

## A Nursing Pre-Transplant Intervention to Reduce Patients' Uncertainty about Allogeneic Hematopoietic Stem Cell Transplantation

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### Abstract

Patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) procedures often experience high levels of uncertainty. In this study, we developed and implemented a nursing intervention program to help patients recognize and reduce pre-transplant uncertainty. This study used a pretest-posttest single-group design without a control group. Eighteen patients undergoing HSCT participated in the intervention program—which included informational support, confirmation that the patients understood the information provided, and emotional support. Outpatients received the intervention at their initial outpatient visits after their procedure dates were determined, while inpatients received it at discharge following their procedures. The Universal Uncertainty in Illness Scale (UUIS), which consists of 26 items and six subscales, was used as the primary outcome measure. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the Hospital Anxiety and Depression Scale were used as secondary outcome measures. The sample included 18 individuals (13 male and five female participants; median age, 52 years). Most participants had acute lymphoblastic leukemia and had previously undergone bone marrow transplantations. Following our intervention, the total UUIS score significantly decreased, from  $80.83 \pm 18.42$  before the intervention to  $63.06 \pm 23.53$  afterward ( $t = 4.98, p < .001$ ). Furthermore, significant post-intervention reductions were observed for all six subscales of the UUIS. There were no significant differences in the functional EORTC QLQ-C30 scale scores; however, the symptom scale showed a significant decrease in fatigue (pre =  $35.19 \pm 19.53$ , post =  $25.93 \pm 17.04$ ,  $Z = -1.99, p < 0.046$ ) and constipation (pre =  $20.37 \pm 20.26$ , post =  $7.41 \pm 14.26$ ,  $Z = -2.11, p = 0.035$ ). There were no significant differences in anxiety and depression levels pre- and post-intervention. Overall, the intervention effectively reduced both UUIS total and subscale scores related to pre-HSCT uncertainties. Assessing uncertainty prior to HSCT is vital to assisting patients in coping with the procedure. Nurses not only provide information but also tailor the information to the patients' cognitive abilities, thereby simplifying their understanding of the disease and its treatment.

**Key words** uncertainty, hematopoietic stem cell transplantation, nursing intervention

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### Introduction

Hematopoietic stem cell transplantation (HSCT) can effectively treat a number of hematologic diseases and malignancies, such as leukemia, malignant lymphoma, and aplastic anemia. In Japan, over 3,500 allogeneic

HSCTs are performed annually, with a 100-day survival rate of approximately 90%. Moreover, bone marrow transplantation has improved over the past decade, yielding comparable results for both related and unrelated HSCT<sup>1</sup>. However, patients scheduled for transplantation often experience physical distress due to side ef-

fects and infections from complete induction therapy, psychological and social distress including emotional responses regarding undergoing the procedure, financial anxiety, and decreased quality of life (QOL)<sup>2, 3</sup>. Additionally, they often face uncertainty related to their illness and its treatment, which can lead to anxiety and depression<sup>4,6</sup>. While HSCT is a curative treatment, patients scheduled to undergo HSCT frequently experience psychosocial distress leading up to the procedure. Recent studies have also found evidence of uncertainty among patients undergoing HSCT<sup>7,9</sup>.

Uncertainty, as defined in Mishel's model of perceived uncertainty in illness, refers to "the inability to determine the meaning of illness-related events"<sup>6, 10</sup>. It encompasses patient anxiety due to the ambiguity of disease status, the complexity of treatment and care, lack of information, inconsistencies regarding differing diagnoses or severity of disease, and the unpredictability of the course and prognosis of a disease<sup>6</sup>. In Colombia, approximately 74% of patients scheduled for HSCT reported a high level of uncertainty before the procedure<sup>7</sup>. Patients scheduled for HSCT often struggle to cope with the abundance and complexity of information surrounding their diseases and treatment options, leading to changes in their daily lives and treatment prospects. They also frequently experience anxiety and fear, hindering their abilities to adopt appropriate coping behaviors<sup>11</sup>.

