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# Anxiety and Depression of the Patients with Hematological Malignancies during Hospitalization for Hematopoietic Stem Cell Transplantation

Ho-Jun Seo[1], Young-Gun Baek[2], Byung-Sik Cho[3], Tae-Suk Kim[4], Yoo Hyun Um[1], and Jeong-Ho Chae[4] ✉

[1]Department of Psychiatry, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, Republic of Korea
[2]Seoul Metropolitan Office of Education, Seoul, Republic of Korea
[3]Department of Hematology, Catholic Blood and Marrow Transplantation Center, Seoul St. Mary's Hospital, Leukemia Research Institute, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea
[4]Department of Psychiatry, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

**Objective** This study aimed to assess the anxiety and depression in patients undergoing hematopoietic stem cell transplantation (HSCT).

**Methods** Eighty-seven adult patients with various hematologic diseases, who were scheduled to receive autologous or allogeneic HSCT, were enrolled. The M.D. Anderson Symptom Inventory and the Hospital Anxiety Depression Scale were applied prospectively at hospital admission (D-14), on the day of transplantation (D day), and at 7 (D7) and 14 days (D14) after transplantation.

**Results** The severity of both anxiety and depressive symptoms increased over time, with a peak at D7, and then showed a downturn at D14. Physical distresses also started with mild intensity at base line, which were continuously aggravated until D7, and then a partial recovery afterwards. Approximately, 52% of the participants had significantly high anxiety or depression before the start of HSCT. The occurrence of aggravation of pain, nausea, shortness of breath, and lack of appetite was associated with the development of anxiety during isolation period. The patients with significant baseline anxiety had higher scores on fatigue and shortness of breath items at D7 compared to those without.

**Conclusion** Our finding suggests the importance of psychiatric approaches, including preventive measures, for the patients undergoing HSCT.

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**Key Words** Hematopoietic stem cell transplantation, Anxiety, Depression, Physical symptom burdens.

## INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a highly aggressive medical therapy among cancer treatments. Patients undergoing HSCT experience critical toxic side effects related to a rigorous conditioning regimen and graft-versus-host disease (GVHD), with the risk of mortality from the procedure itself.[1] HSCT requires a long hospital stay with isolation of at least 4 weeks and frequent extended recovery periods. Most patients already have experiences of several treatment failures and a relapse of cancer and seem to suffer from physical and psychological distress even before the start of HSCT.[2,3] Due to these specific issues for HSCT, several studies have directly focused on symptoms of anxiety and depression and the occurrence of psychological morbidity during HSCT, rather than assessing global quality of life as is generally used for patients with cancer.[4-9]

Previous researches have shown that approximately 20% of patients develop clinically significant psychiatric disorders, such as depressive disorder, anxiety disorder, or adjustment disorder with anxiety or depressed mood during hospitalization for HSCT.[6,10] In addition to deleterious effects on quality of life,[9,11] anxiety and depression seem to negatively affect subjective symptom burden, compliance with medical treatment, and length of hospital stay in patients undergoing HSCT.[12,13] Major depression during hospitalization is also predictive of higher mortality 1- and 3 year after HSCT.[14] A recent research reported that many patients experienced the hospitalization as

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✉ **Correspondence:** Jeong-Ho Chae, MD
Department of Psychiatry, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea
**Tel:** +82-2-2258-6083, **Fax:** +82-2-594-3870, **E-mail:** alberto@catholic.ac.kr

a traumatic event and approximately 30% of HSCT patients meet the criteria for PTSD at 6 months after HSCT.[15]

