Health-related quality of life before and after hematopoietic stem cell transplant: evidence from a survey in Suzhou, China

Yongchun Lianga, Haifang Wangb, Meie Niua, Xiaming Zhub, Jianzheng Cai and Xiubei Wanga

aDepartment of Nursing, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, People’s Republic of China; bDepartment of Hematology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, People’s Republic of China

ABSTRACT
Objectives: The aim of our longitudinal study was to explore changes in HRQOL over a 6-month period and to identify factors associated with the HRQOL of HSCT recipients.
Method: Our study comprised 191 HSCT patients; their data were collected before transplantation and at 30, 90, and 180 days posttransplantation. The Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) questionnaire was used to assess HRQOL. We also evaluated the patients’ demographic characteristics and clinical histories to determine the relative contributions of these factors to HRQOL outcomes.
Results: Before HSCT, the patients reported a mean overall HRQOL of 110.31 (SD, 14.99); this reached a minimum of 105.07 (SD, 18.85) at day 30 after HSCT and increased steadily over time to 106.71 (SD, 18.34) at day 90 and 108.16 (SD, 18.34) at day 180 after HSCT. Compared with baseline, overall HRQOL changed with the mean of −5.24 (SE 1.55; P = .001), and −3.60 (SE 1.55; P = .022), respectively, at 30 days and 90 days after HSCT. Overall HRQOL returned to near pretransplant levels at 180 days after HSCT (SE 1.47; P = .146). Generalized estimating equation (GEE) models showed that household income (β = 6.590; P < .001), transplant-related complications (β = −6.101; P < .001), and patient age (β = 0.243; P = .045) were associated with HRQOL.
Conclusion: The patients’ overall HRQOL was severely impaired in the early stages of posttransplantation, and patients experienced the worst HRQOL at 30 days. They had improved significantly by 180 days posttransplantation. We also found that household income, transplant-related complications, and age were independent predictors of early HRQOL. We therefore concluded that the HRQOL of HSCT patients in the early stages posttransplantation deserved more attention.

Introduction
Hematopoietic stem cell transplantation (HSCT) is the most effective way of treating hematologic malignancies [1]. Before treatment, patients undergoing HSCT undergo high-dose chemotherapy and radiotherapy in order to eradicate tumor cells and abnormally proliferating cells. Thereafter, donor hematopoietic stem cells are injected and the patient’s hematopoietic system is eventually rebuilt. More than 60,000 individuals worldwide undergo allogeneic or autologous HSCT each year, with a concomitant rise in the number of survivors [2]. Advances in HSCT techniques and supportive care have led to dramatic improvements in relapse mortality in patients with high-risk hematologic malignancies. Nearly 60% of HSCT recipients exhibit long-term survival with no disease [1,3].

HSCT has greatly improved the survival of patients; however, this procedure has severe toxic effects, both physiological and psychological, which cannot be ignored [4–9]. The advent of reduced-intensity conditioning regimens has improved patients’ tolerance, yet side effects still occur. These effects – caused by high-dose cytotoxic drugs, immunosuppressive drugs, and systemic irradiation – include nausea, emesis, mucositis, cystitis, and diarrhea [10,11]. They severely inhibit the immune system and increase the individual’s susceptibility to infection. Posttransplantation complications include acute or chronic graft-versus-host disease (GVHD), severe infection, hemorrhagic cystitis, pneumonia, relapse, cataracts, and infertility [12–16]. Acute or chronic GVHD is the major and most common complication, with an incidence of 50% to 70% and 30% to 50%, respectively [17]. The physiological side effects result in decreased physical performance, thus negatively affecting patients’ HRQOL. In addition, patients undergoing HSCT often experience psychological effects – fear, anxiety, and uncertainty – as well as financial difficulties [4,18,19]. All these have psychosocial consequences that influence life satisfaction and HRQOL.

HRQOL is generally conceptualized as a multidimensional construct referring to patients’ perceptions of the impact of a disease and its treatment on their physical, psychological, and social functioning and well-being [20]. In recent years, HRQOL has gradually
become an important part of the evaluation and management of HSCT recipients before and after transplantation [4–6,20–27]. However, studies addressing HRQOL in HSCT patients are subject to overreliance on cross-sectional surveys, diverse research designs, different types of patients studied, variations in methods of HRQOL assessment, and differences in the time points at which HSCT recipients were studied, resulting in great heterogeneity between studies. In addition, we found that authors paid more attention to the trajectory of HRQOL during the longer term in longitudinal studies and that few authors have focused on HRQOL at the early stages of transplantation. However, we regard this period as of great clinical significance, as patients’ bone marrow is affected, leading to increased susceptibility to infection and other complications. These developments are conducive to physiologic and psychological distress and likely to reduce HRQOL.

