared depending on

measurement level and distribution using the Student's T-Test, the Mann-Whitney U-Test and the Chi-Square Test. Comparison of the numbers of symptoms reported by autologous and allogeneic patients used the Mann-Whitney U-Test. Differences between the two groups' responses to individual items were examined with the Chi-Square-Test. Regarding the numbers of physical and psychological symptoms, as well as appraisals of regained pre-transplant performance, differences between groups with different follow up times were examined respectively with the Kruskall-Wallis H-test and the Chi-Square test. Statistical significance was set at alpha=0.05. In order to control for multiple testing and to keep the proportion of false-positive results under 5%, we calculated Q-values in a series of post-hoc tests in which we compared the prevalence of single symptoms in autologous and allogeneic patients [25]. Data analysis was performed using SPSS 16.0.

Results

Patient characteristics

In total, 326 eligible patients visited the outpatient clinic for annual follow-up consultations in 2008. Of these, 226 (69.3%) returned completed surveys. There was only one significant difference between patients who responded to the survey (226/326) and those who did not (100/326): a clear majority of responders spoke German or French as a native language (71.9% (German or French) versus 57.1% (all others); p=0.03). Responders also tended to have shorter follow-up times than non-responders (median 6 years, IQR 7.94, versus a median of 6; IQR 10.75; p=0.066). Medical characteristics and demographics of included patients are shown in table 2 and 3.

Physical well-being (49 items on physical symptoms)	
Skin/hair	Dry skin, skin itching, alopecia/hair loss, skin rash, skin changes
Eyes	Dry eyes, light sensitivity, blurred vision, burning eyes
Otolaryngology	Common cold, hardness of hearing, sinusitis, ear pain
Mouth	Dry mouth, caries, loss of taste, mouth ulcers, tongue burning, fever blisters, toothache, open lesions, gum bleeding
Lung	Breathing difficulty, cough, increased sputum
Cardiovascular	Hypertension, irregular pulse, chest pain on exertion, swollen legs
Gastrointestinal	Diarrhoea, abdominal pain, nausea/vomiting, pyrosis, loss of appetite, constipation, weight loss, rectal bleeding
Urogenital	Incontinence, burning on urination, haematuria, cystitis, nephritis
Neurological	Nervousness, insomnia, shivering, dizziness, palsy
Single symptom items	Fatigue, infections treated with antibiotics
Psychological well-being (5 items on psychological symptoms)	
	Listlessness; diminished emotional capacity; increased aggression; anxiety regarding relapse, sadness
Social well-being (3 items)	
	• Have there been changes in your spousal relationship due to HSCT? • If yes, what kind of changes have you experienced? (text) • Do you have problems in connecting with social groups?
Vocational and financial status (4 items)	
	• Re-uptake of employment post-HSCT; • Change of profession resulting from HSCT; • Occupational re-training done; • Desire to speak with an aide about financial problems after HSCT
Cognitive functioning (1 item)	
	Disturbance of memory
Infertility & Sexuality (Female: 5 items; male: 1 item; addressing both gender: 3 items)	
Female	Diminished vaginal lubrication, itching of vagina, increased vaginal efflux, painful intercourse, hot flashes
Male	Erectile dysfunction
Both genders	Loss of desire; desire to have children; wish to speak with an expert about problems concerning sexuality

Table 1: List of items requested by the follow-up questionnaire.

Self-reported symptoms and concerns

Physical symptoms: One or more physical symptoms were reported by 90.3% of patients (204/226), with a median number of 5 (IQR 6). Patients in their first two years post-HSCT reported a median of 7 (IQR 6) symptoms; with 3 to 5 years, the median fell to 5 (IQR 8.25) symptoms; and while the 6 to 9 year patients reported a median of 6 (IQR 9) physical symptoms, the group with 10 or more years of follow-up experienced a median of only 4 (IQR 7) (p=0.256) (Figure 2).

Sorted by organ system, the patient sample reported symptoms relating to skin and hair (60.6%); eye (59.3%); oral/dental (49.1%) neurological (44.7%); cardiovascular (38.9%); gastrointestinal (37.2%); lung (32.3%), otolaryngological (32.3%) or urological (12.4%) symptom (Table 4).

Three of the ten most frequently reported physical symptoms were indicated by over 40% of all patients: dry skin (47.8%), dry eyes (42%) and tiredness (42%). Seven more symptoms were reported by more than 20% of all patients: mouth dryness (28.3%), breathing difficulty (24.3%), light sensitivity (23.9%), blurred vision (23%), infections treated with antibiotics (22.1%), common cold (21.7%) and burning eyes (20.4%).