Although numerous studies have reported the quality of life and physical or psychological burden of the survivors of HSCT, prospective data which examine the experience of patients during hospitalization for HSCT remain scarce.[4,5,8,9] Although there is a general acceptance that an aggravation of physical condition is expected to affect psychological burden during HSCT, the association has not been well recognized. Previously, Anderson et al.[16] prospectively assessed the severity of individual symptoms during hospitalization in detail with specific measures designed for HSCT patients. This research found that most physical symptoms were most intense at 3−10 days after transplantation. Contrary to consistent findings of physical burden, prospective studies have shown inconsistent results on time course of anxiety and depression during hospitalization.[4,5,8,9] Especially, depression and anxiety each has shown slightly different patterns according to studies.[5,8,9] Moreover, besides physical and psychological burden related to HSCT and isolation, several researches have shown that substantial portion of patients already experience intense distress even before the start of HSCT. Prieto et al.[13] found that 46 of 220 (21%) patients met the criteria for depressive, anxiety or adjustment disorder at the day of hospital admission. Two cross sectional studies found that more than half of patients exceeded the threshold for clinically significant level of anxiety and/or depression at the pre-transplant assessments.[2,3] A previous study found that anxiety and depression before hospitalization were predictors of high anxiety and depression during isolation periods.[8] However, data are still insufficient to examine the relationship between patient's baseline psychological distress and their physical and psychological burdens during hospitalization.

We conducted a prospective longitudinal study to assess psychological and physical symptom burdens experienced by patients during hospitalization for HSCT. In this study, we also aimed to identify the association between aggravation of anxiety and depressive symptoms and that of physical symptom burdens. We also sought to investigate the impact of anxiety and depression before the start of HSCT on the clinical course of psychological and physical distress during hospitalization.

## METHODS

### Participants

The subjects were 87 patients with hematologic disease who were scheduled to receive autologous or allogeneic HSCT at St. Mary's Hospital, The Catholic University of Korea in Seoul, Korea. The patients were recruited from the outpatient clinic after they decided to undergo HSCT treatment following a clinician's recommendation. Inclusion criteria were transplant eligible patients with hematologic diseases, at least 18 years of age, and the ability to understand the research and to give consent to participate in the study. Of the 116 eligible patients, 93 agreed to participate and provided informed consent. Six could not be assessed due to a change in treatment schedule or a withdrawal from participation. Finally, 87 patients participated in the first assessment.

All patient transplants were performed in laminar airflow, high-efficiency particulate air-filtered rooms until engraftment. In cases of allogeneic HSCT, GVHD prophylaxis was attempted with cyclosporine (for sibling donors) or tacrolimus (for unrelated donors) and short-course methotrexate. Granulocyte-colony-stimulating factor was administered subcutaneously to all patients from day 7 after the transplant until neutrophil recovery. Low-dose heparin or lipo-prostaglandin E1 was administered with ursodiol to prevent veno-occlusive disease. Antimicrobial prophylaxis consisted of ciprofloxacin and intraconazole started at the beginning of the conditioning treatment. Cytomegalovirus prophylaxis consisted of high-dose IV acyclovir until engraftment for all patients. Every patient received Pneumocystis jirovecci prophylaxis with sulfamethoxazole/trimethoprim after engraftment until discontinuation of the immunosuppressant.

Among the 87 participants, 14 dropped out by day 14 (six at D day, seven at D7, and one at D14). Participants were lost due to compromised medical status (n=6, including one death) or a withdrawal from participation (n=8).

This study was approved by the Institutional Review Board of St. Mary's Hospital, The Catholic University of Korea. All participants signed an informed consent form after receiving a full explanation of the procedure. All research was undertaken in accordance with the latest version of the Declaration of Helsinki (SCMC070T047).

### Study procedures

Demographic and baseline clinical characteristics were assessed at pre-visit interviews before admission for HSCT. The study instruments were applied at hospital admission (D-14, day-10 to day-14 prior to transplantation, depending on the conditioning regimen), and subsequently on a weekly basis from the day of transplantation (D day) until discharge. Assessments were performed within 2 days of the scheduled interview. Similar to previous studies, only the data of D-14, D day, D7, and D14 were used in the analysis due to high drop-out rates from discharge.[4,5]

The M.D. Anderson Symptom Inventory (MDASI)[17] and Hospital Anxiety Depression Scale (HADS)[18] were used to assess multiple symptoms and emotional problems during HSCT.

