Comparison of quality of life and depression between hematopoietic stem cell transplantation survivors and their spouse caregivers

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Background
Hematopoietic stem cell transplantation (HSCT) is an exhausting process that impacts both the patient and caregiver.

Methods
This was a cross-sectional, HSCT survivor-spouse caregiver matching study to determine quality of life (QoL) and depression among HSCT survivors and their caregivers. QoL and depression were measured with the World Health Organization Quality of Life: Brief Version (26 items) and the 9-item Patient Health Questionnaire, respectively. Data from 97 married couples were analyzed.

Results
There were no significant differences in overall QoL and psychological, social, and environmental health between survivors and spouse caregivers (P=0.345, 0.424, 0.415, and 0.253); however, physical QoL was better in the spouse caregiver group (P=0.011). There was no difference in mean depression scale scores (5.3 vs. 5.1, P=0.812) or proportion of severe depression (15.6% vs. 13.7%, P=0.270) between the two groups. We found that family income had a significant impact on overall QoL and environmental health among spouse caregivers (P=0.013 and 0.023), and female gender, co-morbidities, and family income were the important factors associated with depression among spouse caregivers (P=0.007, 0.017 and 0.049).

Conclusion
This study found that there were no significant differences in QoL or level of depression between HSCT survivors and their spouse caregivers. Family income, gender, and co-morbidities showed significant association with spouse caregiver distress.

Key Words
Hematopoietic stem cell transplantation, Survivor, Caregiver, Quality of life, Depression

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) offers a chance of cure to patients with fatal hematologic diseases [1, 2]. Over the past few decades, there have been remarkable advances in transplantation techniques and supportive care strategies, which directly translates into a significant improvement in survival after HSCT [3-5]. Seventy to eighty percent of survivors at first 2 years after HSCT are believed to become long-term survivors [3-5]. Due to the increasing survival rates for HSCT recipients, long-term health conditions and quality of life (QoL) among this population have been gaining more attention, and several studies have addressed these issues [6, 7]. However, far less studies have investigated QoL among caregivers of HSCT survivors.

Due to the nature of the hematologic malignancy or bone marrow failure syndrome, which can be potentially cured after treatment, patients are more likely to be exposed to intensive protocols that yield significant toxicities during
the treatment period. The disease itself is also commonly associated with dangerous medical conditions such as pancytopenia and severe infection. Therefore, patients with hematologic diseases who are being actively treated often require close monitoring and management by their primary caregivers [8, 9]. Thus, it can be expected that these caregivers experience high levels of mental distress and physical strain [10]. One previous Japanese study demonstrated that mothers of children with leukemia requiring hospital care have poor health-related QoL and were at a greater risk for deteriorated mental health, social functioning, and depression [11].

The focus of this study was on spouse caregivers of HSCT survivors. Hematopoietic stem cell transplantation is an exhausting process. Patients typically undergo multiple rounds of chemotherapy before HSCT for disease control. Although HSCT is often used as the final step of a treatment strategy for the cure, the results are not always satisfactory. Sometimes, though they achieve a cure, patients may suffer from chronic complications for several years after HSCT [12]. During this whole process, the caregiver is often the sole provider of physical and psychological support for the patients, and has to bear the burden of caring for these fragile patients for a long time. These details suggest that caregivers inevitably suffer from exhaustion and that not only HSCT survivors but their caregivers may be vulnerable physically or psychologically. Thus, we conducted a cross-sectional, HSCT survivor-spouse caregiver matching study to assess QoL and depression among the spouse caregivers.