In view of the foregoing, we chose to focus our study more on HRQOL in the early stages of transplantation. We investigated 191 HSCT recipients’ HRQOL before transplantation and on days 30, 90, and 180 posttransplantation. Our aim was to identify the trajectory of HRQOL during the early stages of transplantation and to determine the most salient influencing factors so as to plan for intervention at the earliest time.

Methods

Participants

All the participants were undergoing an allogeneic/autologous bone marrow or peripheral blood stem cell transplant for a hematologic malignancy. Patients were included if they were 18 years old or older and were willing to participate in the study. Patients with mental illness or cognitive impairment were excluded, as were those who experienced graft failures, whose illness was recrudescent, who were too sick to participate, or who died. Participants were recruited from 22 July 2016, to 30 April 2017. Sample size calculations were based on the detection of medium effect sizes (power = 0.8) with an a priori estimation of 10–15 predictor variables: a sample size of 120 was required [28]. Finally, a total of 191 participants were enrolled in the study and each completed the questionnaires before transplantation. The number of participants on days 30, 90, and 180 was 182, 162, and 138, corresponding to participation rates of 95.3%, 84.8%, and 72.3%, respectively (Figure 1). This study was approved by the ethics committee of our hospital and all subjects provided informed consent in accordance with the Declaration of Helsinki.

Study measures

Health-related quality of life

HRQOL was measured by the Functional Assessment of Cancer Therapy – Bone Marrow Transplant (FACT-BMT, V4.0) questionnaire [29], which includes 5 domains: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB), and BMT-specific concerns (BMTS). Responses were ranked from 0 to 4 (0, not at all; 1, a little bit; 2, somewhat; 3, quite a bit; 4, very much). The 5 domain scores were summed to generate a total score. The total scores ranged from 0 to 148, and the higher the score, the better the HRQOL. The reliability coefficients range from 0.86 to 0.89 [29].

Sociodemographic characteristics

Sociodemographic characteristics included age, sex, marital status, residence, education level, and household income [19,23,26,30]. For analysis, marital status included both unmarried and married; and there was no category for divorce or separation in this study. Area of residence was categorized as rural or nonrural. Education was determined according to the highest level attained, including junior high school or below, high school, baccalaureate degree, and above). Household income was divided into 4 categories, from low to high (Table 1).

Clinical data collection

Clinical materials included disease diagnosis (acute leukemia/nonacute leukemia), stem cell source (allogeneic/autologous), preparative regimen (busulfan and cyclophosphamide or not), platelets (the level of platelet measured when patients got out of the
purifying ward), and transplant-related complications (including infection, GVHD, urocystitis, etc.) [4,27,31–33] (Table 1). We obtained this information from the HSCT follow-up group, which was responsible for the follow-up of HSCT patients in the department of hematology.

Statistical analysis

Data analysis was carried out using IBM SPSS Statistics 19. Data were presented as mean ± SD, for continuous variables and count (percentage) for categorical variables. Repeated measures ANOVA was used to assess the changes between different time points and the LSD method for comparison between different measurement points. The GEE method was used to identify the risk factors for HRQOL. All statistical assessments were evaluated with a 2-sided alpha level of 0.05.

Results

Sample baseline characteristics

A total of 138 patients provided serial HRQOL data. The mean age of participants was 33.31 ± 11.40 years (range, 18–62). Of the 138 patients, 82 (59.4%) were male and 56 (40.6%) were female. Only 10 (7.2%) of the 138 patients underwent autologous transplantation; the others 128 (92.8%) received allogeneic transplantation. Table 1 describes the characteristics of the study participants at different points in the treatment process. The dropout sample size was 53 (27.7%). Of these 53 patients, 18 died of serious GVHD, 6 stopped the transplant temporarily owing to serious complications while undergoing pretreatment, 3 experienced graft failures, 5 relapsed, and 5 were too sick to complete the questionnaires. Twelve refused to complete the questionnaires, as most thought that filling out the questionnaires would not help them in any way, and 4 could not be contacted (Figure 1). We compared the baseline characteristics of the missing sample (n = 53) and the rest of the samples (n = 138), which came from patients who completed all the measurements at the 4 time points and found that there was no statistical difference in characteristics between the 2 groups (Table 2). Therefore the missing values were ignored in our data analysis.

