

### まとめ：基盤整備の議論の際には区別

- ▣ ローカル と セントラル
- ▣ 製薬企業に魅力的な領域 と そうでない領域
- ▣ 早期開発のリソース と 後期開発のリソース
- ▣ 単施設の試験 と 多施設の試験

16

これは最後のまとめです。今日、議論の際に区別して頂きたい点です。ローカルの話とセントラルの話に分けましょう。製薬企業に魅力的な領域とそうでない領域は、基盤整備の考え方は変えましょう。早期開発のリソースと後期開発のリソースを区別して議論しましょう。単施設の試験と多施設の試験では、必要なリソース、ノウハウ、スキルは違うということを踏まえて議論して頂きたいと思います。どうぞご清聴ありがとうございました。(拍手)

(野口先生)

どうもありがとうございます。後のディスカッションに多大な宿題を頂いたようで、今から頭を悩ましながら考えさせられる内容でございました。

## Factors related to anxiety and depression in women with breast cancer and their husbands: role of alexithymia and family functioning

Tomoyuki Mantani · Toshinari Saeki · Shinichi Inoue · Hitoshi Okamura · Minako Daino · Tsuyoshi Kataoka · Shigeto Yamawaki

Received: 18 September 2006 / Accepted: 20 December 2006 / Published online: 10 January 2007  
© Springer-Verlag 2007

### Abstract

**Goals of work** The purpose of this study was to explore alexithymia, family functioning, and other factors that might affect anxiety and depression levels in women with breast cancer and in their husbands.

**Patients and methods** A cross-sectional study was undertaken in 46 postsurgical ambulatory women with breast cancer and their husbands. Documented informed consent

for the study was obtained from each subject. All subjects completed the Zung self-rating anxiety scale (SAS), the Zung self-rating depression scale (SDS), the 20-item Toronto alexithymia scale (TAS-20), and the family assessment device (FAD).

**Main results** Multiple regression analysis revealed that a high degree of alexithymia in patients correlated with a high degree of patient anxiety. Patient perceptions of inappropriate affective responsiveness among family members correlated with a high degree of depression. Among husbands, a high degree of anxiety was correlated with their own high level of alexithymia or low level of education, and with the occurrence of adjuvant therapy in their wives. Husband perceptions of inappropriate sharing of roles among family members, their own low education level, and a large number of family members correlated with high degrees of depression among them.

**Conclusions** The present study revealed that alexithymia and family functioning are associated with anxiety and depression, respectively, in both women with breast cancer and in their husbands. Individual traits such as alexithymia and family functioning should be taken into account when we intervene to treat anxiety and depression in breast cancer patients and their husbands.

**Keywords** Breast cancer · Couple · Anxiety · Depression · Alexithymia · Family functioning

T. Mantani · S. Yamawaki (✉)

Department of Psychiatry and Neurosciences, Division of Frontier Medical Science, Programs for Biomedical Research, Graduate School of Biomedical Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan  
e-mail: yamawaki@hiroshima-u.ac.jp

T. Saeki

Department of General Medicine, Hiroshima University Hospital, Hiroshima, Japan

S. Inoue

Senogawa Hospital, Hiroshima, Japan

H. Okamura

Department of Psychosocial Rehabilitation, Graduate School of Health Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan

M. Daino

Graduate School of Nursing, Asahikawa Medical College, Asahikawa, Japan

T. Kataoka

Department of Health Care for Adults, Graduate School of Health Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan

### Introduction

Anxiety and depression are important and prevalent problems affecting the quality of life of women with breast cancer. A frequently cited study by Derogatis and

colleagues [13], involving 215 randomly selected adult inpatients and outpatients being treated for three different types of cancer, found that 47% were having psychiatric disorders. Among the 47%, more than two-thirds (68%) had “reactive” or situational anxiety and depression (adjustment disorders with anxious or depressed mood), and 13% had major depression.