**MATERIALS AND METHODS**

**Subjects and purpose of the study**

The present study was part of a wider cross-sectional study investigating the dyadic concordance of sexuality among HSCT patients and their partners [13]. For the present study, HSCT survivors and their partners were recruited through the post-HSCT registry from Samsung Medical Center and the Korea Blood Cancer Association. The inclusion criteria were as follows: female or male subjects aged at least 20 years, had undergone autologous or allogenic HSCT, had an Eastern Cooperative Oncology Group performance status of 0 to 2, was able to communicate well with the investigators and to understand and fill out the questionnaire, and provided written informed consent prior to study enrollment. Patients presenting with any of the following were not eligible to participate in the study: had no sexual partner, had undergone autologous HSCT in the past 3 months and allogenic HSCT in the past 6 months, and was medically incapable of sexual activity (e.g., past history of genitourinary surgery). Partners of the included subjects were also recruited in the study. For the present study, some adjustments were made to the inclusion criteria of the original study. The original study included patients who had undergone autologous HSCT in the past 3 months and allogenic HSCT in the past 6 months and excluded patient-partner pairs who were not married. From September 2013 to March 2015, a total of 106 HSCT patient-partner pairs were administered a set of questionnaires for the assessment of sexual activity, QoL, depression, fear of recurrence, body image, and caregiver burden. This study was approved by the institutional review boards of Samsung Medical Center. All procedures were carried out in accordance with the Declaration of Helsinki.

The present study focused on the analysis of QoL and depression among spouse caretakers of HSCT survivors. The co-primary end points were i) differences in QoL and depression between caregiver spouses and HSCT survivors and ii) factors associated with QoL and depression among caregiver spouses. Among a total of 106 HSCT patient-partner pairs, the data from 97 married couples were used in the analysis (Fig. 1).

**Data collection and study measures**

The questionnaires for the patients and spouse caregivers were identical, and each consisted of six parts. Each part of the questionnaires contained items on sexual activity, QoL, depression, fear of recurrence, body image, and caregiver burden. Among these items, QoL and depression were of primary interest in this analysis, and assessment measures for each were as follows:

- **Quality of life:** The World Health Organization Quality of Life: Brief Version (26 items) (WHOQOL-BREF 26) was used to assess QoL. The WHOQOL-BREF 26 measures 4 QoL domains: physical health (7 items), psychological health (6 items), social relationships (3 items), and environmental health (8 items). The WHOQOL-BREF 26 also contains QoL and general health items. The mean score of items within
QoL and depression in spouse caregivers

Co-morbidity was defined as the presence of cerebrovascular or cardiovascular disease; diabetes mellitus; hypertension; or pulmonary, hepatic, gastrointestinal, renal, musculoskeletal, gynecological, or ophthalmic disorder.

| Characteristics | Survivor-spouse caregiver pair |
|----------------|-------------------------------|
|                | Survivor, N=97 (%) | Spouse caregiver, N=97 (%) |
| Age (yr), mean (SD) | 51.6 (9.4) | 49.7 (9.9) |
| Gender          |                          |                             |
| Male            | 65 (67.0) | 32 (33.0) |
| Female          | 32 (33.0) | 65 (67.0) |
| Marital status, married | 97 (100.0) | 97 (100.0) |
| Education       |                          |                             |
| High school graduate | 44 (48.9) | 45 (46.4) |
| More than college | 46 (51.1) | 52 (53.6) |
| Employment status |                        |                             |
| Employed        | 16 (16.5) | 22 (22.7) |
| Self-employed   | 10 (10.3) | 24 (24.7) |
| Leave of absence | 20 (20.6) | 6 (6.2) |
| Retired         | 12 (12.4) | 4 (4.1) |
| Housewife       | 15 (15.5) | 29 (29.9) |
| Student         | 1 (1.0)   | 1 (1.0)  |
| Unemployed      | 20 (20.6) | 5 (5.2)  |
| Etc.            | 3 (3.1)   | 6 (6.2)  |
| Family income ($) |                   |                             |
| < $2,000         | 29 (29.9) | 27 (28.1) |
| $2,000–$4,000    | 35 (36.1) | 36 (37.5) |
| > $4,000         | 33 (34.0) | 33 (34.4) |
| Co-morbidity (yes) | 40 (41.2) | 53 (55.2) |
| Taking any medication (yes) | 51 (54.8) | 24 (25.3) |
| Taking psychiatric medication other than sleeping pills (yes) | 7 (7.2) | 5 (5.2) |