Although, on average, allogeneic recipients stated slightly more physical symptoms than autologous recipients (median 6, IQR 8 vs. median 4.5, IQR 6.77; p=0.64), the observed difference was not significant. Furthermore, as shown in figure 3, no notable differences were found between transplant groups regarding individual physical symptom items (Figure 3).

Characteristics	Total (N=226)	Allo (n=188)	Auto (n=38)
Age at last HSCT; mean (SD)	40.1 (15.0)	38.15 (14.39)	49.83 (14.44)
Years after HSCT; median (Range)	6 (1-26)	6 (2-11)	5 (2.75 -8.25)
Gender; male	122 (54%)	102 (54.3%)	20 (52.6%)
Marital status			
Married/cohabiting	154 (68.2%)	128 (68.1%)	26 (68.4%)
Single/widowed/separated	50 (22.1%)	43 (22.9%)	7 (18.4%)
Not documented	22 (9.7%)	17 (9%)	5 (13.2%)
Native Language			
German	181 (80.1%)	150 (79.8%)	31 (81.6%)
French	13 (5.7%)	11 (5.9%)	2 (5.3%)
Other	32 (14.2%)	27 (14.3%)	5 (13.1%)
Current working status			
Full time[a]	73 (32.3%)	65 (34.6%)	8 (21.1%)
Part-time	61 (27%)	54 (28.7%)	7 (18.4%)
Homemaker	22 (9.7%)	16 (8.5%)	6 (15.8%)
Not working	33 (14.6%)	32 (17%)	1 (2.6%)
Retired	19 (8.4%)	9 (4.8%)	10 (26.3%)
Not documented	18 (8%)	12 (6.4%)	6 (15.8%)
Receiving disability insurance[b]			
No disability insurance	197 (87.2%)	161 (85.6%)	36 (94.8%)
Full Disability insurance	21 (9.3%)	20 (10.6%)	1 (2.6%)
Partial Disability insurance	8 (3.5%)	7 (3.7%)	1 (2.6%)

Abbreviation: SD, standard deviation
[a]Full-time engagement means working at least 33 hours per week.
[b]Disability insurance includes paid sick leave, short-term disability benefits and long-term disability benefits.

Table 2: Demographic characteristics (N=226).

	Total (N=226)	Allo (n=188)	Auto (n=38)
Initial Diagnosis			
AML	40.1 (15.0)	56 (29.8%)	4 (10.5%)
ALL	30 (13.3%)	27 (14.4%)	3 (7.9%)
CML	41 (18.1%)	39 (20.7%)	2 (5.3%)
CLL	9 (4%)	4 (2.1%)	5 (13.2%)
Plasma cell disorder	28 (12.4%)	10 (5.3%)	18 (47.8%)
Hodgkin or Non Hodgkin lymphoma	24 (10.6%)	21 (11.2%)	3 (7.9%)
Myelodysplastic syndrome	14 (6.2%)	13 (6.9%)	1 (2.6%)
Myeloproliferative syndrome	7 (3.1%)	7 (3.7%)	0
Aplastic anaemia	10 (4.4%)	10 (5.3%)	0
Autoimmune disease or inborn error	3 (1.3%)	1 (0.5%)	2 (5.3%)
Source of transplant			
Bone marrow	57 (25.2%)	56 (29.8%)	1 (2.6%)
Peripheral blood	168 (74.3%)	131 (69.7%)	37 (97.4%)
Umbilical cord blood	1 (0.4%)	1 (0.5%)	0
Total Body Irradiation[a]			
Yes	115 (50.9%)	111 (59%)	4 (10.5%)
No. of transplantations			
1	18 (8%)	12 (6.4%)	6 (15.8%)
> 1	45 (19.9%)	39 (20.7%)	6 (15.8%)
Donor relationship in allogeneic patients (n=188)			
Identical sibling or matched related		127 (67.6%)	NA
Syngen		6 (3.2%)	NA
Missmatched related		11 (5.9%)	NA
Unrelated		44 (23.4%)	NA
Active chronic GvHD (n=188)[b]			
Yes		72 (38.3%)	NA
No		102 (54.3%)	NA
Unclear or not documented		14 (7.4%)	NA
Karnofsky Score[c]			
100%	137 (60.6%)	112 (59.6%)	25 (65.8%)
90-99%	63 (27.9%)	55 (29.3%)	8 (21%)
80-89%	16 (7.1%)	12 (6.4%)	4 (10.6%)
<80	6 (2.7%)	5 (2.6%)	1 (2.6%)
Not documented	4 (1.8%)	4 (2.1%)	

Abbreviations: AML: Acute Myeloid Leukaemia; ALL: Acute Lymphoblastic Leukaemia, CML: Chronic Myeloid Leukaemia; CLL: Chronic Lymphocytic Leukaemia; GvHD: Graft versus Host Disease.