Family members are typically regarded as caregivers for cancer patients. In family studies of adult cancer patients, the patients’ spouses, in particular, have been the focus of attention as a valued source of emotional support [4, 5, 29]. However, in some studies, spouses reported having as much distress as the patients themselves [42, 44] or even more [4, 29]. Thus, spouses can be considered “second-order patients”, and they may require some form of medical attention.

On the other hand, many studies have been conducted to determine who is at greatest risk of adjustment problems so that support services can be targeted to them. Thus far, social support has been reported to play an important role in the adjustment of both breast cancer patients and their spouses [7, 21, 40, 41] and has attracted considerable attention as a feasible target of treatment. However, some researchers have indicated the limited usefulness of the social support concept for designing preventive or therapeutic interventions and have proposed the importance of focusing on more specific and more detailed processes [11, 12, 49].

Other studies, meanwhile, have focused on the association between communication and distress in couples. These studies have consistently indicated that a breast cancer patient’s partner is a valuable source of emotional support: patients usually want to talk about their concerns with their partner and often find it problematic when they and their partner are not communicating well [31, 38, 46]. Also, empathy has been believed to play a particularly important role in good communication [19, 23, 32, 48].

Rarely, however, few researchers have tried to explain why empathetic communication is poor in some cancer patients and families. Empathy is known to include an ability to identify another’s emotions and to express one’s own emotions. On the other hand, it has been reported that the people who do not express their emotions can hardly obtain support and ruin their psychological health [45, 52]. That is, cancer patients or their families who do not express their emotions may increase not only patient distress but also their own. To avoid this, it is very important to examine why some people in this situation do not express their emotions. Regarding this problem, some researchers have focused on the emotional control involved in conscious restraint against the expression of emotion [22, 59]. Besides emotional control, however, other explanations of why it is difficult for some people to express emotions have not been examined.

Alexithymia is a famous psychological characteristic involving difficulty in expressing emotions and in identifying their own feelings or those of others. The concept initially evolved from clinical observations of patients with psychosomatic disorders; the term was introduced by Nemiah and Sifneos during the early 1970s [37]. The salient features of this construct are as follows: (1) difficulty identifying and describing subjective feelings; (2) difficulty distinguishing between feelings and bodily sensations of emotional arousal; (3) constricted imaginal capacities; and (4) an externally oriented cognitive style [37]. Alexithymia is a common condition, existing in about 10% of healthy people. It has been reported to exist at even higher rates not only in individuals with psychosomatic disease but also in those with panic disorder, posttraumatic stress disorder (PTSD), eating disorder, substance abuse disorder, and so on [58]. It is now considered a possible risk factor in various psychiatric diseases. Moreover, it is difficult for alexithymic people to comprehend the feelings of other people and to make empathic responses [58]. So, we thought it might be important to investigate the relationship between distress and the degree of alexithymia in breast cancer patients and their spouses.

Meanwhile, family members have various functions besides communication. Recently, well-validated questionnaires for evaluating family functioning have been developed, through which several researchers have reported the relationship between poor family functioning and psychological distress in families with cancer patients (e.g., [27, 28]). The concept of family functioning also may be useful for clarifying who is at greatest risk of adjustment problems among these subjects.

The purpose of this study was to explore alexithymia, family functioning, and other factors that might influence anxiety and depression levels in women with breast cancer and in their husbands.

## Materials and methods

### Study sample and procedure

Patients meeting the following criteria were drawn consecutively from the outpatient population of the Mammary Gland Dispensary of Hiroshima University Hospital during the 6-month period from October 1999 to March 2000:

- (1) diagnosis of stage I or II breast cancer followed by surgery for it;
- (2) having been informed of this diagnosis,
- (3) 20 years of age or older,
- (4) interval of more than 3 months between the initial surgery for breast cancer and the interview for the present study,

- (5) married woman living with her husband,
- (6) well enough physically to complete several questionnaires,
- (7) Eastern Cooperative Oncology Group performance status (PS) of 0–2,
- (8) absence of cognitive impairment,
- (9) no active concomitant malignancy.

