




ORIGINAL ARTICLE

# Changes in depressive symptoms among family caregivers of patients with cancer after bereavement and their association with resilience: A prospective cohort study

Yoichi Shimizu<sup>1,2</sup>  | Akitoshi Hayashi<sup>3</sup> | Isseki Maeda<sup>4</sup> | Tomofumi Miura<sup>5</sup> | Akira Inoue<sup>6</sup> | Mayuko Takano<sup>7</sup> | Maho Aoyama<sup>2</sup>  | Yutaka J. Matsuoka<sup>8</sup>  | Tatsuya Morita<sup>9</sup> | Yoshiyuki Kizawa<sup>10</sup> | Satoru Tsuneto<sup>11</sup> | Yasuo Shima<sup>12</sup> | Kento Masukawa<sup>2</sup> | Mitsunori Miyashita<sup>2</sup>

<sup>1</sup>Department of Nursing, National Cancer Center Hospital, Tokyo, Japan

<sup>2</sup>Department of Palliative Nursing, Health Sciences, Tohoku University Graduate School of Medicine, Sendai, Japan

<sup>3</sup>Department of Palliative Care, St. Luke's International Hospital, Tokyo, Japan

<sup>4</sup>Department of Palliative Care, Senri-Chuo Hospital, Toyonaka, Japan

<sup>5</sup>Department of Palliative Medicine, National Cancer Center Hospital East, Kashiwa, Japan

<sup>6</sup>Department of Palliative Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

<sup>7</sup>Department of Nursing, St. Luke's International Hospital, Tokyo, Japan

<sup>8</sup>Division of Health Care Research, Center for Public Health Sciences, National Cancer Center Japan, Tokyo, Japan

<sup>9</sup>Division of Palliative and Supportive Care, Seirei Mikatahara General Hospital, Hamamatsu, Japan

<sup>10</sup>Department of Palliative Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

<sup>11</sup>Department of Human Health Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan

<sup>12</sup>Department of Palliative Medicine, Tsukuba Medical Center Hospital, Tsukuba, Japan

## Correspondence

Yoichi Shimizu, Department of Nursing, National Cancer Center Hospital, Tokyo, Japan.

Email: [yo-shimiz@umin.ac.jp](mailto:yo-shimiz@umin.ac.jp)

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## Abstract

**Objectives:** To elucidate changes in depressive symptoms after bereavement and the impact of pre-loss resilience on such changes and on the extent of complicated grief and posttraumatic growth.

**Methods:** Prospective cohort surveys were provided to family caregivers of patients with cancer in four palliative care units (PCUs) before and after bereavement. Pre-loss Connor–Davidson Resilience Scale scores, pre- and post-loss Patient Health Questionnaire-9 scores, post-loss Brief Grief Questionnaire scores, and the expanded Posttraumatic Growth Inventory scores were determined.

**Results:** Out of 186 bereaved family caregivers, 71 (38.2%) responses were analyzed, among which 47% pre-loss and 15% post-loss responses suggested to be a high risk for major depressive disorder (MDD). Approximately 90% of family caregivers at a high risk for post-loss MDD were already at a high risk for pre-loss MDD.

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Even after adjustment of the background variables as covariates, the interaction effect between family caregivers' pre-loss depressive symptoms and resilience on post-loss depressive symptoms was observed ( $F = 7.29$ ;  $p < 0.01$ ). Moreover, pre-loss resilience was not associated with other bereavement outcome measures.

**Conclusions:** Among family caregivers of patients with cancer in PCUs, 47% and 15% had high risk for MDD before and after bereavement, respectively. Moreover, pre-loss resilience mitigated post-loss depressive symptoms among family caregivers who had high risk for MDD before bereavement. However, considering the study's small sample size, further research is needed.

#### KEYWORDS

bereavement, caregivers, depression, neoplasms, palliative care, psychological posttraumatic growth, psychological resilience, psycho-oncology

## 1 | BACKGROUND

Bereavement causes a decline in the quality of life and mental health, as well as high risks for suicide, cardiovascular mortality, and overall mortality.<sup>1</sup>

Previous studies have shown that between 10% and 26% of bereaved caregivers of patients with cancer develop major depressive disorder (MDD).<sup>1-3</sup> Predictors for depression include pre-loss depressive symptoms, being a partner, younger age, being female, lower educational level, less patient impairment, shorter caregiving duration, pre-loss objective caregiving load, poor preparation for patients' death, less social support, and pre-loss non-hopeful attitude, among others.<sup>3-8</sup>

In Japan, 41% of family caregivers of moribund patients with cancer in the palliative care unit (PCU)<sup>9</sup> and 17% of bereaved family caregivers of patients with cancer<sup>5</sup> have a high risk for MDD. However, changes in severity of depressive symptoms among bereaved family caregivers have yet to be clarified.