Abbreviations: GVHD, chronic graft versus host disease; HSCT, hematopoietic stem cell transplantation.
More than half of the spouse caregivers (N=53, 55.2%) reported that they had co-morbidities, whereas less than half of the HSCT survivors (N=40, 41.2%) manifested these problems. More HSCT survivors (N=51, 54.8%) than spouse caregivers (N=24, 25.3%) were taking medication at the time of survey. The numbers of HSCT survivors and spouse caregivers on psychiatric medication other than sleeping pills were 7 and 5 (7.2% and 5.2%), respectively.

Hematopoietic stem cell transplantation survivors’ clinical characteristics

Among patients, mean duration since diagnosis was 4.3 years at the time of survey, ranging from 0.6 to 26.7 years, and acute myeloid leukemia was the most common reason for undergoing HSCT (N=36, 38.3%) (Table 1). There were more patients who had undergone autologous HSCT (N=67, 68.7%) than patients who had undergone allogeneic HSCT (N=30, 31.3%) in this study. At the time of survey, 33 patients (35.1%) were taking immune suppressive agent, and the numbers of patients who responded that they experienced acute and chronic graft versus host disease was 26 (26.8%) and 51 (52.6%), respectively.

Assessment of quality of life and depression: comparison between hematopoietic stem cell transplantation survivors and caregivers

Table 2 shows the results of the comparison of QoL and depression between HSCT survivors and their spouse caregivers. In our comparison of QoL between the two groups, we found that there were no significant differences in overall QoL and general health. Among the 4 QoL domains, psychological, social, and environmental health showed no significant differences between HSCT survivors and their spouse caregivers. Whereas physical health was found to be better in spouse caregivers compared with HSCT survivors (14.2 vs. 13.1; P=0.011). With regard to depression, HSCT survivors suffered slightly more from depression than spouse caregivers (5.3 vs. 5.1 for the mean scale; 15.6% vs. 13.7% for the proportion of severe depression), but the difference was not statistically significant.

Factors associated with quality of life and depression among spouse caregivers

The results of the multivariate analysis of factors associated with QoL and depression among spouse caregivers are shown in Table 3. After adjusting for both HSCT survivor and spouse caregiver factors, we found that spouse caregivers of survivors who had higher monthly family incomes (>4,000) were more likely to have better overall QoL and environmental health [by 3.24 (standard error, SE=1.27) and 2.24 (SE=1.27) points] compared with spouse caregivers of survivors who had lower monthly family incomes (<4,000). This finding was statistically significant (P<0.05). With regard to depression, spouse caregivers who were caring for female survivors were less likely to have depression [by 8.22 (SE=3.69) points] compared with spouse caregivers who were caring for male survivors (P<0.05). Spouse caregivers of survivors who had higher monthly family incomes (>4,000) were less likely to have depression [by 2.78 (SE=1.38) points] compared with spouse caregivers of survivors who had lower monthly family incomes (<4,000). This finding was statistically significant (P<0.05). Gender was among the spouse caregiver factors associated with higher rates of depression [females, by 10.24 (SE=3.67) points, compared with males]. This finding was statistically significant (P<0.05). Spouse caregivers without comorbid conditions were less likely to have depression [by 2.58 (SE=1.06) points] compared with spouse caregivers with comorbid conditions (P<0.05).