We selected patients who had undergone surgery for breast cancer at least 3 months before the interview because an earlier report showed that most patients can psychologically adapt to bad news within 3 months after learning of it [1]. Eligible patients and their husbands were asked to complete several questionnaires, provided both the patient and her husband gave written consent to participate in the study. Patient characteristics and data on the severity of pain in each patient were obtained by a brief interview conducted by a trained psychologist. The pain severity was measured by a four-point Likert scale (1 “not at all” to 4 “very much”). Medical data regarding Eastern Cooperative Oncology Group performance status (PS), treatment regimen, and months elapsed after surgery were collected from patient records. All data were determined at the date of the interview. This study was approved by the Institutional Review Board and the Ethics Committee of Hiroshima University Hospital, Japan.

#### Psychological measurement

##### *Zung self-rating anxiety scale SAS*

The degree of anxiety was measured by the Japanese version of the Zung self-rating anxiety scale. The SAS is a self-report questionnaire with 20 items rated on a four-point scale [61]. A previous study by our colleagues suggested that the Japanese version of the SAS has high validity and reliability [43]. A high score indicated a high degree of anxiety.

##### *Zung self-rating depression scale SDS*

The degree of depression was measured by the Japanese version of the Zung self-rating depression scale. The SDS is a self-report questionnaire with 20 items rated on a four-point scale [60]. Fukuda and Kobayashi [16] suggested that the Japanese version of the SDS has high validity and reliability. A high score indicated a high degree of depression.

##### *The 20-item Toronto alexithymia scale (TAS-20)*

The degree of alexithymia was measured using the Japanese version of the TAS-20. The TAS-20 is a self-report questionnaire with 20 items rated on a five-point scale with

a three-factor structure: (1) difficulty in identifying feelings; (2) difficulty in describing feelings; (3) externally oriented thinking. Previous studies have suggested that the TAS-20 has adequate validity and reliability [2, 3] and that the Japanese version of the TAS-20 also has high construct validity and reliability [18]. In this study, the TAS-20 total score was used as an index of the degree of alexithymia. A high score indicated a high degree of alexithymia.

##### *Family assessment device (FAD)*

Family functioning was assessed by using the Japanese version of the family assessment device (FAD), a 60-item self-report questionnaire designed to assess seven dimensions of family functioning based on the McMaster model of family functioning [34]. Six of the scales on the FAD reflect the dimensions of family functioning outlined in the MMFF [14]: problem solving, communication, roles, affective responsiveness, affective involvement, and behavior control. The seventh scale of general functioning assesses overall health/pathology. Low scores indicated good functioning, whereas high scores denoted poorer functioning. A previous study by our colleagues demonstrated that the Japanese version of the FAD is valid and reliable [54].

#### Statistical analysis

First, we performed a univariate analysis between the SAS or the SDS scores and investigated sociodemographic, psychosocial, and medical factors to determine possible independent variables by the Mann–Whitney *U*-test or Spearman’s rank correlation coefficient, in patients and in husbands, respectively. Dummy variables were used when independent variables were categorical. Then, we determined the final risk factors by applying stepwise multiple regression analysis with patients’ and husbands’ SAS or SDS scores as the dependent variables, entering all independent variables investigated in this study. All *p* values reported here are two-tailed. We used SPSS Version 10.0J statistical software (SPSS, Chicago, IL, USA) for all of the data analyses.

#### Results

##### Patient characteristics

Of the 67 eligible couples, 19 (28.4%) declined to participate in the study. Of the 48 participating couples, 2 patients did not complete the SAS scale. Thus, the data available for the 46 couples (68.7%) who responded were used in the analysis. The mean ages of the 46 participating patients and the 21 nonparticipating patients were  $52.3 \pm 10.5$  [standard deviation (SD)] and  $55.6 \pm 10.1$  years, respectively.