The MDASI was developed to measure the symptom burden during daily life in patients with cancer, including symptom severity and symptom-related interference with daily life. The MDASI assesses a patient's health status within the 24 hours prior to evaluation and includes individual symptom items for measuring symptom intensity and items that assess symptom-related interference. Each item is rated on a scale of 0 (not at all) to 10 (as bad as you can imagine or completely interferes). The validity and reliability of the MDASI and the Korean version of the MDASI have been established.[17,19] For the current study, 6 physical symptom items which are common in patients undergoing HSCT were used in the analysis.[16,20] It includes pain, fatigue, nausea, shortness of breath, lack of appetite, and disturbed sleep. The HADS is a self-rating scale designed to screen for psychiatric morbidity in patients with medical illness. The HADS does not include the numerous somatic items found in the usual psychiatric measures that assess anxiety and depression. The HADS consists of two separate scales for anxiety and depressive symptoms, with seven items for each scale. Each item has a four-point Likert scale from 0 to 3, and the total score for anxiety or for depressive symptoms ranges from 0 to 21. HADS has been used frequently in patients with cancer, and the validity and reliability of the original version and the Korean version of HADS have been established.[18,21,22] For the current study, the HADS assessed a patient's status within the 24 hours prior to evaluation and used a cutoff score of 7.

### Data analysis

Descriptive statistics were calculated for demographic and clinical characteristics of the participants. A mixed model for repeated measurement (MMRM) analysis was used to evaluate changes in HADS and MDASI symptom intensities and to evaluate group differences between those who had significant anxiety or depression prior to HSCT and those not, with diagnoses, HSCT methods, gender, and age as covariates. Pairwise logistic regression models were used to assess the association of MDASI symptom items with the occurrence of new anxiety and depression during HSCT. The individual MDASI symptoms item score at D7 was compared between the patients with and without significant anxiety/depression at D-14 using an analysis of covariance (ANCOVA) with the baseline scores, diagnoses, HSCT methods, gender, and age as covariates. All statistical tests were performed using SAS version 8.0 (SAS, Inc., Cary, NC, USA), with a two-tailed value of 0.05, and the power of the sample to detect an effect size was 80%.

## RESULTS

### Participants' characteristics

The sociodemographic and disease-related characteristics of the subjects are given in Table 1. The mean age of the subjects was 38.1 years (SD=14.1), and the proportion of females was 42.5%. The median time since diagnosis was 6 months

**Table 1.** Sociodemographic and disease-related characteristics of the participants (N=87)

| Characteristic | N | % |
|---|---|---|
| Age, years | | |
| Mean (SD): 38.1(14.1) | | |
| Range: 18−65 years | | |
| Gender | | |
| Male | 50 | 57.5 |
| Female | 37 | 42.5 |
| Marital status | | |
| Married | 54 | 62.1 |
| Unmarried | 30 | 34.5 |
| Divorced or widowed | 3 | 3.4 |
| Religion | | |
| None | 39 | 44.8 |
| Protestant | 17 | 19.5 |
| Buddhism | 12 | 13.8 |
| Catholic | 18 | 20.7 |
| Others | 1 | 1.1 |
| Education | | |
| Less than high school | 13 | 14.9 |
| High school degree | 32 | 36.8 |
| Above college | 42 | 48.3 |
| Economic status (below 2/3 of median wage) | | |
| Previous psychiatric treatment | 21 | 24.1 |
| Time since diagnosis, months | 3 | 3.4 |
| Median: 6 | | |
| IQR: 5−15 | | |
| Diagnosis | | |
| Acute myelogenous leukemia | 22 | 25.3 |
| Acute lymphoblastic leukemia | 26 | 29.9 |
| Multiple myeloma | 16 | 18.4 |
| Non-Hodgkin's lymphoma | 2 | 2.3 |
| Severe aplastic anemia | 10 | 11.5 |
| Myelodysplastic syndromes | 8 | 9.2 |
| Chronic myelogenous leukemia | 3 | 3.4 |
| Type of HSCT | | |
| Autologous | 31 | 35.6 |
| Allogeneic | 56 | 64.4 |
| Conditioning regimen | | |
| Chemotherapy only | 28 | 32.2 |

IQR: interquartile range, HSCT: hematopoietic stem cell transplantation

(interquartile range, 5 to 15). Of the 87 patients, 26 suffered from acute lymphoblastic leukemia, 22 from acute myelogenous leukemia, 16 from multiple myeloma, 10 from severe aplastic anemia, 8 from myelodysplastic syndromes, 3 from chronic myelogenous leukemia, and 2 from non-Hodgkin's lymphoma. Approximately 68% of the subjects were conditioned with chemoradiotherapy, and the other 32.2% with chemotherapy only. Approximately, 64% of the subjects underwent allogeneic HSCT, and the remaining 35.6% underwent autologous HSCT.

