Original Article

Post-traumatic stress disorder and its risk factors in Japanese patients living with implantable cardioverter defibrillators: A preliminary examination

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ABSTRACT

Background: Trauma reactions, including post-traumatic stress disorder (PTSD), in patients with implantable cardioverter defibrillators (ICDs) have recently garnered increased attention. The aim of this preliminary study was to examine the incidence of and risk factors for PTSD and to assess its impact on psychosocial distress and health-related quality of life (QOL) in Japanese patients with ICD.
Methods: Seventy-four outpatients with ICD (63 men, 11 women; age 59.3 ± 13.6 years) completed a questionnaire comprising a modified PTSD Checklist Specified for a stressor that included arrhythmias and ICD shocks, the Zung Self-Rating Depression Scale (SDS), the State-Trait Anxiety Inventory (STAI)-State scale, and Medical Outcomes Study 36-item Short-Form (SF-36) for health-related QOL. We compared relevant sociodemographic and medical variables of patients with and without PTSD. The mean number of days since ICD implantation was 2471 ± 703.
Results: Of 74 patients, 28 (37.8%) had received ICDs for secondary prevention, 42 (56.8%) had experienced ICD shocks, 36 (48.6%) had experienced ≥1 appropriate ICD shock, and 12 (16.2%) had experienced electrical storms. We diagnosed 19 patients (25.8%) with PTSD. Compared with the non-PTSD group, the PTSD group had significantly higher SDS and STAI-S scores and significantly lower scores in all eight subscales of the SF-36. Multiple logistic regression analysis identified experiencing ≥1 appropriate ICD shock (odds ratio [OR]: 6.0, 95% confidence interval [CI]: 1.45–24.63, and p < 0.013) and anxiolytic use (OR: 15.0, 95% CI: 3.38–66.26, and p < 0.001) as independent risk factors for PTSD.
Conclusions: Our study shows that PTSD in patients with ICD has significant psychosocial impact with associated impairment of both physical and mental QOL and suggests that, in particular, patients who experience appropriate ICD shocks or take anxiolytics require psychiatric/psychological intervention.
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1. Introduction

Implantable cardioverter defibrillators (ICD) are an established form of therapy for both primary and secondary prevention of lethal cardiac arrhythmias [1]. Previous studies have shown that ICD implantation improves the quality of life (QOL) of most patients with ICD [2,3]. However, underlying diseases or comorbidity, poor social support, or ICD-specific problems such as frequent shocks and poor understanding of ICD therapy can increase anxiety and depressive symptoms and reduce QOL in patients with ICD [2,4,5]. Ten percent to 41% of the patients with ICD experience significant depressive symptoms, whereas general or ICD-specific anxiety occurs in 13–38% [6]. Some preliminary studies have suggested that psychological distress can precipitate arrhythmic events [7,8]. Moreover, a vicious cycle may ensue, characterized by ICD implantation leading to anxiety and depression, which in turn precipitates arrhythmic events, leading to further distress [9].

Recently, trauma reactions, including post-traumatic stress disorder (PTSD), have garnered increased attention as a form of psychosocial distress that partly overlaps depressive symptoms or anxiety in patients with ICD [6,10–18]. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [19], PTSD occurs in people who have been exposed to a traumatic event that involves actual or threatened death (criterion A). PTSD symptomatology is categorized into: (1) "intrusive recollection" (persistent re-experiencing of the traumatic event, criterion B); (2) "avoidant/numbing" (persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness that was

not present before the trauma, criterion C); and (3) "hyper-arousal" (persistent symptoms of increasing arousal that were not present before the trauma, criterion D).

ICD shocks are potential traumatic stressors in patients with ICD because they may act as continuous reminders of having a potentially fatal disease [10,11]. Traumatic events experienced by patients with ICD vary widely and are complex. Furthermore, even being told that they are at risk for life-threatening arrhythmias that could lead to sudden cardiac death (i.e., ICD implantation for primary prevention) may be traumatic for patients [6]. Therefore, threats to patients' lives and well-being are not isolated events, but are persistent and enduring. Patients with PTSD symptoms may be particularly stressed by agonizing rumination and involuntary preoccupation with the underlying disease process [13].

To our knowledge, five published studies have assessed the incidence of PTSD after ICD implantation and estimated it at 7.6–26% [13–16]. However, these studies used disparate definitions of criterion A of PTSD (i.e., exposure to a traumatic event that involves actual or threatened death), presenting a methodological problem. Some reports classified rapid onset of the cardiac condition (cardiac arrest or acute myocardial infarction) as criterion A [13,15], whereas another used arrhythmia or its treatment (i.e., having an ICD) [14]. In the former, researchers excluded patients receiving ICDs for primary prevention. To cover patients with ICDs for both primary and secondary prevention, we believe that rapid onset of the cardiac condition, life-threatening arrhythmia, and ICD shocks should all separately qualify as meeting criterion A.

The aim of this preliminary study was to examine PTSD incidence and risk factors and to assess its impact on psychosocial distress and health-related QOL of Japanese patients with ICD.

2. Method

2.1. Participants and procedures

This preliminary study was conducted as a component of routine care in a clinical setting where patients with ICD had been recognized as experiencing psychosocial difficulties. During the 4 months from February to May, 2006, collaborative care between cardiologists and psychologists was offered to patients attending the ICD clinic of the Department of Cardiology, Tokyo Women's Medical University. During this period, psychologists assessed patients with ICD for psychosocial problems. Informed consent for this assessment was obtained from all participating patients; all were aged over 18 years and able to communicate in Japanese. The patients completed self-completing questionnaires (in the same order for all patients) to assess the psychological and health-related factors under investigation on the same day as their cardiological assessment. To ensure that they did not miss any questions and to help them understand the items, an experienced psychologist (S.K.) was present while the patients completed the questionnaires, which took 20–30 min. Where psychosocial problems were suspected, the psychologist recommended that the participant receive psychosocial care. The 72 patients who completed their questionnaires during the study period were retrospectively evaluated.

2.2. Measures

2.2.1. Assessment of post-traumatic stress symptoms
PTSD symptoms were assessed with a modified PTSD Checklist Specified for a stressor (PCL-S) [20]. The specified stressor was "potentially fatal cardiac arrhythmias or ICD shocks, both appropriate and inappropriate". The PCL-S is a widely used, self-reporting, extensively validated 17-item Likert scale that corresponds to the DSM-IV [19] criteria for PTSD. Participants were asked to rate

specific PTSD symptoms resulting from their potentially fatal cardiac arrhythmias or ICD shocks. To make the PCL-S easier to complete, the checklist was modified from a 5-point ("not at all", "a little bit", "moderately", "quite a bit", and "extremely") to a four-point response scale ("not at all or a little of the time", "some of the time", "good part of the time", and "most of the time") to match the format of the other questionnaires. A presumptive PTSD diagnosis was made when a participant met the DSM-IV symptom criteria, namely, at least one item from criterion B (intrusive recollection), three items from criterion C (avoidant/numbing), and two items from criterion D (hyper-arousal). Symptoms those were rated as "some of the time" or above (responses three through four for individual items) were classified as present.

2.2.2. Assessment of other psychological/health-related variables
The Zung Self-Rating Depression Scale (SDS) was used to screen for depression and to measure the severity of the depression in numerous settings [21]. The SDS is a self-reporting scale for assessing the psychological and somatic symptoms of depression. It contains 20 questions and is used to assess depression in clinical studies on cardiovascular disease [22,23].

The State-Trait Anxiety Inventory (STAI) was used to measure anxiety symptoms [24]. As state anxiety is characterized as a temporary change in a patient's emotional state due to medical illness or other external cause and because state anxiety has previously been used in clinical studies on cardiovascular disease [25,26], only the state scale measurement was used in this study. STAI scores range 20–80; higher scores indicate greater degrees of anxiety.

The Medical Outcomes Study 36-item Short-Form (SF-36) [27,28] was used to assess health-related QOL. This is a widely used self-reporting measure of general physical and mental health functioning across eight domains that include physical functioning; role-physical (limitations in the kinds/amount of work/activities due to physical functioning); bodily pain; general health; vitality; social functioning; role-emotional (limitations in the kinds/amount of work/activities due to emotional functioning); and mental health. Higher scores are indicative of greater health-related QOL. A number of validation studies have been conducted in the general and various medically ill populations. The Japanese version has demonstrated good reliability and validity in the general population of Japan [27,28].

2.3. Clinical variables associated with implantable cardioverter defibrillators

Data on the relevant clinical characteristics of the participants and the conditions under which their ICDs were implanted were obtained from medical records. The collected data included indications for ICDs, underlying heart disease, New York Heart Association functional class, shock therapy history (times of shocks, both appropriate and inappropriate; electrical storm [ES] experiences, defined as the occurrence of ≥3 separate episodes of ventricular tachycardia or ventricular fibrillation within 24 h; days since ICD implantation; days since last shock), medications, living with/without family, and employment status.

2.4. Statistical analyses

Student's t-test was used to identify differences in continuous variables between groups, and categorical variables were compared by the χ^2 test. To identify independent risk factors for PTSD, the variables were analyzed in two steps. In the first step, univariate analysis was performed. In the second step, multiple logistic regression analysis was performed, with forward stepwise

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variable selection. In the regression analysis, data sets that were significantly ($p < 0.05$) or almost significantly ($p < 0.25$) associated with the PTSD group were used in the first step. Regression coefficients were used to calculate the odds ratio (OR) and 95% confidence interval (CI) of the OR. In all statistical analyses, $p < 0.05$ was taken to indicate statistical significance. Data analyses were performed by using SPSS (version 16, SPSS, Chicago, IL, USA).

3. Results

3.1. Relevant clinical and other characteristics of participants

The relevant clinical and other characteristics of the study group are listed in Table 1. In all, 74 patients (63 men and 11 women; age, 59 ± 14 years [mean $\pm$ SD]) completed the surveys. Eight patients (11%) lived alone and 35 (47%) were not working at the time of the survey. The underlying heart disease was coronary artery disease in 19% of cases. Twenty-eight patients (38%) underwent ICD implantation for secondary prevention. The mean number of days since ICD implantation was 2471 ± 703 days. Of the 74 patients, 42 (57%) had experienced ICD shocks and 12 (16%), ES. No patients in had received non-pharmacological therapy,

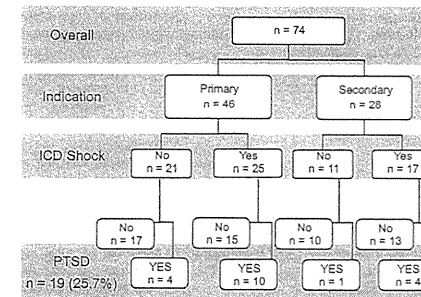such as cognitive behavioral therapy (CBT), for any psychiatric condition.

3.2. Incidence of post-traumatic stress disorder and its effect on psychological distress and health-related quality of life

Nineteen of the 74 patients (25.8%) were diagnosed with PTSD. The incidence of PTSD according to the indication for ICD and ICD shock experience is shown in Fig. 1. No differences in incidence of PTSD were found between patients who received ICD for primary prevention and those who received ICD for secondary prevention (Table 1). Remarkably, of the 21 patients with ICDs for primary prevention who had never experienced ICD shocks, four (21.1%) were diagnosed with PTSD.

Analyses of SDS and STAI-S scores as well as the eight subscales of the SF-36 are shown in Table 2. Compared with the non-PTSD group, the PTSD group had significantly higher SDS and STAI-S scores and significantly lower scores in all eight subscales of the SF-36.

3.3. Risk factors for post-traumatic stress disorder

Table 1 also lists the results of the univariate analysis performed in the first step to identify risk factors for PTSD. Compared

Table 1
Characteristics of subjects with or without PTSD.

	Overall ($n=74$)	PTSD ($n=19$)	No PTSD ($n=55$)	p
Male	63(85.1)	18(94.7)	45(81.8)	0.16
Age in years	59.3 ± 13.6	61.3 ± 11.8	58.6 ± 14.2	0.47
Indication for ICD				
Primary prevention	46(62.2)	14(73.7)	32(58.2)	
Secondary prevention	28(37.8)	5(26.3)	23(41.8)	0.18
Underlying heart disease				
Coronary artery disease	14(18.9)	4(21.1)	10(18.2)	
Idiopathic dilated cardiomyopathy	14(18.9)	5(26.3)	9(16.4)	
Hypertrophic cardiomyopathy	11(14.9)	4(21.1)	7(12.7)	
Arrhythmogenic right ventricular cardiomyopathy	2(2.7)	0(0.0)	2(3.6)	
Unclassified cardiomyopathy	2(2.8)	1(5.3)	1(1.8)	
Valvular heart disease	3(4.1)	2(10.5)	1(1.8)	
Idiopathic VF/long QT syndrome	22(29.7)	3(15.8)	19(34.5)	
Others	6(8.1)	0(0.0)	6(10.9)	0.28
NYHA functional class				
I	51(68.9)	10(52.6)	41(74.5)	
II	22(29.7)	8(42.1)	14(25.5)	
III	1(1.4)	1(5.3)	0(0.0)	0.03
Clinical variance				
≥ 1 ICD shock, total*	42(56.8)	14(73.7)	28(50.9)	0.07
≥ 1 ICD shock, appropriate	36(48.6)	14(73.7)	22(40.0)	0.01
≥ 1 ICD shock, inappropriate, never appropriate	6(8.1)	0(0.0)	6(10.9)	0.33
Number of shocks (in those receiving shocks)	13.5(21.7)	12.3(22.2)	6.1(15.6)	0.13
≥ 1 Electrical storm	12(16.2)	8(42.1)	4(7.2)	0.00
Days since ICD implantation	2471.2 ± 702.5	2519 ± 727.5	2454 ± 699.6	0.73
Days since last shock		806.4 ± 749.6	1226 ± 1018.3	0.18
Medications				
β-Blockers	35(47.3)	10(52.6)	25(45.5)	0.39
ACE inhibitors/ARBs	36(48.6)	9(47.4)	27(49.1)	0.56
Amiodarone/sotalol	34(37.8)	11(57.9)	23(41.8)	0.17
Antidepressants	4(5.4)	3(15.8)	1(1.8)	0.05
Anxiolytics	15(20.3)	10(52.6)	5(9.1)	0.00
Hypnotics	10(13.5)	5(26.3)	5(9.1)	0.07
Not living with family	8(10.8)	3(15.8)	5(9.1)	0.33
Unemployed/retired	35(47.3)	13(68.4)	22(40.0)	0.09

Values indicate number of patients (%) or the mean $\pm$ SD.
ACE, angiotensin-converting enzyme; ARB, angiotension II receptor blocker; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; PTSD, post-traumatic stress disorder; and VF, ventricular fibrillation.

* Appropriate and inappropriate shocks.

Fig. 1. The prevalence of PTSD according to indications for ICD and ICD shock experience. ICD, implantable cardioverter defibrillator and PTSD, post-traumatic stress disorder.

Table 2
Scores for psychological distress and health-related QOL with and without PTSD.

	Overall ($n=74$)	PTSD ($n=19$)	No PTSD ($n=55$)	t	p
SDS	39.7 ± 10.4	48.5 ± 8.4	36.3 ± 9.1	5.05	0.00
STAI-state	41.6 ± 12.7	49.1 ± 14.0	39.0 ± 11.2	3.17	0.00
SF-36					
Physical functioning	71.5 ± 22.3	61.9 ± 17.5	74.6 ± 22.9	-2.15	0.04
Role physical	73.5 ± 27.2	57.0 ± 28.8	79.1 ± 24.5	-3.17	0.00
Bodily pain	74.9 ± 25.0	65.8 ± 22.7	77.9 ± 25.2	-1.81	0.08
General health	46.5 ± 19.0	32.4 ± 15.2	51.1 ± 17.9	-3.98	0.00
Vitality	58.9 ± 19.8	47.4 ± 16.3	62.4 ± 19.5	-2.86	0.01
Social functioning	71.1 ± 27.0	52.1 ± 28.8	77.3 ± 23.5	-3.73	0.00
Role emotional	74.6 ± 26.6	56.9 ± 26.4	80.8 ± 24.1	-3.53	0.00
Mental health	70.7 ± 21.3	52.2 ± 18.0	76.7 ± 18.6	-4.85	0.00

PTSD, post-traumatic stress disorder; SDS, Zung Self-Rating Depression Scale; SF-36, Medical Outcomes Study 36-item Short-Form; and STAI, State-Trait Anxiety Inventory.

with the non-PTSD group, the PTSD group had significantly higher New York Heart Association functional class ($p < 0.028$), more frequent ES ($p < 0.001$), experienced ≥ 1 appropriate ICD shocks ($p < 0.01$), and more frequent use of antidepressants ($p < 0.05$) and anxiolytics ($p < 0.0001$). According to multiple logistic regression analysis, experiencing ≥ 1 appropriate ICD shock and anxiolytic use were significant independent risk factors (Table 3). The OR for experiencing ≥ 1 appropriate ICD shock was 6.0 (95% CI: 1.45–24.63, and $p < 0.013$); that for anxiolytic use was 15.0 (95% CI: 3.38–66.26, and $p < 0.001$).

4. Discussion

This cross-sectional study obtained three major findings. First, the incidence of PTSD, estimated by using the modified PCL-S for cardiac arrhythmia or ICD shock, was 25.8% in Japanese patients with ICD. Second, the PTSD was associated with significantly impaired QOL in patients with ICD for both physical and mental subscales. Third, independent risk factors for PTSD were experiencing ≥ 1 appropriate ICD shock and anxiolytic use. To our knowledge, this is the first study to evaluate PTSD in Japanese patients with ICD.

Table 3
Logistic regression analysis of risk factors for PTSD.

Variable	B	p	Odds ratio	95% Confidence interval
Anxiolytic use	2.706	0.013	14.98	3.38–66.26
≥ 1 appropriate ICD shock	1.787	0.000	5.97	1.45–24.63

-2 log likelihood $= 62.092$; $\chi^2 = 22.214$ ($p < 0.0001$); and Nagelkerke $R^2 = 0.381$.
PTSD, Post-traumatic stress disorder and ICD, implantable cardioverter defibrillator.

4.1. Incidence of post-traumatic stress disorder in patients with implantable cardioverter defibrillators

Five studies estimated the incidence of PTSD in patients with ICD to be 7.6–26% [13–17]. This variation may be caused by several factors, including PTSD diagnostic procedure and study population characteristics such as underlying disease. In the United States, the underlying diseases in 81% of patients with ICD are ischemic heart diseases such as myocardial infarction or angina pectoris, whereas in Japan, the underlying diseases in patients with ICD are ischemic heart diseases, cardiomyopathies, and idiopathic ventricular fibrillation (arrhythmia) in 34%, 35%, and 19%, respectively [29]. In the present study, 38% of the participants received ICDs for secondary prevention. Of the 28 patients who received ICDs for secondary prevention, five developed PTSD. This finding appears consistent with those of previous studies of patients with ICDs for secondary prevention: 26% in the Living with an Implanted Cardioverter Defibrillator study [13] or 19% at baseline (average of 2 years after implantation) and 12% at final follow-up (5.5 years) in a longitudinal study [15]. As was true of our study, Kapa et al. studied patients with ICD with both primary and secondary prevention indications (51% for secondary) [14]. They found that the incidence of PTSD at 2, 6, and 12 months after implantation was 21%, 12%, and 13%, respectively.

The diagnostic procedure for PTSD also affects the apparent incidence of PTSD. It remains controversial whether patients who have received ICDs for primary prevention and have not experienced ICD shocks meet criterion A for a PTSD diagnosis (exposure to a traumatic and life-threatening event) [19]. However, in the present study, 4/21 (19%) of such patients did develop PTSD. Despite the small number of subjects, this finding suggests that even being told that they are at risk of life-threatening arrhythmias and having an ICD implanted may result in the development of PTSD symptoms in some patients. PTSD occurring after receiving diagnoses of other life-threatening diseases such as HIV [30] has been reported.

The gold standard for diagnosing PTSD is a structured clinical interview such as the Clinician-Administered PTSD Scale [31]. However, in all previous studies evaluating PTSD in patients with ICD, self-reporting questionnaires such as the Impact of Events Scale-Revised [13–15,32] or the Post-traumatic Stress Diagnostic Scale [16,17,33] have been used to make a presumptive diagnosis. Although the PCL-S used in this study reflects the DSM-IV symptoms of PTSD, it also provides only a presumptive diagnosis. Further studies using a structured interview procedure for a more accurate PTSD diagnosis are needed.