DISCUSSION

In this study of 97 HSCT survivor and spouse caregiver pairs, we identified that caregiver QoL was generally com-

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Table 2. Comparison of quality of life and depression between HSCT survivors and their spouse caregivers.

| Quality of life | Patient, mean (SD) | Caregiver, mean (SD) | P |
|----------------|-------------------|---------------------|---|
| Overall quality of life and general health | 11.3 (4.4) | 11.8 (3.8) | 0.345 |
| Physical health | 13.1 (3.7) | 14.2 (3.0) | 0.011 |
| Psychological | 13.3 (3.4) | 13.0 (3.1) | 0.424 |
| Social relationships | 11.7 (3.8) | 12.1 (3.6) | 0.415 |
| Environment | 12.5 (3.2) | 12.1 (2.8) | 0.253 |
| Depression | | | |
| Mean (SD) | 5.3 (4.5) | 5.1 (4.8) | 0.812 |
| Severity of depression (N, %) | | | |
| Normal (0–9) | 81 (84.4) | 82 (86.3) | 0.270 |
| Abnormal (10–27) | 15 (15.6) | 13 (13.7) | |

1 "strongly disagree", 2 = "disagree", 3 = "neither", 4 = "agree", 5 = "strongly agree", Thus, a higher mean indicates better quality of life. 1 "not at all", 2 = "a little", 3 = "quite a bit", 4 = "very much", Thus, a higher mean indicates more severe depression.

Abbreviations: HSCT, hematopoietic stem cell transplantation; SD, standard deviation.
Table 3. Factors associated with quality of life and depression among spouse caregivers.a,b)

| Characteristics                        | WHOQOL-BREF 26 | Depression | coefficient (SE) |
|----------------------------------------|----------------|------------|------------------|
|                                        | Overall health | Physical    | Psychological   | Social            | Environmental     |
|                                        | coef. (SE)     | coef. (SE) | coef. (SE)      | coef. (SE)       | coef. (SE)       |
| HSCT survivor factor                   |                |            |                 |                  |                  |
| Age                                    | -0.03 (0.13)   | 0.11 (0.12)| 0.07 (0.11)     | 0.04 (0.14)      | 0.01 (0.10)      | 0.26 (0.16)      |
| Gender (ref. male)                     |                |            |                 |                  |                  |                  |
| Female                                 | 0.81 (2.87)    | -2.70 (2.49)| -1.20 (2.43)    | 1.01 (3.05)      | 0.62 (2.25)      | -8.22 (3.69)     |
| Employment status (ref. employed)      |                |            |                 |                  |                  |                  |
| Unemployed                             | 1.18 (1.03)    | 0.44 (0.90)| 1.55 (0.89)     | -0.22 (1.14)     | 0.19 (0.82)      | 0.50 (1.20)      |
| Income ($) (ref. $2,000)               |                |            |                 |                  |                  |                  |
| 2,000–4,000                            | 2.25 (1.24)    | 1.13 (1.04)| 0.54 (1.01)     | 1.55 (1.27)      | 0.77 (0.94)      | 0.96 (1.27)      |
| 4,000+                                 | 3.24 (1.27)    | 1.27 (1.04)| 0.64 (1.05)     | 1.75 (1.32)      | 2.24 (0.96)      | -2.78 (1.38)     |
| Co-morbidity (ref. yes)                |                |            |                 |                  |                  |                  |
| No                                     | 1.16 (0.97)    | -0.37 (0.78)| 0.59 (0.81)     | -0.24 (1.00)     | 0.08 (0.73)      | 0.82 (1.08)      |
| Disease at diagnosis (ref. etc.)       |                |            |                 |                  |                  |                  |
| AML                                    | 1.38 (0.95)    | 0.21 (0.81)| 0.38 (0.81)     | 0.50 (1.04)      | -0.15 (0.75)     | -0.91 (1.23)     |
| Type of transplantation (ref. Auto)    |                |            |                 |                  |                  |                  |
| Allo                                   | -0.26 (1.55)   | 0.34 (1.30)| -0.05 (1.32)    | 1.37 (1.65)      | 2.40 (1.21)      | -0.75 (1.65)     |
| Chronic GVHD (ref. no)                 |                |            |                 |                  |                  |                  |
| Yes                                    | -1.08 (1.21)   | -1.20 (1.04)| -0.54 (1.04)    | -1.63 (1.29)     | -1.02 (0.96)     | 2.21 (1.52)      |
| Spouse caregiver factor                |                |            |                 |                  |                  |                  |
| Age                                    | 0.10 (0.13)    | -0.07 (0.12)| -0.03 (0.11)    | -0.01 (0.13)     | 0.01 (0.10)      | -0.20 (0.14)     |
| Gender (ref. male)                     |                |            |                 |                  |                  |                  |
| Female                                 | -2.21 (2.87)   | 0.66 (2.45)| -1.18 (2.45)    | -1.52 (3.07)     | -1.99 (2.27)     | 10.24 (3.67)     |
| Employment status (ref. employed)      |                |            |                 |                  |                  |                  |
| Unemployed                             | 0.28 (0.93)    | 1.06 (0.81)| 1.32 (0.84)     | 1.23 (1.01)      | -0.39 (0.74)     | 1.68 (1.12)      |
| Co-morbidity (ref. yes)                |                |            |                 |                  |                  |                  |
| No                                     | 1.66 (0.92)    | 1.42 (0.80)| 1.11 (0.81)     | 1.29 (1.02)      | 0.31 (0.73)      | -2.58 (1.06)     |