### Anxiety and depression during isolation period

Figure 1 shows the mean scores of HADS and anxiety or depression cases with a cutoff score of 7 across the four time points. The severity of both anxiety and depressive symptoms increased over time, with a peak at D7, and then showed a downturn at D14. Depression showed a sharper increase over time compared with anxiety level. A significant main effect of time was observed for depression, but not for anxiety (p=0.003 and p=0.100, respectively). The number of HADS anxiety and depression cases across four time points showed a similar trend to the time course of mean HADS scores, with a peak occurrence at D7. Before the start of HSCT, as many as 33.3% and 43.7% of the subjects were already included in the HADS anxiety and depression cases, respectively, and 51.7% of the participants had significantly high anxiety or depression at baseline.

### The physical symptom burdens during isolation period

Table 2 provides mean scores of 6 physical symptom items of MDASI across four time points. All symptom items showed a similar pattern of symptom change: mild symptom intensity at baseline, continuously aggravated symptoms until D7, and then a partial recovery. Significant main effects of time were observed for all of these symptoms.

### The associations between newly developed anxiety or depression and aggravation of physical symptoms

Table 3 presents the results of pairwise logistic regression

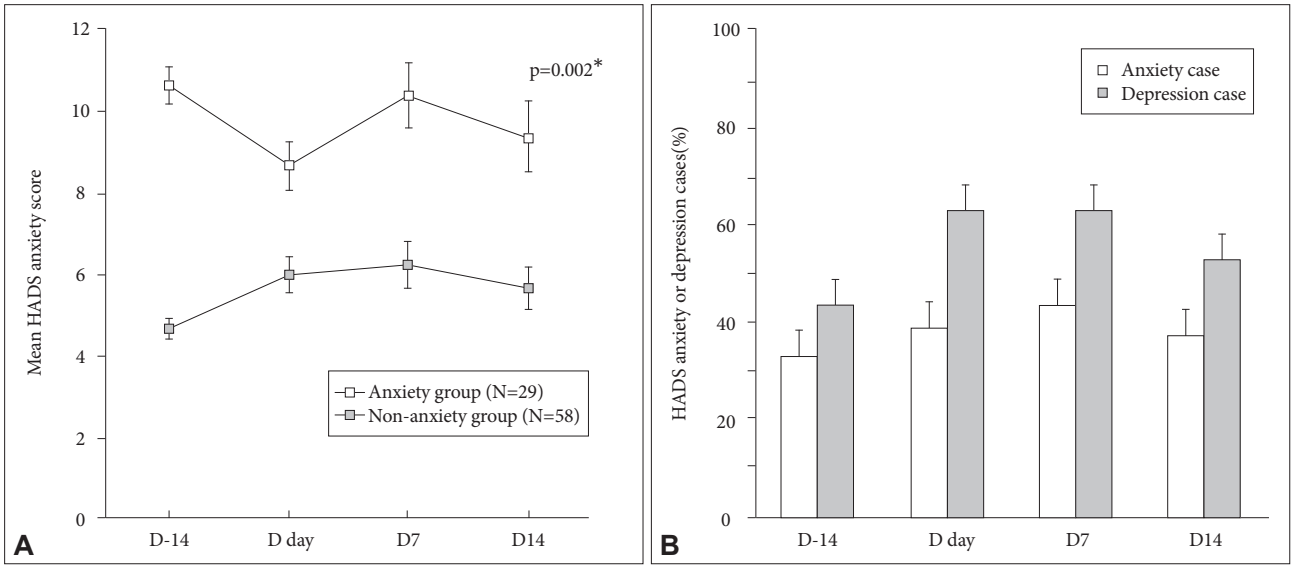


**Figure 1.** Mean scores and cases (%) of HADS at different stage of the isolation periods*. A: HADS anxiety or depression cases were defined as HADS anxiety or depression scores>7, respectively. B: The main time effect in MMRM analysis. HADS: Hospital Anxiety Depression Scale.