4.2. Factors associated with post-traumatic stress disorder

The following key risk factors for depression or anxiety in patients with ICD have been identified: < 50 years of age, being female, premorbid psychiatric diagnosis, poor social support, and > 5 defibrillations (appropriate or inappropriate) [6]. However, information on the risk factors for PTSD in such patients has been limited.

Table 4
PTSD symptom clusters and presentation in patients with ICD[c].

Criterion A (exposure): All
- Cardiac event, SCA[a], ICD[b] implantation, shock, or electrical storm is perceived as deadly or threatening
- There is a perception of fear, helplessness, or horror

Criterion B (persistent re-experiencing): ≥1
- Recalling the cardiac event repeatedly
- Dreaming about getting shocked
- Truly believing or feeling shock is recurring (e.g., phantom shock)
- Exposure to cues that remind them of the event (e.g., couch they were on when shocked) creates psychological distress
- Exposure to cues that remind them of the event (e.g. heart racing) causes the body to react

Criterion C (persistent avoidance): ≥3
- Avoiding discussion of the event (this may include avoidance of an office visit or repeated no-shows)
- Cannot remember the event (e.g., SCA or shock)
- Avoidance of engagement in activities because of fear of shock
- Feeling estranged from family or friends following cardiac trauma
- Restricted range of affect (inability to express a range of emotions) following SCA or shock
- Belief that shock is an indicator of cardiac health and foreshortened future

Criterion D (increased arousal): ≥2
- Following cardiac trauma (e.g., surgery, SCA, shock, electrical storm)
  - Trouble falling or staying asleep
  - More irritable and angry
  - Difficulty concentrating
  - Exaggerated startle response
- Hyper-vigilant: preoccupied with heart rate, gastrointestinal and chest pain, and other bodily sensations

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[a] SCA, sudden cardiac arrest.
[b] ICD, implantable cardioverter-defibrillator.
[c] Modified from Sears et al. [6].

The effect of ICD shocks on the development of PTSD has been evaluated in five studies [13–17]; their findings are controversial. In three of the five studies, ICD shocks were associated with PTSD diagnoses [14–16]. Kapa et al. found that patients who had experienced ES had significantly higher PTSD scores within 2 months after implantation; however, they reported no difference in PTSD scores between patients who had experienced appropriate ICD shocks and those who had not [14]. Von Kanel et al. found that experiencing at least five ICD shocks (appropriate or inappropriate) was a predictor of PTSD [15]. Versteeg et al. found that ICD shock (appropriate or inappropriate) was the strongest determinant of PTSD at 3 months post-implantation, but was not associated with PTSD at 6 months post-implantation.

The role of inappropriate ICD shocks on the development of PTSD was not evaluated in the five studies mentioned above [13–17]. In the present study, inappropriate ICD shocks were not associated with PTSD. Due to the possibility of various backgrounds being associated with the development of PTSD, a more accurate role of ICD therapy as the cause of PTSD should be evaluated in different study designs, including a control population.

Psychological distress, especially PTSD symptoms, evokes sympathetic nervous system activity, which might be a trigger for a lethal arrhythmia. Although depression has been reported as a predictor for appropriate shocks (subsequent occurrence of lethal arrhythmias) among patients with ICD [34]; such a predictive effect of PTSD remains unknown. In the present study, experiencing ≥1 appropriate ICD shock was associated with PTSD, but a causal relationship cannot be inferred from this cross-sectional study.

In addition, we identified anxiolytic use as an independent risk factor. Versteeg et al. and Habibovic et al. found that baseline anxiety predicts PTSD independently [16,17]. Subjective cardiac symptoms [13] or ICD concerns [16] are reportedly associated with PTSD. It is reasonable to presume that anxiety or perceived sensitivity to cardiac conditions may lead to the subsequent prescription of anxiolytics. First-line standard pharmacologic treatment for PTSD is a selective serotonin reuptake inhibitor (SSRI), not an anxiolytic [35]. Furthermore, non-pharmacologic treatment such as CBT is generally effective for PTSD [36], and may be useful for patients with ICD [37,38]. Although the effect of SSRIs on decreasing ICD intervention is unknown, preliminary studies have reported that a SSRI [39] or SSRI in combination with CBT [40] is associated with reduced ventricular arrhythmia in patients with ICD.

Clinicians need to consider the possibility of PTSD; it is desirable to consult psychiatrists when it is suspected. We have provided examples of how PTSD symptoms may be expressed in patients with ICD according to the description of Sears et al. [6] (Table 4). Formal diagnosis requires that the disturbance (symptoms in criteria B, C, and D) last longer than 1 month and cause clinically significant distress or impairment in social, occupational, or other important areas of functioning [19].

4.3. Limitations of this study

This preliminary study has several limitations. First, there were possible design flaws in that it did not enroll consecutive patients, which may have created bias. Moreover, it was retrospective, of cross-sectional design, and involved a single center. Second, we used a modified version of the PCL-S, a self-reporting questionnaire, as a diagnostic tool. As explained in Section 4.1, this tool only provides a presumptive diagnosis. Furthermore, modification of the PCL-S may have influenced its discriminant properties. Third, because the number of subjects in this study was relatively small, subgroup analysis was not feasible. To clarify these issues, we suggest that further prospective clinical investigations, including a control population, must be carried out.

5. Conclusions

The present preliminary study shows that PTSD has a significant psychosocial impact with associated impairment of both physical and mental QOL in patients with ICD. In particular, our findings suggest that patients who have experienced appropriate ICD shocks or are taking anxiolytics require psychiatric/psychological intervention.

References

[1] Goldberger Z, Lampert R. Implantable cardioverter-defibrillators. Expanding indications and technologies. JAMA 2006;295:809–18.
[2] Sears SF, Conti JB. Quality of life and psychological functioning of ICD patients. Heart 2002;87:488–93.
[3] Spurrell P, Mitchell A, Kamalvand K, et al. Quality of life after use of the patient activated atrial defibrillator. Int J Clin Pract 2003;57:30–4.
[4] Thomas SA, Friedmann E, Kao CW, et al. Quality of life and psychological status of patients with implantable cardioverter defibrillators. Am J Crit Care 2006;15:389–98.
[5] Jacq F, Foulldrin G, Savouré A, et al. A comparison of anxiety, depression, and quality of life between device shock and nonshock groups in implantable cardioverter defibrillator recipients. Gen Hosp Psychiatry 2009;31:266–73.
[6] Sears SF, Hauf JD, Kirian K, et al. Posttraumatic stress and the implantable cardioverter-defibrillator patient: what the electrophysiologist needs to know. Circ Arrhythmia Electrophysiol 2011;4:242–50.
[7] Whang W, Albert CM, Sears Jr. SF, et al. Depression as a predictor for appropriate shocks among patients with implantable cardioverter-defibrillators: results from the Triggers of Ventricular Arrhythmias (TOVA) study. J Am Coll Cardiol 2005;45:1090–5.
[8] Heller SS, Ormont MA, Lidagoster L, et al. Psychosocial outcome after ICD implantation: a current perspective. Pacing Clin Electrophysiol 1998;21:1207–15.
[9] Pedersen SS, Van den Broek KC, Sears SF. Psychological intervention following implantation of an implantable defibrillator: a review and future recommendations. Pacing Clin Electrophysiol 2007;30:1546–54.
[10] Hamner M, Hunt N, Gee J, et al. PTSD and automatic implantable cardioverter defibrillators. Psychosomatics 1999;40:82–5.
[11] Neel M. Posttraumatic stress symptomatology in patients with automatic implantable cardioverter defibrillators: nature and intervention. Int J Emergency Ment Health 2000;2:259–63.
[12] Prudente LA, Reigle J, Bourguignon C, et al. Psychological indices and phantom shocks in patients with ICD. J Interventional Card Electrophysiol 2006;5:185–90.
[13] Ladwig KH, Baumert J, Marten-Mittag B, et al. Posttraumatic stress symptoms and predicted mortality in patients with implantable cardioverter-defibrillators: results from the prospective living with an implanted cardioverter-defibrillator study. Arch Gen Psychiatry 2008;65:1324–30.
[14] Kapa S, Rotondi-Trevisan D, Mariano Z, et al. Psychopathology in patients with ICDs over time: results of a prospective study. Pacing Clin Electrophysiol 2010;33:198–208.
[15] von Kanel R, Baumert J, Kolb C, et al. Chronic posttraumatic stress and its predictors in patients living with an implantable cardioverter defibrillator. J Affect Disord 2010;31:344–52.
[16] Versteeg H, D.A.M.J. Theuns, Erdman RAM, et al. Posttraumatic stress in implantable cardioverter defibrillator patients: the role of preimplantation distress and shocks. Int J Cardiol 2011;3:438–9.
[17] Habibović M, van den Broek KC, Alings M, et al. Posttraumatic stress 18 months following cardioverter defibrillator implantation: shocks, anxiety, and personality. Health Psychol 2012;31:186–93.
[18] Bilanovic A, Irvine J, Kovacs AH, et al. Uncovering phantom shocks in cardiac patients with an implantable cardioverter defibrillator. Pacing Clin Electrophysiol 2013;36:673–83.
[19] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington: American Psychiatric Association; 1994 ([Revised]).
[20] Weathers F.W., Litz B.T., Herman D.S., et al. The PTSD checklist: reliability, validity, & diagnostic utility. Paper presented at the Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio, Texas; 1993.
[21] W.W.K. Zung. A self-rating depression scale. Arch Gen Psychiatry 1965;12:63–70.
[22] Shiotani I, Sato H, Kinjo K, et al. The Osaka Acute Coronary Insufficiency Study (OACIS) group. Depressive symptoms predict 12-month prognosis in elderly patients with acute myocardial infarction. J Cardiovasc Risk 2002;9:153–60.
[23] Pihl E, Jacobsson A, Fridlund B, et al. Depression and health-related quality of life in elderly patients suffering from heart failure and their spouses: a comparative study. Eur J Heart Fail 2005;7:583–9.
[24] Spielberger CD, Gorssuch RL, Lushene PR, et al. Manual for the State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press; 1983.
[25] Kamphuis HC, de Leeuw JR, Derksen R, et al. Implantable cardioverter defibrillator recipients: quality of life in recipients with and without ICD shock delivery: a prospective study. Europace 2003;5:381–9.
[26] van den Broek KC, Nyklícek I, van der Voort PH, et al. Risk of ventricular arrhythmia after implantable defibrillator treatment in anxious type D patients. J Am Coll Cardiol 2009;54:531–7.
[27] Fukuhara S, Bito S, Green J, et al. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. J Clin Epidemiol 1998;5:1037–44.
[28] Fukuhara S, Ware JE, Kosinski M, et al. Psychometric and clinical tests of validity of the Japanese SF-36 Health Survey. J Clin Epidemiol 1998;51:1045–53.
[29] The Japanese Circulation Society, The Japanese Association for Thoracic Surgery, The Japanese Society for Artificial Organs, The Japanese Society for Cardiovascular Surgery, The Japanese College of Cardiology, The Japanese Society of Electrocardiology, The Japanese Heart Failure Society, The Japanese Heart Rhythm Society. Guidelines for the Diagnosis and Treatment of Cardiovascular Diseases; 2005.
[30] Nightingale VR, Sher TG, Mattson M, et al. The effects of traumatic stressors and HIV-related trauma symptoms on health and health related quality of life. AIDS Behav 2011;15:1870–8.
[31] Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician-Administered PTSD Scale. J Traumatic Stress 1995;8:75–90.
[32] Weiss DS, Marmar CR. The impact of event scale-revised. In: Wilson J, Keane T, editors. Assessing Psychological Trauma and PTSD. New York: Guilford; 1997 pp. 344–62.
[33] Foa E, Cashman L, Jaycox L, et al. The validation of a self-report measure of posttraumatic stress disorder: the posttraumatic diagnostic scale. Psychol Assess 1997;9:445–51.
[34] Whang W, Albert CM, Sears Jr. SF, et al. Depression as a predictor for appropriate shocks among patients with implantable cardioverter-defibrillators: results from the Triggers of Ventricular Arrhythmias (TOVA) study. J Am Coll Cardiol 2005;45:1090–5.
[35] Stein DJ, Ipser J, McAnda N. Pharmacotherapy of posttraumatic stress disorder: a review of meta-analyses and treatment guidelines. CNS Spectrums 2009;14 (1 Suppl 1):25–31.
[36] Mendes DD, Mello MF, Ventura P, et al. A systematic review on the effectiveness of cognitive behavioral therapy for posttraumatic stress disorder. Int J Psychiatry Med 2008;38:241–59.
[37] Frizelle DJ, Lewin RJP, Kaye G, et al. Cognitive-behavioral rehabilitation programme for patients with an implanted cardioverter defibrillator: a pilot study. Brit J Health Psychol 2004;9:381–92.
[38] Sears SF, Sowell LDV, Kuhl EA, et al. The ICD shock and stress management program: a randomized trial of psychosocial treatment to optimize quality of life in ICD patients. Pacing Clin Electrophysiol 2007;30:858–64.
[39] Leftheriotis D, Flevari P, Ikonomidis I, et al. The role of the selective serotonin re-uptake inhibitor sertraline in nondepressive patients with chronic ischemic heart failure: a preliminary study. Pacing Clin Electrophysiol 2010;33:1217–23.
[40] Kuijpers PM, Honig A, Wellens HJ. Effect of treatment of panic disorder in patients with frequent ICD discharges: a pilot study. Gen Hosp Psychiatry 2002;24:181–4.
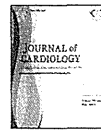
Original article

Impact of clustered depression and anxiety on mortality and rehospitalization in patients with heart failure☆

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ABSTRACT

Background: Anxiety is often present in patients with depression. The aim of this study was to evaluate the impact of clustered depression and anxiety on mortality and rehospitalization in hospitalized patients with heart failure (HF).
Methods: A total of 221 hospitalized patients with HF, who completed the questionnaires, were analyzed in this prospective study (mean age 62 ± 13 years; 28% female). One-third patients had implanted cardiac devices. Depression was defined as a Zung Self-Rating Depression Scale index score of ≥60 and anxiety was defined as a State-Trait Anxiety Inventory score of ≥40 (male) or ≥42 (female). The primary outcome was the composite of death from any cause or rehospitalization due to worsened HF and refractory arrhythmia.
Results: Of the 221 HF patients, 29 (13%) had depression alone, 80 (36%) had anxiety alone, and 46 patients (21%) had both depression and anxiety. During an average follow-up of 41 ± 21 months, patients with depression alone and those with clustered depression and anxiety were at an increased risk of the primary outcome [hazard ratio (HR) 2.24, 95% confidence interval (CI): 1.17–4.28, p = 0.01 and HR 2.75, 95% CI: 1.51–4.99, p = 0.01, respectively] compared to patients with no symptoms. Multivariate analysis after adjusting for age, gender, New York Heart Association functional class, B-type natriuretic peptide, device implantation, renal dysfunction, and left ventricular dysfunction showed that clustered depression and anxiety, but not depression alone or anxiety alone, was an independent predictor of the primary outcome (HR 1.96, 95% CI: 1.00–3.27, p = 0.04).
Conclusions: Our results showed that clustered depression and anxiety were associated with worse outcomes in patients with HF.

Introduction

Heart failure (HF) is caused from most types of heart diseases and is a chronic and progressive condition that is a major cause of morbidity and mortality [1]. The psychological issues, particularly emotional distress including depression and anxiety, are common in patients with HF [1–5]. Several studies have focused on the role of depression and suggested that depression is a possible risk factor for adverse outcomes in patients with HF [4–7]. The prevalence of depression is reported to be approximately 15–40% in patients with HF, and depression is independently associated with poor outcomes [5–13]. A meta-analysis showed that depression is common among patients with HF, and substantially higher rates of clinically significant depression are present among patients with more severe HF [4].

There have been fewer studies regarding anxiety in patients with HF. A previous report showed that 18.4% of patients with

HF had an anxiety disorder [14]. Another report showed that the score for anxiety symptoms was higher in patients with HF than in healthy controls [15]. However, this issue has remained controversial [1]. In some studies, no association has been found between anxiety symptoms and cardiac events in patients with HF [16–19].

Recently, van den Broek et al. [20] focused on the impact of clustering psychosocial risk factors on clinical outcomes in patients with implantable cardioverter defibrillators (ICDs) and showed that ICD patients with both anxiety and Type D personality were at an increased risk of ventricular arrhythmia. In that study, the risk factors were clustered because psychological risk factors often occurred together, but not individually, and the clustering of psychological risk factors may pose a high-risk factor for clinical events than would a single risk factor in cardiac patients [20,21]. Although depression and anxiety have been discussed separately as psychological factors, they frequently cluster within a patient [22]. The signs and symptoms of anxiety are often present in patients with depression, and the two conditions may play a partial role in a pathophysiological process of HF [23]. Some studies have shown that the clustered depression and anxiety worsened patients' health status following myocardial infarction or percutaneous coronary intervention [24,25]. From this viewpoint, clustered depression and anxiety may be clinically valuable as an indicator of psychological distress in patients with HF. However, a few studies have investigated this issue. The aim of this study was to evaluate the effect of clustered depression and anxiety on mortality and rehospitalization in patients with HF.

Methods

We conducted a substudy of the prospective observational study comprising hospitalized patients with cardiovascular disease, who were admitted to the Cardiology Department of Tokyo Women's Medical University Hospital between June 2006 and April 2008. Patients with dementia, delirium, or other conditions (e.g. unconsciousness, intensive care, and end stage of another life-threatening disease) that make completing self-reported written questionnaires difficult were excluded. Among them, 221 patients with a New York Heart Association (NYHA) functional class ≥2 on admission, who were diagnosed with HF, and who completed the questionnaires were included in this study (Fig. 1). The details of

the study have been reported elsewhere [26]. The protocol was approved by the institutional review board of Tokyo Women's Medical University. All patients gave written informed consent.

Assessment of depression and anxiety

The majority of patients received the psychological questionnaires within 3 days (2 ± 1 days) after their admission to the hospital. For patients who initially required intensive treatment, these questionnaires were received after their transfer to the general cardiology ward. The Zung Self-Rating Depression Scale (SDS) was used to screen for depression and to measure the severity of the depression in a number of settings [27–31]. The Zung SDS is a self-reported scale containing 20 questions that assess the psychological and somatic symptoms. The Zung SDS score has been reported to be a primary discriminating variable in distinguishing depressed from non-depressed persons and indicates likelihood ratio positive for major depression as 3.3 [95% confidence interval (CI): 1.3–8.1] and likelihood ratio negative as 0.35 (95% CI: 0.2–0.8) [29]. The Zung SDS score has also been used to assess depression in clinical studies on cardiovascular diseases [32–36]. A cutoff index score of 60 has been shown to detect clinical depression while avoiding an abundance of false positives in sick patients [37–40]. In this study, depression was defined as a Zung SDS index score of ≥60.

The State-Trait Anxiety Inventory (STAI) was used to measure anxiety symptoms [41]. In this study, only the state-scale measurement was used because state anxiety is characterized as a temporary change in each patient's emotional state due to medical illness or other external cause, the measurement has also been used in clinical studies on cardiovascular diseases [16,20,42]. The STAI comprises 20 items, and each item is scored on a four-point scale from 1 (not at all) to 4 (very much so). The STAI scores range from 20 to 80, with higher scores indicating greater levels of anxiety. Anxiety was defined as a score of ≥40 (male) or ≥42 (female) [43,44].

Follow-up

After discharge, patients were seen as outpatients at our hospital or their general practitioner's clinic at 1- to 3-month intervals until October 2011. Patients receiving pacing device therapy, including pacemakers, cardiac resynchronization therapy (CRT), and ICD, were also followed every 3–6 months at our pacemaker/ICD clinic. The information about deceased patients was obtained from the medical records, family members, their general practitioners, and the admitting hospital.