a) For coefficients, a negative value indicates a negative relationship between the variables. b) $P < 0.05$. c) $P = 0.013$. d) $P = 0.023$. e) $P = 0.032$. f) $P = 0.049$. g) $P = 0.007$. h) $P = 0.017$.

Abbreviations: coef., coefficient; GVHD, chronic graft versus host disease; HSCT, hematopoietic stem cell transplantation; ref., reference; SE, standard error; WHOQOL-BREF 26, World Health Organization Quality of Life: Brief Version (26 items).

parable to, but not better than that of HSCT survivors. There was also no difference between HSCT survivors and spouse caregivers with respect to the level of depression or the proportion of participants whose depression was considered to be severe. In addition, it was observed that several physical and psychosocial factors were associated with QoL and depression among spouse caregivers. Family income was an important factor affecting distress among caregivers, and caregivers with higher family income exhibited better overall QoL, and were less depressed. Among spouse caregivers, being female and having co-morbidities was significantly linked to depression.

Not surprisingly, this was not the first study to investigate the psychosocial health of HSCT survivors and their caregivers, and various measures have been used to assess distress among this population [14-18]. Our study used the WHOQOL-BREF 26 [19-21] to assess QoL and the PHQ9 [22-25] to assess depression. Both measures have been widely used to investigate other medical conditions [26-29]; however, they have scarcely been introduced in HSCT conditions. Though the tools used in previous studies varied considerably, the results analyzed from previous studies and those observed in the present study were substantially consistent with regard to comparable QoL and depression between caregivers and HSCT survivors, and negative impact of female gender and health problems on caregiver outcome [14, 18]. Although family income, as a great contributor to the QoL and depression of partners, has rarely been addressed before, the importance of social support was suggested based on a finding that poor social support negatively affects the QoL and post traumatic growth of partners [18].

It is also worthy to note that the caregivers frequently experienced physical health problems [30]. Although physical health-related QoL was reported to be better in spouse caregivers when they were compared with HSCT survivors, more than half of partners (55.2%) in this study responded that they had one or more co-morbidities at the time of survey. This percentage was surprisingly high considering that the percentage of HSCT survivors who reported that they had co-morbidities was 41.2%. Because the questionnaire for the assessment of co-morbid conditions consists of a broad range of items that are ambiguous and potentially permit subjective interpretation, it is highly likely that many subjective symptoms were considered co-morbidities in this
study. For example, when evaluating the presence of digestive diseases, mild “dyspepsia” could be answered as either “yes” or “no,” by the subject, depending on his or her perspective. This ambiguity was also present in items on musculoskeletal disorders; myalgia or arthralgia could be arbitrarily regarded as having or not having a musculoskeletal disorder by individual responders. Given that emotional distress and burnout may manifest as nonspecific symptoms, the high percentage of spouse caregivers reporting that they had co-morbidities may indicate not only physical but mental health concerns. In fact, the psychological, social, and environmental health problems and depression observed in spouse caregivers were almost equal to that assessed in HSCT survivors.