Changes in HRQOL scores over time

Overall HRQOL

Before HSCT, patients reported a mean overall HRQOL of 110.31 (SD, 14.99); it reached a minimum of 105.07 (SD, 18.85) at day 30 after HSCT and increased steadily over time to 106.71 (SD, 18.34) at day 90 and 108.16...
Compared with baseline, overall HRQOL changed with the mean of $-5.24$ (SE 1.55; $P = .001$), and $-3.60$ (SE 1.55; $P = .022$), respectively, at 30 days and 90 days after HSCT. Overall HRQOL had returned to near pretransplant levels 180 days after HSCT (SE 1.47; $P = .146$) (Table 3).

Patients reported a mean PWB HRQOL of 22.14 (SD, 4.05) at baseline, 20.38 (SD, 5.47) at day 30, and 21.58 (SD, 4.46), 21.92 (SD, 4.12) at days 90 and 180 after HSCT. Patients experienced the worst physical function at 30 days after transplantation. The deterioration from baseline had no statistical significance at 90 (SE, 0.44; $P = .208$) and 180 days (SE, 0.42; $P = .603$) (Table 3).

SWB HRQOL

SWB HRQOL showed a continuous decline with means 23.63 (SD, 4.16), 22.24 (SD, 4.88), 21.90 (SD, 4.35), 21.29 (SD, 5.45) at baseline and at 30, 90, and 180 days, respectively. Within SWB HRQOL, the decrease from baseline was significant at 30 (SE, 0.38; $P < .001$), 90 ($P = .001$), and 180 days ($P < .001$) (Table 3).

### Table 2. Baseline characteristics comparison of the missing sample with the rest of the sample.

| Characteristics               | The missing sample ($n = 53$) | The rest of the sample ($n = 138$) | $\chi^2/t$  | $P$ value  |
|------------------------------|------------------------------|-----------------------------------|-------------|------------|
| Mean age at referral, (mean ± SD) | 35.57 ± 12.94               | 33.31 ± 11.40                    | 1.206       | 0.229      |
| Gender, n (%)                | Male 35 (66.0)               | Female 18 (34.0)                 | 0.707       | 0.401      |
| Marital status, n(%)         | Unmarried 16 (30.2)          | Married 37 (69.8)                | 0.004       | 0.948      |
| Residence, n (%)             | Rural 20 (37.7)              | Nonrural 33 (62.3)               | 0.263       | 0.877      |
| Education, n (%)             | Junior high school and below | 15 (28.3)                        | 0.005       | 0.943      |
| Household income, n (%)      | Less than 5000 yuan/month    | 13 (24.5)                        | 0.860       | 0.650      |
| Disease diagnosis, n (%)     | Acute leukemia 34 (64.2)     | Nonacute leukemia 19 (35.8)      | 0.107       | 0.744      |
| Stem cell source, n (%)      | Allogeneic 49 (92.5)         | Autologous 4 (7.5)               | 1.399       | 0.237      |
| Preparative regimen, n (%)   | Bu/Cy 44 (83.0)              | Non-Bu/Cy 9 (17.0)               | 0.014       | 0.904      |
| platelets, n(%)              | <20 × 10^9/L 10 (18.9)       | ≥20 × 10^9/L 43 (81.8)           | 0.005       | 0.048      |
| Transplant related complications, n (%) | Yes 36 (67.9) | No 17 (32.1)                     | 0.290       | 0.590      |

Note: HSCT, hematopoietic stem cell transplantation; Bu/Cy, busulfan and cyclophosphamide; platelets, the level of platelet measured when patients got out of the purifying ward; transplant-related complications, infection, graft-versus-host disease, urocystitis, etc.

### Table 3. Functional assessment of cancer therapy–bone marrow transplantation (FACT-BMT) and its dimensions and mean scores at 4 different time points and tests of difference for patients before HSC, and at 30, 90, and 180 days post transplantation.