Clinical outcomes

The primary outcome was the composite of death from any cause and rehospitalization due to worsened HF and refractory arrhythmia from the time of enrollment to the first event. Worsened HF was defined by signs and symptoms, such as dyspnea, rales, and ankle edema, as well as by the need for treatment with diuretics, vasodilators, positive inotropic drugs, or an intra-aortic balloon pump. Refractory arrhythmia was defined as supraventricular or ventricular tachyarrhythmia that required external defibrillation or pacing, intravenous antiarrhythmics, such as amiodarone and nifekalant, catheter ablation, or implantation of an ICD, or bradyarrhythmia that required implantation of a pacemaker. Both supraventricular and ventricular arrhythmias are common in patients with HF, and cause symptoms, hemodynamic instability, and morbidities such as stroke and sudden death. Therefore, we included rehospitalization for refractory arrhythmia in
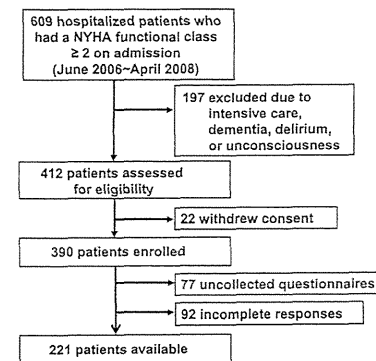
Fig. 1. The flow diagram of study subjects. NYHA, New York Heart Association.

609 hospitalized patients who had a NYHA functional class ≥ 2 on admission (June 2006~April 2008)

→ 197 excluded due to intensive care, dementia, delirium, or unconsciousness

412 patients assessed for eligibility

→ 22 withdrew consent

390 patients enrolled

→ 77 uncollected questionnaires
→ 92 incomplete responses

221 patients available

the primary endpoint. The second outcome was death from any cause.

Data analysis

The data are presented as either mean ± standard deviation (SD) or number of patients. We created four groups on the basis of depression and anxiety: (1) depression alone, (2) anxiety alone, (3) clustered depression and anxiety, and (4) no symptoms (no depression nor anxiety). Baseline clinical data were compared between the groups using analysis of variance (ANOVA). The Cox proportional hazards model was used to assess the relationship of depression, anxiety, and the cluster of both with clinical outcomes. We first assessed the unadjusted relationship of the following variables at discharge with the primary outcome: female gender, age $\geq$65 years, NYHA functional class, plasma B-type natriuretic peptide (BNP) concentration >250 pg/ml [45,46], implantation of an ICD/CRT with a defibrillator (CRT-D), left ventricular ejection fraction (LVEF) $\leq$35%, estimated glomerular filtration rate (eGFR) by the Modification of Diet in Renal Disease formula [47] <60 ml/min/1.73 m^2, depression, anxiety, and clustered depression and anxiety. Then, we assessed the relationship of depression, anxiety, and the cluster of both with the primary outcome after controlling for gender, age $\geq$65 years, NYHA functional class, BNP >250 pg/ml, implantation of an ICD/CRT-D, LVEF $\leq$35%, and eGFR <60 ml/min/1.73 m^2. The cumulative event-free rates were calculated using the Kaplan–Meier method. The data analyses were performed with SPSS (Statistical Package for the Social Sciences) statistical software (version 11.01, SPSS Inc., Chicago, IL, USA). A p-value of <0.05 was considered significant.
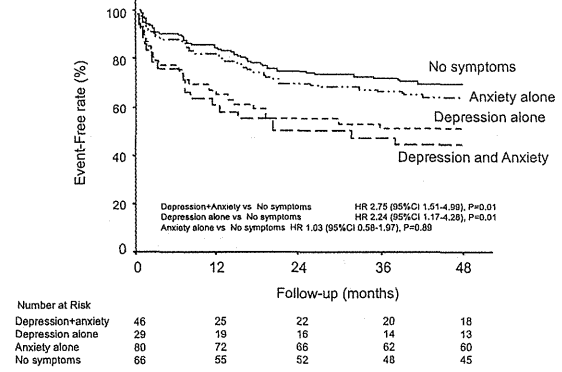
Results

Patients

A total of 221 patients with HF who completed both the Zung SDS and STAI were included in this analysis. More than half of the patients (64%) had a non-ischemic etiology, and one-third had implanted cardiac devices. Five patients (2%) who were diagnosed with major depression by a psychiatrist had taken antidepressants (Table 1). In our sample, none of the patients with depression received non-pharmacological treatment such as cognitive behavior therapy.

Psychological distress and outcomes

Overall, 75 patients (34%) were diagnosed as having depression and 126 patients (57%) as having anxiety. Among them, 29 patients (13%) had depression alone, 80 patients (36%) had anxiety alone, and 46 patients (21%) had both depression and anxiety (Table 1).

During an average follow-up of 41 ± 21 months, 69 patients (31%) met the primary outcome: 31 patients died and 38 patients required rehospitalization due to worsened HF or refractory arrhythmia. Kaplan–Meier curves for the primary outcome in the four groups are shown in Fig. 2. Patients with depression alone and those with clustered depression and anxiety were at an increased risk of the primary outcome [hazard ratio (HR) 2.24, 95% CI: 1.17–4.28, p = 0.01 and HR 2.75, 95% CI: 1.51–4.99, p = 0.01, respectively] compared to patients with no symptoms. Causes of death and rehospitalization are shown in Table 2. Kaplan–Meier curves for death from any cause are shown in Fig. 3. Patients with clustered depression and anxiety were at an increased risk of death

Table 1
Patient characteristics.

	Depression alone (n = 29)	Anxiety alone (n = 80)	Depression + anxiety (n = 46)	No symptoms (n = 66)	p value
Age (years)	61 ± 10	62 ± 14	60 ± 12	62 ± 12	0.18
Female	7 (24%)	22 (28%)	14 (30%)	19 (25%)	0.91
Underlying heart disease					0.01
Coronary artery disease	7 (24%)	20 (25%)	5 (11%)	39 (59%)	
Non-ischemic cardiomyopathy	11 (38%)	23 (29%)	37 (80%)	44 (67%)	
Valvular heart disease	10 (34%)	20 (25%)	2 (4%)	7 (11%)	
Congenital heart disease	0 (0%)	1 (1%)	2 (4%)	2 (3%)	
BNP on admission (pg/ml)	269 (84–709)	275 (4–2254)	349 (8–5271)	152 (4–8454)	0.01
BNP at discharge (pg/ml)	236 (48–826)	242 (18–1478)	288 (15–2326)	120 (5–4926)	0.01
NYHA functional class on admission (II/III/IV)	25/4/0	67/15/0	23/22/1	56/10/0	<0.01
NYHA functional class at discharge (II/III/IV)	27/2/0	77/3/0	30/15/1	64/2/0	<0.01
LVEF (%)	35 ± 10	38 ± 12	35 ± 15	39 ± 16	0.21
eGFR (ml/min/1.73 m^2)	72 ± 36	76 ± 38	70 ± 43	80 ± 38	0.16
Implanted cardiac devices					
Pacemaker/CRT-P	3 (10%)	5 (6%)	7 (15%)	7 (11%)	0.20
ICD/CRT-D	7 (24%)	18 (23%)	15 (33%)	15 (23%)	0.16
Comorbidities					
Hypertension	10 (34%)	31 (39%)	18 (39%)	25 (38%)	0.16
Diabetes	3 (10%)	27 (34%)	11 (24%)	28 (42%)	0.05
Major depression	1 (3%)	0 (0%)	3 (7%)	1 (2%)	0.04
Medications at discharge					
Beta-blockers	21 (72%)	59 (74%)	33 (72%)	43 (65%)	0.76
ACE inhibitors/ARBs	25 (86%)	69 (86%)	42 (91%)	59 (89%)	0.57
Spironolactone/eplerenone	16 (55%)	38 (48%)	30 (65%)	31 (47%)	0.15
Calcium channel blockers	16 (55%)	55 (69%)	19 (41%)	43 (65%)	<0.01
Aspirin	10 (34%)	29 (36%)	15 (33%)	33 (50%)	0.09
Warfarin	16 (55%)	42 (53%)	32 (70%)	22 (33%)	0.11
Amiodarone	11 (38%)	22 (28%)	20 (43%)	9 (14%)	<0.01
Antidepressants	1 (3%)	0 (0%)	3 (7%)	1 (2%)	0.16
Married	26 (90%)	73 (91%)	36 (78%)	64 (97%)	<0.01
Employed	13 (45%)	40 (50%)	13 (28%)	34 (52%)	0.04

Values are n (%) or mean ± SD or median (range).
ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BNP, B-type natriuretic peptide; CRT, cardiac resynchronization therapy; CRT-D, CRT with a defibrillator; CRT-P, CRT with a pacemaker; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Fig. 2. Kaplan–Meier curve for the primary outcome (death from any cause or rehospitalization due to worsened heart failure or refractory arrhythmia) in the four heart failure patient groups on the basis of depression and anxiety. HR, hazard ratio; CI, confidence interval.

Table 2
Causes of death and rehospitalization for cardiac events.

	Depression alone (n = 29)	Anxiety alone (n = 80)	Depression + anxiety (n = 46)	No symptoms (n = 66)	p value
Death from any cause	8 (28%)	4 (5%)	17 (37%)	2 (3%)	<0.01
Cardiac death	8 (28%)	4 (5%)	16 (35%)	2 (3%)	<0.01
Sudden death	2 (7%)	1 (1%)	1 (2%)	0 (0%)	0.96
Heart failure	6 (21%)	3 (4%)	15 (33%)	2 (3%)	<0.01
Non-cardiac death	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0.06
Hospitalization for heart failure	7 (24%)	15 (19%)	5 (11%)	4 (6%)	0.90
Hospitalization for refractory arrhythmia	3 (10%)	2 (3%)	1 (2%)	1 (2%)	0.29

Values are n (%).

from any cause (HR 5.59, 95% CI: 2.84–10.90, p < 0.01) compared to patients with no symptoms.

The univariate analysis showed that in addition to NYHA functional class, implantation of an ICD/CRT-D, LVEF $\leq$35%, BNP at discharge >250 pg/ml, eGFR <60 ml/min/1.73 m^2, depression alone, and a combination of depression and anxiety, but not anxiety alone, were significant predictors for the primary outcome (Table 3).
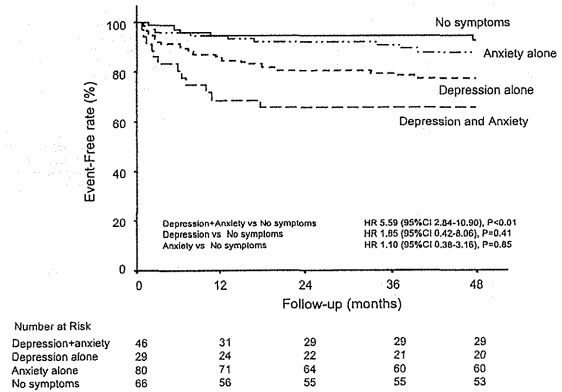
Fig. 3. Kaplan–Meier curve for death from any cause in the four heart failure patient groups on the basis of depression and anxiety. HR, hazard ratio; CI, confidence interval.

Table 3
Univariate predictors for the primary outcome.

	Hazard ratio (95% CI)	p value
Female gender	0.70 (0.43–1.15)	0.16
Age ≥65 years	0.89 (0.56–1.42)	0.64
NYHA functional class at discharge	3.97 (2.61–6.04)	<0.01
Implantation of an ICD/CRT-D	4.26 (2.56–7.07)	<0.01
eGFR <60 ml/min/1.73 m^2	2.88 (1.81–4.59)	<0.01
BNP at discharge >250 pg/ml	2.95 (1.80–4.81)	<0.01
LVEF ≤35%	1.99 (1.24–3.19)	<0.01
Depression	2.59 (1.56–4.20)	<0.01
Anxiety	1.71 (0.98–2.98)	0.05
Depression and anxiety	2.63 (1.56–4.41)	<0.01

BNP, B-type natriuretic peptide; CRT-D, cardiac resynchronization therapy with a defibrillator; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Table 4
Relationship of depression and anxiety with the primary outcome after adjusting for age, gender, New York Heart Association class, device implantation, estimated glomerular filtration rate, B-type natriuretic peptide, and left ventricular ejection fraction.

	Hazard ratio (95% CI)	p value
Depression	1.69 (0.97–2.95)	0.06
Anxiety	1.46 (0.80–2.65)	0.21
Depression and anxiety	1.96 (1.00–3.27)	0.04

The relationship between depression and anxiety with the primary outcome after adjusting for age, gender, NYHA class, device implantation, eGFR, BNP, and LVEF revealed that patients with clustered depression and anxiety had an increased risk of the primary outcome, but depression alone was not related to the primary outcome (Table 4).

Discussion

Our study revealed that the prevalence of clustered depression and anxiety was 20% in hospitalized patients with HF. Furthermore, we found that patients with both depression and anxiety were at an increased risk of the primary composite outcome: death from any cause and rehospitalization due to worsened HF and refractory arrhythmia. Finally, clustered depression and anxiety, but not depression or anxiety alone, were shown to be independent factors associated with worsening clinical outcomes.

Several studies have shown that depression is an independent predictor of mortality in patients with HF [1–13]. In our study, depression was a risk factor in the univariate analysis but was not an independent factor after adjusting for clinical variables at discharge related to the primary outcome. There are a number of possible reasons for the differences in our results compared with those in the previous reports. First, our study had a high prevalence (one-third) of patients with an ICD/CRT-D. At present, an ICD is the principle therapy in HF patients for preventing sudden cardiac death. It is increasingly used due to the extended indication for primary prevention. However, ICD-specific problems, such as frequent shocks and a poor understanding of ICD therapy, increase depressive symptoms and reduce the quality of life for the ICD patients [39,48–50]. Our main study showed that an ICD implantation was significantly associated with depression [26]. Furthermore, the prevalence of depression increased as the NYHA functional class grade increased [4]. In our study, 18 of 23 patients (78%) with NYHA class III/IV at discharge were diagnosed with depression by the Zung SDS. The presence of an ICD/CRT-D and NYHA functional class III/IV may have confounded the association

between depression and the primary outcome. Therefore, depression alone was thought not to be a predictor in this study after adjusting for multiple variables.

State anxiety is a transient mental or emotional reaction to several stressors, including medical illness. In a sense, it is thought to be a normal reaction in hospitalized patients and an inevitable result of hospitalization. A Japanese report showed that anxiety has been reported to be independently associated with rehospitalization due to worsened HF in outpatients with stable HF [44]. However, in general, an association between anxiety and mortality or long-term cardiac events in patients with HF has not been found [16–19]. Katon et al. suggested that the combination of depression and anxiety is associated with poor treatment adherence and increased medical complications in patients with chronic medical illness, which may be a severe consequence [51]. Anxiety and depression are different disorders, and the way in which their mechanisms may interact in the development of cardiac events or death are not understood. In the real world, however, psychological factors may cluster together within individuals to increase the risk of subsequent medical events [21]. There is a possibility that patients with higher psychological distress are selected by combining anxiety with depression.

In our study, HF was a major cause of death, and the rate of HF was significantly higher in patients with both depression and anxiety than in those with either depression or anxiety only or those with no symptoms. Although its pathophysiologic mechanisms are not completely understood, psychological distress may affect the treatment adherence behavior in patients with HF [52]. Poor adherence to treatment is associated with increased morbidity and mortality in patients with HF [53]. Clustered depression and anxiety can be a stronger predictive marker of the severity of the illness or poor prognosis than depression alone in hospitalized patients with HF. This cluster may also be an important marker for psychological distress, particularly in hospitalized patients with HF.

Study limitations

There were some limitations in this study. First, this was a single-center cohort study. The clinical characteristics of our patients might not reflect those of general cardiovascular patients with HF. Second, the patients admitted to our hospital were not consecutively enrolled in our main study. Many patients who received emergent or intensive care were not enrolled because they could not complete the questionnaires. Third, the questionnaires were not completed prior to discharge. The primary aim of our main study was to evaluate the prevalence and distribution of depression in hospitalized patients. Moreover, the length of the hospital stay in our patients ranged from a few days to several months because the severity of HF or comorbidities was heterogeneous. For a long-term prognosis, the assessment just before discharge might be more appropriate. However, previous studies have demonstrated that depression at the time of hospitalization, not prior to discharge, is associated with a poorer prognosis in patients with cardiovascular disease [54–57]. Fourth, the number of subjects was relatively small. Therefore, subgroup analysis was not feasible.

Conclusions

Our results showed that clustered depression and anxiety were predictors of death from any cause or rehospitalization due to worsened HF and refractory arrhythmia in patients with HF. This cluster may be an important marker for poor outcomes in patients with HF.

Conflict of interest

None declared.