[a]Prevalence of patients who had a total body irradiation in the conditioning regime with 12 Gray.

[b]The GvHD grading scheme developed by the National Institutes of Health consensus development project on criteria for clinical trials in chronic GvHD, was used by rating physicians.

[c]Karnofsky Performance status (KPS) was rated by the physician at the annual follow-up visit and comprises an individual's health and physical functionality, based on a criteria related performance index rated from 100% (normal function) to 10% (moribund).

Table 3: Medical characteristics (N=226).

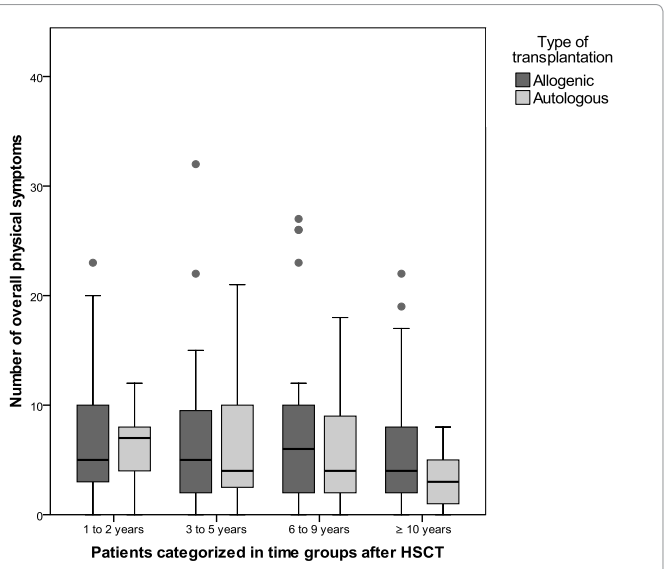


Figure 2: Median number of physical symptoms related to time-period of follow-up. Boxes include the distribution of numbers of symptoms between the 75th and the 25th percentile, with the thick line in each box representing the median number of symptoms. The lines extending above and below the boxes indicate the 90th and 10th percentile, respectively. Outliers are designated as '•'. Patients are grouped by transplant type (allogeneic/autologous) and by period post-HSCT (1 to 2 years (n=58); 3 to 5 years (n=54); 6 to 9 years (n=54) and ≥ 10 (n=60)).

	Patients reporting ≥ 1 symptom in one organ group a; n (%)	Percentages of patients classified by their reported number of symptoms Auto (n=38)		
		1-2	3-4	≥5
Skin & hair (5 items)	137 (60.6 %)	51.8%	6.6%	2.2%
Eyes (4 items)	134 (59.3%)	46.5%	12.8%	0
Otolaryngology (4 items)	73 (32.3%)	31%	1.3%	0
Oral/dental (9 items)	111 (49.1%)	37.6%	8%	3.5%
Lungs (3 items)	73 (32.3%)	31%	1.3%	0
Cardiovascular (4 items)	88 (38.9%)	35.8%	3.1%	0
Gastrointestinal (8 items)	84 (37.2%)	28.3%	7.1%	1.8%
Urological (5 items)	28 (12.4%)	11.1%	1.3%	0
Neurological (6 items)	101 (44.7%)	34.5%	8.4%	1.8%

[a]Percentage is based on total population (N=226)

Table 4: demonstrates numbers and prevalence of the symptoms indicated by patients regarding symptom groups.

Psychological well-being: One or more psychological concerns were indicated by 45.6% of patients (104/226). The most common, claimed by 23.9% of patients, was managing stressful emotional situations, followed by anxiety regarding relapse (22.1%) and sadness (13.7%). Listlessness and increased aggression were mentioned by 11.1% each. Autologous and allogeneic patients did not differ regarding the median number of overall psychological symptoms (p=0.507). However, with increased follow-up time, patients of both transplant types reported fewer psychological concerns. While in the first two years post-HSCT, 60.3% of patients reported at least one psychological concern (mean number of concerns 1.06, SD 1.18), that number fell after 3 to 5 years to 53.7% (mean 1, SD 1.32), after 6 to 9 years to 37% (mean 0.78, SD 1.28) and after ten or more years to 31.7% (mean 0.47, SD 0.83) (p=0.007).