The difference in age between participating and nonparticipating patients was not significant ( $t=-1.180$ ;  $df=65$ ;  $p=0.242$ ). The mean intervals between the initial surgery for breast cancer and the date of the interview of the 46 participating patients and the 21 nonparticipating patients were  $18.3\pm 11.7$  and  $22.8\pm 13.2$  months, respectively. The

difference between participating and nonparticipating patients regarding the interval between the initial surgery for breast cancer and the date of the interview was not significant ( $t=-1.413$ ;  $df=65$ ;  $p=0.162$ ).

The participating patients' characteristics (Table 1) include the following: 48% had at least 12 years of education;

**Table 1** Univariate analysis of the factors associated with SAS and SDS in patients

Patient characteristics	n (%)	SAS		SDS	
		Mean score (SD)	<i>p</i> value	Mean score (SD)	<i>p</i> value
<b>Sociodemographic factor</b>					
Age <sup>a</sup> 52.3±10.5 years (34–75)	46 (100)	$r=0.117$	0.439	$r=0.093$	0.538
Education <sup>b</sup>					
≤12 years	23 (52)	31.0 (5.4)		38.5(8.6)	
>12 years	21 (48)	31.9 (6.0)	0.841	37.1(5.8)	0.724
Employment status <sup>b</sup>					
Unemployed	29 (63)	32.1 (5.9)		39.0(7.7)	
Employed	17 (37)	30.9 (5.1)	0.438	36.1(6.1)	0.214
Socioeconomic status <sup>a</sup> 36.7±15.0 (15.0–73.0)	46 (100)	$r=0.113$	0.453	$r=0.183$	0.224
Number of family members <sup>a</sup> 3.30±1.26 (2–6)	46 (100)	$r=-0.070$	0.642	$r=-0.045$	0.766
Children younger than 18 years <sup>b</sup>					
No	30 (67)	31.8 (5.2)		37.7(7.7)	
Yes	16 (33)	31.4 (6.5)	0.636	38.3(6.5)	0.890
<b>Psycho-social factors</b>					
TAS-20 total score <sup>a</sup>					
Patients 49.6±9.6 (29.0–72.0)	46 (100)	$r=0.336$	0.023	$r=0.375$	0.010
Husbands 49.9±8.3 (32.0–68.0)	46 (100)	$r=0.076$	0.622	$r=0.222$	0.143
FAD					
Patients					
Problem Solving <sup>a</sup> 2.07±0.45 (1.17–3.17)	46 (100)	$r=0.243$	0.104	$r=0.260$	0.081
Communication <sup>a</sup> 2.04±0.47 (1.00–3.00)	46 (100)	$r=0.305$	0.039	$r=0.390$	0.007
Roles <sup>a</sup> 1.92±0.35 (1.18–2.55)	46 (100)	$r=-0.062$	0.682	$r=0.152$	0.315
Affective responsiveness <sup>a</sup> 2.21±0.53 (1.33–3.50)	46 (100)	$r=0.343$	0.020	$r=0.502$	<0.001
Affective involvement <sup>a</sup> 2.15±0.41 (1.29–3.14)	46 (100)	$r=0.170$	0.259	$r=0.251$	0.092
Behavior control <sup>a</sup> 2.11±0.38 (1.00–2.89)	46 (100)	$r=0.120$	0.426	$r=0.329$	0.025
General functioning <sup>a</sup> 1.89±0.52 (1.00–3.50)	46 (100)	$r=0.208$	0.165	$r=0.364$	0.013
Husbands					
Problem Solving <sup>a</sup> 1.92±0.55 (1.00–3.50)	46 (100)	$r=-0.080$	0.598	$r=0.137$	0.363
Communication <sup>a</sup> 1.99±0.42 (1.11–2.89)	46 (100)	$r=0.016$	0.915	$r=0.209$	0.162
Roles <sup>a</sup> 1.84±0.40 (1.00–2.73)	46 (100)	$r=-0.133$	0.380	$r=0.107$	0.477
Affective responsiveness <sup>a</sup> 2.10±0.52 (1.00–3.50)	46 (100)	$r=0.032$	0.831	$r=0.166$	0.271
Affective involvement <sup>a</sup> 1.95±0.41 (1.14–3.14)	46 (100)	$r=-0.028$	0.852	$r=0.027$	0.860
Behavior control <sup>a</sup> 1.97±0.42 (1.00–2.56)	46 (100)	$r=-0.157$	0.299	$r=0.143$	0.341
General functioning <sup>a</sup> 1.82±0.40 (1.00–2.58)	46 (100)	$r=0.005$	0.974	$r=0.258$	0.083
SAS (husbands) <sup>a</sup> 32.4±7.1 (21–64)	46 (100)	$r=0.169$	0.260	$r=0.235$	0.115
SDS (husbands) <sup>a</sup> 36.4±7.4 (20–50)		$r=0.042$	0.783	$r=0.260$	0.081
<b>Medical factors</b>					
Months elapsed after surgery <sup>b</sup> 18.3±11.7 months (3–47 months)	46 (100)	$r=0.035$	0.817	$r=-0.125$	0.406
Pain <sup>b,c</sup>					
0	14 (30)	29.4 (5.8)		34.7 (6.3)	
1,2,3	32 (70)	32.6 (5.3)	0.087	39.3 (7.3)	0.046
Type of surgery <sup>b</sup>					
Mastectomy	24 (57)	31.2 (5.6)		37.9 (7.6)	
Lumpectomy	18 (43)	32.6 (6.2)	0.541	37.5 (7.5)	0.760
Adjuvant therapy (radiation, chemotherapy, or hormone therapy) <sup>b</sup>					
None	6 (13)	28.3 (3.9)		36.3 (8.4)	
One or more	40 (87)	32.2 (5.7)	0.094	38.2 (7.1)	0.707
Past history of psychiatric treatment <sup>b</sup>					
No	43 (93)	31.7 (5.7)		37.7 (7.4)	
Yes	3 (7)	31.7 (5.5)	0.947	40.7 (3.2)	0.410