In the post-loss grief process, psychological adjustment is needed.<sup>10-12</sup> Resilience may facilitate psychological adjustment to the psychological burden of caring for an ill family member.<sup>11,13</sup> Resilience is the dynamic capacity of an individual to maintain or regain mental health following a stressful or traumatic exposure.<sup>14</sup> According to the cross-sectional study of Hwang et al., high resilience among family caregivers is associated with low depression in palliative settings.<sup>15</sup> A longitudinal research is required to confirm whether resilience is indeed a protective factor against bereavement-related psychological distress. We hypothesized that despite the increase in depressive symptoms due to psychological burden before bereavement, high resilience promotes psychological adaptation and improved depressive symptoms after bereavement. Therefore, this study aimed to test the interaction effect between pre-loss depressive symptoms and resilience on post-loss depressive symptoms.

Another psychological distress after bereavement is complicated grief (CG), which is different from MDD.<sup>2</sup> Complicated grief is an

intense feeling of grief that is unusually severe and prolonged, characterized by difficulty adapting to loss.<sup>16</sup> Some bereaved family caregivers often report some degree of growth through the grieving process.<sup>17,18</sup> In addition, higher resilience is reportedly associated with a greater degree of Posttraumatic Growth (PTG).<sup>13,19</sup> Therefore, we hypothesized that resilience may act protectively against bereavement distress and promote psychological adaptation, thereby reducing the risk for CG and facilitating PTG. However, the relationship between pre-loss resilience, CG and PTG remains poorly explored. Thus, this study also aimed to examine the association between pre-loss resilience, grief reaction, and PTG.

Taken together, the present study aimed to (1) reveal patterns of changes in Japanese family caregivers' depressive symptoms after bereavement, (2) clarify the interaction effect between pre-loss depressive symptoms and resilience on post-loss depressive symptoms, and (3) examine the association between pre-loss resilience, PTG, and grief reaction.

## 2 | METHODS

In this cohort study, we recontacted the participants involved in the pre-loss survey. We collected their baseline data recorded for the pre-loss survey at four PCUs between December 2016 and January 2018 and collected the follow-up data in July and August of 2018 for the post-loss survey, named as the fourth Japan HOspice and Palliative Evaluation (J-HOPE4) study.<sup>20</sup>

### 2.1 | Participants and procedure

As the baseline data, potential participants were family caregivers of patients with terminal cancer admitted to four PCUs. The inclusion criteria were (1) primary family caregivers; (2) both patients and family caregivers aged 20 years or above; and (3) patients admitted to the PCUs before 29 January 2018. The exclusion criteria were (1)

family caregivers suffering from serious psychological symptoms as determined by the primary physician; (2) family caregivers incapable of completing the self-report questionnaire due to linguistic and health issues (e.g., cognitive impairment or visual deficit); and (3) length of stay <48 h. All participants provided written informed consent prior to study inclusion. The researchers asked the participants to return the completed questionnaire to the research office by mail.

For the follow-up survey, questionnaires were sent to pre-loss survey participants whose patients had died by 31 January 2018. Non-responders were sent reminders to submit the questionnaire after 1 month. Documents explaining the aims and procedures of the J-HOPE4 study, as well as this follow-up survey, were sent along with the questionnaire. Returning a completed questionnaire without checking the “no participation” box implied consent to participate in the study. However, we excluded those subjects whose age, gender, and relationship did not match between pre-loss and post-loss surveys, possibly because another family member might have already responded.

The pre-loss and post-loss surveys were approved by the Institutional Review Board (IRB) of Tohoku University School of Medicine (IRB approval ID: 2016-1-409, 2017-2-236-1) and all participating institutions (St. Luke's International Hospital, Gratia Hospital, and National Cancer Center).

## 2.2 | Measurements

### 2.2.1 | The Patient Health Questionnaire-9

The severity of the participants' depression was measured using the Patient Health Questionnaire-9 (PHQ-9)<sup>21,22</sup> during the pre- and post-loss surveys. This instrument consists of nine items focused on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM) 4th Edition for MDD, and is validated in Japanese.<sup>23</sup> Participants were asked regarding the frequency of the nine depressive symptoms throughout the preceding 2 weeks, with choices ranging from “0” (not at all) to “3” (nearly every day).<sup>21,22</sup> Scores  $\geq 10$ , representing the valid cutoff point for MDD,<sup>21,23</sup> was used to categorize participants into those at high (PHQ-9 score  $\geq 10$ ) or low (PHQ-9 score <10) risk for MDD. The Cronbach's  $\alpha$  were 0.86 and 0.88 in the pre-loss and post-loss surveys, respectively.

### 2.2.2 | Connor–Davidson resilience scale

During the pre-loss survey, individual resilience was measured using the 25-item scale Connor–Davidson Resilience Scale (CD-RISC)<sup>24,25</sup> wherein each item was rated using a 5-point Likert scale (from 0 [not true at all] to 4 [true nearly all of the time]); the higher the scores, the higher the resilience (range, 0–100). The scale was rated according to how the respondent felt over

the past month regarding “Able to adapt to change,” “Can deal with whatever comes,” “See the humorous side of things,” among others.<sup>24</sup> This scale, as well as its Japanese version, has been confirmed to be reliable and valid.<sup>24,25</sup> The Cronbach's  $\alpha$  of this study was 0.94.