A recent systematic review of illness uncertainty management interventions for patients with cancer and their families found that informational support was the usual approach, provided both in-person and via telephone, along with emotional, appraisal, and instrumental support<sup>12</sup>. While gathering information is helpful in the early stages of the disease, obtaining and interpreting accurate information can be challenging. Therefore, it is important to provide accurate information on HSCT and ensure that patients fully understand the information, to help them cope with pre-treatment uncertainty<sup>13</sup>.

Nursing interventions should start before hospitalization for HSCT, to help patients recognize and reduce their uncertainties associated with the procedure<sup>7, 14</sup>. In recent years, most nursing intervention studies have focused on post-HSCT follow-up; however, to the best of our knowledge, there have been no reports in the literature on nursing intervention studies specifically targeting pre-HSCT patients to help them cope with uncertainties before undergoing the procedure<sup>15-17</sup>. Therefore, this study aimed to develop and assess the effectiveness of a nursing intervention program that would help patients scheduled to undergo HSCT recognize and reduce pre-transplant uncertainty, ultimately leading to more successful procedures. The expected study outcome was

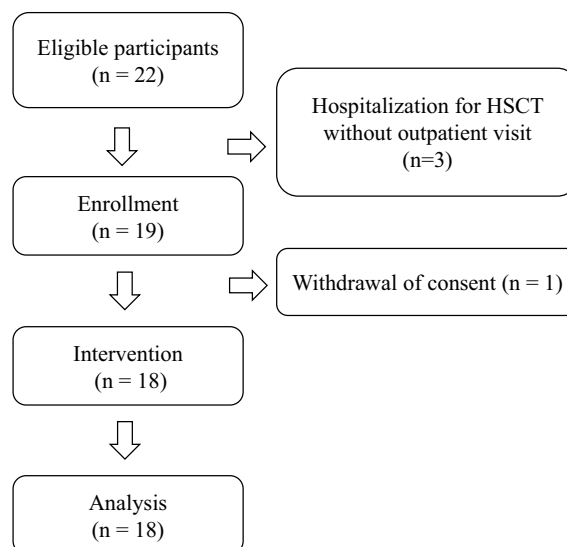


Figure 1. Recruitment flow chart

that patient uncertainty would decrease post-intervention.

## Methods

### Study design

This study used a pretest-posttest single-group design, without a control group.

### Sample size

The sample size was calculated using GPower 3.1.9.7. Based on Cohen's criteria of feasibility<sup>18</sup>, the effect size was set at 0.8, the  $\alpha$  error at 0.05, and the test power  $1-\beta$  at 0.8. The necessary sample size was calculated to be 15 participants. We estimated that 25% of participants would refuse or withdraw their consent owing to physical or emotional difficulties. Therefore, we set the desired sample size at 20. Twenty-two participants enrolled in the study, but the final sample size was 18. This was because the timing of the intervention was not suitable for three patients, who were suddenly discharged from the hospital and admitted for HSCT without an outpatient visit. One other patient withdrew their consent owing to difficulty completing the study questionnaires (Figure 1).

### Recruitment

This study enrolled patients who were scheduled to undergo allogeneic HSCT at Tokushima University Hospital in Japan between July 2020 and July 2022. Our inclusion criteria were as follows: patients 20 years of age or older, undergoing their first allogeneic HSCT, who had received final consent from the donor for the transplantation, and who had been given permission to participate in the study by their attending physician.

**Table 1. Structure of the nursing intervention program to reduce uncertainty**

Structure	Informational support	Confirming understanding of information	Emotional support
Purpose	To provide information and knowledge related to HSCT	To confirm understanding of information related to HSCT	To reduce anxiety associated with HSCT
UUIS and contents of support	Unpredictability of Daily Life	Shown the course of HSCT in Figure, scheduling and job prospects from admission to discharge for HSCT with the nurse. (Included in pamphlet)	To confirm what the patient did not understand about the information they obtained through informational support (Done one week after the intervention by telephone). To provide positive feedback when the patient was coping with uncertainty.
	Complexity of Interpretation of Information	To explain complex information about HSCT according to the patient's cognitive abilities, including basic knowledge of HSCT and acquiring self-care skills such as physical activity and infection prevention in a defensive environment. (Included in pamphlet)	To hear to patients' anxiety regarding HSCT. To provide patients a sense of security and treat them with empathy.
	Instability of Self-confidence in Carrying on a Struggle against Illness	Explained advice from the success stories of patients who had undergone HSCT. In particular, describe what they were aware of during their HSCT. (Included in pamphlet)	
	Unpredictability Recovery from Illness	Scheduling the prospect of treatment, such as upcoming conditioning regimen and HSCT transplantation methods, with the nurse. (Included in pamphlet)	
	Ambiguity of Characteristics of Illness		To confirm how they perceived their illness, the treatment they have received, and the treatment they will receive. (Done face-to-face)
	Lack of Cues Finding Meaning in Illness		To confirm the perception of the meaning of one's illness, the treatment the patients have received, and the treatment they will receive. (Done face-to-face)