**Table 2.** Mean (SD) scores of 6 physical symptom items of MDASI at different stage of the isolation periods

| Items of MDSAI | D-14 | D day | D7 | D14 | p† |
|---|---|---|---|---|---|
| Pain | 2.58 (3.20) | 4.22 (2.85) | 5.95 (3.14) | 4.93 (3.24) | <0.001* |
| Fatigue | 3.63 (2.89) | 4.55 (2.88) | 5.39 (2.83) | 4.70 (2.65) | <0.001* |
| Nausea | 2.10 (2.89) | 5.21 (2.19) | 5.51 (3.62) | 4.13 (3.34) | <0.001* |
| Shortness of breath | 1.54 (2.51) | 2.11 (2.54) | 2.90 (3.04) | 2.06 (2.73) | 0.001* |
| Lack of appetite | 3.13 (3.25) | 4.71 (3.20) | 5.07 (3.36) | 4.70 (3.03) | <0.001* |
| Disturbed sleep | 3.46 (3.33) | 4.78 (3.19) | 4.87 (3.19) | 4.08 (3.10) | <0.001* |

*p<0.01, †the main time effect in MMRM analysis. MDASI: M.D. Anderson Symptom Inventory

analysis of newly developed anxiety/depression and the aggravation of physical symptoms during isolation period. After the start of HSCT, anxiety and depression newly developed in 24 (27.6%) and 32 (36.8%) cases, respectively. The occurrence of significant aggravation of symptoms such as pain, nausea, shortness of breath, and lack of appetite was associated with the development of anxiety. In contrast, no physical symptom on MDASI was associated with the development of depression.

**Table 3.** The association between newly developed anxiety or depression and aggravation of physical symptoms during isolation periods*

| Items of MDSAI | New anxiety | | New depression | |
|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI |
| Pain | 3.30 | 1.16−9.41 | - | - |
| Fatigue | - | - | - | - |
| Nausea | 4.55 | 1.39−14.82 | - | - |
| Shortness of breath | 4.90 | 1.79−13.40 | - | - |
| Lack of appetite | 5.41 | 1.79−16.34 | - | - |
| Disturbed sleep | - | - | - | - |

*new anxiety/depression and aggravation of physical symptoms were defined as a case of HADS anxiety/depression scores>7 and scores of each symptom item in MDASI >5, respectively. MDASI: M.D. Anderson Symptom Inventory, HADS: hospital anxiety depression scale, OR: odds ratio, CI: confidence interval

## Comparison between patients with significant anxiety or depression at baseline and those without

Patients were divided into two groups, those who had significant anxiety or depression prior to HSCT (anxiety group or depression group) and those who did not (non-anxiety group or non-depression group), and their physical symptom scores on MDASI at D7, which was the most critical time point of distress, were compared (Table 4). When a ANCOVA was performed with baseline scores, diagnoses, HSCT methods, gender and age as covariates, the anxiety group had higher scores on individual symptom items of fatigue and shortness of breath compared to the non-anxiety group

**Table 4.** Comparison of mean scores (SD) of physical symptom burdens at D7 between the patients who had significant anxiety/depression prior to HSCT (anxiety/depression group) and not (no anxiety/no depression group)†

| Items of MDSAI | Anxiety group | Non-anxiety group | p | Depression group | Non-depression group | p |
|---|---|---|---|---|---|---|
| Pain | 6.60 (2.70) | 5.60 (3.30) | 0.164 | 6.16 (3.12) | 5.68 (3.18) | 0.452 |
| Fatigue | 6.55 (2.25) | 4.81 (2.94) | 0.009** | 5.04 (2.83) | 5.84 (2.81) | 0.241 |
| Nausea | 6.28 (3.26) | 5.12 (3.75) | 0.186 | 5.67 (3.48) | 5.29 (3.83) | 0.690 |
| Shortness of breath | 3.93 (3.31) | 2.38 (2.78) | 0.020* | 2.53 (2.83) | 3.37 (3.27) | 0.198 |
| Lack of appetite | 5.52 (3.31) | 4.84 (3.39) | 0.365 | 4.90 (3.29) | 5.29 (3.49) | 0.589 |
| Disturbed sleep | 5.03 (3.64) | 4.79 (2.97) | 0.405 | 4.96 (2.81) | 4.76 (3.66) | 0.411 |