### 2.2.3 | Family APGAR

Family function was assessed using the Family APGAR during the pre-loss survey.<sup>26</sup> Considering that family function can affect both pre-loss resilience<sup>27,28</sup> and pre-loss depressive symptoms,<sup>28,29</sup> it needed to be adjusted as a covariate. This five-item questionnaire measures satisfaction with social support from the family according to five constructs, namely “Adaptability,” “Partnership,” “Growth,” “Affection,” and “Resolve.” The scores for each item ranged from 0 (“hardly ever”) to 2 (“almost always”); the higher the total scores, the higher the family function level (range, 0–10). This scale, as well as its Japanese version, has been confirmed to be reliable and valid.<sup>26,30</sup> In this study, the Cronbach's  $\alpha$  was 0.93.

### 2.2.4 | Brief Grief Questionnaire

The severity of participants' grief reaction after bereavement was measured using the Brief Grief Questionnaire (BGQ).<sup>31</sup> The BGQ is a self-report instrument that assesses the severity of CG-related grief reactions using five questions regarding the difficulty in accepting a loved one's death, grief interfering with daily life, troubling images or thoughts about the deceased, and avoiding things related to the deceased; it is also validated in Japanese.<sup>32</sup> Each item was scored from 0 (“not at all”) to 2 (“a lot”).<sup>31</sup> In this study, the Cronbach's  $\alpha$  was 0.71.

### 2.2.5 | Japanese version of the expanded Posttraumatic Growth Inventory

The degree of positive changes experienced by the participants after a traumatic event, that is, the death of a loved one in this study, was determined using the Japanese version of the expanded PTG Inventory (PTGI-X-J)<sup>33</sup> during the post-loss survey. The PTGI-X-J is a 25-item scale created by adding four items regarding spiritual–existential change into the PTG Inventory (PTGI) and is validated in Japanese.<sup>33</sup> Participants were asked regarding the extent to which they experienced each of the 25 particular positive changes following traumatic events, with choices ranging from 0 (“I did not experience”) to 5 (“I experienced to a very great degree”). The Cronbach's  $\alpha$  of this study was 0.97. This scale measures five domains of growth: “Appreciation of Life” (three items), “Personal Strength” (four items), “New Possibilities” (five items), “Relating to Others” (seven items), and “Spiritual and

Existential Change" (six items).<sup>33</sup> In this study, the Cronbach's  $\alpha$  of each domain was 0.83, 0.83, 0.94, 0.93, and 0.90, respectively. Due to the difference in the number of items for each domain, this scale was interpreted using the average total score and average score for each domain.

## 2.2.6 | Participant and patient characteristics

We asked the participants their sociodemographic information, including age; gender; relationship with the patient (partners, children, etc.); education level; religious beliefs; belief in the survival of the soul after physical death; whether they lived with the patient; frequency of their attendance; perceived social support (feelings of being loved and cared for and perception that their concerns or problems are being recognized); and psychotropic drug use or psychiatric counseling, and also asked their patients' sociodemographic information, including age; gender; marital status; household income; and length of cancer diagnosis.

## 2.3 | Statistical analyses

First, descriptive analyses of the demographic characteristics, degree of individual resilience assessed using the CD-RISC, and severity of depression assessed using the PHQ-9 during both the pre- and post-loss surveys were conducted. For the PHQ-9, changes in total scores and those for each item were described.

Thereafter, mixed model analysis was performed with the post-loss PHQ-9 scores as the dependent variables and pre-loss PHQ-9 scores, CD-RISC scores, and their interaction term (pre-loss PHQ-9 scores  $\times$  CD-RISC scores) as the independent variables. This model was then adjusted as covariates through the following background variables: family caregivers' age; gender; relationship with the patient; education level; perceived social support; duration following bereavement; duration after the patients' diagnosis; family function; belief in the survival of the soul after physical death; availability of another person who could stay with the patient; and preparation for bereavement. These covariates were selected according to the possibility of confounding from previous studies.<sup>3-8,27,29,34,35</sup> The required sample size was 92, with a moderate effect size ( $|p| = 0.4$ ),  $\alpha$  at 0.05, and detection power at 0.8. However, the required sample size was not reached; thus, the detection power calculated by ad hoc was 0.77.

To visually understand the significant interaction between pre-loss PHQ-9 and CD-RISC scores, we used boxplots to illustrate the changes in PHQ-9 scores before and after loss; the scores were stratified by higher/lower resilience and presence/absence of high risk for pre-loss MDD. The higher and lower resilience classifications were quantified by the median CD-RISC score.

To determine associations among pre-loss resilience, grief reaction and PTG, we calculated the Pearson correlation coefficients between CD-RISC scores and BGQ scores, and PTGI-X-J scores.

All tests were two-tailed with a  $p$  value  $< 0.05$  indicating statistical significance. All statistical analyses were performed using SAS Ver.9.4 (SAS Institute Inc.).