Cognitive functioning: Memory disturbance was reported by 21.2% of patients. No differences in the prevalence of memory problems were found between autologous and allogeneic transplant recipients (p=0.368), or between groupings based on follow-up length (p=0.173).

Vocational and financial well-being: After a median 5 years of follow-up, illness-related job changes were reported by 11% of patients (range: 1-25 years of follow-up), and participation in occupational retraining was noted by 8.4% (range 1-20 years of follow-up). A small minority (5.3%) claimed current financial difficulties requiring the support of a social worker.

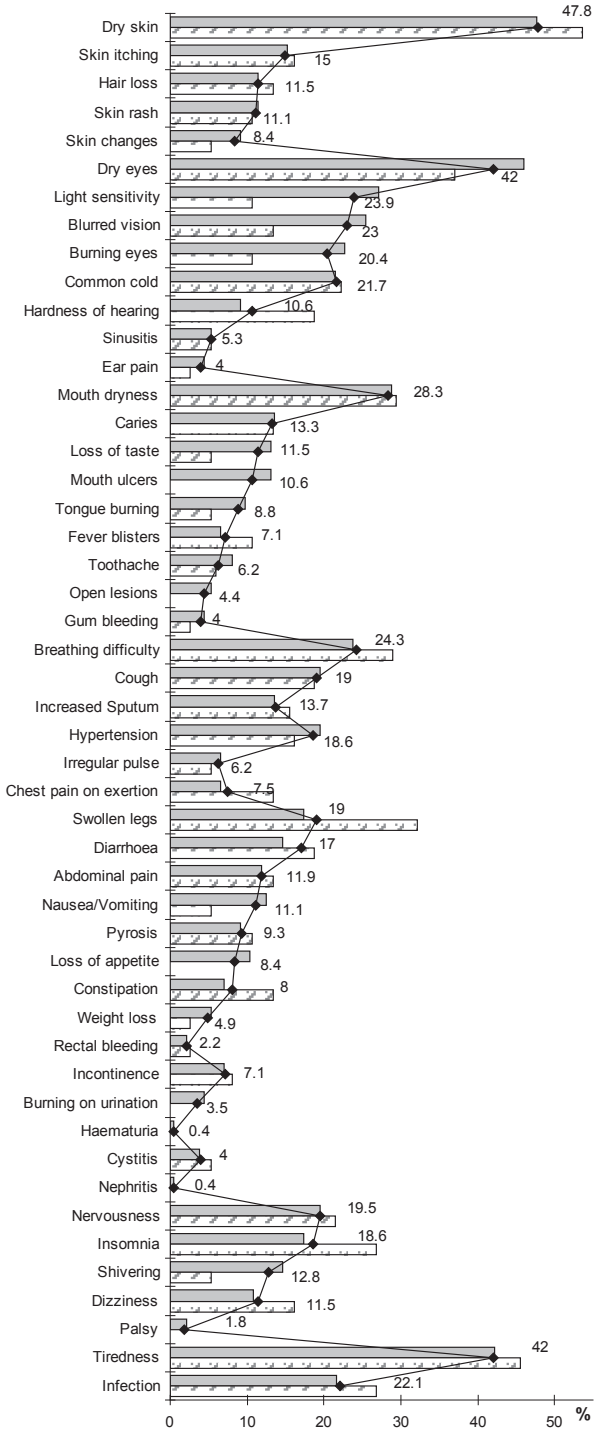


Figure 3: Percentages of physical symptoms in allogeneic patients (n = 188; grey bars), autologous patients (n = 38; hatched bars) and in the total sample (N = 226; line graph with rhombus). Numbers adjacent each data point indicate the percentage distribution of a symptom in the whole sample.

Social well-being: Only 13 patients (5.8%) reported problems connecting with social groups, although 15% (34/226) reported post-HSCT changes in marital satisfaction. Of thirty who supplied details of the changes affecting them and their significant others most, 5 cited illness, 7 separation, 8 problems with sexuality or fertility, and 10 decreases in mutually beneficial emotional exchanges.