*p<0.05, **p<0.01, †ANCOVA was performed with baseline scores, diagnoses, HSCT methods, sex and age as covariates. HSCT: hematopoietic stem cell transplantation

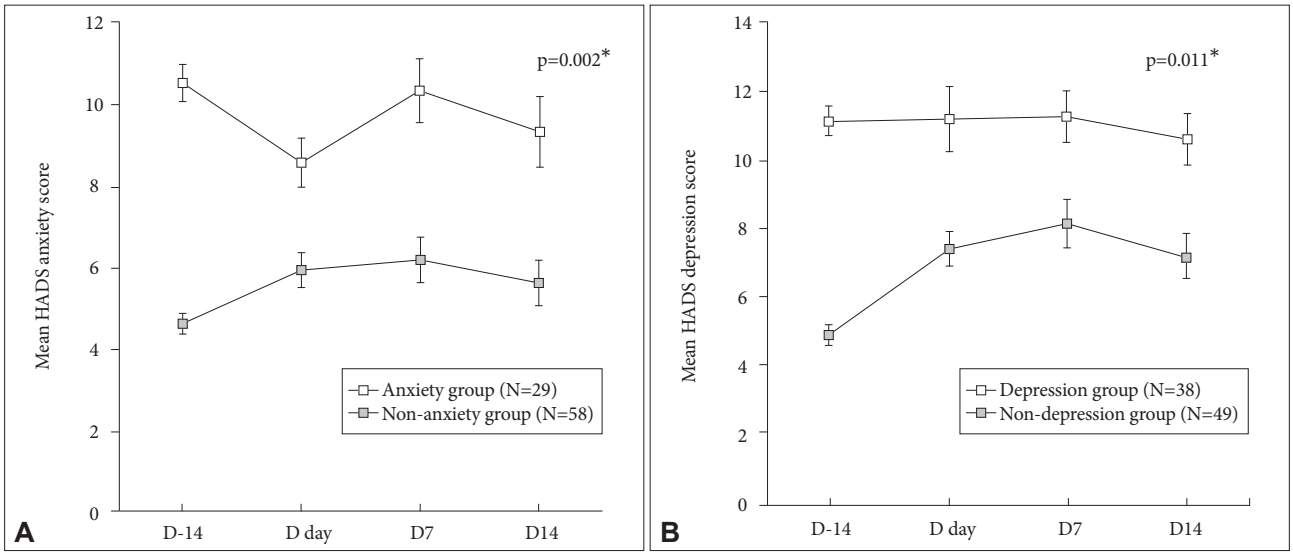


**Figure 2.** HADS anxiety and depression scores across 4 time points by anxiety and non-anxiety group and by depression and non-depression group. A: HADS anxiety scores of anxiety and non-anxiety group. B: HADS depression scores of depression and non-depression group. *time by group effects in MMRM analysis using diagnoses, HSCT method, gender, and age as covariates. HADS: hospital anxiety depression scale, HSCT: hematopoietic stem cell transplantation.

(p=0.009 and p=0.020, respectively). However, there was no significant difference between the depression group and the non-depression group.

Figure 2A illustrates the varying patterns of anxiety during isolation period in the anxiety and the non-anxiety groups. The anxiety level of those in the anxiety group was highest at baseline, decreased at D-day, was aggravated at D7, and slightly recovered at D14. However, only minimal changes in anxiety over time were observed in the non-anxiety group. The course of anxiety revealed a significant difference between the anxiety and non-anxiety groups using diagnoses, HSCT method, gender, and age as covariates (time by group interaction, p=0.002). Depression severity also revealed a significant difference between the depression and non-depression groups (time by group interaction, p=0.011) (Figure 2B) The depression group reported a high level of depression continuously throughout the study period, with minimal change over time. In contrast, the non-depression group reported mild depression at baseline, but showed a sharp increase in severity of depression until D7, which partially recovered at D14. Despite the fact that their global depression level was lower than that in the depression group, the non-depression group experienced quite a severe aggravation of depression over time compared with the depression group.