## 3 | RESULTS

A total of 291 (69.8%) of 417 family caregivers replied to the pre-loss survey, while 108 (58.1%) of 186 bereaved family caregivers replied to the post-loss survey. After matching the respondents' age, gender, and relationship, 71 (38.2%) responses were analyzed (Figure S1).

### 3.1 | Patients' and primary family caregivers' characteristics

Patients' and caregivers' characteristics are summarized in Table 1. Patients, 59.2% of whom were male, had a mean age of 72.7 (Standard deviation [SD]: 12.2) years. Bereaved family caregivers, 77.5% of whom were female, had a mean age of 63.4 (SD: 13.2) years, and 60% of them were spouses or partners of the patient. The mean (SD) duration following bereavement was 376 (109.0) days, and the time interval between the pre- and post-loss surveys was 409 (105.6) days. Furthermore, 12 (17.4%) caregivers used psychotropic drugs or psychiatric counseling.

The mean CD-RISC score was 58.7 (SD: 16.5), while the mean PHQ-9 scores at the pre- and post-loss surveys were 9.2 (SD: 5.7) and 4.4 (SD: 4.5), respectively (Table 1).

### 3.2 | Patterns of changes in family caregivers' depressive symptoms after bereavement in Japan

Among the family caregivers of moribund patients with cancer in the PCUs, 47% and 15% had high risks for pre-loss and post-loss MDD, respectively. Of the caregivers with a high risk for post-loss MDD, only 40% reported to have used psychotropic drugs or psychiatric counseling.

The patterns of changes in family caregivers' depressive symptoms after bereavement were as follows: "improvement" (high risk for pre-loss MDD to low risk for post-loss MDD) in 33%, "consistently low" (low risk for pre-loss MDD to low risk for post-loss MDD) in 52%, "persistently depressed" (high risk for pre-loss MDD to high risk for post-loss MDD) in 14%, and "worsening" (low risk for pre-loss MDD to high risk for post-loss MDD) in 1.5%.

Figure 1 shows the changes of each PHQ-9 item. The proportion of caregivers with depressive mood and lack of interest, which are the core symptoms of depression, decreased after bereavement from 75% to 50% ( $p < 0.01$ ) and from 75% to 54% ( $p < 0.01$ ), respectively. However, self-perception and thoughts of suicide before and after bereavement were not improved significantly ( $p = 0.11$ ,  $p = 1.0$ ).

TABLE 1 Demographic characteristics of patients and caregivers

Family characteristics		n = 71	
Age			
Mean (SD)	72.7	(12.2)	
Sex, n (%)			
Male	42	(59.2)	71
Female	29	(40.8)	
Primary tumor sites, n (%)			
Lung	10	(14.1)	71
Liver, gallbladder, pancreas	15	(21.1)	
Upper digestive tract	12	(16.9)	
Lower digestive tract	13	(18.3)	
Head and neck	4	(5.6)	
Uterus, ovary	2	(2.8)	
Breast	7	(9.9)	
Kidney, bladder	2	(2.8)	
Hematological malignancy	1	(1.4)	
Others	5	(7.1)	
Marital status, n (%)			
Married	49	(69.0)	71
Single	3	(4.2)	
Widowed	16	(22.5)	
Divorced	3	(4.2)	
Number of people living in the same house, n (%)			
0	10	(14.3)	70
1	34	(48.6)	
≥2	26	(37.1)	
Duration after the patient's diagnosis, n (%)			
≥3 years	22	(31.4)	70
≥1 year, <3 years	26	(37.1)	
≥6 months, <1 year	4	(5.7)	
≥3 months, <6 years	10	(14.3)	
<3 months	8	(11.4)	
History of palliative care team visit, n (%)			
Presence	57	(81.4)	70
Absence	9	(12.9)	
Unknown	4	(5.7)	
Medical expenditure during the last month, n (%)			
<100,000 yen	11	(15.7)	70
≥100,000 yen, <200,000 yen	11	(15.7)	
≥200,000 yen, <400,000 yen	18	(25.7)	
≥400,000 yen, <600,000 yen	13	(18.6)	
≥600,000 yen	17	(24.3)	

TABLE 1 (Continued)