UUIS, Universal Uncertainty in Illness Scale; HSCT, Hematopoietic stem cell transplantation

The sole exclusion criterion was having a psychiatric disorder. The attending physician or hematopoietic cell transplant coordinator (HCTC) selected eligible patients and verbally explained the study's purpose to them. After obtaining verbal informed consent, each patient was referred to one of the nurses on the research team. The nurse provided a written and oral explanation of the study's purpose and obtained written informed consent from each patient.

**Intervention program**

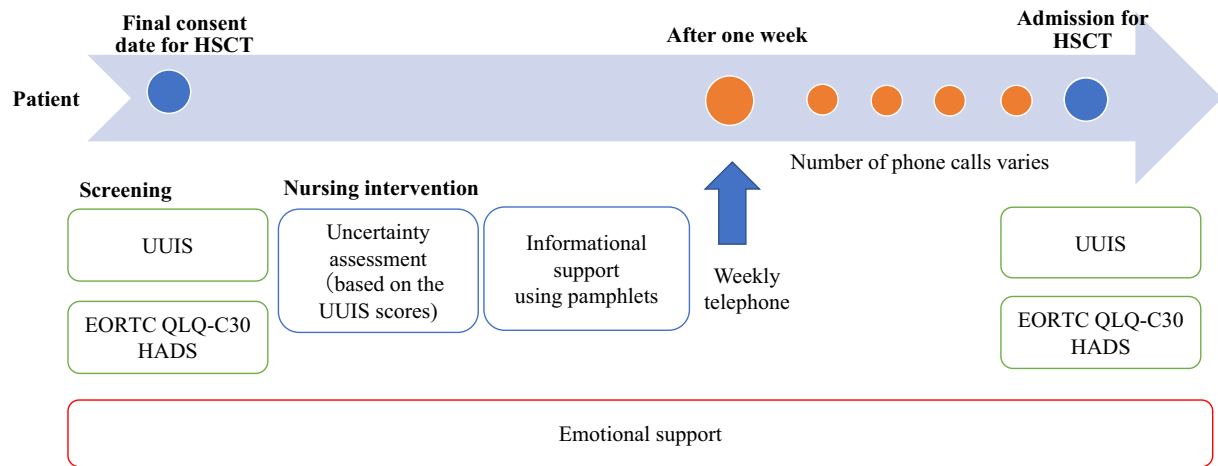
***Theoretical framework for Pre-HSCT uncertainty and coping***

This study developed a theoretical framework for pre-transplantation uncertainty in patients undergoing HSCT, based on Mishel's model of perceived uncertainty in an illness<sup>6</sup>. Before undergoing HSCT, patients face various uncertainties concerning factors such as the disease itself, treatment options, symptoms, treatment course, and treatment environment. Nurses delivered information concerning HSCT to patients in a manner

that matched their cognitive abilities. This was done to reduce pre-transplant uncertainty and help the patients deal with the challenges that transplantation presents. The expected outcomes for the patients included improved pre-HSCT QOL and reduced levels of anxiety and depression.