Infertility and sexuality: Approximately 20% of women (21/104) and men (24/122) reported decrease in sexual interest. Of 104 female responders, 37.5% claimed diminished vaginal lubrication, with increased vaginal discharge reported by 9.6%. Hot flashes were indicated by 25% of women, who had an average age of 45.38 (SD=11.14). Painful intercourse was reported by 18.3% of women. Only 4 reported itching of the vagina. Comparing the occurrence of single symptoms in autologous and allogeneic transplanted women and between the different post-HSCT time groups, no differences were found.

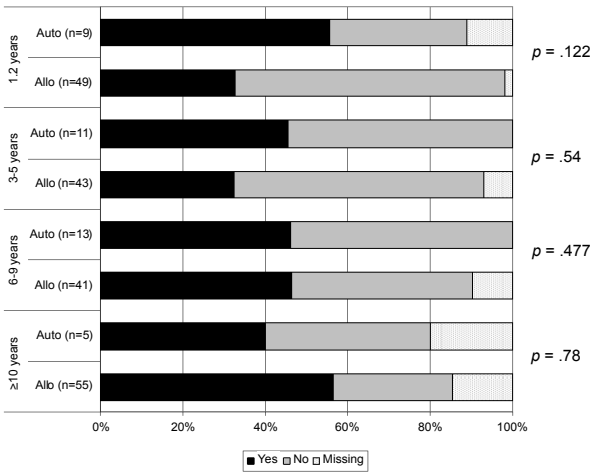
Regarding male sexuality, 23.8% of 122 male responders reported erectile dysfunction. The mean age in this group was 51 (SD 11.9), compared to 47 years (SD 13.5) in men reporting no erectile dysfunction. Erectile dysfunction was reported equally in autologous and allogeneic transplant recipients (p = 0.665) and in the four post-HSCT time groups (p = 0.444).

Questions concerning the desire to conceive were noted by three men (mean age 40.6 years, SD 6.4) and four women (mean age 26.5 years SD 7.2). Of the entire sample, 8 patients (3.5%) wished to have advice from an expert in sexuality and/or fertility matters.

Appraisal of returning to normal performance regarding time span after allogeneic or autologous HSCT: As shown in figure 4, concerning appraisals of 'having returned to normal' there were no significant differences between allogeneic and autologous patients either within or between post-HSCT time spans.

Discussion

This study is one of the few to report findings generated by patient self-report instruments used in clinical follow-up and focusing on post-HSCT symptoms and concerns. The high number of symptoms and concerns observed here illustrates the diversity of this patient population's needs. In light of the Institute of Medicine's latest 'From Cancer Patient to Cancer Survivor: Lost in Transition' report [26], it highlights transplant centers' responsibility to provide ongoing surveillance, care and information on available psychosocial and



[a]Chi Square Test

Figure 4: The response of patients (N = 226) to the question `Do you feel completely back to normal and able to meet the daily demands required to do your job or housework? ´ is shown, dependent on transplant type and length of follow up. In view of follow-up time, no significant differences were found between allogeneic and autologous patients[a]

practical resources. It is becoming increasingly clear that complex care for HSCT patients requires a chronic care follow-up model that integrates comprehensive management not only of medical but also of psychosocial aspects, while reinforcing continuity of care and support regarding patient self-management and decision making. This contrasts with the acute care model currently prevalent, which has thus far failed to adequately address such issues [27].

In contrast to a number of earlier studies, we found no notable differences in the number of physical and emotional symptoms reported by autologous and allogeneic patients [28-30], thereby adding to a growing evidence base that the two patient groups have equal needs for long-term follow-up care [4,15]. One possible explanation for the equal number of symptoms between groups detected by our study might be the significantly higher age of autologous HSCT patients (~10 years) as well as the smaller sample size of this group. Higher age at transplantation remains a risk factor linked with more severe late effects and shorter post-transplant survival [31]. Due to the increasing relaxation of upper age limits for HSCT, the proportion of survivors with multiple morbidities is growing. Considering the ongoing discussion regarding differences in follow-up needs between allogeneic and autologous recipients, our results indicate the need for life-long follow-up of both groups.

The data reported in this study describes no notable differences in numbers of symptoms depending on time post-transplantation. Several studies, both cross-sectional and longitudinal in design, support our findings, as they also indicate significant proportions of patients suffering persistent symptoms and/or developing new ones. [4,15,32,33] In comparison to control groups, HSCT recipients experience significantly more long-term symptoms that might result in inability to work, financial or insurance problems, and barriers to resuming normal everyday lives [34]. A cumulative burden of chronic health conditions evolving with increasing time after transplantation might account for the stable number of symptoms detected in our study. This explanation is supported by a recent cross-sectional case-control study showing that the incidence of any given chronic health condition in 1022 allogeneic and autologous stem cell transplant recipients increased from 32% at 2 years post-transplant to 59% at 10 years [35]. Overall, survivors were twice as likely as their matched siblings to develop a chronic condition, and 3.5 times more likely to develop a severe/life threatening condition.