<b>Family characteristics</b>	<b>n = 71</b>		
Annual income during care: n (%)			70
<1 million yen	7	(10.0)	
≥1 million yen, <2 million yen	11	(15.7)	
≥2 million yen, <4 million yen	23	(32.9)	
≥4 million yen, <6 million yen	13	(18.6)	
≥6 million yen, <8 million yen	6	(8.6)	
≥8 million yen	10	(14.3)	
<b>Family characteristics</b>	<b>n = 71</b>		
Age			
At pre-loss Mean (SD)	62.3	13.2	
At post-loss Mean (SD)	63.4	13.2	
Sex, n (%)			71
Male	16	(22.5)	
Female	55	(77.5)	
Relationship with the patient, n (%)			71
Spouse or partner	44	(62.0)	
Child	21	(29.6)	
Sibling	2	(2.8)	
Daughter-in-law or son-in-law	2	(2.8)	
Parents	2	(2.8)	
Others	0	(0)	
Duration following bereavement			
Days, mean (SD)	375.9	(109.0)	71
<6 months, n (%)	0	(0)	
6–12 months, n (%)	33	(46.5)	
1–1.5 years, n (%)	31	(43.7)	
1.5–2 years, n (%)	7	(9.9)	
2–2.5 years, n (%)	0	(0)	
Education, n (%)			71
Elementary to junior high school	5	(7.0)	
High school	21	(29.6)	
Vocational school, junior college	22	(31.0)	
Undergraduate, graduate	23	(32.4)	
Caregiver's physical health status during the last admission, n (%)			71
Good	16	(22.5)	
Moderate	44	(62.0)	
Not good	11	(15.5)	
Bad	0	(0)	
Caregiver's mental health status during the last admission, n (%)			70
Good	7	(10.0)	

(Continues)

TABLE 1 (Continued)

Family characteristics	<i>n</i> = 71	
Moderate	34	(48.6)
Not good	23	(32.9)
Bad	6	(8.6)
Time spent with patient during the final week, <i>n</i> (%)		71
Every day	56	(78.9)
4–6 days/weeks	9	(12.7)
1–3 days/weeks	6	(8.5)
None	0	(0)
Availability of another person who could stay with the patient, <i>n</i> (%)		70
Presence	44	(62.9)
Absence	26	(37.1)
Perceived social support (how people listen to one's worries or problems), <i>n</i> (%)		71
A great deal	18	(25.4)
Quite a bit	24	(33.8)
Somewhat	25	(35.2)
A little	4	(5.6)
Not at all	0	(0)
Religious belief, <i>n</i> (%)		68
None	31	(45.6)
Buddhism	31	(45.6)
Christianity	4	(5.9)
Shinto	1	(1.5)
Others	1	(1.5)
Preparedness for bereavement, <i>n</i> (%)		70
Not at all	2	(2.9)
Not enough	9	(12.9)
Somewhat prepared	46	(65.7)
Prepared	13	(18.6)
Household income, <i>n</i> (%)		68
<1 million yen	5	(7.4)
≥1 million yen, <2 million yen	14	(20.6)
≥2 million yen, <4 million yen	25	(36.8)
≥4 million yen, <6 million yen	6	(8.8)
≥6 million yen, <8 million yen	8	(11.8)
≥8 million yen	10	(14.7)
Belief in the survival of the soul after physical death, <i>n</i> (%)		70
Agree	25	(35.7)
Somewhat agree	23	(32.9)
Somewhat disagree	14	(20.0)
Disagree	8	(11.4)

TABLE 1 (Continued)

Family characteristics	n = 71		
Experience in using psychotropic drugs or psychiatric counseling, n (%)			69
Absence	57	(82.6)	
Continued use before bereavement	9	(13.0)	
Started using after bereavement	3	(4.4)	
Cohabitation status with patients before their death, n (%)			71
Lived together	57	(82.6)	
Not lived with them	12	(17.4)	
Time interval between pre- and post-loss surveys			71
Days, mean (SD)	409.0	(105.6)	
The scales <sup>a</sup>			
PHQ-9			
At pre-loss Total score, mean (SD)	9.2	(5.7)	66
At post-loss Total score, mean (SD)	4.4	(4.5)	66
CD-RISC			
Total score, mean (SD)	58.7	(16.5)	66
Family APGAR, mean (SD)			71
Total score	7.7	(2.7)	
Adaptability, mean (SD)	1.6	(0.6)	
Partnership, mean (SD)	1.6	(0.5)	
Growth, mean (SD)	1.5	(0.7)	
Affection, mean (SD)	1.5	(0.7)	
Resolve, mean (SD)	1.5	(0.6)	

Abbreviations: CD-RISC, Connor–Davidson Resilience Scale; PHQ-9, Patients Health Questionnaire-9; SD, standard deviation.

<sup>a</sup>PHQ-9, CD-RISC.

### 3.3 | Interaction effect between family caregivers' pre-loss resilience and depressive symptoms on their post-loss depressive symptoms

The interaction effect was observed between family caregivers' pre-loss resilience and depressive symptoms on the severities of post-loss depressive symptoms even after the background variables were adjusted as covariates ( $F = 7.29$ ;  $p < 0.01$ ) (Table 2).

Among the participants with a high risk for pre-loss MDD, the depressive symptoms of the higher resilience group improved better than the lower resilience group (average changes in the PHQ-9 scores were  $-8.5$  [SD: 4.4] and  $-6.8$  [SD: 5.6], respectively; Cohen's  $d = 0.33$ ). Conversely, among the participants with a low risk for pre-loss MDD, depression improvement was similar between the resilience groups (average changes in PHQ-9 scores were  $-2.2$  [SD: 3.4] and  $-2.2$  [SD: 2.9], respectively; Cohen's  $d = 0.02$ ) (Figure 2).