***Structure and content of the program***

The Universal Uncertainty in Illness Scale (UUIS), developed by Nogawa<sup>19</sup> and based on Mishel's theory, was used in the nursing intervention program to help patients who were scheduled for HSCT reduce their levels of uncertainty. Pre-HSCT uncertainty was defined using the definitions of the UUIS subscales, and nursing intervention methods were established after reviewing relevant literature<sup>19, 20</sup>. Reinforcing knowledge with information has been proven to be effective in reducing uncertainty, and emotional support also helps promote psychosocial adjustment<sup>21</sup>. Thus, the nursing intervention program in this study: 1) provided informational support, 2) obtained confirmation of each patient's understanding of the information provided, and 3) provided emotional support (**Table 1**).



**Figure 2. Implementation of the intervention**

Informational support was provided via a pamphlet developed specifically for this study. The pamphlet contained information regarding HSCT, and the nurses used it to explain complex information to the patients based on each one's cognitive abilities<sup>20</sup>. It included basic knowledge regarding HSCT, advice on acquiring skills for physical activity and infection prevention in a defensive environment, success stories of other patients who had undergone the procedure, and recommendations regarding books and internet-based resources on HSCT. The nurses also discussed each patient's schedule from admission to discharge with the patient themselves, as well as prospective treatment schedules, upcoming conditioning regimens, and the HSCT transplantation methods their procedures would use. Each patient's HSCT progress was planned individually using an illustration provided in the pamphlet. Confirmation of each patient's understanding of the information helped to identify any aspects that were not understood. The nurses provided positive feedback to the patients to help reduce their uncertainty. The process also revealed how patients understood their illnesses and treatments as explained by their physicians, and their perceptions of their illnesses and treatment options<sup>2</sup>. As HSCT involves psychological distress, the intervention provided both informational and psychological support. Emotional support was provided to alleviate the anxiety associated with HSCT and provide a sense of security.

#### **Content Validity of the Intervention**

The intervention program was validated by a certified HSCT physician, an HCTC, and two nursing researchers. The validity of the pamphlet was confirmed by a certified HSCT physician and an HCTC. Finally, the pamphlet's content was reviewed by an HSCT survivor and the language was modified to enhance clarity.

#### **Implementation of the Intervention**

Please refer to **Figure 2** for a full visual overview of

how the intervention was implemented.

#### **Uncertainty assessment (Pre-Intervention)**

First, patients filled out the UUIS. Then, a nurse with a minimum of five years of experience in a hematology ward and an in-depth understanding of nursing patients with cancer conducted an uncertainty assessment. The assessment used the data collected from the UUIS questionnaire, and the patients were queried regarding the factors that contributed to their high scores if they scored 4 or 5.

#### **Practical intervention methods**

The nurse administering the UUIS explained it to the patient using pamphlets for approximately an hour, to provide information regarding HSCT. The nurse then confirmed the patient's understanding of their disease, the treatment they received, and the type of HSCT they were scheduled to undergo—as well as their perceptions of the disease and the significance of HSCT. One week later, the nurse called the patient to check if there were any aspects of HSCT that they still did not understand. The nurse also inquired about the patient's ability to address uncertainty, and provided positive feedback. Each patient received at least one support call by telephone from the same nurse. Thereafter, calls were made once per week, depending on each patient, until their admission to the hospital for their HSCT procedure. The number of phone calls varied for each patient.

#### **Timing of the intervention**

The intervention was conducted with outpatients and inpatients at different time points. Outpatients received the intervention during their earliest outpatient visit after their HSCT date was set, while inpatients received the intervention upon discharge after their HSCT date was set.

## Data collection

### *Patient demographics*

Data regarding the age, sex, disease, transplantation method, employment, and family structure of each patient were collected from their medical records.

### *Measures*

The impact of the intervention was measured using the UUIS, European Organization for Research and Treatment of Cancer QOL Questionnaire (EORTC QLQ-C30), and the Hospital Anxiety and Depression Scale (HADS).

### *Universal uncertainty in illness scale*

The UUIS consists of 26 items and six subscales: the unpredictability of daily life, the complexity of interpreting information, lack of cues to find meaning in the illness, ambiguous characteristics of the illness, unpredictability regarding recovery from the illness, and lack of self-confidence in carrying on the struggle against the illness<sup>19</sup>. The alpha confidence coefficient for the scale was 0.94. Scoring was based on a 5-point Likert-type scale, with higher levels of uncertainty leading to higher scores. The UUIS does not have a specific cutoff value. This study compared patient scores before and after the intervention, and a decrease in UUIS score was considered to be associated with a decrease in uncertainty.