Another important observation arising from the current study was that, as follow-up time increases, though the number of patients who gave positive appraisals of their performance and 'returning to normality' increased, a considerable proportion still reported not having regained their pre-transplant performance. The low rate of positive agreement to this question (32.7% - 56.4%) contrasts somehow with findings from an earlier longitudinal study in which 63% to 68% of two year survivors 'felt that they had returned to old selves' [15]. Besides the wording and scoring differences between the two studies' questionnaire items, we suggest that our study's low positive response rate reflected the dynamic that, with increasing time post-transplant, survivors increasingly accept that they might never again experience the 'normality of pre-transplant life'. This possibility has recently been a topic of considerable discussion among clinicians and researchers, some of whom have suggested that negative changes and restrictions due to long-term effects of prior or chronic health conditions are outweighed by the survivors' gratitude for being alive [36,37].

Integrating a self-report survey into clinical follow-up care to assess symptoms and concerns might provide a more complete picture of patients' health status, particularly regarding late effects and co-morbidities. For instance, in our study, eye-related symptoms were frequently mentioned by patients (59.3%). These might be associated with common late effects such as sicca syndrome, retinopathy or cataract, for which early recognition and treatment could be extremely beneficial [38]. At present, the systematic use of self-reports in HSCT follow-up is rare. However, according to our clinical experience and increasing evidence from different oncology disciplines, while patient self-reports in follow-up care are arguably both feasible and beneficial, a need remains for research demonstrating their impacts on patient outcomes [39].

This study's findings should be interpreted in light of the following limitations. This was a single-centre cross-sectional study examining a heterogeneous sample of HSCT patients regarding disease, treatment history and co-morbidities. We admittedly did not perform multivariate analyses, which would have accounted for the simultaneous effects of diverse variables on the responses of interest. Also, non-German or non-French native speakers were under-represented in the sample, as the questionnaires were only available in these two languages. In order to enhance the participation of foreign language speakers known to be at risk for health disparities [40], we suggest supplying multi-lingual questionnaires and the assistance of professional interpreters as appropriate.

Critical comparison of this study's survey with the HSCT Assist model showed that the Assist model's domains and their subordinated indicators were only partially addressed. For example, the domains of health behaviour and spiritual well-being were completely missing and, in view of other domains, including physical-well being, for example, no assessment was included of muscle cramps, numbness and joint pain, although these are possible indicators of common musculoskeletal late effects such as myopathy, fibromyalgia, osteoporosis, scleroderma, strictures, fasciitis or neuropathy [41] The lack of such important issues calls for an adaptation of the survey before any future use.

The U.S. Food and Drug Administration outline new standards for self-report endpoints in clinical studies [42]. The generation of self report items should be based on qualitative work, i.e., derived from patient interviews, expert opinion and evidence in the literature. For example, the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) provides a solid basis for the development of self-report measures assessing acute or late adverse effects of treatment from the patient's perspective. To develop the PRO-CTCAE symptom item bank based on the well-established CTCTAE terminology, Basch et al. [43] employed rigorous research steps, including the development of a conceptual framework, item selection and refinement via cognitive patient interviews and an expert survey, along with careful psychometric testing.

Optimally, the follow-up of HSCT patients should be based on a combination of systematic self-reporting and objective diagnostics. This approach would contribute to patient care quality by detecting health changes and nascent problems undetectable via clinical testing, leading to early treatment and hence to improved patient outcomes, e.g., reduced symptoms, increased health-related quality of life and enhanced patient satisfaction [6].

Conclusion

A clinical self-report questionnaire used in the follow-up of HSCT recipients showed high frequencies of diverse symptoms and patient related concerns. However, no significant differences could be found between autologous and allogeneic recipients. The results indicate a need for continuous monitoring of both groups, which will allow timely and effective interventions to prevent or alleviate late effects following HSCT.

Acknowledgements

We give special thanks to the patients receiving follow-up care at the USB and the healthcare team of the USB outpatient clinic. We are also grateful to Isabel Lehmann for her help with data collection, and to Professor Dr. Catherine Nissen for her thoughtful review of an earlier version of this manuscript.

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