| Time          | Overall HRQOL | PWB HRQOL | SWB HRQOL | EWB HRQOL | FWB HRQOL | BMTS HRQOL |
|---------------|---------------|-----------|-----------|-----------|-----------|------------|
| $T_1 (n=138)$ | 110.31 ± 14.99| 22.14 ± 4.05| 23.63 ± 4.16| 18.85 ± 3.77| 14.93 ± 6.53| 30.76 ± 4.59|
| $T_1$ (n = 138): Before HSCT* | 110.31 ± 14.99 | 22.14 ± 4.05 | 23.63 ± 4.16 | 18.85 ± 3.77 | 14.93 ± 6.53 | 30.76 ± 4.59 |
| $T_2 (n = 138):30 Days$ | 105.07 ± 18.85 | 20.38 ± 5.47 | 22.24 ± 4.88 | 19.57 ± 3.70 | 13.43 ± 6.58 | 29.45 ± 4.39 |
| $T_3 (n=138):90 Days$ | 106.71 ± 18.34 | 21.58 ± 4.46 | 21.90 ± 4.83 | 19.76 ± 3.45 | 13.89 ± 5.72 | 29.58 ± 4.78 |
| $T_4 (n=138):180 Days$ | 108.16 ± 18.34 | 21.92 ± 4.12 | 21.29 ± 5.45 | 20.04 ± 3.28 | 14.88 ± 5.47 | 30.02 ± 4.73 |
| F             | 4.572         | 6.226     | 12.730    | 4.351     | 3.794     | 3.995      |
| Sig           | 0.005*        | 0.001*    | <0.001*   | 0.007*    | 0.013*    | 0.048*     |
| Change over time |                |           |           |           |           |            |
| $T_2$–$T_1$   | −5.24 (1.55)  | −1.75 (0.46)| −1.39 (0.38)| 0.72 (0.38)| −1.51 (0.59)| −1.31 (0.43)|
| Day 30-baseline| 0.001*        | <0.001*   | <0.001*   | 0.061     | 0.012*    | 0.003*     |
| $T_3$–$T_1$   | −3.60 (1.55)  | −0.59 (0.44)| −1.73 (0.41)| 0.91 (0.40)| −1.04 (0.57)| −1.18 (0.49)|
| Day 90-baseline| 0.022*        | 0.208     | <0.001*   | 0.024*    | 0.068     | 0.017*     |
| $T_4$–$T_1$   | −2.15 (1.47)  | −0.22 (0.42)| −2.34 (0.45)| 1.20 (0.36)| −0.05 (0.57)| −0.74 (0.43)|
| Day 180-baseline| 0.146        | 0.603     | <0.001*   | 0.001*    | 0.929     | 0.086      |

Note: HSCT, hematopoietic stem cell transplantation; HRQOL, health-related quality of life; PWB, physical well-being; SWB, social/family well-being; EWB, emotional well-being; FWB, functional well-being; BMTS, bone marrow transplantation–specific concerns.

*Indicates statistical significance.
90 (SE, 0.41; \( P < .001 \)), and 180 (SE, 0.45; \( P < .001 \)) days after HSCT (Table 3).

**EWB HRQOL**

On the other hand, EWB HRQOL showed a rising trend, with means 18.85 (SD, 3.77), 19.57 (SD, 3.70), 19.76 (SD, 3.45) and 20.04 (SD, 3.28) at baseline and at 30, 90, and 180 days, respectively. The improvement at day 30 was not significant (SE, 0.38; \( P = .061 \)). However, it was significant at days 90 (SE, 0.40; \( P = .024 \)) and 180 (SE, 0.36; \( P = .001 \)) after HSCT (Table 3).

**FWB HRQOL**

The score of FWB HRQOL also changed dynamically at different time points (\( F = 3.794; P = 0.013 \)). It reached its highest level before HSCT, with a mean of 14.93 (SD, 6.53) and then descended to its lowest level, to 13.43, at 30 days after HSCT (SD,6.58). These changes were significant (SE, 0.59; \( P = .012 \)). Improvement began at 90 days, with a mean of 13.89 (SD, 5.72) after HSCT, representing a change of \(-1.04\) (SE, 0.57; \( P = .068 \)). It then and returned nearly to baseline level (SE, 0.57; \( P = .929 \)) at 180 days after HSCT (Table 3).

**BMTS HRQOL**

Last, BMTS HRQOL was highest before HSCT, with a mean of 30.76 (SD, 4.59). Patients experienced the most serious damage at 30 days after HSCT, with a mean of 29.45 (SD, 4.39); this decline was statistically significant (SE, 0.43; \( P = .003 \)). And there was a mean of 29.58 (SD, 4.78) at 90 days after HSCT, still lower than pretransplant levels (SE = 0.49; \( P = .017 \)). But patients began to recover at 180 days after HSCT, with a mean change of \(-0.74\) (SE = 0.43; \( P = .086 \)) from baseline (Table 3).

**Factors associated with HRQOL 180 days after HSCT**

Table 4 summarizes the GEE model to find risk factors for HRQOL. Household income (\( \beta = 6.590; P < .001 \)), transplant-related complications (\( \beta = -6.101; P < .001 \)), and patient age (\( \beta = 0.243, P = .045 \)) were associated with HRQOL.