### *The european organization for research and treatment of cancer QOL questionnaire*

The EORTC QLQ-C30 was developed by Aaronson, and has been tested for both reliability and validity<sup>22</sup>. It consists of 30 items, including five functional scales (physical, role, social, emotional, and cognitive functioning), three symptom scales (fatigue, pain, and nausea/vomiting), six single-item scales (dyspnea, appetite loss, sleep disturbance, constipation, diarrhea, and financial impact), and a global health status scale. The scores on all scales and single-item measures range from 0-100. Higher scores on the global QOL and functioning scales indicate better health and functioning. Higher scores on the symptom and single-item scales indicate a poorer health status.

### *Hospital anxiety and depression scale*

The HADS was developed by Zigmond<sup>23</sup>, and it was translated into Japanese by Kugaya. It consists of 14 items: seven anxiety items (HADS-A) and seven depression items (HADS-D). The Cronbach's alpha coefficient was 0.77 for the anxiety scale and 0.79 for the depression scale. Each item is rated on a 4-point Likert-type scale ranging from 0-3. Anxiety or depression scores range from 0-21 (0-7: none; 8-10: doubtful; 11-21: definite). Higher scores indicate more severe anxiety or depression.

## Statistical analysis

Patient demographics were analyzed using descriptive statistics. For the UUIS and HADS, paired Student's *t*-tests were performed after confirming the normality of data distribution in pre- and post-tests. The EORTC QLQ-C30 was scored according to the EORTC Scoring Manual, and a Wilcoxon signed-rank sum test was performed. All statistical tests were two-tailed, and the level of statistical significance was set at  $p = 0.05$ . Statistical analyses were performed using SPSS version 29.0 (Armonk, NY, US).

## Ethical approval

The study protocol was approved by the ethics committee of Tokushima University Hospital (approval no. 3757), and the study was performed in accordance with the latest version of the Helsinki Declaration. The intervention was conducted after enrollment of the study in the UMIN Clinical Trials Registry (UMIN000040421). All patients received informational pamphlets and provided written informed consent before the intervention. To protect patient privacy, all interventions were conducted in private rooms.

## Results

### Patient demographics

Eighteen patients (13 male and five female participants) with a median age of 52 years participated in the study. All of the patients were undergoing HSCT for the first time. Seven patients had acute lymphoblastic leukemia, and 13 were scheduled for bone marrow transplantations. Most of the patients were employed, and all had family members living with them. Three of the patients were refused a transplant from their first or second donor. The average number of intervention days was 26 (range, 10-75) days, the average number of telephone interventions was three (range, 1-8), and the average duration of each telephone call was 19.78 min (**Table 2**).

### The UUIS

The total UUIS score decreased significantly, from  $80.83 \pm 18.42$  pre-intervention to  $63.06 \pm 23.53$  post-intervention ( $t = 4.98$ ,  $p < 0.001$ ). All six subscales of the UUIS also decreased significantly post-intervention: unpredictability of daily life decreased from  $28.67 \pm 7.40$  pre-intervention to  $22.00 \pm 8.02$  post-intervention ( $t = 4.52$ ,  $p < 0.001$ ); ambiguous characteristics of the illness decreased from  $12.33 \pm 3.52$  pre-intervention to  $9.67 \pm 4.69$  post-intervention ( $t = 3.83$ ,  $p = 0.001$ ); and complexity of interpreting information decreased from  $10.22 \pm 3.39$  pre-intervention to  $7.78 \pm 2.98$  post-intervention ( $t = 3.72$ ,  $p = 0.002$ ; **Table 3**).