## DISCUSSION

In the current study, the courses of physical symptom burden of the patients undergoing HSCT showed a gradual increase in symptom intensity from baseline to a peak at 7 days after transplantation. It is consistent with the majority of prospective studies which used similar assessment time points.[5,9,16] We found the severity of anxiety and depression symptoms were also continuously aggravated until 7 days after transplantation, and both were partially recovered by 14 days after transplantation. The previous prospective findings of anxiety and depression have somewhat varied across studies. Fife et al.[4] (n=97) found that both anxiety and depressive symptoms increased from baseline, with the highest intensity at 1 day before transplantation, and then decreased gradually until 14 days after transplantation. In contrast, Prieto et al.[5] (n=220) found discrepancies between the time courses of anxiety and depressive symptoms. The score for anxiety was highest at hospital admission and decreased gradually throughout HSCT, whereas depression showed a sharp increase from baseline until 7 days after transplantation and decreased after that. Tecchio et al.[8] (n=107) and El-Jawahri et al.[9] (n=90) found a sharp aggravation of depression from baseline until 1 week after transplantation, while the severity of anxiety was stable from baseline throughout the study periods. It is interesting to note that despite varied findings of the temporal trajectory of anxiety from a stable course to a reduction over the HSCT periods, depression level is relatively concordant, which is usually severe during the isolation periods. Consistent with previous findings, depression level in the current study showed a steeper increase compared to anxiety. The MMRM showed significant main effect of time for depression, but not for anxiety. The rates of patients with HADS depression scores>7 climbed from 42.7% up to 63.2% until 7 days after transplantation, whereas the rates of those with HADS anxiety scores>7 changed only from 33.3% to 39.1%.

In the current study, substantial number of patients already had significant level of anxiety and depression even before the start of transplantation. We found approximately half of the participants had HADS anxiety or depression scores>7 at baseline. This finding is notable given that only 3 participants had the past psychiatric history. Our finding seems rather higher compared to previous prospective findings.[4,5,8,9] The reason is unclear. However, compared with previous studies, the participants of the current study had relatively a short median time since diagnosis (6 months), which might be not enough to accept and cope with their disease. Whereas, consistent with our finding, previous studies of pre-transplantation evaluation found that more than half of the patients had clinically significant anxiety or depression level.[2,3] High pre-transplant anxiety or depression is a predictive factor for emotional distress during HSCT, and anxiety or depression before or during HSCT is also predictive of earlier mortality of HSCT.[11,14,23] Our findings suggest that the cumulative psychological burden from the course of chemotherapy for induction and consolidation could lead some vulnerable patients to a significant level of distress even before the start of HSCT.

It is interesting to note the difference of time course of emotional distress between patients with baseline anxiety or depression and those without. Figure 2 shows that patients with baseline anxiety experienced their most severe anxiety at the moment of admission, which might reflect their uncertainty and fearfulness confronted with the highly aggressive medical therapy.[5] Since then, the anxiety level was decreased at the day of transplantation, then aggravated again at 7 days after transplantation, and then slightly recovered at 14 days after transplantation, which might follow the pattern of physical burden. Whereas, only a slight change in anxiety was observed in patients without baseline anxiety. It suggests patients without severe anxiety at the beginning of transplant procedure might handle their anxiety well during isolation period. With regards to depression, patients with baseline depression reported a high level of depression continuously with minimal change throughout HSCT. On the other hand, the de-

pression level in patients without baseline depression was mild at the moment of admission, but showed rather a sharp increase until 7 days after transplantation, and then partially decreased. This finding suggests that even patients who do not have significant depression at the start of HSCT might experience quite severe aggravation of depression during HSCT. Interestingly, previous studies have found that rather than biomedical variables, non-biological variables such as personality trait, pre-transplant anxiety or depression, and past psychiatric history to be the most independent predictors for emotional distress during HSCT.[8,10,12,13] Focusing on the patients with high anxiety or depression at the very beginning of transplant procedure might be a useful method to screen a possible case at risk of developing severe anxiety or depression during HSCT. Our finding also suggests that in contrary to anxiety, attention is needed even in the patients without high baseline depression. Empirical data from future studies are needed for the confirmation of this finding.