### 3.4 | Association among pre-loss resilience, PTG, and grief reaction

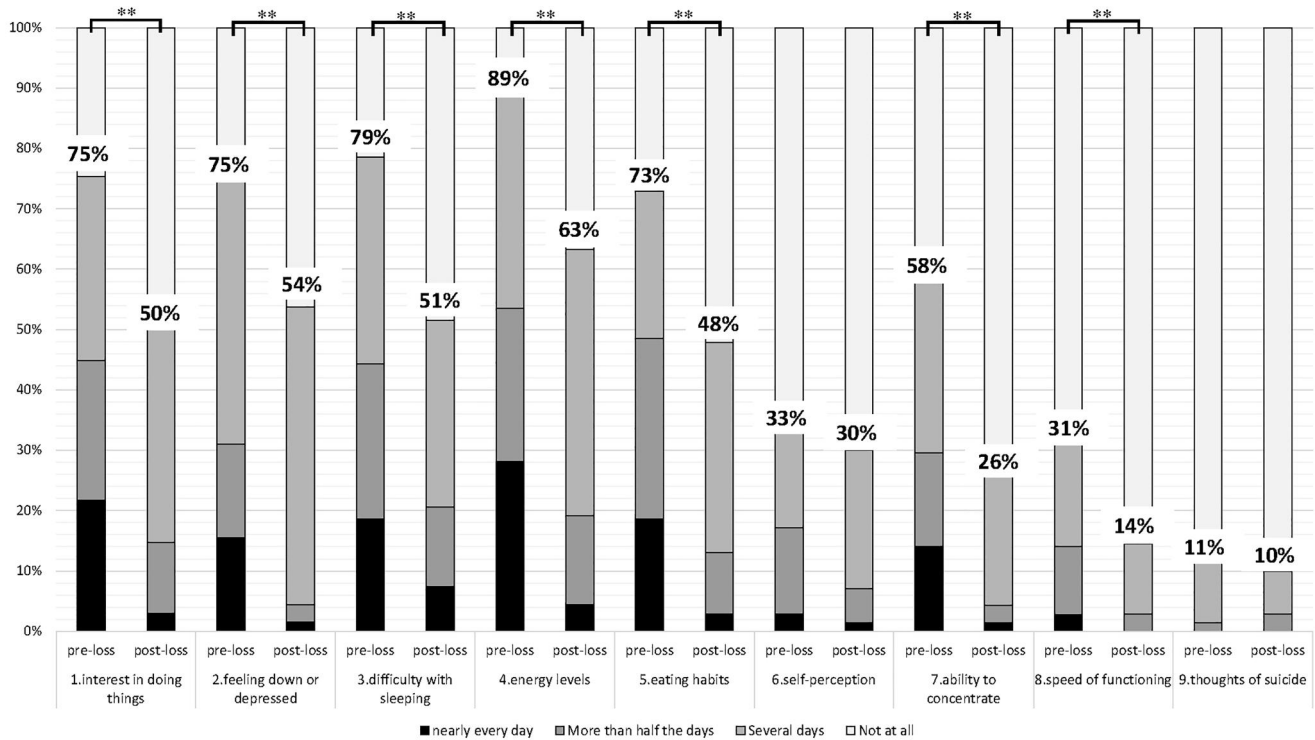
Participants had a mean BGQ score of 5.3 (SD: 2.0), with 16.2% having possible CG. The mean total PTGI-X-J score was 47.2 (SD: 28.7), with each domain having an average score of 1.9 (Table S1).

After adjusted by their pre-loss depressive symptoms, their pre-loss resilience was not associated with their severity of grief reaction ( $r = -0.07$ ,  $p = 0.63$ ). In addition, pre-loss resilience was not associated with PTG, either in total score or in any subdomains (See Tables S1 and S2).

## 4 | DISCUSSION

This study presents the following major findings: (1) among the family caregivers of patients with cancer, 47% and 15% had high risks for pre-loss and post-loss MDD, respectively; (2) in the group with a high





\*\* Wilcoxon signed rank test p<0.01

FIGURE 1 Changes in scores for each Patient Health Questionnaire-9 item after bereavement

TABLE 2 Mixed model analysis for variables predicting changes in PHQ-9 scores following bereavement

Variables <sup>a</sup>	Adjusted model by background variables <sup>b</sup>				Non-adjusted model without the interaction term				Non-adjusted model with the interaction term			
	Coefficient	Std. error	F value	p	Coefficient	Std. error	F value	p	Coefficient	Std. error	F value	p
Intercept	2.47	2.94			3.82	1.61			-0.89	2.30		
PHQ-9 score at pre-loss	0.85	0.19	20.8	<0.01	0.40	0.06	43.2	<0.01	0.94	0.20	21.7	<0.01
CD-RISC score	0.03	0.03	0.86	0.36	-0.05	0.02	5.32	0.02	0.03	0.03	0.66	0.42
Interaction:												
PHQ-9 at the pre-loss × CD-RISC	-0.01	0.003	7.29	<0.01					-0.01	0.003	7.84	<0.01

Abbreviations: CD-RISC, Connor-Davidson Resilience Scale; PHQ-9, Patients Health Questionnaire-9.