**Table 2. Demographics**

Item	Sub-group	Sub-total	Mean (±SD)	Median	Range
Age (years)				52	23-65
	21-30	1			
	31-40	2			
	41-50	4			
	51-60	8			
	61-65	3			
Sex	Male	13			
	Female	5			
Disease	ALL	7			
	AML	3			
	MDS	3			
	ATLL	2			
	CML	2			
	CLL	1			
Transplant types	BMT	13			
	PBSCT	3			
	CBT	2			
Working status	Employed	17			
	Unemployed	1			
Family living together	Yes	18			
	No	0			
Doner refused transplant	Once	2			
	Twice	1			
Period of intervention			26.2 (±21.4)		10-75
Number of telephone interventions			3 (±2.4)		1-8
	1	6			
	2	5			
	3	2			
	4	0			
	5	2			
	6	1			
	7	0			
	8	2			

ALL, Acute lymphoblastic leukemia; AML, Acute myeloid leukemia; MDS, Myelodysplastic syndrome; ATLL, Adult T-cell Leukemia/Lymphoma; CML, Chronic myeloid leukemia; CLL, Chronic lymphocytic leukemia; BMT, Bone marrow transplantation; PBSCT, Peripheral hematopoietic stem cell transplantation; CBT, Umbilical cord blood transplantation.

**The EORTC QLQ-C30**

The functional EORTC QLQ-C30 scale scores did not differ significantly. The symptom scale showed a significant decrease in fatigue (pre = 35.19 ± 19.53, post = 25.93 ± 17.04, Z = -1.99, p < 0.046) and constipation (pre = 20.37 ± 20.26, post = 7.41 ± 14.26, Z = -2.11, p = 0.035), but no significant differences in the other symptoms. Similarly, global health status/QOL

did not differ significantly (Table 4).

**The HADS**

The total HADS score decreased significantly, from 13.17 ± 5.04 pre-intervention to 10.89 ± 5.95 post-intervention (t = 2.38, p = 0.029); however, there was no significant difference in anxiety (pre = 7.06 ± 3.56, post = 5.89 ± 3.18, t = 1.70, p = 0.108). There was no

**Table 3. Universal Uncertainty in Illness Scale (UIIS)**

	Pre-test Mean±SD	Post-test Mean±SD	t	p
Total	80.83±18.42	63.06±23.53	4.98	<0.001
Subscales				
Unpredictability of Daily Life	28.67±7.40	22.00±8.02	4.52	<0.001
Ambiguity of Characteristics of Illness	12.33±3.52	9.67±4.69	3.83	0.001
Complexity of Interpretation of Information	10.22±3.39	7.78±2.98	3.72	0.002
Lack of Cues Finding Meaning in Illness	11.94±5.01	9.56±4.31	3.20	0.005
Instability of Self-confidence in Carrying on a Struggle against Illness	9.22±3.35	7.11±3.23	2.83	0.011
Unpredictability Recovery from Illness	8.39±2.93	6.94±3.10	2.78	0.013

**Table 4. European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30)**

	Pre-test Mean±SD	Post-test Mean±SD	Z	p-value
Functional scales				
Physical functioning	82.59±13.94	82.59±19.29	0.98	0.325
Role functioning	79.63±23.95	79.63±26.54	0.00	1.000
Emotional functioning	82.41±14.26	82.41±16.39	0.32	0.752
Cognitive functioning	83.33±17.15	87.96±17.90	0.95	0.343
Social functioning	70.37±28.33	75.93±30.90	0.63	0.531
Symptom scales/items				
Fatigue	35.19±19.53	25.93±17.04	-1.99	0.046
Nausea and vomiting	2.78±6.39	0.93±3.93	-1.41	0.157
Pain	12.96±24.63	10.19±18.20	-0.81	0.417
Dyspnea	16.67±17.15	12.96±16.72	-0.71	0.480
Insomnia	24.07±22.30	14.81±23.49	-1.89	0.059
Appetite loss	22.22±28.01	9.26±19.15	-1.89	0.070
Constipation	20.37±20.26	7.41±14.26	-2.11	0.035
Diarrhoea	11.11±19.80	12.96±23.26	0.33	0.739
Financial difficulties	33.33±41.22	29.63±32.11	-0.84	0.399
Global health status/QOL	70.37±21.62	75.46±20.90	1.23	0.218
Summary score	81.00±9.94	85.70±11.27	1.83	0.067

QOL, Quality of Life

**Table 5. Hospital Anxiety and Depression Scale (HADS)**

	Pre-test Mean±SD	Post-test Mean±SD	t	p-value
Anxiety and depression (HADS Total)	13.17±5.04	10.89±5.95	2.38	0.029
Anxiety (HADS-A)	7.06±3.56	5.89±3.18	1.70	0.108
Depression (HADS-D)	6.22±2.53	5.22±3.46	1.89	0.076

significant difference in depression as well (pre = 6.22 ± 2.53, post = 5.22 ± 3.46,  $t = 1.89$ ,  $p = 0.076$ ). None of the patients scored more than 11 points in terms of anxiety or depression (**Table 5**).