Particularly, we noticed that the percentage of HSCT survivors and spouse caregivers exhibiting abnormal depression levels was considerably high, which were 15.6% and 13.7%, respectively (P=0.270). According to the 2014 Korea National Health & Nutrition Examination Survey, 6.6% of the general population has significant depression defined by a PHQ9 score of 10 or higher. Although the spouse caregiver is not the person who undergoes chemotherapy or HSCT and may be considered to be of normal health, he or she suffers from more depression than the general population. This finding has also been well-demonstrated in a previous study [18], where survivor acquaintances were enrolled as matched controls. In that study, survivors and partners reported more depressive symptoms than controls (P<0.001), and risk of depression for partners was nearly 3.5 times that of controls (P<0.002). Importantly, despite a substantial rate of depression, only 7 patients (7.2%) and 5 caregivers (5.2%) responded that they were taking psychiatric medication in the present study. Taken together, these findings suggest that there are unmet needs for psychosocial interventions in HSCT survivors as well as in their spouse caregivers; however, there have been no data on the effectiveness of interventions in these populations [31].

In this study, it was remarkable that family income highly impacted both caregiver QoL and depressive symptoms. To the best of our acknowledge, income as a contributing factor in psychosocial health, has not been previously analyzed. However, it can be assumed that the family of a patient who undergoes HSCT experiences significant loss of income due to medical expense during an entire course of treatment. This study found that only 26.8% of HSCT survivors earned an income, whereas approximately half of caregivers earned an income through paid employment or self-employment. Considering the composition of gender in each patient and caregiver group, where the dominance of male and female was shown per each, and that the economically active population in South Korea is mostly male, it is highly likely that the main income earner before the diagnosis was the HSCT survivor in the majority of families and that this role shifted to the partner over time. Our findings suggest that HSCT may affect the patient’s ability to work and that difficulties on return to work related to social factors such as employment discrimination, should also be considered. Although spouses are able to work, they are often exhausted from caring for the HSCT survivors; it has also been found that the transplant process also affects the caregiver’s ability to work, which leads to a significant loss of income [32]. Income is an important factor in determining psychosocial health. Many factors inevitably contribute to the decrease or loss of income in the family of HSCT survivors. Factors in society that interrupt return to work among HSCT survivors, should be identified and addressed, and social and financial support is needed for the families at risk.

This study had several limitations. One of the major weaknesses was the absence of a control group to confirm the higher level of distress in caregiver participants compared with the general healthy population. Although we could find QoL reports that used the WHOQOL-BREF 26 and examined the general population [33, 34] (in which overall QoL as well as all sub-domains of QoL were much better in the general population than in the caregivers of our study), the comparison was limited by different nationality and research period; QoL differs from country to country and can change over time. In addition, we only considered spouse caregivers in this analysis although spouses cannot be the representatives of all caregivers. Because caregiving may also be provided by other family members, such as parents or children of a patient, relatives, or paid caregivers, interpretation of the result of this study should be limited to spouse caregivers.

In conclusion, the present study identified that there was no significant difference in QoL and the level of depression between HSCT survivors and spouse caregivers. In addition, gender, co-morbidities, and family income were the important factors associated with caregiver QoL and depression. We suggest that clinical psychosocial interventions that target both survivors and caregivers is needed, and that social support to families who are financially challenged has to be considered.

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Authors’ Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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