References

[1] Pelle AJM, Gidron YY, Szabó BM, Denollet J. Psychological predictors of prognosis in chronic heart failure. J Card Fail 2008;14:341–50.
[2] MacMahon KM, Lip GY. Psychological factors in heart failure: a review of the literature. Arch Intern Med 2002;162:509–16.
[3] Caro MA, Sowden GL, Mastromauro CA, Mahnks S, Beach SR, Januzzi JL, Huffman JC. Risk factors for positive depression screens in hospitalized cardiac patients. J Cardiol 2012;60:72–7.
[4] Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527–37.
[5] Jiang W, Alexander J, Christopher EJ, Kuchibhatla M, Gaulden LF, Cuffe MS, Blazing MA, Davenport C, Califf RM, Krishnan RR, O'Connor CM. Relationship of depression to increase risk of mortality and rehospitalization in patients with congestive heart failure. Arch Intern Med 2001;161:1849–56.
[6] Vaccarino V, Kasl S, Abramson J, Krumhoz H. Depressive symptoms and risk of functional decline and death in patients with heart failure. J Am Coll Cardiol 2001;38:199–205.
[7] Kato N, Kinugawa K, Shiga T, Hatano M, Takeda N, Imai Y, Watanabe M, Yao A, Hirata Y, Kazuma K, Nagai R. Depressive symptoms are common and associated with adverse clinical outcomes in heart failure with reduced and preserved ejection fraction. J Cardiol 2012;60:23–30.
[8] Whooley MA. Depression and cardiovascular disease: healing the brokenhearted. JAMA 2006;295:2874–81.
[9] Havranek EP, Ware MG, Lowes BD. Prevalence of depression in congestive heart failure. Am J Cardiol 1999;84:348–50.
[10] Guck TP, Elsasser GN, Kavan MG, Barone EJ. Depression and congestive heart failure. Congest Heart Fail 2003;9:163–9.
[11] Kato N, Kinugawa K, Yao A, Hatano M, Shiga T, Kazuma K. Relationship of depressive symptoms with hospitalization and death in Japanese patients with heart failure. J Card Fail 2009;15:912–9.
[12] Lesman-Leegte I, Jaarsma T, Sanderman R, Linssen G, van Veldhuisen DJ. Depressive symptoms are prominent among elderly hospitalized heart failure patients. Eur J Heart Fail 2006;8:634–40.
[13] O'Connor CM, Abraham WT, Albert NM, Clare R, Stough WG, Gheorghiade M, Greenberg BH, Yancy CW, Young JB, Fonarow GC. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). Am Heart J 2008;156:662–73.
[14] Haworth JE, Moniz-Cook E, Clark AL, Wang M, Waddington R, Cleland JG. Prevalence and predictors of anxiety and depression in a sample of chronic heart failure patients with left ventricular systolic dysfunction. Eur J Heart Fail 2005;7:803–8.
[15] De Jong M, Moser DK, An K, Chung ML. Anxiety is not manifested by elevated heart rate and blood pressure in acutely ill cardiac patients. Eur J Cardiovasc Nurs 2004;3:247–53.
[16] Jiang W, Kuchibhatla M, Cuffe MS, Chung ML. Prognostic value of anxiety and depression in patients with chronic heart failure. Circulation 2004;110:3452–6.
[17] Friedmann E, Thomas SA, Liu F, Morton PG, Chapa D, Gottlieb SS. Relationship of depression, anxiety, and social isolation to chronic heart failure outpatient mortality. Am Heart J 2006;152, 940.e1–8.
[18] Konstam V, Salem D, Pouleur H, Kostis J, Gorkin L, Shumaker S, Mottard I, Woods P, Konstam MA, Yusuf S. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure: SOLVD Investigations (Studies of Left Ventricular Dysfunction Investigators). Am J Cardiol 1996;78:890–5.
[19] Domen NL, Pelle AJ, Szabó BM, Pederson SS. Symptoms of anxiety and cardiac hospitalizations at 12 months in patients with heart failure. J Gen Intern Med 2012;27:345–50.
[20] van den Broek KC, Nyklíček I, van der Voort PH, Alings M, Meijer A, Denollet J. Risk of ventricular arrhythmia after implantable defibrillator treatment in anxious type D patients. J Am Coll Cardiol 2009;54:531–7.
[21] Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. J Am Coll Cardiol 2005;45:637–51.
[22] Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implication for therapy. Circulation 1999;99:2192–217.
[23] Kop WJ, Synowski SJ, Gottlieb SS. Depression in heart failure: biobehavioral mechanisms. Heart Fail Clin 2011;7:23–38.
[24] Pederson SS, Denollet J, Spindler H, Ong AT, Serruys PW, Erdman RA, van Dombrug RT. Anxiety enhances the detrimental effect of depressive symptoms on health status following percutaneous coronary intervention. J Psychosom Res 2006;61:783–9.
[25] Martens EJ, Smith OR, Denollet J. Psychological symptom clusters, psychiatric comorbidity and poor self-reported health status following myocardial infarction. Ann Behav Med 2007;34:87–94.
[26] Suzuki T, Shiga T, Kuwahara K, Kobayashi S, Suzuki S, Nishimura K, Suzuki A, Omori H, Mori F, Ishigooka J, Kasanuki H, Hagiwara N. Depression and outcomes in hospitalized Japanese patients with cardiovascular disease – prospective single-center observational study. Circ J 2011;75:2465–73.
[27] Zung WWK. A self-rating depression scale. Arch Gen Psychiatry 1965;12:63–70.
[28] Zung WW. The differentiation of anxiety and depressive disorders: a biometric approach. Psychosomatics 1971;12:380–4.
[29] Williams Jr JW, Noel PH, Cordes JA, Ramirez G, Pignone M. Is this patient clinically depressed? JAMA 2002;287:1160–70.
[30] Schrag A, Barone P, Brown RG, Leentiens AFG, McDonald WM, Starkstein S, Weintraub D, Poewe W, Rascol O, Sampaio C, Stebbins GT, Goetz CG. Depression rating scales in Parkinson's disease: critique and recommendations. Mov Disord 2007;22:1077–92.
[31] Zung WWK, Richards CB, Short MJ. Self-rating depression scale in an outpatient clinic. Arch Gen Psychiat 1965;13:508–15.
[32] Shiotani I, Sato H, Kinjo K, Nakatani D, Mizuno H, Ohnishi Y, Hishida E, Kijima Y, Hori M, Sato H, the Osaka Acute Coronary Insufficiency Study (OACIS) group. Depressive symptoms predict 12-month prognosis in elderly patients with acute myocardial infarction. J Cardiovasc Risk 2002;9:153–60.
[33] Pihl E, Jacobsson A, Fridlund B, Strömberg A, Mårtensson J. Depression and health-related quality of life in elderly patients suffering from heart failure and their spouses: a comparative study. Eur J Heart Fail 2005;7:583–9.
[34] Kourea K, Parissis JT, Farmakis D, Paraskevaidis I, Panou F, Filippatos G, Kremastinos DT. Effects of darbepoetin-alpha on quality of life and emotional stress in anemic patients with chronic heart failure. Eur J Cardiovasc Prev Rehabil 2008;15:365–9.
[35] Parissis JT, Nikolaou M, Farmakis D, Bistola V, Paraskevaidis IA, Adamopoulos S, Filippatos G, Kremastinos DT. Clinical and prognostic implications of self-rating depression scales and plasma B-type natriuretic peptide in hospitalized patients with chronic heart failure. Heart 2008;94:585–9.
[36] Barefoot JC, Helms MJ, Mark DB, Blumenthal JA, Califf RM, Haney TL, O'Connor CM, Siegler IC, Williams RB. Depression and long-term mortality risk in patients with coronary artery disease. Am J Cardiol 1996;78:613–7.
[37] Suzuki T, Shiga T, Kuwahara K, Kobayashi S, Suzuki S, Nishimura K, Suzuki A, Ejima K, Manaka T, Shoda M, Ishigooka J, Kasanuki H, Hagiwara N. Prevalence and persistence of depression in patients with implantable cardioverter defibrillator: a 2-year longitudinal study. Pacing Clin Electrophysiol 2010;33:1455–61.
[38] Okimoto JT, Barnes RF, Veith RC, Baskind MA, Inui TS, Carter WB. Screening for depression in geriatric medical patients. Am J Psychiatry 1982;139:799–802.
[39] Passik SD, Kirsh KL, Donaghy KB, Theobald DE, Lundberg JC, Holtsclaw E, Dugan Jr WM. An attempt to employ the Zung Self-Rating Depression Scale as a "Lab Test" to trigger follow-up in ambulatory oncology clinics: criterion validity and detection. J Pain Symptom Manage 2001;21:273–81.
[40] Raison CL, Borisov AS, Broadwell SD, Capuron L, Woolwine BJ, Jacobson IM, Nemeroff CB, Miller AH. Depression during pegylated interferon-alpha plus ribavirin therapy: prevalence and prediction. J Clin Psychiatry 2005;66:41–8.
[41] Spielberger CD, Gorssuch RL, Lushene PR, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press Inc.; 1983.
[42] Kamphuis HC, de Leeuw JR, Derksen R, Hauer RN, Winnubst JA. Implantable cardioverter defibrillator recipients: quality of life in recipients with and without ICD shock delivery: a prospective study. Europace 2003;5:381–9.
[43] Nakazato K, Shimonaka Y. The Japanese State-Trait Anxiety Inventory: age and sex differences. Percept Motor Skills 1989;69:611–7.
[44] Tsuchihashi-Makaya M, Kato N, Chishaki A, Takeshita A, Tsutsui H. Anxiety and poor social support are independently associated with adverse outcomes in patients with mild heart failure. Circ J 2009;73:280–7.
[45] Valle R, Aspromonte N, Giovinazzo P, Carbonieri E, Chiatto M, di Tano G, Feola M, Milli M, Fontebasso A, Barro S, BardelIotto S, Milani L. B-type natriuretic peptide-guided treatment for predicting outcome in patients hospitalized in sub-intensive care unit with acute heart failure. J Card Fail 2008;14:219–24.
[46] van Veldhuisen DJ, Linssen GC, Jaarsma T, van Gilst WH, Hoes AW, Tijssen JG, Paulus WJ, Voors AA, Hillege HL. B-type natriuretic peptide and prognosis in heart failure patients with preserved and reduced ejection fraction. J Am Coll Cardiol 2013;61:1498–506.
[47] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461–70.
[48] Sears SF, Conti JB. Quality of life and psychological functioning of ICD patients. Heart 2002;87:488–93.
[49] Thomas SA, Friedmann E, Kao CW, Inguito P, Metcalf M, Kelley FJ, Gottlieb SS. Quality of life and psychological status of patients with implantable cardioverter defibrillators. Am J Crit Care 2006;15:389–98.
[50] Jacq F, Fouldrin G, Savouré A, Anselme F, Baguelin-Pinaud A, Cribier A, Thibaut F. A comparison of anxiety, depression and quality of life between device shock and nonshock groups in implantable cardioverter defibrillator recipients. Gen Hosp Psychiatry 2009;31:266–73.

[51] Katon W, Lin EHB, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. Gen Hosp Psychiatry 2007;29:147–55.

[52] DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 2000;160: 2101–7.

[53] Wu JR, Moser DK, Chung ML, Lennie TA. Objectively measured, but not self-reported, medication adherence independently predicts event-free survival in patients with heart failure. J Card Fail 2008;14:203–10.

[54] Ahern DK, Gorkin L, Jeffrey JA, Tierney C, Hallstrom A, Ewert C, Capone RJ, Schron E, Kornfeld D, Herd JA, Richardson DW, Follick MJ. Biobehavioral variables and mortality or cardiac arrest in the Cardiac Arrhythmia Pilot Study (CAPS). Am J Cardiol 1990;66:59–62.

[55] Ladwig KH, Kieser M, Konig J, Breithardt G, Borggrefe M. Affective disorders and survival after acute myocardial infarction. Eur Heart J 1991;12:959–64.

[56] Frasure-Smith N, Lesperance F, Talajic M. Depression following myocardial infarction. JAMA 1993;270:1819–25.

[57] Frasure-Smith N, Lesperance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. Circulation 1995;91:999–1005.

Characteristics of Elderly Cancer Patients' Concerns and Their Quality of Life in Japan: A Web-based Survey

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Objective: Cancer incidence and the number of cancer patients are increasing in today's aging society. The purpose of this study was to investigate the characteristics of elderly cancer patients' concerns and examine the association between their concerns and quality of life.
Methods: This was a cross-sectional web-based survey completed by ambulatory cancer patients aged 20 years or older. The questionnaire on cancer patients' concerns, comprehensive concerns assessment tool and the European Organization for Research and Treatment of Cancer QLQ-C30 were distributed to the subjects. Multiple regression analysis was conducted to determine which patients' concerns significantly contributed to their quality of life.
Results: The final study population consisted of 807 cancer patients, among whom 243 (30%) were elderly (65 years or older). Elderly cancer patients had particular difficulty with self-management, psychological symptoms and medical information, and the prevalence of their concerns was generally lower than that of younger patients, with the exception of physical symptoms. Multiple types of elderly patients' concerns were independently associated with quality of life.
Conclusions: We found that elderly cancer patients suffered from various concerns, thus multidisciplinary intervention is important for providing them with optimal care. The results of this study suggest that elderly cancer patients' quality of life will improve if their concerns are properly handled.

Key words: psycho-oncology — supportive care — public health — quality of life

INTRODUCTION

Since aging is a major risk for the development of cancer (1,2), elderly people are more likely to develop cancer than younger people (3,4). As the average life expectancy increases, the elderly population is growing, with the result that the number of older cancer patients is increasing. In 2013 in Japan, the elderly population aged 65 years or older was estimated to be 32 270 000 and the rate of aging 25.3% (as of 1 February 2014, provisional estimates) (5,6). In 2008 in Japan, the number of cancer incidence cases in patients over 65 years old was 538 061, among which 331 150 were males and 206 911 females (7,8). More and more elderly individuals will need cancer treatment in the near future.

However, there are a number of problems with the treatment of elderly cancer patients. Older patients tend to develop complications due to organ dysfunction and vulnerability (1,3,9–11), and their poor physical condition influences their tolerance to cancer therapy and increases the mortality risk (12–14). In general, cognitive impairment and depression are common disorders in elderly persons (15,16), and especially patients with cognitive dysfunction tend to develop delirium (11,17), which may hinder their ability to make proper decisions on their treatment (15). Moreover, according to a previous study, older people usually do not talk directly about their concerns (18), and another study indicates that cancer patients are reluctant to disclose their psychosocial concerns, so healthcare professionals hesitate to express their concerns (19,20). It seems to be difficult for medical staff to identify elderly cancer patients' problems and provide them with the necessary information and optimal support (20). On the other hand, elderly cancer patients need various forms of support such as understanding medical information, ameliorating physical symptoms, dealing with financial problems and coping with anxiety about the future (21,22). The Japanese government requires designated cancer care hospitals nationwide to establish a cancer care support and information service center in their hospitals based on the 'Basic Plan to Promote Cancer Control Act' of 2007 (23). The cancer care support and information service centers are intended to meet the needs of cancer patients without having to visit other institutions (24) and any cancer patient can use them freely, but their needs have not been handled appropriately (21,22). It is also reported that elderly cancer patients have economic limitations and have difficulty taking part in social activities, are physically and emotionally unstable, and are liable to feel lonely (11).

Previous Western studies found that older adults experienced significantly lower occurrence rates compared with younger adults in almost 50% of various physical and psychological symptoms associated with cancer and its treatment (25), an elderly cancer patient group showed a lower physical functioning score compared with the younger cancer patient group in the quality of life (QOL) domains (26), and that there was a moderate-to-strong association between patients' needs and psychological distress and/or QOL (27). To the best of our knowledge, few studies in Japan have comprehensively investigated and assessed elderly cancer patients' concerns including physical and psychological symptoms, medical treatment and daily life, even though these findings are essential for providing optimal care for elderly Japanese cancer patients.

The purposes of this study were: (i) to investigate what kind of concerns elderly cancer patients have, (ii) to compare elderly with younger cancer patients' concerns to clarify the characteristics of the elderly and (iii) to examine the association between elderly cancer patients' concerns and their QOL. We hypothesized that elderly cancer patients' concerns are multidimensional, that they had fewer concerns than younger cancer patients, and that there is a significant association between elderly cancer patients' concerns and their QOL.

METHODS

SUBJECTS

This survey was conducted via the Internet using Lyche-web of INTAGE Inc., Tokyo, Japan. The company recruited and registered monitors who could use the Internet through advertisement. We extracted potential participants who met the eligibility criteria and performed a questionnaire investigation from 22–24 October 2012.

The eligibility criteria for inclusion in this study were as follows: (i) subjects of 20 years or older, (ii) subjects who were diagnosed with cancer (any primary site and clinical stage, at any time point after diagnosis) and under treatment and (iii) subjects who have been to the hospital for cancer treatment for at least 1 year. The exclusion criteria were: (i) workers of mass media, advertisement agencies, market research companies and (ii) healthcare providers such as doctors, nurses, social workers and so on. Monitors were paid with points in return for participating in this investigation, that is, they could earn points if they answered all questions, and then they could exchange points for cash, net points or donation to some organization.

This study was approved by the Institutional Review Board and Ethics Committee of the National Cancer Center Hospital, Japan. The return of completed forms was considered consent.

PROCEDURE

This was a cross-sectional survey by internet to examine the characteristics of elderly cancer patients' concerns and the association between their concerns and QOL. We defined 65 years or older as the elderly in this investigation. The subjects were asked to fill out the online self-administered questionnaire. Inappropriate returns such as duplicate responses from the same terminal, mismatch between registered information and answer contents and inappropriate response time were deleted. As the participants were required to answer all questions, there should be no missing values in this investigation. The questionnaire consisted of the three sections described below.

INSTRUMENTS

CANCER PATIENTS' CONCERNS: COMPREHENSIVE CONCERNS ASSESSMENT TOOL (CCAT)

This self-reported questionnaire was developed to comprehensively assess cancer patients' concerns for our investigation, and its validity and reliability have been confirmed in Japanese cancer patients (28). The questionnaire includes four different types of concerns: physical symptoms (five items), psychological symptoms (five items), daily living (six items), self-management (three items), medical information (five items) and two symptoms: pain (one item) and constipation (one item). Participants were asked to respond to this questionnaire which evaluated the level or frequency of their concerns in the previous week on a four-point Likert scale

(1: no concerns, 2: slight concerns [once or twice a week], 3: moderate concerns [more than half of a week], 4: serious concerns [Every day]). We defined a rating of 3 or 4 as the presence of concerns.

QOL: EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER QUALITY OF LIFE QUESTIONNAIRE-CORE 30

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) is a 30-item cancer-specific questionnaire for assessing the general health-related QOL of cancer survivors (29). The questionnaire includes five functional scales (physical, role, emotional, cognitive and social) and nine symptom scales (fatigue, pain, nausea and vomiting and others) and a global health status/QOL scale. The reliability and validity of the Japanese version of the EORTC QLQ-C30 has been confirmed in a previous study (30). The present study uses a global health status score of 0–100, with a higher score indicating a higher QOL.

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS

An *ad hoc* self-administered questionnaire was used to obtain information on the patients' sociodemographic status, including age, sex, marital status, educational level, cancer site (all cancer types), clinical stage (the presence of recurrence or metastasis), anti-cancer treatment (surgery, chemotherapy, hormonal therapy and radiation therapy), duration since diagnosis (<6 months, 6 months to 5 years and ≥5 years), employment status (full-time/part-time or unemployed). As to the performance status (PS) defined by the Eastern Cooperative Oncology Group (ECOG), we described physical symptoms clearly in the questionnaire and asked participants to assess themselves using a rating from 0 (no symptoms) to 4 (bedridden).

STATISTICAL ANALYSES

First, we conducted an unpaired *t*-test to show the demographic differences between elderly (≥65 years old) and younger (<65 years old) cancer patients. Second, we calculated the prevalence of concerns in each subscale and item of CCAT among elderly and younger cancer patients, respectively. We regarded a rating of 3 or 4 on the four-point Likert scale as the presence of concern for each item, and we defined the presence of concern as having one or more items of concern in each subscale. We subsequently conducted an unpaired *t*-test to investigate the differences between elderly and younger cancer patients' concerns. Lastly, we conducted a multiple regression analysis to examine the association between elderly cancer patients' concerns and their QOL. In this analysis, the global health status score of EORTC QLQ-C30 was entered as a dependent variable, and the concerns present in the seven subscales were entered as independent variables. Age, sex, marital status (two groups: married or others), clinical stage (two groups: presence or non-presence of recurrence/metastasis), duration since diagnosis (three groups: <6 months,

6 months to 5 years, ≥5 years), employment status (two groups: full-time/part-time or unemployed), educational level (two groups: more than high school graduate or others) were also entered as independent variables for adjustment.

All *P* values were two-sided, and a *P* value of <0.05 was regarded as being statistically significant. All statistical procedures were conducted using SPSS software for Windows (Version 21.0 J, SPSS Inc., 2012).

RESULTS

PATIENT CHARACTERISTICS

A total of 1009 cancer patients were recruited in this study and data were available for 807 cancer patients. The response rate was 80.0%. The patients' sociodemographic and clinical characteristics are shown in Table 1. Based on the data collected, 243 subjects (30%) were over 65 years old; mean (±SD) and median age were 71.3 (±4.7) and 71 years, respectively. More than 90% were married, male, and did not have any impairment of physical functioning (PS 0 or 1). About 40% were prostate cancer and ~30% were diagnosed with recurrent/metastatic cancer. The background characteristics of the two age-specific subject groups were significantly different in sex, marital status, employment status, cancer site, history of anti-cancer treatment and global health status score, as shown in Table 1.

PREVALENCE OF CONCERNS AND DIFFERENCES BETWEEN ELDERLY (≥65 YEARS) AND YOUNGER (<65 YEARS) SUBJECTS

The most commonly perceived concerns among the elderly cancer patients were self-management, containing 'Want to know what I can do in poor health' (46.1%), 'Want to know what I can do for curing disease by myself' (45.3%), 'Want to know what I can do to take care of myself' (35.0%), followed by psychological symptoms 'Insomnia' (34.6%) and medical information 'Want to know about other treatments' (34.2%). We also found differences between older and younger cancer patients' concerns using univariate analysis, as shown in Table 2. The elderly subject group suffered significantly more from 'Loss of weight' (*P* = 0.04) in Physical symptoms but suffered less from 'Not being insightful' (*P* = 0.01), 'Feeling down and/or depressed' (*P* < 0.01) in psychological symptoms compared with the younger subject group. The elderly group also had significantly less difficulty with self-management (*P* = 0.03), daily living (*P* < 0.01) and constipation (*P* = 0.02) compared with the younger group.