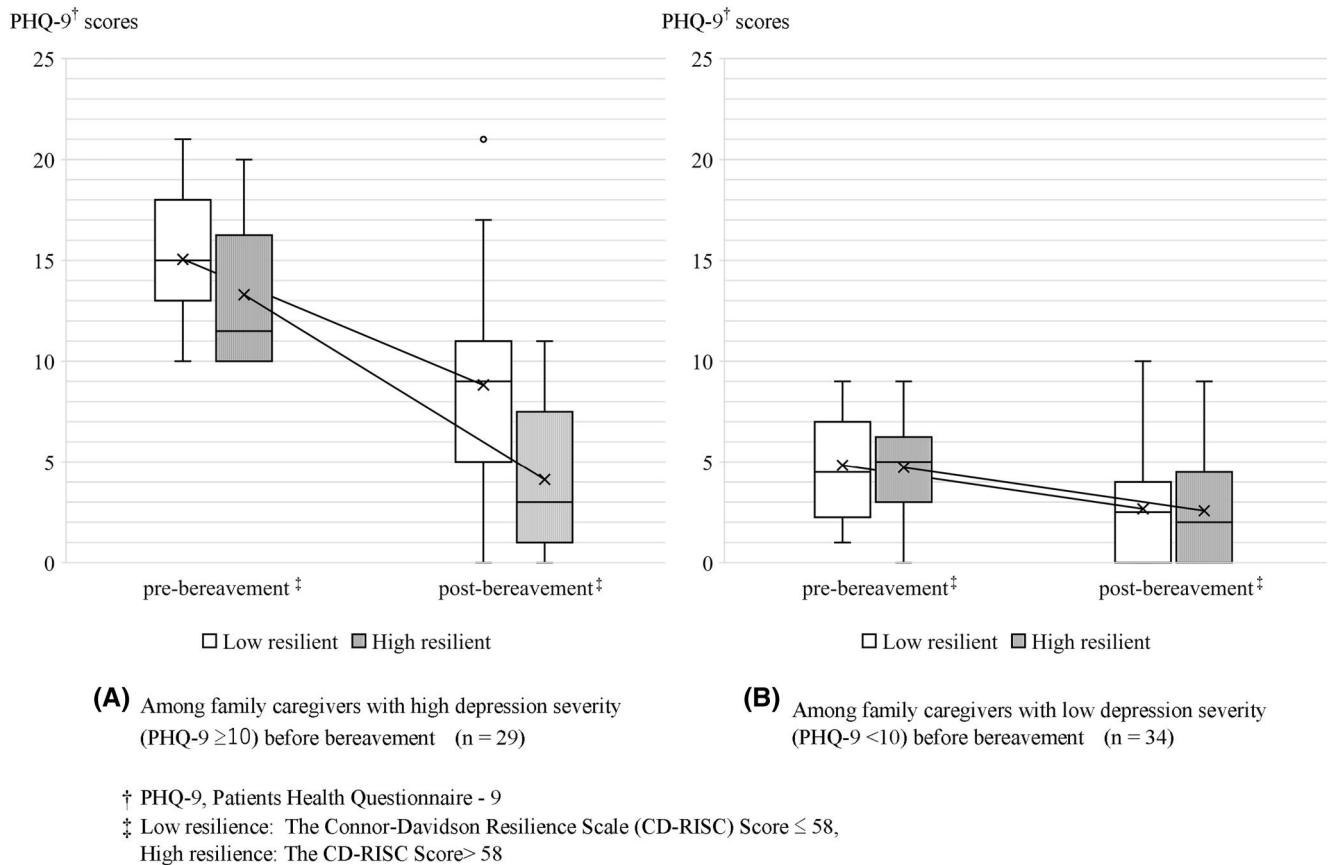
<sup>a</sup>PHQ-9, CD-RISC.

<sup>b</sup>Adjusted according to background variables, including Family APGAR scores; family caregivers' age, gender, relationship, education level, and perceived social support; belief in the survival of the soul after physical death; duration following bereavement; duration after the patient's diagnosis; availability of another person who could stay with the patient; and preparedness for bereavement.

risk for pre-loss MDD, those with greater pre-loss resilience experienced improved depressive symptoms after bereavement; and (3) pre-loss resilience was not associated with the severity of grief reaction and PTG.

This is the first cohort study in Japan to show patterns of changes in depressive symptoms after bereavement among family caregivers of patients with cancer, with the percentage of caregivers with high MDD risk decreased from 47% to 15% after bereavement. Such findings were similar to those presented in the previous cross-

sectional studies wherein the percentage was 41%<sup>9</sup> before bereavement and 17%<sup>2</sup> after bereavement. Notably, improvements in the scores for two items in the PHQ-9 regarding “depressive mood” and “loss of interest,” two core symptoms in the criteria for MDD according to the DSM-V,<sup>36</sup> had been observed after bereavement. This might suggest that increased fatigue and sleep problems due to caregiving-related exhaustion had contributed to the increase in PHQ-9 scores and that strong distress before bereavement might have also affected the caregiver's mood.