Patients with baseline anxiety experienced significantly higher distress in the MADSI items of fatigue and shortness of breath at D-7, the most critical time point for distress from HSCT. No significant difference was observed between patients with baseline depression and those without. Additionally, aggravation of various symptoms, such as pain, nausea, shortness of breath, and lack of appetite were associated with newly emerged anxiety during isolation periods, whereas no MADSI symptom items were associated with newly-emerging depression. Numerous studies in cancer patients found that physical symptom intensity is associated with psychological factors such as anxiety and depression.[24-27] Modulations of pain signal, expectation of pain, ability to cope/self-efficacy, personality traits and sleep have been known as possible mediating factors between physical symptom and anxiety/depression.[28] However the relationships are complex and difficult to fully characterize. To our knowledge, few studies have examined the distinct impact of anxiety and depression on the perception of physical stimuli. A previous study in 405 patients with cancer, which included three subgroups of depression and anxiety, depression but not anxiety, and neither, revealed that anxiety and depression had additive and independent effects on somatic symptom burden.[29] Nevertheless, the reason of our finding that the distress from various physical symptoms had a stronger association with anxiety than with depression is unclear. A recent literature highlighted the importance of the meaning of events to an individual as an important factor in making cancer patients anxious.[30] Supposing that patients undergoing HSCT might already know well and worry about their treatment related mortality and life-threatening complications, those with higher anxiety might be more sensitive to their physical reactions during HSCT and feel more distressed. Moreover, emerging side effects may be interpreted more catastrophically, thereby worsening their anxiety rather than depression as an acute response. Further data is needed to replicate this finding in the future.

The current study had several limitations. Generalization of the results should be restricted because the sample size was small, and the study was performed at a single institution. The medication such as benzodiazepines and hypnotics were prescribed on an as-needed basis for patients, which could have affected the response to the assessments of psychological and physical distress. In the current study, to minimize patient burden during HSCT, only two subjective measures were used to assess distress during HSCT. Therefore, only small amounts of data were provided compared with previous prospective studies. However, considering the great degree of side effects such as fever, nausea, and GVHD, even a small amount of paperwork may have been difficult for the patients. Even in healthy populations, the number of questions in scales negatively influences the accuracy of answers.[31] The simplicity of the assessments in the current study may have had positive effects on the reliability of the data compared with the previous prospective studies.[4,5,8,9]

Despite these limitations, the current study has significant meanings. It contributes to the prospective data of patients who are most difficult to engage in studies due to the considerable burden of side effects. The current results highlight the importance of the psychological distress in patients with hematologic disease and provide a basis for further studies on the benefits of the psychiatric treatment prior to the start of HSCT. Studies examining the efficacy and safety of psychiatric approaches such as medication and psychotherapy before the start of HSCT and studies to distinguish patients who experience persistent psychological symptoms after HSCT are needed.

## Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

## Author Contributions

Conceptualization: Ho-Jun Seo, Tae-Suk Kim, Jeong-Ho Chae. Data curation: Ho-Jun Seo, Young-Gun Baek. Formal analysis: Ho-Jun Seo, Jeong-Ho Chae. Investigation: Ho-Jun Seo, Young-Gun Baek. Methodology: Ho-Jun Seo, Byung-Sik Cho, Jeong-Ho Chae. Project administration: Ho-Jun Seo, Jeong-Ho Chae. Resources: Ho-Jun Seo, Byung-Sik Cho. Supervision: Byung-Sik Cho, Jeong-Ho Chae. Validation: Ho-Jun Seo, Yoo Hyun Um. Visualization: Ho-Jun Seo. Writing—original draft: Ho-Jun Seo. Writing—review & editing: Yoo Hyun Um, Jeong-Ho Chae.

## ORCID iDs

Jeong-Ho Chae https://orcid.org/0000-0002-6070-9324
Ho-Jun Seo https://orcid.org/0000-0003-1661-1394

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