ASSOCIATION BETWEEN ELDERLY CANCER PATIENTS' CONCERNS AND QOL

The results of the multiple regression analysis are shown in Table 3. Five subscales other than medical information and self-management were significantly associated with the elderly cancer patients' QOL, among which the most significantly associated was pain (*P* < 0.01), followed by physical

Table 1. Demographics and clinical characteristics of all participants

Characteristics	All		≥65 years		<65 years		P
	N	%	N	%	N	%	
No.	807	100.0	243	30.1	564	69.9	
Age	Mean: 57.6 (SD = 11.6)		Mean: 71.3 (SD = 4.7)		Mean: 51.7 (SD = 8.3)		
	Median: 57 (range, 23–86)		Median: 71 (range, 65–86)		Median: 52 (range, 23–64)		
Sex							
Male	433	53.7	219	90.1	214	37.9	0.00
Female	374	46.3	24	9.9	350	62.1	
Marital status							
Married	640	79.3	221	90.9	419	74.3	0.00
Education							
>12 years	513	63.5	139	57.2	374	66.3	0.93
Employment status							
Full-time/part-time	365	45.2	49	20.2	316	56.0	0.00
Cancer site							
Breast	237	29.4	8	3.3	229	40.6	0.00
Prostate	126	15.6	102	42.0	24	4.3	
Colon	58	7.2	20	8.2	38	6.7	
Stomach	48	5.9	22	9.1	26	4.6	
Lung	34	4.2	13	5.3	21	3.7	
Bladder	31	3.8	12	4.9	19	3.4	
Uterus	31	3.8	0	0.0	31	5.5	
Hematopoietic system	29	3.6	5	2.1	24	4.3	
Liver	23	2.9	10	4.1	13	2.3	
Rectum	22	2.7	10	4.1	12	2.1	
Esophagus	15	1.9	7	2.9	8	1.4	
Head and neck	12	1.5	1	0.4	11	2.0	
Kidney	10	1.2	5	2.1	5	0.9	
Ovary	10	1.2	0	0.0	10	1.8	
Pancreas	9	1.1	6	2.5	3	0.5	
Biliary system	5	0.6	2	0.8	3	0.5	
Undiagnosed	9	1.1	3	1.2	6	1.1	
Others	98	12.1	17	7.0	81	14.4	
Clinical stage							
Recurrence/metastasis	213	26.4	66	27.2	147	26.1	0.75
History of anti-cancer treatment[a]							
Surgery	678	84.0	175	72.0	503	89.2	0.00
Chemotherapy	384	47.6	94	38.7	290	51.4	0.00
Hormonal therapy	318	39.4	83	34.2	235	41.7	0.05
Radiation therapy	293	36.3	64	26.3	229	40.6	0.00

Table 1. Continued

Characteristics	All		≥65 years		<65 years		P
	N	%	N	%	N	%	
ECOG performance status							
0	453	56.1	144	59.3	309	54.8	0.44
1	323	40.0	88	36.2	235	41.7	
2	25	3.1	9	3.7	16	2.8	
3	5	0.6	2	0.8	3	0.5	
4	1	0.1	0	0.0	1	0.2	
Duration since diagnosis							
<6 months	45	5.6	19	7.8	26	4.6	0.61
≥6 months to <1 year	112	13.9	32	13.2	80	14.2	
≥1 year to <2 years	190	23.5	50	20.6	140	24.8	
≥2 years to <5 years	288	35.7	92	37.9	196	34.8	
≥5 years	172	21.3	50	20.6	122	21.6	
EORTC QLQ-C30	Mean: 62.2 (SD = 22.7)		Mean: 64.7 (SD = 22.3)		Mean: 61.2 (SD = 22.8)		0.04
Global health status score	Median: 66.7 (range, 0–100)		Median: 66.7 (range, 0–100)		Median: 66.7 (range, 0–100)		

ECOG, Eastern Cooperative Oncology Group; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30.
[a]Multiple choice.

symptoms ($P < 0.01$), constipation ($P < 0.01$), psychological symptoms ($P = 0.01$) and daily living ($P = 0.01$), after adjusting for age, sex, marital status, clinical stage, duration since diagnosis, employment status and educational level. As the coefficient of determination (R^2) in this survey was 0.31, we could not sufficiently estimate QOL from the concerns of elderly cancer patients.

DISCUSSION

As to the elderly cancer patients' concerns, about half of them had difficulty with self-management, psychological symptoms and medical information. In terms of self-management, it appears that they would like to decide their own treatment and they are likely to do something on their own without relying on others. As for psychological symptoms and medical information, a previous study reported that the prevalence of unmet needs among cancer patients aged over 70 years was high in the Psychological and Health system and Information domains and slightly >50% of them appeared to be unsatisfied (26), which is consistent with our findings. This indicates that they have not obtained sufficient information for living with medical treatment, even though cancer care support and information service centers play an important role in providing cancer patients and their families with useful information such as how to deal with side effects at home, available treatment or treatment options and interpersonal communication. The reasons for this are that many cancer patients are still not

familiar with the centers (31), or older patients with cognitive dysfunction might not be able to approach the centers because of their inadequate health literacy (32), so it may be necessary to simply remind them about the centers. With regard to psychological symptoms of older cancer patients such as insomnia, medical staff must handle this properly, for example, by regularly making assessments in clinical practices and objectively asking the families or visiting nurses about the patient's home life (33). Moreover, it would be necessary for oncologists to receive training on the primary approach for dealing with psychological symptoms of older cancer patients (34).

With respect to the comparison between elderly and younger cancer patients' concerns, a previous study reported that the elderly had less trouble with psychological symptoms and social functioning than younger cancer patients (25), and another study suggested that the elderly showed lower physical functioning scores in the QOL domains compared with the younger cancer patients (26), and these results are in agreement with our study. The reason for this seems to be that older cancer patients in Japan receive their pension or financial support from their children, which alleviates concerns about money. In addition, since they have finished raising their children and are retired from work, they have fewer demands on their time and resources compared with younger cancer patients (35,36). Since younger individuals still have work and family responsibilities, they seem to have more difficulty with psychosocial problems, financial problems, social functioning and so on (35,36). Regarding QOL, it is generally considered

Table 2. Prevalence of concerns[a] and differences between elderly (≥65 years) and younger (<65 years) cancer patients—univariate analysis

Concerns	All		≥65 years		<65 years		P
	n = 807	%	n = 243	%	n = 564	%	
Physical symptoms (having one or more concerns in the following five items)	123	15.2	39	16.0	84	14.9	0.68
Loss of weight	51	6.3	22	9.1	29	5.1	0.04
Loss of appetite	49	6.1	16	6.6	33	5.9	0.69
Dyspnea	43	5.3	9	3.7	34	6.0	0.18
Diarrhea	35	4.3	12	4.9	23	4.1	0.58
Nausea and/or vomiting	21	2.6	6	2.5	15	2.7	0.88
Psychological symptoms (having one or more concerns in the following five items)	391	48.5	114	46.9	277	49.1	0.57
Insomnia	257	31.8	84	34.6	173	30.7	0.28
Being tired and/or feeling sluggish	226	28.0	51	21.0	175	31.0	0.00
Not being insightful	146	18.1	31	12.8	115	20.4	0.01
Feeling down and/or depressed	123	15.2	21	8.6	102	18.1	0.00
Feeling agitated and/or nervous	71	8.8	16	6.6	55	9.8	0.15
Daily living (having one or more concerns in the following six items)	241	29.9	51	21.0	190	33.7	0.00
Concerns about medical fees	179	22.2	35	14.4	144	25.5	0.00
Inability to do job	133	16.5	18	7.4	115	20.4	0.00
Inability to do housework and/or to take care of family	69	8.6	12	4.9	57	10.1	0.02
Concerns about nursing care insurance	66	8.2	24	9.9	42	7.4	0.25
Inability to take care of oneself	58	7.2	11	4.5	47	8.3	0.06
Having no means of going to hospital	37	4.6	7	2.9	30	5.3	0.13
Self-management (having one or more concerns in the following three items)	494	61.2	135	55.6	359	63.7	0.03
Want to know what I can do for curing of disease by myself	423	52.4	110	45.3	313	55.5	0.01
Want to know what I can do in poor health	414	51.3	112	46.1	302	53.5	0.05
Want to know what I can do to take care of myself	334	41.4	85	35.0	249	44.1	0.02
Medical information (having one or more concerns in the following five items)	373	46.2	103	42.4	270	47.9	0.15
Want to know about other treatments	289	35.8	83	34.2	206	36.5	0.52
Want to know about other hospitals	235	29.1	73	30.0	162	28.7	0.71
Unable to understand explanation about disease and/or treatment	149	18.5	54	22.2	95	16.8	0.07
Unable to communicate well with doctor	140	17.3	42	17.3	98	17.4	0.98
Want to know about fertility	66	8.2	15	6.2	51	9.0	0.17
Pain							
Painful	142	17.6	41	16.9	101	17.9	0.72
Constipation							
Constipated	126	15.6	27	11.1	99	17.6	0.02

[a]Rated 3 or 4 on the four-point Likert scale on each item of the comprehensive concerns assessment tool.

to be lower in elderly compared with younger cancer patients, because the physical functions of elderly patients are weakened and they tend to have more comorbidities than younger patients (37), and the severity of comorbidities adversely affects QOL (38). In a previous study, however, the QOL of elderly cancer patients was the same degree as in younger cancer patients after adjustment for PS (39), and another study reported that QOL was not significantly different between

elderly and younger cancer patients (26). In our study, QOL was higher in the elderly than in the younger cancer patients. One of the reasons for this seems to be that older cancer patients are better able to adapt to severe situations compared with younger patients, although the elderly are more strongly affected by cancer itself or the treatment (40,41).

Regarding the association between concerns and QOL of elderly cancer patients, we found that there is a significant

Table 3. Association between elderly cancer patients' concerns and quality of life[a]—multiple regression analysis[b]

Concerns	Coefficient (B)	Standardizing coefficient (β)	T	P	Partial R^2
Physical symptoms	−11.77	−0.19	−3.23	0.00	0.14
Psychological symptoms	−6.70	−0.15	−2.53	0.01	0.11
Daily living	−8.34	−0.15	−2.53	0.01	0.11
Self-management	−4.67	−0.10	−1.61	0.11	0.08
Medical information	−3.44	−0.08	−1.20	0.23	0.06
Pain	−12.23	−0.21	−3.64	0.00	0.11
Constipation	−11.96	−0.17	−3.07	0.00	0.05
					Total R^2 = 0.31

[a]Global health status score of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30.
[b]Adjusted for age, sex, marital status (two groups), clinical stage (two groups), duration since diagnosis (three groups), employment status (two groups) and educational level (two groups).

association, but self-management and medical information, which are highly prevalent concerns among the elderly subjects, do not significantly contribute to QOL. Nevertheless, elderly subjects have great difficulty with these two subscales. On the other hand, the other five subscales that are significantly associated with QOL do not pose much difficulty for the elderly cancer patients. Therefore, we consider it important to comprehensively intervene in their multiple concerns. Several previous studies have suggested that the more adequate information cancer patients obtain, the more satisfied they are (20), and the more able they are to adapt to their psychological and emotional states (42); therefore the QOL of elderly cancer patients is expected to improve with multifaceted intervention and the provision of sufficient information about their concerns.

The present study has several limitations. First, there was the potential for selection bias in that the subjects were outpatients, over 90% of them were diagnosed >6 months earlier, ~90% of them were male and 40% were prostate cancer, and moreover, they were all able to participate in this internet survey. Based on these factors, it was estimated that most of the subjects were physically and mentally stable, and they had little cognitive dysfunction and high health literacy because they were capable enough to use the internet. As more men than women use the internet in general, it is believed that most subjects in this study were men. That is to say, subjects in this study were not representative elderly cancer patients in Japan. Further investigations need to be conducted other than through the internet, such as by interviews with not only outpatients but inpatients in clinical sites, in the future. In addition, we should point out that there was a possibility that most of the study subjects had normal cognitive function. In fact, the number of cognitive deficit patients in Japan was estimated to be 4 620 000 in 2013 (43), and many elderly cancer patients have cognitive impairment. Therefore, we should evaluate the cognitive function of elderly cancer patients first, positively detect their concerns including concerns of patients with cognitive dysfunction by using assessment tool like

comprehensive geriatric assessment (CGA) after that, and examine whether we can clarify their concerns.

Second, the CCAT questionnaire for cancer patients' concerns proved to be valid and reliable in a previous study, but it is not specific to elderly cancer patients (28). Finally, since our investigation was cross-sectional in design, we cannot conclude the causal relationship between patients' concerns and their QOL. This problem needs further investigation in a longitudinal study; for example, we should reinvestigate after an interval of several months. In addition, further research needs to focus on various patients and clinical characteristics such as age, sex, cancer type, PS and so forth.

Despite these limitations, this study has several strengths. To our knowledge, it is the first study to comprehensively assess elderly cancer patients' concerns in Japan; in doing so, we could understand the characteristics of elderly cancer patients' concerns in detail. The response rate of this study was 80%, which was considered to be relatively high.

In today's aging society, multidisciplinary intervention and training for healthcare professionals will be required to deal with different and complex concerns of elderly patients with cancer. We should also make an active effort to investigate concerns of elderly cancer patients who do not complain, predict their possible problems such as upset, and intervene in them. This will make it possible to provide them with optimal oncological care to improve their QOL.

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Conflict of interest statement

None declared.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* 2010;60:277–300.
2. Yancik R, Ries LA. Cancer in older persons: an international issue in an aging world. *Semin Oncol* 2004;31:128–36.
3. Hurria A, Browner IS, Cohen HJ, et al. Senior adult oncology. *J Natl Compr Canc Netw* 2012;10:162–209.
4. Balducci L, Beghe C. Cancer and age in the USA. *Crit Rev Oncol Hematol* 2001;37:137–45.
5. Statistics Bureau, Ministry of Internal Affairs and Communications, Estimates, Japan. Available from: http://www.stat.go.jp/data/jinsui/new.htm (28 February 2014, date last accessed) (in Japanese).
6. Office for Policies on Cohesive Society, Cabinet Office, Government of Japan, 2012 Available from: http://www8.cao.go.jp/kourei/whitepaper/w-2012/gaiyou/ (28 February 2014, date last accessed) (in Japanese).
7. Foundation for Promotion of Cancer Research CANCER STATISTICS IN JAPAN 2012 The Editorial Board of the Cancer Statistics in Japan 2012 (in Japanese).
8. Center for Cancer Control and Information Services, National Cancer Center, Japan (October 2013 Last Updated) Available from: http://ganjoho.jp/professional/statistics/statistics.html#02 (in Japanese).
9. Rao AV, Seo PH, Cohen HJ. Geriatric assessment and comorbidity. *Semin Oncol* 2004;31:149–59.
10. Lichtman SM. Chemotherapy in the elderly. *Semin Oncol* 2004;31:160–74.
11. Rao A, Cohen HJ. Symptom management in the elderly cancer patient: fatigue, pain, and depression. *J Natl Cancer Inst Monogr* 2004;32:150–7.
12. Jacobs LA, Vaughn DJ. In the clinic. Care of the adult cancer survivor. *Ann Intern Med* 2013;11:158.
13. Meyerhardt JA, Catalano PJ, Haller DG, et al. Impact of diabetes mellitus on outcomes in patients with colon cancer. *J Clin Oncol* 2003;21:433–40.
14. Satariano WA, Ragland DR. The effect of comorbidity on 3-year survival of women with primary breast cancer. *Ann Intern Med* 1994;120:104–10.
15. Extermann M. Older patients, cognitive impairment, and cancer: an increasingly frequent triad. *J Natl Compr Canc Netw* 2005;3:593–6.
16. Polyakova M, Sonnabend N, Sander C, et al. Prevalence of minor depression in elderly persons with and without mild cognitive impairment: a systematic review. *J Affect Disord* 2013.
17. Martinez VN, Franco JG. Subsyndromal delirium in elderly patients: a systematic review. *Rev Esp Geriatr Gerontol* 2013;48:122–9.
18. Murray J, Banerjee S, Byng R, et al. Primary care professionals' perceptions of depression in older people: a qualitative study. *Soc Sci Med* 2006;63:1363–73.
19. Arora NK. Interacting with cancer patients: the significance of physicians' communication behavior. *Soc Sci Med* 2003;57:791–806.
20. Neumann M, Wirtz M, et al. Identifying and predicting subgroups of information needs among cancer patients: an initial study using latent class analysis. *Support Care Cancer* 2011;19:1197–209.
21. Hansen DG, Larsen PV, Holm LV, et al. Association between unmet needs and quality of life of cancer patients: a population-based study. *Acta Oncol* 2013;52:391–9.
22. Lundstrom LH, Johnsen AT, Ross L, Petersen MA, Groenvold M. Cross-sectorial cooperation and supportive care in general practice: cancer patients' experiences. *Fam Pract* 2011;28:532–40.
23. Division of Cancer Control and Health Promotion, Health Services Bureau, Ministry of Health, Labour and Welfare.
24. Rutten LJ, Arora NK, Bakos AD, Aziz N, Rowland J. Information needs and sources of information among cancer patients: a systematic review of research (1980–2003). *Patient Educ Couns* 2005;57:250–61.
25. Cataldo JK, Paul S, Cooper B, et al. Differences in the symptom experience of older versus younger oncology outpatients: a cross-sectional study. *BMC Cancer* 2013;13:6.
26. Akechi T, Okuyama T, Uchida M, et al. Perceived needs, psychological distress and quality of life of elderly cancer patients. *Jpn J Clin Oncol* 2012;42:704–10.
27. Akechi T, Okuyama T, Endo C, et al. Patient's perceived need and psychological distress and/or quality of life in ambulatory breast cancer patients in Japan. *Psychooncology* 2011;20:497–505.
28. Yokoo M, Akechi T, Ogawa A, et al. Comprehensive assessment of cancer patients' concerns and the association with quality of life (in submission).
29. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–76.
30. Kobayashi K, Takeda F, Teramukai S, et al. A cross-validation of the European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) for Japanese with lung cancer. *Eur J Cancer* 1998;34:810–5.
31. The minutes of the Cancer Control Promotion Council, Ministry of Health, Labour and Welfare. Available from: http://www.mhlw.go.jp/stf/shingi/2r9852000000008fcb.html (28 February 2014, date last accessed) (in Japanese).
32. Safeer RS, Keenan J. Health literacy: the gap between physicians and patients. *Am Fam Physician* 2005;72:463–8.
33. Cheng Karis KF, Thompson DR, Ling WM, Chan Carmen WH (2005) Measuring symptom prevalence, severity and distress of cancer survivors. *Clin Effectiveness Nurs* 2005;9:154–60.
34. Kalsi T, Payne S, Brodie H, et al. Are the UK oncology trainees adequately informed about the needs of older people with cancer? *Br J Cancer* 2013;108:1936–41.
35. Mor V, Allen S, Mallin M. The psychosocial impact of cancer on older versus younger patients and their families. *Cancer* 1994;74:2118–27.
36. Baker F, Denniston M, Smith T, West MM. Adult cancer survivors: how are they faring? *Cancer* 2005;104:2565–76.
37. Puts MT, Monette J, Girre V, et al. Quality of life during the course of cancer treatment in older newly diagnosed patients. Results of a prospective pilot study. *Ann Oncol* 2011;22:916–23.
38. Chen RC, Royce TJ, Extermann M, Reeve BB. Impact of age and comorbidity on treatment and outcomes in elderly cancer patients. *Semin Radiat Oncol* 2012;22:265–71.
39. Sanson-Fisher R, Girgis A, Boyes R, et al. The unmet supportive care needs of patients with cancer. Supportive Care Review Group. *Cancer* 2000;88:226–37.
40. Overcash J, Extermann M, Parr J, Perry J, Balducci L. Validity and reliability of the FACT-G scale for use in the older person with cancer. *Am J Clin Oncol* 2001;24:591–6.
41. Berg CA, Upchurch R. A developmental-contextual model of couples coping with chronic illness across the adult life span. *Psychol Bull* 2007;133:920–54.
42. Repetto L, Piselli P, Raffaele M, Locatelli C. Communicating cancer diagnosis and prognosis: when the target is the elderly patient—a GIOGer study. *Eur J Cancer* 2009;45:374–83.
43. Ministry of Health, Labour and Welfare. Available from: http://www.mhlw.go.jp/houdou_kouhou/kaiken_shiryou/2013/dl/130607-01.pdf (28 February 2014, date last accessed) (in Japanese).

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Comprehensive Assessment of Cancer Patients' Concerns and the Association with Quality of Life

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Objective: Comprehensive assessment of perceived concerns can be used to guide supportive care appropriate to individual cancer patients. This study sought to determine the prevalence of cancer patients' concerns and the degree to which these concerns contribute to patients' quality of life.
Methods: Participants were patients with all types of cancer, who completed an Internet survey questionnaire regarding comprehensive concerns about physical, psychological, psychosocial and economic aspects of having cancer. The questionnaire was based on the newly developed Comprehensive Concerns Assessment Tool and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire.
Results: We obtained complete data from 807 patients. Factors related to 'self-management' concerns were the most common (61.2%), followed by concerns about 'psychological symptoms' (48.5%), 'medical information' (46.2%), 'daily living' (29.9%), 'pain' (17.6%), 'constipation' (15.6%) and other 'physical symptoms' (15.2%). Multiple regression analysis revealed that all concerns except those about 'medical information' significantly contributed to quality of life.
Conclusions: Cancer patients' concerns were shown to be multidimensional and significantly associated with quality of life. Thus, assessment of patients' concerns should be multidimensional in nature, and a multidisciplinary care team should help patients improve their quality of life.

Key words: quality of life − patient care team − social support − needs assessment

INTRODUCTION

Cancer patients face various symptoms and problems in daily life that involve the physical, psychological and socio-economic effects of treatment complications and extended survival.