**Conclusion**

This prospective study has evaluated changes in the HRQOL of patients with hematologic and lymphoid malignancies treated with hematopoietic stem cell transplantation with a follow-up of 6 months and has also recognized factors associated with HRQOL in the early stages following transplantation. We found that patients’ overall HRQOL was severely impaired early – that is, they experienced the worst HRQOL at 30 days posttransplantation – but they experienced a significant improvement by 180 days posttransplantation. We also have confirmed that better HRQOL was associated with higher household income, absence of transplant-related complications, and older age.

We concluded that the HRQOL of patients in the early stages of transplantation should receive more attention. The deterioration in patients’ HRQOL in the early stages of transplantation has many causes. The main one is that the immune and hematopoietic systems are not yet completely rebuilt in the early stages of recovery. This reduces the body’s power of resistance and can lead to infections and other complications. Distressing symptoms of reduced physical performance and functioning and increased high levels of fatigue affect patients’ HRQOL negatively [34]. Furthermore, the long period of hospitalization can produce social isolation and a lack of social support, resulting in anxiety and depression [6,35]. With the recovery of hematopoietic function, the HRQOL gradually begins to increase, reaching a statistically higher level by 180 days posttransplantation. However, the recovery process is very long and difficult. Study [36] has confirmed that the HRQOL in HSCT patients after an average of 20 years posttransplantation is still below that of the general population.

Another fact that should arouse attention is the trajectory of social/family well-being. There was a continuous deterioration in social/family well-being during the study period. After transplantation, a deterioration in social function is a common problem [37–39]. Research [37] has found that 48%, 23%, and 16% of patients had reduced social function at 6 months, 1 year, and 2 years after transplantation, respectively. In addition, reemployment after transplantation is an important part of the restoration of social function. Gruber et al. [40] have confirmed that reemployed patients experience less anxiety and depression and have fewer sleep problems than unemployed patients.

Measures should be taken to help patients return to normal life as soon as possible after transplantation. The results of our multivariate analyses show that transplant-related complications, household income, and

**Table 4. Factors predicting health-related quality of life.**

| Parameter                          | \( \beta \) | SE  | 95% Wald CI        | Wald \( \chi^2 \) | Sig. |
|-----------------------------------|-------------|-----|--------------------|-----------------|-----|
| Intercept                         | 95.519      | 8.230 | 79.388–111.650    | 134.702         | <.001|
| Household income                  | 6.590       | 1.519 | 3.612–9.567       | 18.817          | <.001|
| Transplant-related complications  | -6.101      | 1.352 | -8.730–-3.451     | 20.367          | <.001|
| Age                               | 0.243       | 0.122 | 0.005–0.481       | 4.000           | .045|

Note: CI, confidence interval.
age were the chief factors affecting patients’ HRQOL. The effects of medical complications on HRQOL have been confirmed [31,41]. Although complications are more difficult to manage via nursing, we still have to do our best to prevent their occurrence. When complications arise, nurses should provide not only the best available care but also use their scientific knowledge to educate patients, informing them of the causes of complications as well as the prognosis and available treatments so as to eliminate patients’ worries and anxiety and improve their compliance and the overall efficacy of treatment.

We also found that higher household income is associated with greater HRQOL. Economic factors affect HRQOL in many ways, since they involve treatment costs, nutritional options, health conditions, and compliance with treatment [19]. HSCT imposes a heavy economic burden to patients and their families even after discharge from the hospital. A survey [42] from China found that economic factors had the greatest impact on the HRQOL of patients; only 15% believed that their economic conditions could meet the requirements of treatment. Similarly, the results of this study suggest that older patients had a better HRQOL. Older patients usually have more stable social networks, better interpersonal skills, more supportive friendships, and more satisfactory marriages [26]; they often have a better state of mind and are more capable of coping with major life changes.

In conclusion, our study sheds light on changes in HRQOL before and after HSCT, suggesting that HRQOL in the initial period of treatment should receive more attention. We also demonstrated that transplant-related complications, household income, and age were risk factors associated with HRQOL. Nevertheless, weaknesses in our study must be acknowledged. One limitation is its relatively small sample size compared with multicenter studies. A second limitation might be that only FACT-BMT was used to assess the patients’ QOL without considering other measurements. Further, we did not discuss the influence of factors including anxiety, depression, caregivers’ roles, rehabilitation treatment, and so on, which may also have an effect on HRQOL. However, the results of this study still have practical value clinically. In the future we will focus more on these other factors and discuss their interactions so as to make the results more useful to the scientific community.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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