## Discussion

The results showed that the UIIS scores decreased significantly post-intervention compared to pre-

intervention. The effects of providing informational support and confirmation that the patients understood the information presented to them are discussed below.

### Effects of providing informational support

During informational support, patients were provided with information regarding HSCT based on their cognitive abilities, through pamphlets. This resulted in decreases in four subscales: unpredictability of daily life,

complexity of interpretation of information, lack of self-confidence in carrying on the struggle against the illness, and unpredictability of recovery from the illness.

Unpredictability of daily life refers to patients not knowing whether they will be able to continue their usual routines and roles following HSCT<sup>19</sup>. This uncertainty was addressed by providing each patient with a pamphlet containing a diagram that explained the HSCT process. The pamphlet also mentioned what to expect throughout the treatment process, starting from the date of admission to discharge. It is important for patients to understand how their treatment will affect their daily lives and work before undergoing HSCT, so this type of information can help them better focus on the transplantation.

The complexity of interpreting the information refers to the uncertainty that patients experience when they lack the necessary information about the disease or HSCT<sup>19</sup>. To address this uncertainty, pamphlets were provided and nurses explained the basics of HSCT and the skills needed, in a safe environment. Providing information is a key strategy for managing uncertainty in patients<sup>24</sup>, but it is also important to help patients meet their informational needs using other sources. Nurses involved with patients can use books and online resources to provide information, solve problems, and offer their patients additional options when they lack information.

Lack of self-confidence in carrying on the struggle against the illness refers to a patient not knowing whether their body will react positively to HSCT<sup>19</sup>. Before treatment, patients experience emotional fluctuations regarding whether they should undergo HSCT. This is because they realize that HSCT is a highly invasive treatment that may result in prolonged hospitalization, and they are uncertain of their chances of survival<sup>2</sup>. It is important for them to learn from patients who have undergone HSCT, to help them achieve a positive perspective on the procedure. For this purpose, we created a pamphlet to explain interventions for this type of uncertainty, which included advice from patients who had successfully undergone HSCT. The purpose of the pamphlet was to assist the patients in this study with viewing HSCT as a necessary step in curing their diseases.

Unpredictability of recovery from the illness refers to a patient being uncertain about the possible outcomes of their disease, such as not being in complete remission or relapsing before undergoing HSCT<sup>4, 20</sup>. To address this form of uncertainty, prospective treatment schedules were arranged between each patient and their nurse. This included upcoming conditioning regimens and transplantation methods. Even when it is difficult to predict the future, having a detailed treatment plan for a

patient's return to normal life before their admission to undergo HSCT can help them get through the procedure without losing hope<sup>25</sup>.

### **Effect of confirmoffing that patients understood the presented information**

Confirming that the patients understood the information they were provided allowed us to identify which aspects of informational support they struggled to comprehend. In addition to providing accurate information using the pamphlet, the nurses also verified whether the patients understood the information, and if they did not understand something the nurses helped explain it, thereby reducing uncertainty preceding HSCT. Confirming each patient's perception of their disease and treatment options via explanations from their doctors can reduce ambiguity surrounding the illness and the lack of clarity surrounding the meanings of illness subscales.

Ambiguous characteristics of the illness refers to patient uncertainties surrounding their illnesses and the prior treatments received<sup>19</sup>. Patients often have an ambiguous understanding of their disease and treatment because the content, amount, and timing of information are not provided in a setting that is appropriate to each patient's ability to understand<sup>26</sup>. In our study, this uncertainty was addressed by identifying how our patients perceived their diseases, the treatments they had previously received, and the treatment that they would receive. For patients who were unable to explain the progress of their disease or treatment, the nurse supplemented explanations with medical records. It is crucial to evaluate how well patients comprehend their diseases and treatments, in order to understand the treatment aspects of HSCT.