Numerous symptoms and problems must be managed, including pain (1), distress (2), insufficient social support (3) and treatment location (4). Almost all of these are reported to be factors significantly related to quality of life (QOL) (5−8). Recent studies have also dealt with a wide range of cancer patients' care needs, and having many needs is one of the factors reported to worsen cancer patients' QOL (9,10). These findings suggest that medical professionals should focus on the various symptoms and problems that cancer patients face in order to better support them.

However, past studies have shown that patients' symptoms and problems are often not appropriately addressed by medical professionals (11−13). Also, patients frequently report that they have not received the support they needed during treatment and follow-up (14−16). These problems result in part from a lack of appropriate, brief assessment tools of symptoms and problems, which leads to insufficient guidance for effective and efficient care. Cancer patients experience one or more symptoms and several problems simultaneously, and how they feel and respond to these symptoms and problems differs between individuals. Therefore, their symptoms and problems must be assessed comprehensively from the patient's viewpoint as 'perceived concerns'. The comprehensive assessment of perceived concerns can offer some advantages. First, patient-important outcomes can be directly assessed. Second, it can help with the prioritization of necessary care by more specifically indicating the support resources needed to improve the patient's QOL. However, as mentioned above, few tools are available for such assessment.

The framework of this study is based on the premise of appropriate supportive care, which is defined as care based on patients' perceived concerns to improve QOL. The study objectives were 3-fold: to develop a questionnaire that comprehensively assesses cancer patients' concerns; to examine the prevalence of concerns in cancer patients; and to explore the contribution of concerns to cancer patients' QOL.

PATIENTS AND METHODS

SUBJECTS

Subjects were patients on the registered cancer patient list of Intage Inc., Tokyo, Japan, a company that specializes in Internet surveys and recruits monitors from among Internet users by advertisements placed on various websites in Japan. From the registered monitors, we selected patients that matched the eligibility criteria of this study. Inclusion criteria were persons aged 20 years or older, who were diagnosed with cancer (any primary cancer site, all stages and at any time point after diagnosis) and had visited a hospital for cancer treatment within the past year. Exclusion criteria were patients who were either healthcare professionals or who worked in the areas of media, advertisement or web investigation. The reward for responding to the questionnaire was given according to a point system. Respondents could save points if they completed all questions. They could then exchange points for money or save their accumulated points.

This study was approved by the Institutional Review Board and Ethics Committee of the National Cancer Center, Japan. Because this was an Internet survey, responding to the survey constituted informed consent to participate in this study.

PROCEDURE

In this cross-sectional study, the survey was conducted over the Internet between 22 and 24 October 2012. In total, 1009 eligible cancer patients were asked to complete the self-administered questionnaires.

We excluded data when answers were transmitted repeatedly from the same terminals, when attributes were different from those of the answer or when the answer time was inappropriate. Missing values were not possible because the web investigation was structured to require participants to answer all of the questions.

INSTRUMENTS

CANCER PATIENTS' CONCERNS

We developed a self-reported questionnaire, which we named the Comprehensive Concerns Assessment Tool (CCAT), to comprehensively assess the concerns of patients across all types of cancer throughout all phases of the cancer experience. After reviewing existing patient and family support sheets compiled by the National Cancer Center Japan and a needs assessment tool [Short-form Supportive Care Needs Survey Questionnaire: SCNS-SF34-J (17)], we selected 50 items encompassing physical, psychological and psychosocial concerns of cancer patients. We then selected 26 of these items using a focus group of experts that included psycho-oncologists, nurses and medical social workers. We explored subcategories by factor analysis and examined the internal consistency of each subscale.

On the CCAT, respondents were asked to indicate the level or frequency of their concerns over the last week. The four response options were (i) no concern, (ii) mild concern (1 or 2 days a week), (iii) moderate concern (more than half the week) and (iv) serious concern (every day).

The CCAT will be published on the homepage (http://pod. ncc.go.jp).

QUALITY OF LIFE

We assessed patient QOL using the European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C 30 (18). The EORTC QOL-C 30 consists of 30 items on self-reported aspects of QOL in cancer patients. The validity and reliability of the Japanese version of the EORTC QLQ-C 30 had been confirmed (17). In this study, we used the Global Health Status score ranging from 0 to 100, with higher scores representing higher QOL.

SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

We used an *ad hoc* self-administered questionnaire to obtain data on the patients' socio-demographic status, including marital status, employment status and educational level. We also obtained other medical information, including primary cancer site, time since diagnosis and presence of recurrence or metastasis from this questionnaire.

STATISTICAL ANALYSIS

First, we evaluated factor validity of the CCAT using factor analysis with Promax rotation. The number of factors was determined by Keiser's criterion (eigenvalue of 1.0 or greater). To evaluate the internal consistency of each factor, we calculated Cronbach's alpha coefficients. We calculated the prevalence of each subscale and each item to clarify the prevalence of each concerns. We defined 'presence of each concern subscale' as the presence of one or more items receiving a score of 3 or 4 on each factor, and 'presence of each concern item' as an item receiving a score of 3 or 4.

Next, to explore the contribution of each concern to cancer patients' QOL, we conducted multiple regression analysis, where the dependent variable was the Global Health Status score of the EORTC QLQ-C 30 and the independent variables were the presence of each concern subscales. In this analysis, age, sex, marital status (married or other), occupation (employed or unemployed), educational level (college graduate or other), time since diagnosis (<6 months, 6 months to <5 years and >5 years) and presence of recurrence or metastasis were entered as independent variables for adjustment, with reference to past studies.

A P value of <0.05 was considered statistically significant, and all reported that P values were two tailed. All statistical analysis was conducted using SPSS 21 version software for Windows (IBM Inc., 2012).

RESULTS

PATIENT CHARACTERISTICS

Complete data were available for 807 patients. The response rate was 80.0%. Table 1 shows the participants' socio-demographic and clinical characteristics. Mean (±SD) and median age of the study population were 57.6 (±11.6) and 57.0 years, respectively. The male–female ratio was about 1 : 1. Approximately 80% were married, and ~60% had a graduate education. As for cancer site, most had breast cancer (~30%), followed by prostate cancer (15.6%) and colorectal cancer (9.9%). A few subjects had lung, stomach or liver cancer. Most subjects were survivors whose time since diagnosis fell within 2–5 years, and 5.6% of participants were in the early stages of cancer treatment. Mean (±SD) and median (range) of the Global Health Status score of EORTC QLQ-C 30 were 62.2 (±22.7) and 66.7 (0–100), respectively.

FACTOR STRUCTURE OF PERCEIVED CONCERNS

Factor analysis indicated a five-factor solution. Table 2 shows the final factor pattern, factor name and internal consistency of each factor (Cronbach's alpha coefficient).

The first six items comprising concerns related to daily living during cancer treatment showed significant loading onto Factor 1. The next five items related to concerns about

Table 1. Characteristics of the study participants ($n = 807$)

Characteristics	No. of participants	%
Age (years)		
Mean: 57.6 (SD = 11.6), median: 57.0, range: 23–86		
Sex		
Man	433	53.7
Woman	374	46.3
Marital status		
Married	640	79.3
Unmarried	90	11.2
Separated/divorced	55	6.8
Widow/widower	22	2.7
Occupation		
Unemployed	442	54.8
Employed	365	45.2
Educational level		
Junior high school	13	1.6
High school	281	34.8
Technical school	60	7.4
Junior college	97	12.0
College	331	41.0
Graduate school	25	3.1
Primary cancer site		
Breast	237	29.4
Prostate	126	15.6
Colon	58	7.2
Stomach	48	5.9
Lung	34	4.2
Urinary bladder	31	3.8
Uterus	31	3.8
Hematologic cancer	29	3.6
Liver	23	2.9
Rectum	22	2.7
Esophagus	15	1.9
Head and neck	12	1.5
Kidney	10	1.2
Ovary	10	1.2
Pancreas	9	1.1
Gall bladder	5	0.6
Not yet diagnosed	9	1.1
Others	98	12.1
Time since diagnosis		
<6 months	45	5.6
6 months to <1 year	112	13.9

Continued

Table 1. *Continued*

Characteristics	No. of participants	%
1 year to <2 years	190	23.5
2 years to <5 years	288	35.7
>5 years	172	21.3
Recurrence/metastasis		
Yes	213	26.4
No	594	73.6

medical information loaded onto Factor 2. Five items including 'being tired and/or feeling sluggish' related to concerns about psychological symptoms loaded onto Factor 3. Three items related to concerns about self-management loaded onto Factor 4, and five other items related to concerns about physical symptoms loaded onto Factor 5. Items for 'pain' and 'constipation' did not belong to any factor. 'Pain' might reflect not only physical symptoms but also various aspects of cancer patients' concerns. 'Constipation' might not have been a symptom related to the kind of cancer and cancer treatment found in this study population. However, pain and constipation are very common and important symptoms for all cancer patients so we included these two items as individual subscales in the other analysis in this study. Factors 1–4 showed good internal consistency ($\alpha > 0.70$), and Factor 5 showed moderate internal consistency ($\alpha = 0.67$).

PREVALENCE OF PERCEIVED CONCERNS

Table 3 shows the prevalence of each subscale and item. The subscale related to concerns about 'self-management' was the most common (61.2%), followed by 'psychological symptoms' (48.5%), 'medical information' (46.2%), 'daily living' (29.9%), 'pain' (17.6%), 'constipation' (15.6%) and 'physical symptoms' (15.2%). Among the items, 'Want to know what I can do for curing the disease by myself' was the most common, followed by 'Want to know what I can do in poor health', and 'Want to know what I can do to take care of myself'. The prevalence of these items was over 40% and all of them belonged to the 'self-management' subscale. Half of the subjects had 'psychological concerns' and one-third of subjects suffered from 'insomnia' and 'being tired and/or feeling sluggish'. About half of the subjects also had some difficulties with 'medical information' and wanted to know about other treatments and hospitals. However, the prevalence of items about communication with medical staff, such as being 'unable to communicate well with doctor', was <20%. About one-third of subjects had some concerns about 'daily living'. Comparatively, more subjects had economic concerns such as 'concerns about medical costs' and an 'inability to work'. The prevalence of the subscale related to concerns about 'physical symptoms' was <20% as was those for 'pain' and 'constipation'.

Table 2. Factor pattern for the questionnaire items and reliability data

	Item number in the questionnaire and item	Factor loadings[a]
Factor 1	Daily living (six items); Cronbach's $\alpha = 0.84$	
C5	Concerns about nursing care insurance	0.78
C3	Inability to take care of oneself	0.73
C2	Inability to do housework and/or to take care of family	0.72
C6	Having no means of going to hospital	0.72
C4	Concerns about medical costs	0.66
C1	Inability to do job	0.62
Factor 2	Medical information (five items); Cronbach's $\alpha = 0.85$	
D2	Unable to communicate well with doctor	0.94
D1	Unable to understand explanation about disease and/or treatment	0.92
D3	Want to know about other hospitals	0.63
D8	Want to know about fertility	0.47
D4	Want to know about other treatments	0.44
Factor 3	Psychological symptoms (five items); Cronbach's $\alpha = 0.79$	
B2	Feeling down and/or depressed	0.98
B3	Feeling agitated and/or nervous	0.72
B4	Being not insightful	0.68
B1	Insomnia	0.47
A3	Being tired and/or feel sluggish	0.37
Factor 4	Self-management (three items); Cronbach's $\alpha = 0.91$	
D6	Want to know what I can do for curing the disease by myself	0.96
D7	Want to know about what I can do in poor health	0.85
D5	Want to know what I can do to take care of myself	0.71
Factor 5	Physical symptoms (five items); Cronbach's $\alpha = 0.67$	
A2	Loss of appetite	0.66
A8	Loss of weight	0.55
A5	Nausea and/or vomiting	0.50
A7	Dyspnea	0.50
A6	Diarrhea	0.47
Factor 6	Pain (one item)[b]	
A1	Painful	
Factor 7	Constipation (one item)[b]	
A4	Constipated	

Loading after Promax rotation ($n = 807$).
[a]Factor loadings for the items where a cross-loading of >0.30 were demonstrated.
[b][Pain] and [constipation] belonged to neither factor in the first factor analysis.

ASSOCIATION BETWEEN PERCEIVED CONCERNS AND QOL

The seven subscales are considered to be independent of each other as multicollinearity was ruled out because tolerances were sufficiently large (0.77–0.93) and variance inflation

Table 3. The prevalence of concerns of the study participants ($n = 807$)

Concerns[a]	No. of participants	%
Physical symptoms		
Having one or more concerns in the following items	123	15.2
1 Loss of weight	51	6.3
2 Loss of appetite	49	6.1
3 Dyspnea	43	5.4
4 Diarrhea	35	4.4
5 Nausea and/or vomiting	21	2.6
Psychological symptoms		
Having one or more concerns in the following items	391	48.5
1 Insomnia	257	31.9
2 Being tired and/or feeling sluggish	226	28.1
3 Being not insightful	146	18.1
4 Feeling down and/or depressed	123	15.2
5 Feeling agitated and/or nervous	71	8.8
Daily living		
Having one or more concerns in the following items	241	29.9
1 Concerns about medical costs	179	22.2
2 Inability to work	133	16.5
3 Inability to do housework and/or to take care of family	69	8.5
4 Concerns about nursing care insurance	66	8.2
5 Inability to take care of oneself	58	7.1
6 Having no means of going to hospital	37	4.6
Self-management		
Having one or more concerns in the following items	494	61.2
1 Want to know what I can do for curing the disease by myself	423	52.4
2 Want to know what I can do in poor health	414	51.3
3 Want to know what I can do to take care of myself	334	41.4
Medical information		
Having one or more concerns in the following items	373	46.2
1 Wanting to know about other treatments	289	35.8
2 Wanting to know about other hospitals	235	29.1
3 Unable to understand explanation about disease and/or treatment	149	18.4
4 Unable to communicate well with doctor	140	17.3
5 Wanting to know about fertility	66	8.2
Pain		
1 Painful	142	17.6
Constipation		
1 Constipated	126	15.6

[a]Rated three or more on the four-point Likert scale on each questionnaire item.

factors were sufficiently small (1.07–1.30). Except for the subscale related to concerns about 'medical information', each subscale contributed to QOL with meaningful variables

Table 4. Concerns associated with the participant's quality of life (QOL)[a] in the multiple regression analysis[b]

Participant's concerns[c]	Coefficient (B)	Standardized coefficient (β)	t	P	Partial R^2 (rank)
Physical symptoms	−11.07	−0.18	−5.46	0.00	0.06 (2)
Psychological symptoms	−10.69	−0.24	−7.25	0.00	0.09 (1)
Daily living	−6.84	−0.14	−4.14	0.00	0.05 (4)
Self-management	−3.72	−0.08	−2.39	0.02	0.03 (5)
Medical information	−2.03	−0.05	−1.35	0.18	0.02 (7)
Pain	−10.77	−0.18	−5.87	0.00	0.06 (2)
Constipation	−5.07	−0.08	−2.67	0.01	0.03 (5)
					Total $R^2 = 0.34$

[a]Global QOL score of the EORTC QLQ-C30.
[b]Adjusted for age, sex, marital status (two groups), educational level (two groups), occupation (two groups), time since diagnosis (three groups) and presence of recurrence/metastasis.
[c]Independent variables are presence of concerns; having one or more items rated three or more on the four-point Likert scale of each subscale.

($P < 0.05$), and explained 33.8% of patients' QOL ($R^2 = 0.34$). The subscale related to concerns about 'psychological symptoms' most contributed to QOL ($\beta = -0.24$), followed by 'physical symptoms' ($\beta = -0.18$), 'pain' ($\beta = -0.18$), 'daily living' ($\beta = -0.14$), 'self-management' ($\beta = -0.08$) and 'constipation' ($\beta = -0.08$) after adjusting for age, sex, marital status, occupation, educational level, time since diagnosis and presence of recurrence/metastasis (Table 4).

DISCUSSION

We began this study by developing a questionnaire to comprehensively assess cancer patients' concerns. The findings support the validity and reliability of the CCAT developed and revealed that patients' concerns are multidimensional (e.g. physical, psychological and social).

In regard to examining the prevalence of concerns as a next step, we found that cancer patients can experience a wide range of perceived concerns. In particular, more than half of our ambulatory cancer patients were concerned about 'self-management'. Indeed, cancer treatment has expanded to include the home setting because of longer survival, the increased number of ambulatory patients treated with chemotherapy and shortened hospital stays. Because cancer patients are primarily responsible for managing their treatment, 'self-management' has become an important factor in cancer self-care. Thus, self-management skills and information on beneficial exercise (19,20) and appropriate nutrition and meal planning should be provided to help patients manage their cancer. The second most prevalent concern was

'psychological symptoms'. About half of the subjects had psychological concerns, and 30% suffered from 'insomnia'. Because insomnia is a common problem in cancer patients (1,21), medical personnel should routinely ask them whether they are suffering from insomnia. Providing information on sleep hygiene (22) is especially recommended as part of a routine care for patients with insomnia. In addition to medication, psychotherapy including cognitive behavioral therapy (23,24) and relaxation therapy (22,25) could offer alternative support if these services are available. Many subjects also had concerns about medical and socio-economic information. Information demand is not limited to the early stages of disease but continues throughout cancer treatment (26,27). Therefore, this information should be easy for patients to obtain and easy to understand. More medical personnel having sufficient knowledge and good communication skills are needed to settle the concern about information. We found a relatively low prevalence of concern about 'physical symptoms', including 'pain' and 'constipation', which might reflect the large majority of participants who were at relatively earlier stage of cancer. It might also reflect concern about 'current' physical symptoms, not about possible 'future' symptoms. Based on our findings, we conclude that there is a need to improve support for cancer patients' self-management, psychiatric concerns and access to information on medical care and daily living.

In relation to our third objective of identifying which concerns contribute to patients' QOL, our findings indicate that all concerns except those related to 'medical information' significantly contributed to QOL. These results suggest that addressing patients' multidimensional concerns can help them effectively improve their QOL. On the other hand, considering the multidimensionality of patients' concerns, intervention would ideally involve multidisciplinary team support for each patient. Multidisciplinary care teams have recently been operating in various contexts of cancer care, including nutrition support teams, rehabilitation and palliative care (28,29). With the aim of improving the quality of cancer treatment that includes QOL, the multidisciplinary care team could consist of, for example, an oncologist, palliative care specialist, psycho-oncologist, expert nurse, pharmacist, dietitian and medical social worker. Because patients' concerns and sense of values have become more diverse with the advancement and diversification of cancer treatment, patients' problems should be screened comprehensively and efficiently, with subjects prioritized, and the right persons placed in the right positions to support them. The Cochrane Database Systematic Review revealed that each psychosocial intervention had only a small effect on QOL of cancer patients, and therefore suggested the need to select the most effective interventions and assign the most appropriate support staff (30).

This study has several limitations. First, patients were recruited over the internet. It was based on relatively little data from patients diagnosed with common cancers (e.g. stomach, colon, lung and liver) and those in the early stages of cancer treatment. The CCAT was only conducted at the website,

namely not face to face. Therefore, our results included the availability of CCAT might not be applicable to patients with all types and all stages of cancer treatment in actual critical scenes. However, data were obtained from patients across the country, minimizing institutional bias. Second, the investigation was cross-sectional in design, which precludes any conclusions about causality between concerns and QOL. Third, the contribution rate of the factor analysis was not extremely high. Thus, other factors might be associated with cancer patients' improved QOL. Future studies are warranted to extend our findings to other cancer sites and cancer treatment stages in actual critical scenes. Also, concrete intervention plans must be prepared when we use this tool and longitudinal study is needed to investigate whether intervention based on the results of cross-sectional studies will affect patients' QOL. Because CCAT is only Japanese version, English version will require future research in order to confirm its utility.

In conclusion, through comprehensive assessment, we have demonstrated the prevalence of cancer patients' concerns. The questionnaire developed in this study can serve as a screening tool to identify cancer patients' concerns. Concerns about psychological symptoms, physical symptoms, daily living, self-management and medical information contributed to patients' QOL directly or indirectly. Intervention by multidisciplinary care teams would be ideal, and experts on these teams should work closely together to support cancer patients.

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Conflict of interest statement

None declared.