**FIGURE 2** Changes in participants' PHQ-9 scores after bereavement. (A) Among family caregivers with high depression severity (PHQ-9  $\geq 10$ ) before bereavement (n = 29); (B) Among family caregivers with low depression severity (PHQ-9 < 10) before bereavement (n = 34)

However, in end-of-life care settings, family caregivers needed care because 14% of them were persistently depressed. In fact, approximately 90% of the bereaved family caregivers with a high risk for post-loss MDD were already at a high risk for MDD before bereavement. Thus, assessing depressive symptoms and identifying high risk individuals during the care period may help identify those who need follow-up after bereavement.

Another important finding was the interaction effect between family caregivers' pre-loss depression and pre-loss resilience on their post-loss depression. This finding suggests that despite the high risk for pre-loss MDD, the higher the caregivers' resilience, the lesser the depressive symptoms after bereavement, and the lower the resilience, the more the depressive symptoms persist without improvement. Considering these results, assessing caregivers' depressive symptoms and resilience and providing appropriate support before bereavement is imperative. Notably, increasing pre-loss resilience may relieve persistent strong depressive symptoms following bereavement. However, considering that observational studies are inconclusive, future research and development of interventions focusing on family caregivers' resilience, such as psychological education based on stress resilience models, are needed to clarify whether increasing resilience can improve persistent strong depression.

On the other hand, resilience was not associated with changes in severity of depressive symptoms among family caregivers with a low

risk for pre-loss MDD. Our study and a previous study<sup>15</sup> both showed that higher resilience among family caregivers was associated with lower depressive symptom severity in end-of-life care settings. Therefore, family caregivers with a low risk for MDD might have had improved depressive symptoms due to the already existing effects of resilience on their distress. Nonetheless, further research is needed.

Moreover, family caregivers' pre-loss resilience was not associated with post-loss CG and PTG. Although the positive association between resilience and PTG was fairly reported previously,<sup>13,19</sup> Levine SZ et al. stated that higher resilience was associated with both lower PTG and lower stress.<sup>37</sup> Thus, resilience might act protectively against distress and promote recovery but might not necessarily promote growth. This finding is consistent with the reports wherein PTG showed a curvilinear relationship with CG<sup>38</sup> and depression.<sup>39</sup> However, considering the small sample size of our study, further research is needed.

#### 4.1 | Study limitations

The current study has several limitations worth noting. First, given the small sample size and high attrition rate, the results of this study remain inconclusive, with limited generalizability. The pre-

loss resilience and depression did not differ between the family caregivers who responded in the post-loss survey and those who did not. On the other hand, those who responded were more likely to live together with the patients than those who did not (See Table S3). Second, this study has a methodological deficit of being a secondary combination of two studies. Nevertheless, the evaluation of the effect of pre-loss resilience in the same subjects is considered a strength of this study. Third, considering that participants were limited to those who had lost a loved one in the HPCJ member facility, our findings cannot be extrapolated to the entire Japanese population. Fourth, we were unable to evaluate the impact of caregivers' experiences before the pre-loss survey on the association between their resilience and pre-loss depression given that resilience during daily life before the patients' cancer diagnosis could not be measured. Fifth, changes in family caregivers' resilience after bereavement could not be ascertained given that resilience was not measured during the post-loss survey. Notably, Markovitz et al. reported that resilience measured using the CD-RISC might be relatively stable trait not affected by adversity.<sup>40</sup> Sixth, given that the bereaved family suffering from psychological distress might not return the questionnaire, their depression and CG could have been underestimated. Finally, CG and depression were assessed using the BGQ and PHQ-9, which are both screening tools and are therefore incapable of providing a full clinical diagnosis.

## 4.2 | Conclusions and implications for practice

The current study primarily found that 47% of family caregivers caring for moribund patients with cancer in PCUs had a high risk for MDD. Although many family caregivers showed improvement in depressive symptoms, 15% of bereaved family caregivers still remained at high risk for MDD. Moreover, our findings showed that pre-loss resilience contributed to recovery of depressive symptoms among family caregivers with a high risk for pre-loss MDD. However, considering the small sample size of our study, further research is needed.

Careful assessment of family caregivers' pre-loss resilience and depressive symptoms is therefore necessary, given that those with a high risk for pre-loss MDD and lower resilience tend to remain at high risk for MDD after bereavement, with more than half of them possibly not receiving appropriate evidence-based care.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Yoichi Shimizu  <https://orcid.org/0000-0002-5154-090X>

Maho Aoyama  <https://orcid.org/0000-0002-6094-0788>

Yutaka J. Matsuoka  <https://orcid.org/0000-0002-8690-8129>

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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