Lack of cues to find meaning in the illness refers to the uncertainty of not knowing the meaning of one's disease or treatment<sup>19</sup>. This uncertainty was addressed by confirming each patient's perception of the meaning of their illness, the treatments they received previously, and the treatment that they would receive. Meaning-making regarding diseases and HSCT has been reported to enhance positive personal growth and adaptive coping<sup>27</sup>. Patients should recognize what it means to undergo HSCT, to enable them to prepare for a long and painful treatment process.

### **Effect on QOL and the HADS**

In this study, reducing uncertainty was predicted to be helpful for improving QOL and decreasing depression and anxiety; however, there were no changes in these indicators following the intervention. Compared to previous studies that applied the EORTC QLQ-C30 prior to HSCT procedures, the patients in this study scored better on the functional and symptom scale



items, suggesting no change resulting from the intervention<sup>28</sup>. Fatigue was reported to be highest during treatment and improved preceding HSCT, after a certain amount of time had elapsed since chemotherapy was last administered. Similarly, constipation also improved in most patients as their HSCT procedures approached, which aligns with findings from previous studies<sup>29</sup>.

Although reported to be high preceding HSCT<sup>30</sup>, our intervention did not seem to affect patient anxiety. It has been reported that approximately 30% of patients are depressed before HSCT<sup>31</sup>. However, in the present study, none of the patients were found to be depressed before HSCT; therefore, there was no change in depression following our intervention. Depression is a factor that impacts QOL; therefore, the prevention of depression is important to improving QOL<sup>14</sup>. It is also important to assess QOL and depression before HSCT, because low levels of problem-solving have been reported to increase depression and decrease QOL<sup>32</sup>.

### Implications for nursing

It is important to assess uncertainty before patients undergo HSCT, so they can better prepare themselves. Nurses can not only provide information to their patients, but also supplement and provide information based on each patient's cognitive status. This helps to resolve the complexity surrounding understanding the disease and its treatment. Useful ways of helping patients deal with uncertainty include confirming their understanding of the information, addressing questions together if they do not understand something, and teaching problem-solving strategies. It is necessary for patients to understand their diseases and treatment options, as well as perceive them in a positive manner, to help cure said diseases and facilitate earlier adaptation to HSCT<sup>33</sup>.

### Limitations

This was a pre-and-post study conducted at a single institution. The number of calls varied depending on each patient's situation (e.g., early admission due to COVID-19, or HSCT donor changes), which affected the results. Moreover, it was not possible to determine whether the patients were able to successfully address their uncertainties; therefore, our results should be interpreted with some caution. Future studies should identify the factors that influence perceptions of uncertainty in a larger cohort, thereby providing a more efficient intervention for patients with low understanding.

### Conclusion

This study examined the effectiveness of a nursing intervention program aimed at reducing patient uncertainty leading up to HSCT. It proved to be successful in

reducing all of the UUIS total and subscale scores for pre-HSCT uncertainties.

### Acknowledgments

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### Author Contributions

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K.N., S.Y., and A.H designed the study. K.N., S.F., A.F., and K. K. screened the patients. S.F obtained informed consent. K.N. collected the data. K.N. and Y.A. analyzed the data. K.N., S.F., A.F., K.K., Y.A., M.A., S.Y., and A. H. wrote the manuscript.

### Conflicts of Interest

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The authors declare no conflict of interest. Disclosure forms provided by the authors are available on the website.

### Funding Statement

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### Ethics Approval

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The study protocol was approved by the ethics committee of Tokushima University Hospital (No. 3757) and was performed in accordance with the latest version of the Helsinki Declaration.

### Informed Consent

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Eighteen patients received the information pamphlets and provided written informed consent before starting the intervention.

## Clinical Trial Number and Registry URL

The intervention was initiated after enrollment in the UMIN Clinical Trials Registry (UMIN000040421).

URL: [https://center6.umin.ac.jp/cgi-open-bin/ctr/ctr\\_view.cgi?recptno=R000046049](https://center6.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000046049)

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