References

1. Pachman DR, Barton DL, Swetz KM, Loprinzi CL. Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. *J Clin Oncol* 2012;30:3687–96.
2. Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. *Psychooncology* 2001;10:19–28.
3. McIllmurray MB, Thomas C, Francis B, Morris S, Soothill K, Al-Hamad A. The psychosocial needs of cancer patients: findings from an observational study. *Eur J Cancer Care (Engl)* 2001;10:261–9.
4. Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. *J Clin Oncol* 2010;28:4457–64.
5. Rodríguez AM, Mayo NE, Gagnon B. Independent contributors to overall quality of life in people with advanced cancer. *Br J Cancer* 2013;108:1790–800.
6. Yamagishi A, Morita T, Miyashita M, et al. Pain intensity, quality of life, quality of palliative care, and satisfaction in outpatients with metastatic or recurrent cancer: a Japanese, nationwide, region-based, multicenter survey. *J Pain Symptom Manage* 2012;43:503–14.

7. Hack TF, Pickles T, Ruether JD, et al. Predictors of distress and quality of life in patients undergoing cancer therapy: impact of treatment type and decisional role. *Psychooncology* 2010;19:606–16.

8. Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. *Psychooncology* 2010;19:734–1.

9. Hansen DG, Larsen PV, Holm LV, Rottmann N, Bergholdt SH, Sondergaard J. Association between unmet needs and quality of life of cancer patients: a population-based study. *Acta Oncol* 2010;52:391–1.

10. Akechi T, Okuyama T, Endo C, et al. Patient's perceived need and psychological distress and/or quality of life in ambulatory breast cancer patients in Japan. *Psychooncology* 2011;20:497–505.

11. Miyajima K, Fujisawa D, Hashiguchi S, et al. Symptoms overlooked in hospitalized cancer patients: impact of concurrent symptoms on overlooked by nurses. *Palliat Support Care* 2013;19:1–6.

12. Werner A, Stenner C, Schuz J. Patient versus clinician symptom reporting: how accurate is the detection of distress in the oncologic after-care? *Psychooncology* 2011;4:503–14.

13. Laugsand EA, Sprangers MA, Bjordal K, Skorpen F, Kaasa S, Klepstad P. Health care providers underestimate symptom intensities of cancer patients: a multicenter European study. *Health Qual Life Outcomes* 2010;8:104.

14. Husain A, Barbera L, Howell D, Moineddin R, Bezjak A, Sussman J. Advanced lung cancer patients' experience with continuity of care and supportive care needs. *Support Care Cancer* 2013;21:1351–8.

15. Puts MT, Papoutsis A, Springall E, Tourangeau AE. A systematic review of unmet needs of newly diagnosed older cancer patients undergoing active cancer treatment. *Support Care Cancer* 2012;20:1377–94.

16. Laugsand EA, Jakobsen G, Kaasa S, Klepstad P. Inadequate symptom control in advanced cancer patients across Europe. *Support Care Cancer* 2011;19:2005–14.

17. Okuyama T, Akechi T, Yamashita H, et al. Reliability and validity of the Japanese version of the Short-form Supportive Care Needs Survey questionnaire (SCNS-SF34-J). *Psychooncology* 2009;18:1003–10.

18. Aaronson NK, Ahmedzai S, Bergman B, et al. The European organization for research and treatment of cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–76.

19. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev* 2012;8:CD008465.

20. Mishra SI, Scherer RW, Geigle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database Syst Rev* 2012;8:CD007566.

21. Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. *J Clin Oncol* 2001;19:895–908.

22. Berger AM, Kuhn BR, Farr LA, et al. One-year outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. *J Clin Oncol* 2009;27:6033–40.

23. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. *J Clin Oncol* 2008;26:4651–58.

24. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part 1: sleep and psychological effects. *J Clin Oncol* 2005;23:6083–96.

25. Rabin C, Pinto B, Dunsiger S, Nash J, Trask P. Exercise and relaxation intervention for breast cancer survivors: feasibility, acceptability and effects. *Psychooncology* 2009;18:258–66.

26. Choi KH, Park JH, Park SM. Cancer patients' informational needs on health promotion and related factors: a multi-institutional, cross-sectional study in Korea. *Support Care Cancer* 2011;19:1495–504.

27. Jenkins V, Fallowfield L, Saul J. Information needs of patients with cancer: results from a large study in UK cancer centres. *Br J Cancer* 2001;84:48–51.

28. Kesson EM, Allardice GM, George WD, Burns HJ, Morrison DS. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. *BMJ* 2012;344:e2718.

29. Boxer MM, Vinod SK, Shafiq J, Duggan KJ. Do multidisciplinary team meetings make a difference in the management of lung cancer? *Cancer* 2001;117:5112–20.

30. Goedendorp MM, Gielissen MF, Verhagen CA, Bleijenberg G. Psychosocial interventions for reducing fatigue during cancer treatment in adults. *Cochrane Database Syst Rev* 2009;21:CD006953.

Prevalence, associated factors and source of support concerning supportive care needs among Japanese cancer survivors

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Abstract

Background: The current study aimed to describe cancer survivors' supportive care needs in Japan, to identify associated factors of unmet needs, and to describe the source of support that are preferred and actually used by cancer survivors.

Methods: Using a web-based questionnaire, we examined unmet supportive needs and its associated factors among 628 adult Japanese cancer survivors. The questionnaire comprised 16 items representing five domains (medical-psychological, financial, social-spiritual, sexual, and physical needs).

Results: Prevalence of unmet need ranged from 5 to 18%, depending on different domains. The prevalence was high in medical-psychological and financial domains and relatively low in physical and sexual domains. Poor performance status, psychiatric morbidity and low income status were associated with unmet needs of most domains. Most cancer survivors preferred and actually sought support from their family and friends. Financial needs were preferred to be provided by non-medical professionals. Call for peer support was intense, especially for medical-psychological, social-spiritual, and sexual needs; however, peer support was not well-provided.

Conclusions: This study illustrated characteristics of Japanese cancer survivors who are likely to have unmet needs. The study demonstrated need for expanded involvement of non-medical professionals and peer support, especially in the domains of medical-psychological, social-spiritual, financial and sexual needs.

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Background

The number of cancer survivors has been increasing because of rising incidence of cancer and advances in cancer treatment [1]. This emphasizes the importance of recognizing concerns among cancer survivors.

Supportive care need is defined as 'requirement of some action or resource that is necessary, desirable, or useful to attain optimal well-being' [2]. Needs are considered unmet if required actions/resources have not been provided. Up to 30 to 50% of cancer survivors have unmet supportive needs [3–7], leading to poor quality of life and psychological distress [8]. Therefore, knowledge about their supportive needs and possible source of support is critical for better patient care and policy making.

The understudied topics in this area include the following [2–11]: First, past studies mostly addressed only specific populations in terms of time from cancer diagnosis – either addressing survivors within 1 year from diagnosis [3,4,7] or long-term survivors [6]. Few studies have examined supportive care needs across the 'stages' of cancer survivorship (active treatment, re-entry, and long-term survivorship [12]). Second, findings have been scarce regarding the sources of support that cancer survivors use to meet their needs. Third, while supportive care services must be considered in cultural and health service contexts [13], only a few surveys have been done in Japan, limited to patients with breast and colorectal cancer, or inpatient settings [8,11,14]. In Japan, the National Basic Plan to Promote Cancer Control Programs [15] came to effect in 2007, aiming to establish basic structure of cancer treatment in the country. The plan, revised in 2012, explicitly describes quality of life of cancer survivors as an important agenda.

Therefore, the current study aimed (1) to describe cancer survivors' unmet supportive care needs in Japan, (2) to identify its associated factors, and (3) to describe the source of support that cancer survivors prefer and actually use.

Methods

Participants and procedure

This study was conducted as a part of a larger study [16,17] that aimed to measure quality of life of short-term and long-term cancer survivors in the community. Participants were eligible if they were diagnosed with cancer within 10 years. The participants were recruited through a nationwide commercial-based website-monitoring system (INTAGE research monitor, Inc., http://intage.co.jp). This is a registry used for multiple purposes, ranging from scientific research to commercial marketing. The registrants were recruited through social media and self-selectively registered. The registrants are reimbursed if they participate in surveys. Approximately 1,300,000 people were registered, among whom 2059 people were registered as having been diagnosed with cancer within 10 years.

We aimed to recruit 600 cancer survivors using a stratified sampling method by gender (male : female = 1 : 1) and time since cancer diagnosis (200 survivors each from the following three categories: within 2 years from cancer diagnosis, 2 to 5 years, and 5 to 10 years). We used a cutoff of 2 years in the assumption that patients with certain types of cancers can take more than 1 year until they complete treatment. A cutoff of 5 years is a widely used definition of long-term cancer survivors [18]. The sample size was set because majority of past studies enrolled up to 200 participants [5]. We randomly selected and invited 900 potential participants, with estimation of 60% response rate (based on the previous statistics of the database). The survey was conducted over a week in December 2012 after approval by the institutional review board of Tohoku University.

Measures

Supportive care need

Prior to this study, we reviewed existing supportive care need questionnaires and identified two well-used questionnaires as candidates – the Supportive Care Needs Survey Questionnaire [19,20] and the Cancer Survivors' Unmet Needs measure [21]. However, the former scale lacks important domains for long-term survivors (e.g. employment issues, financial burden, fertility). The latter scale is highly inclined to psycho-social and existential issues and included domains that are not relevant to most Japanese cancer survivors (e.g. parking issue). Furthermore, it has not been validated in Japan. Therefore, we decided to develop an original scale.

We developed a questionnaire based on the items of the Quality of Life Cancer Survivors Instrument (QOL-CS) [22], which was used as an outcome measure in a part of this survey. The QOL-CS comprises 41 items representing four domains (physical, social, psychological, and spiritual well-being) of cancer-specific quality of life. Because the QOL-CS contains multiple items that cover similar concepts and for the purpose of reducing burden of respondents, the research team elaborately rephrased and merged these 41 items into 16 items. We merged six items of physical symptoms (fatigue, appetite, pain, constipation, nausea and overall physical health) into a single item 'physical problems, such as fatigue, appetite, pain, constipation, nausea'. We replaced ten items on psychological well-being (e.g. coping, quality of life, anxiety and depression) by a single item 'psychological issues provoked by cancer'. We merged three items assessing level of distress during each stage of treatment (initial diagnosis, cancer treatments, and time after treatment completion) into one item 'level of distress through cancer diagnosis and treatments'. We merged four items assessing level of fear toward diagnostic tests, cancer recurrence, metastasis and secondary cancer, into a single item of 'your level of fear on diagnostic tests and cancer progression or recurrence'. We replaced seven items assessing spiritual well-being by two items of 'interpersonal and social issues' and 'religious and spiritual issues'. This item was rephrased as such because concept of spirituality was considered unfamiliar to most Japanese survivors, and meaning of life is generally described in societal and interpersonal perspectives [23]. The rest of the items were left unchanged, which included eight items on social concerns (e.g. personal relationship, sexuality, employment, and financial burden), menstrual changes or fertility, and sleep.

Responses to these questions were adopted from Zebrack's web-based need surveys [24,25]. Respondents were asked to endorse one of the following responses: (a) 'Have not used any service and have not had need in that domain', (b) 'Have already used a service and have no further need', (c) 'Have not used any service so far but would like to use in the future', and (d) 'Have used service(s) and would like to use more'. Participants who answered (a) were categorized as having no need. Participants who answered (b) or (d) were categorized as participants with 'service used'. Participants who answered (c) were categorized as having 'unmet need'.

We conducted an exploratory factor analysis in the current sample to see the structure of the questionnaire using the principal component analysis with promax rotation. Based on the scree plot, we considered five-component structure as appropriate. Those five factors were named medical-psychological needs (four items, Cronbach's alpha coefficient = 0.88), financial needs (three items, 0.78), social-spiritual needs (five items, 0.83), sexual needs (two items, 0.80), and physical needs (two items, 0.62). The

correlation coefficients between each factor were weak to moderate ($r = 0.40-0.79$). (Supplementary table)

Source of support — preference and actual use

We asked the participants who had used any service before the survey (i.e. those who answered either (b) or (d)) about the source of support they had used. We asked those who had any needs at the time of survey (i.e. those who answered either (c) or (d)) about the kind of support they would like to use further. The participants were allowed to choose as many answers as they liked from among (1) medical professionals, (2) non-medical professionals, (3) peer support, and (4) family or friends.

Psychological distress

Psychological distress was measured using the K6 scale [26], a self-rated six-item questionnaire exploring the frequency of psychological distress during the past 30 days. The K6 scores range from 0 to 24. Those who scored 15 or more were classified as having psychiatric morbidity [27].

Perceived social support

Participants' perceived social support was assessed with the short-version Multidimensional Scale of Perceived Social Support [28]; a well-validated seven-item questionnaire with seven-point scales. The participants were divided into two groups according to the median score.

Demographic and medical characteristics

We asked the participants of their demographic and clinical information, as listed in Table 1.

Statistical analysis

First, we conducted descriptive analyses to characterize the overall study sample, summarizing the proportions of patients indicating no need, service used and unmet need in each of the 16 need areas. Ratios of service used : unmet need were calculated for each need to describe proportion of participants who received appropriate services. Also, we compared prevalence of unmet needs according to time since last treatment, using chi-squared test and Fisher's exact test where appropriate. Second, we conducted binary logistic regression analyses to explore associated factors of unmet needs. Demographic and clinical variables, psychiatric morbidity and social support, were entered as independent variables. A backward stepwise selection method was used to reduce non-significant variables from the models, with a p-value of <0.1 on the Wald statistics. Participants with missing values were excluded from this analysis. Further, we conducted descriptive analyses on source of support which the participants (1) preferred

and (2) actually used. Data were analyzed with the SPSS version 21.0 (IBM). All the tests were two-tailed, with p-value of <0.05.

Table 1. Demographic background (n = 628)

Characteristics		n	%
Age	<50	190	30.3
	50–64	267	42.5
	≥65	171	27.2
Gender	Male	314	50
	Female	314	50
Marital status	Married	502	79.9
	Single or divorced/ widowed	126	20.1
Having child(ren)	Yes	464	73.9
	No	164	26.1
Age of youngest child	<College graduation	164	35.3
(n = 464)	≥College graduation	300	64.7
Household size	Living alone	70	11.1
	Two or more	558	88.9
Occupational status	Employed	277	44.1
	Unemployed	351	55.9
Annual income	<4m yen	214	34.1
	≥4m yen	368	58.6
	Unknown	46	7.3
Change in income status	No change	397	63.2
	Decreased	216	34.4
	Increased	15	2.4
Cancer site	Lung	23	3.7
	Gastrointestinal	163	26.0
	Breast	165	26.3
	Urological	126	20.0
	Gynecological	44	7.0
	Other	107	17.0
Years since diagnosis	<2 years	211	33.6
	2–5 years	208	33.1
	5–9 years	209	33.3
Performance status	0	413	65.8
	1	200	31.8
	2	13	2.1
	3	2	0.3
Received treatment (absolute number)	Surgery	530	84.4
	Radiation therapy	194	30.9
	Chemotherapy	248	39.5
	Hormonal therapy	201	32
Treatment combination	Surgery (=Sur) only	187	30
	Radiation therapy (=Rt) only	8	1
	Chemotherapy (=Cx) only	12	2
	Hormonal therapy (=Hor) only	11	2
	Sur + Rt + Cx + Hor	52	8
	Sur + Rt + Cx	39	6
	Sur + Rt + Hor	49	8
	Sur + Rt	26	4
	Sur + Cx + Hor	28	4
	Sur + Cx	104	17
	Sur + Hor	45	7
	Rt + Cx + Hor	1	0
	Rt + Cx	8	1
	Rt + Hor	11	2
	Cx + Hor	4	1
	No treatment	43	7

Results

Participants' characteristics

Of 900 candidate participants, 628 responded and completed the questionnaire (response rate: 69.7%). Data of 46 survivors with missing values were excluded from the logistic analysis. The participants' mean age was 56 years. Most participants were in good performance status. Type of cancer was skewed toward breast and prostate cancers, and proportion of lung and gastric cancers were smaller than Japanese general population sample [29] (Table 1).

Prevalence of no need, service used, and unmet need

Approximately 5 to 18% of the participants had unmet need in any of the 16 areas of needs (Table 2). The prevalence was generally high in medical-psychological and financial domains and low in physical and sexual domains. Ninety-five participants (15.1%) endorsed one domain of unmet needs, and 162 participants (25.7%) endorsed two or more domains (data not shown). The ratio of service used : unmet need shows that services were relatively well used for medical-psychological needs, social-spiritual needs, and physical needs and relatively less for sexual needs (Table 2). The prevalence of unmet needs was constant after treatments (Table 3).

Associated factors of unmet needs

Table 4 shows the associated factors of unmet needs of each domain. Poor performance status and psychiatric morbidity were associated with unmet needs of most domains. Gender, marital status, cohabitants, change in income, and social support were not associated with unmet needs. Employed survivors were more likely to have unmet medical-psychological needs. Unmet sexual needs are remarkable among younger survivors, survivors of urological cancer, and survivors who passed long after surgery. Presence of young children was associated with unmet social-spiritual needs. Lower income was associated with unmet medical-psychological, financial, and social-spiritual needs. Prevalence of unmet needs did not differ among groups in terms of time since cancer diagnosis for any domain of needs.

Preference and actual use of support

In Figure 1, we illustrated both actual and preferred source of support. Most cancer survivors preferred and actually sought support from their family and friends, except for physical problems. Support from medical professionals was preferred for most of the needs except for financial needs. Non-medical professionals (e.g. social welfare, labor union, job-coordination center, professional helpers, and insurance company) were the preferred source of support for financial needs. Call for peer support was intense,

Table 2. Prevalence of no need, service used and unmet need

	No need		Service used		Unmet need		Service used :
	n	%	n	%	n	%	Unmet need
Factor 1: medical-psychological needs							
Concerns about illness or treatment	373	59.4	174	27.7	81	12.9	2.1:1
Psychological problems	386	61.5	166	26.4	76	12.1	2.2:1
Fear of recurrence	306	48.7	213	33.9	109	17.4	2:1
Concerns about family	344	54.8	209	33.3	75	11.9	2.8:1
Factor 2: financial needs							
Financial burden	338	53.8	178	28.3	112	17.8	1.6:1
Interference in employment	401	63.9	136	21.7	91	14.5	1.5:1
Interference in home activities	388	61.8	185	29.5	55	8.8	3.4:1
Factor 3: social-spiritual needs							
Personal relationship problems	408	65.0	178	28.3	42	6.7	4.2:1
Religious and spiritual problems	530	84.4	69	11.0	29	4.6	2.4:1
Support from other people	268	42.7	318	50.6	42	6.7	7.6:1
Social problems	420	66.9	123	19.6	85	13.5	1.4:1
Isolated feeling	411	65.4	154	24.5	63	10.0	2.4:1
Factor 4: sexual needs							
Menstrual changes and fertility	508	80.9	64	10.2	56	8.9	1.1:1
Sexuality	481	76.6	84	13.4	63	10.0	1.3:1
Factor 5: physical needs							
Sleep problems	460	73.2	117	18.6	51	8.1	2.3:1
Physical problems	440	70.1	144	22.9	44	7.0	3.3:1

Table 3. Prevalence of unmet needs according to time since latest treatments

Time since last administration of each type of treatment	None n (%)	<3 months n (%)	3 months–1 year n (%)	1–5 years n (%)	5–10 years n (%)
Factor 1: medical-psychological needs					
Surgery	22 (22.4)	9 (16.4)	27 (28.7)	58 (22.8)	26 (20.5)
Chemotherapy	88 (23.2)	17 (28.3)	8 (21.1)	22 (21.8)	7 (14.3)
Hormonal therapy	91 (21.3)	25 (24.5)	5 (26.3)	14 (26.4)	7 (25.9)
Radiation therapy	98 (22.6)	9 (33.3)	6 (24)	21 (21)	8 (19)
Factor 2: financial needs					
Surgery	20 (20.4)	16 (29.1)	24 (25.5)	71 (28)	27 (21.3)
Chemotherapy*	85 (22.4)	21 (35)	15 (39.5)	29 (28.7)	8 (16.3)
Hormonal therapy	101 (23.7)	30 (29.4)	4 (21.1)	18 (34)	5 (18.5)
Radiation therapy	102 (23.5)	11 (40.7)	7 (28)	30 (30)	8 (19)
Factor 3: social-spiritual needs					
Surgery	19 (19.4)	10 (18.2)	17 (18.1)	59 (23.2)	25 (19.7)
Chemotherapy	74 (19.5)	15 (25)	9 (23.7)	21 (20.8)	11 (22.4)
Hormonal therapy	88 (20.6)	22 (21.6)	4 (21.1)	13 (24.5)	3 (11.1)
Radiation therapy	85 (19.6)	8 (29.6)	7 (28)	21 (21)	9 (21.4)
Factor 4: sexual needs					
Surgery	7 (7.1)	5 (9.1)	11 (11.7)	35 (13.8)	20 (15.7)
Chemotherapy	42 (11.1)	7 (11.7)	6 (15.8)	15 (14.9)	8 (16.3)
Hormonal therapy	46 (10.8)	12 (11.8)	4 (21.1)	11 (20.8)	5 (18.5)
Radiation therapy	51 (11.8)	5 (18.5)	3 (12)	11 (11)	8 (19)
Factor 5: physical needs					
Surgery	9 (9.2)	6 (10.9)	9 (9.6)	38 (15)	16 (12.6)
Chemotherapy	44 (11.6)	10 (16.7)	1 (2.6)	17 (16.8)	6 (12.2)
Hormonal therapy	53 (12.4)	15 (14.7)	1 (5.3)	7 (13.2)	2 (7.4)
Radiation therapy	52 (12)	5 (18.5)	4 (16)	12 (12)	5 (11.9)

*$p < .05$; chi-squared test and Fisher's exact test.

Table 4. Associated factors of unmet needs ($n = 582$)

	Factor 1: medical-psychological needs		Factor 2: financial needs		Factor 3: social-spiritual needs		Factor 4: sexual needs		Factor 5: physical needs	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Age (reference: ≥65)										
<50	—	—	—	—	—	—	2.49*	1.03–6.00	—	—
Age of youngest child (reference: ≥college graduation)										
<College	—	—	—	—	2.12**	1.22–3.70	—	—	—	—
Employment status: employed (reference: unemployed)	1.90**	1.23–2.94	—	—	—	—	—	—	—	—
Annual income: <4m yen (reference: ≥4m yen)	1.99**	1.27–3.13	2.26***	1.51–3.38	1.93**	1.20–3.12	—	—	—	—
Cancer site (reference: others)										
Urological	—	—	—	—	—	—	4.67**	1.71–12.79	—	—
Time since latest surgery (reference: no surgery)										
5–10 years	—	—	—	—	—	—	3.46*	1.30–9.25	—	—
Performance status (PS): ≥1 (reference: PS = 0)	2.02**	1.31–3.13	2.25***	1.48–3.42	2.85***	1.80–4.50	—	—	4.24***	2.43–7.35
Psychiatric morbidity (K6 ≥ 15)	3.55***	2.29–5.46	1.72*	1.12–2.64	4.65***	2.95–7.35	2.59**	1.49–4.52	2.72***	1.59–4.65
Cox-Snell R2	0.114		0.108		0.160		0.068		0.087	
Nagelkerke R2	0.176		0.160		0.254		0.130		0.166	

Only significant variables were demonstrated.
OR, odds ratio.
*$p < .05$
**$p < .01$
***$p < .001$

Figure 1. Preference and actual use of support

especially for medical-psychological, social-spiritual, and sexual needs; however, peer support was generally not well-provided.

Discussion

This survey demonstrated prevalence of unmet supportive care needs among Japanese cancer survivors as 4.6 to 17.8%, depending on different domains. These figures are lower than those of survivors who are under treatment [3–5,7] and are comparable with those of long-term cancer survivors [6]. The prevalence was high in psychological domain and low in sexual domain. Prevalence of unmet needs was generally not different either according to time since cancer diagnosis or since last administration of treatments. Cancer survivors should be examined for their unmet needs long after cancer diagnosis and completion of treatment.

Medical professionals and family/friends are the two major sources of support. In contrast, gaps between preference and actual use of peer support and support by non-medical professionals were remarkable. Call for support by non-medical professionals is remarkable for financial needs. In Japan, approximately 30% of patients with

cancer quit their job after cancer diagnosis, and the large proportion of the rest was obliged to change their work status from full-time to part-time employment [30,31]. As conceptualized in the reviews by Feuerstein et al. [32] and Mehnert [33], cancer survivors need multifactorial support for employment by multiple disciplines [30,31,34].

Need for peer support has long been questioned in Japan because Japanese people have been considered as less likely to share their illness experience with others [35]. Only 20% of all designated cancer centers in Japan are equipped with peer support programs as of 2013, despite the recommendation in Japanese Basic Plan to Promote Cancer Control Programs [15,36,37]. Our results argue for further promotion of peer support programs. Peer support is expected to supplement professional psychological services, where patients with cancer are often reluctant to consult [38].

Cancer survivors with unmet sexual needs are frequently not provided with any service. Sex-related issues are infrequently discussed in clinical practice in Japan [39], and increasing clinicians' awareness and clinical skills are imperative. Considering that cancer survivors perceive family and friends as an important source of
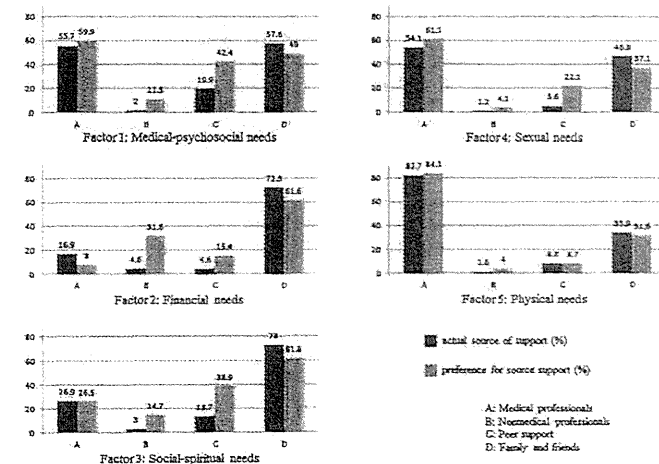
support, proactive education to family can be helpful. Topics including treatment-induced sexual challenges and intercouple communication should be covered in family education [40] and probably in peer support as well.

The strength of our study is relatively large sample size with well-balanced distribution of participants in regards to time since their cancer diagnoses. Use of web-based survey is also advantageous because this

enabled to access cancer survivors who do not come to clinics on regular basis.

The most important study limitation is representativeness of the sample. The participants were limited to those who have internet literacy and those who were self-selectively registered to a database. Distribution in age and type of cancers is slightly different from that of general cancer population in Japan. The participants were limited to those in good performance status; therefore, we may have underestimated unmet needs. No difference was made between survivors during and past primary treatment. The second limitation is that our need assessment instrument has not been validated. The items of interest were selected somewhat arbitrarily, although they were derived from a validated quality-of-life instrument and have been selected on agreement of multidisciplinary study team. The questionnaire lacked items on information needs, which have been listed as an important domain of needs in other need instruments. Majority of participants endorsed multiple domains of unmet needs, suggesting need for investigating the impact of different need combinations. Finally, the cross-sectional design provides no information on causal relationship. In particular, variables of time since cancer diagnosis/last treatment should be examined further in longitudinal studies.

Conclusions

Despite its limitations, our study is noteworthy because this is the first study in Japan that assessed unmet needs of cancer survivors along with preference and usage of service. The study depicted survivors at risk for unmet needs in different domains. The study also highlighted need for continued and expanded involvement of non-medical professionals and peer support in the care of cancer survivors, especially in the domains of medical-psychological, social-spiritual, financial and sexual needs.

Acknowledgements

Conflict of interest

The authors have declared no conflicts of interest.

References

1. Katanoda K, Matsuda T, Matsuda A, et al. An updated report of the trends in cancer incidence and mortality in Japan. Jpn J Clin Oncol 2013;43(5):492–507.

2. Sanson-Fisher R, Girgis A, Boyes A, et al. The unmet supportive care needs of patients with cancer. Support Care Rev Group Cancer 2000;88:226–237.

3. Armes J, Crowe M, Colbourne L, et al. Patients' supportive care needs beyond the end of cancer treatment: a prospective, longitudinal survey. J Clin Oncol 2009; 27(36):6172–6179.

4. Boyes AW, Girgis A, D'Este C, et al. Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a population-based cross-sectional study. BMC Cancer 2012;12:150.

5. Harrison JD, Young JM, Price MA, et al. What are the unmet supportive care needs of people with cancer? A systematic review. Support Care Cancer 2009; 17(8):1117–1128.

6. Harrison SE, Watson EK, Ward AM, et al. Primary health and supportive care needs of long-term cancer survivors: a questionnaire survey. J Clin Oncol 2011; 29(5):2091–2098.

7. McDowell ME, Occhipinti S, Ferguson M, et al. Predictors of change in unmet supportive care needs in cancer. Psycho-Oncology 2010;19(5):508–516.

8. Akechi T, Okuyama T, Endo C, et al. Patient's perceived need and psychological distress and/or quality of life in ambulatory breast cancer patients in Japan. Psycho-Oncology 2011;20(5):497–505.

9. Sanders SL, Bantum EO, Owen JE, et al. Supportive care needs in patients with lung cancer. Psycho-Oncology 2010;19(5):480–489.

10. Ream E, Quennell A, Fincham L, et al. Supportive care needs of men living with prostate cancer in England: a survey. Br J Cancer 2008;98(12):1903–1909.

11. Fujisawa D, Park S, Kimura R, et al. Unmet supportive needs of cancer patients in an acute care hospital in Japan--a census study. Support Care Cancer 2010;18(11): 1393–1403.

12. Stanton AL. What Happens Now? Psychosocial Care for Cancer Survivors After Medical Treatment Completion. J Clin Oncol 2012;30:1215–1220.

13. Lam WW, Au AH, Wong JHF, et al. Unmet supportive care needs: a cross-cultural comparison between Hong Kong Chinese and German Caucasian women with breast cancer. Breast Cancer Res Treat 2011;130: 531–541.

14. Fielding R, Lam WW, Shun SC, et al. Attributing variance in supportive care needs during cancer: culture-service, and individual differences, before clinical factors. PLoS One 2013;8(5):e65099.

15. Japanese Ministry of Health Labor and Welfare. Cancer Control Measures. http://www. mhlw.go.jp/english/wp/wp-hw5/dl/23010222e. pdf [as accessed on 06/24/2014].

16. Fujisawa D, Fujimori M, Umezawa S, et al. Survey on quality of life among long-term cancer survivors. Annual report of Clinical Cancer Research Grant, Japanese Ministry of Health Labor and Welfare 2013;41–45 [Japanese].

17. Fujisawa D, Umezawa S, Basaki-Tange A, et al. Smoking status, service use and associated factors among Japanese cancer survivors-a web-based survey. Support Care Cancer 2014; May 22. DOI: 10.1007/s00520-014-2284-2.

18. Jefford M, Rowland J, Grunfeld E, et al. Implementing improved post-treatment care for cancer survivors in England, with reflections from Australia, Canada, and the USA. Brit J Cancer 2012;108:14–20.

19. Boyes A, Girgis A, Lecathelinais C. Brief assessment of adult cancer patients' perceived needs: development and validation of the 34-item Supportive Care Needs Survey (SCNS-SF34). J Eval Clin Pract 2009;15(4): 602–606.

20. Okuyama T, Akechi T, Yamashita H, et al. Reliability and validity of the Japanese version of the Short-form Supportive Care Needs Survey questionnaire (SCNS-SF34-J). Psycho-Oncology 2009;18(9):1003–1010.

21. Hodgkinson K, Butow P, Hunt GE, et al. The development and evaluation of a measure to assess cancer survivors' unmet supportive care needs: the CaSUN (Cancer Survivors' Unmet Needs measure). Psycho-Oncology 2007;16(9):796–804.

22. Ferrell BR, Dow KH, Grant M. Measurement of the quality of life in cancer survivors. Qual Life Res 1995;4(6):523–531.

23. Morita T, Tsunoda J, Inoue S, et al. An exploratory factor analysis of existential suffering in Japanese terminally ill cancer patients. Psycho-Oncology 2000;9(2):164–168.

24. Zebrack B. Information and service needs for young adult cancer survivors. Support Care Cancer 2009;17(4):349–357.

25. Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. Cancer 2013;119(1):201–214.

26. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002;32(6): 959–976.

27. Furukawa TA, Kawakami N, Saitoh M, et al. The performance of the Japanese version of the K6 and K10 in the World Mental Health Survey Japan. Int J Methods Psychiatr Res 2008;17(3):152–158.

28. Dahlem NW, Zimet GD, Walker RR. The Multidimensional Scale of Perceived Social Support: a confirmation study. J Clin Psychol 1991;47(6):756–761.

29. Matsuda A, Matsuda T, Shibata A, et al. Cancer Incidence and Incidence Rates in Japan in 2008: A Study of 25 Population-based Cancer Registries for the Monitoring of Cancer Incidence in Japan (MCIJ) Project. Jpn J Clin Oncol 2013;44(4):388–396.

30. Yamaguchi K. The views of 7885 people who faced up to cancer: Towards the creation of a database of patients' anxieties: A report on research into the anxieties and burdens of cancer sufferers. Joint Study Group on the Sociology of Cancer. http://www.scchr.jp/cancerqa.html 2004 [as accessed on 04/25/2014].

31. Takahashi M, Saito N, Muto K, et al. Survey on medical treatment and employment. http://first.cancer-work.jp/wp-content/uploads/2012/08/investigation_report2012.pdf [as accessed on 04/25/2014] [Japanese].

32. Feuerstein M, Todd B, Moskowitz M, et al. Work in cancer survivors: a model for practice and research. J Cancer Surviv 2010;4:415–437.

33. Mehnert A. Employment and work-related issues in cancer survivors. Crit Rev Oncol Hematol 2011;77:109–130.

34. Mehnert A, de Boer A, Feuerstein M. Employment challenges for cancer survivors. Cancer 2013;119(11Suppl):2151–2159.

35. Ohnuki-Tierney E. Illness and culture in contemporary Japan. Cambridge University Press: NY, 1984;51–74.

36. National Cancer Center information service website. http://hospdb.ganjoho.jp/kyotendb.nsf/fTopSoudan?OpenForm [as accessed on 10/21/2013] [Japanese].

37. Kawakami S, Yanagisawa A, Konishi T, et al. Agenda for dissemination of peer support by cancer survivors. Jpn J Cancer Chemother 2014;41(1):31–35 [Japanese].

38. Endo C, Akechi T, Okuyama T, et al. Patient-perceived barriers to the psychological care of Japanese patients with lung cancer. Jpn J Clin Oncol 2008;38(10): 653–660.

39. Takahashi M, Kai I, Hisata M, et al. Attitudes and practices of breast cancer consultations regarding sexual issues: a nationwide survey of Japanese surgeons. J Clin Oncol 2006;24(36):5763–5768.

40. Takahashi M, Ohno S, Inoue H, et al. Impact of breast cancer diagnosis and treatment on women's sexuality: a survey of Japanese patients. Psycho-Oncology 2008;17(9):901–907.

Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site.

ディジーズマネジメント

❶ がん緩和：がんとうつ病の関係

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「がん対策基本法」が2007年に施行され，2012年にはがん対策のマスタープランである「がん対策推進基本計画」が改定され，実地の声を反映させるべく各都道府県での医療計画も作成された．今回の基本計画の改定では，がん患者・家族の強い意向を反映して，「早期からの緩和ケア」が「診断時からの緩和ケア」とより明確に示された点と，「精神心理的苦痛の軽減」がより明確に掲げられた．患者・家族の精神的苦痛を軽減するために，うつ病への対策をはじめ，精神心理的ケアの充実が求められている．本稿では，がん領域のうつ病への対策の現状を紹介したい．

臨床をとらえなおし，患者を全人的にとらえるためにbiological（生物学的），psychological（心理学的），social（社会的）と多層的な視点からアプローチを試みる分野が精神腫瘍学（サイコオンコロジー；psycho-oncology）である．

これらの臨床・研究の成果を踏まえ，がんに関連する心理・社会的問題への障壁を取り払い，等しくケアが提供されることを目標にして，米国のNCCN（National Comprehensive Cancer Network）は心理・社会的問題を「Distress（つらさ）」として包括し，評価と治療のガイドラインを作成・公開している[2]．

がん患者と心理・社会的問題

がん患者とその家族は様々な精神的，心理・社会的問題を抱えている．実際にがん患者の20〜40％に重度の心理・社会的問題が認められ，その問題に対して適切な援助が提供されている患者は10％にも満たない[1]．適切な提供がなされていない背景には，「精神的」や「心理的」，「感情の問題」といった言葉にスティグマ，負のイメージがついてまわり，患者が医療者に対して相談を躊躇すること，多忙な診察のなかで医師が患者に心理・社会的問題について尋ねる余裕のないことが指摘されている[2]．その反省を受け，がんの

うつ状態・うつ病

がん治療全般をとおして，様々な精神症状が出現する．がん患者のおよそ30〜40％に何らかの精神医学的問題が認められる．特に頻度の高い疾患は，せん妄と大うつ病，適応障害である[3]．抑うつ状態はがんの原発部位にかかわらず，あらゆる時期に出現する．わが国の有病率調査では，大うつ病は約5％で，適応障害が15〜25％であった．がん医療において，うつ病の診断・治療の重要性が繰り返し指摘される背景には，いくつかの原因があげられる．

抑うつ状態は一般的であるにもかかわらず，しばしば見落とされる

がん患者においても，うつ病の主たる身体症状は不眠，食欲不振，全身倦怠感である．これらの症状はがん自体で生じる症状や，がん治療の有害事象と重なるため，患者自身も医療者も抑うつ状態に伴う身体症状と考えず，見落とされることが知られている[4]．

また，抑うつ状態は喪失体験による心理的反応に伴い出現することも多い．そのため，「喪失体験があるならば，抑うつ状態に陥っても当然である」といった医療者側の誤解も生じやすい．加えて，医療者の知識不足による抑うつ症状の過小評価，医療者が精神症状を評価することをためらうことにより，抑うつ状態が見落とされ，誤った対応をされがちであることも知られている[5]．

QOLの低下を招く

抑うつ症状自体がQOLの低下を招くと同時に，無価値感や自責感により積極的ながん治療を拒否することをとおして，身体治療の成績にも影響する[6]．また，患者が抑うつ状態であること自体が家族の精神的苦痛を悪化させる．

器質的な原因が重畳する

がん患者の抑うつ状態の背景を評価する際に，ストレス因子など心理的要因との関連に注意が向きがちだが，同時に原疾患による脳転移や腫瘍随伴症候群，高カルシウム血症，医原的な要因の強い薬剤性（ステロイドや抗悪性腫瘍薬，降圧薬），全脳照射も抑うつ状態を引き起こす．抑うつ状態を評価するときには，治療内容の変化との時間関係や治療効果，今後の治療計画を総合的に評価することが重要である．

疼痛との関連

疼痛が適切に緩和されていないと，抑うつ状態を生じることが示されている．疼痛が緩和されないために，「生きる価値がない，生きていてもしかたがない」と感じ，希死念慮を生じることがある．疼痛の軽減を図ることで抑うつも軽減することができるため，うつ病を疑う場合には身体症状の評価も同時に行う必要がある．

自殺

がん患者の自殺率は一般人口に比べて高く，特に告知後1週間以内では12倍，1年以内でも3倍に及ぶ[7]．がん患者が自殺企図や希死念慮を訴える背景には，抑うつ状態の合併や疼痛の合併，進行がん，診断から早期（3〜6か月以内），貧弱なソーシャルサポートがあることが指摘されている．特に絶望感は抑うつ状態とは独立した要因である．自殺を予防するために，たとえば進行がんの初回治療時から精神症状緩和をはじめ，身体症状緩和，ソーシャルサポートの構築など，身体症状・精神症状・社会的問題に対する包括的な支援が必要である．

高齢がん患者の抑うつ状態

加齢は発がんのリスクであると同時に，うつ病や自殺のリスク因子でもある．高齢者の抑うつ状態は，若年者と異なり抑うつ気分を自覚・訴えることは少ない．代わりに興味の喪失や認知機能の低下（記憶力の低下，集中困難），身体不定愁訴を訴えることが多い．

スクリーニング

臨床的な問題として，主治医や看護師など多忙なプライマリーチームは抑うつ状態を見落としが