<sup>a</sup> Univariate analysis was performed on Spearman's rank correlation coefficient

<sup>b</sup> Univariate analysis was performed on the Mann–Whitney *U*-test

<sup>c</sup> Coded as 0 = not at all, 1 = mild, 2 = moderate, 3 = very severe

63% were not employed; 33% had one or more children younger than 18; 70% reported having pain; 87% had undergone or were undergoing one or more adjuvant forms of therapy, such as radiation treatment, chemotherapy, and hormone therapy; and 7% had a history of psychiatric treatment. The husbands' characteristics (Table 2) include

the following: a mean age of  $54.4 \pm 11.6$  years (range 31–82); 48% had at least 12 years of education; 87% were employed; and 2% had a history of psychiatric treatment. Because the patients were enrolled consecutively during a 6-month period, the study was not biased for the patient characteristics, and thus, it can be assumed that the

**Table 2** Univariate analysis of the factors associated with SAS and SDS in husbands

Husband characteristics	n (%)	SAS		SDS	
		Mean score (SD)	<i>p</i> value	Mean score (SD)	<i>p</i> value
<b>Sociodemographic factor</b>					
Age <sup>a</sup> $54.4 \pm 11.6$ years (31–82)	46 (100)	$r=0.14$	0.344	$r=0.187$	0.214
Education <sup>b</sup>					
$\leq 12$ years	24 (52)	34.7 (8.7)		38.4 (8.1)	
$>12$ years	22 (48)	29.9 (3.6)	0.018	34.1 (5.9)	0.042
Employment status <sup>b</sup>					
Unemployed	6 (13)	30.4 (2.7)		40.3 (8.3)	
Employed	40 (87)	32.7 (7.6)	0.601	35.8 (7.2)	0.196
Socioeconomic status <sup>a</sup> $36.7 \pm 15.0$ (15.0–73.0)	46 (100)	$r=0.03$	0.822	$r=0.153$	0.311
Number of family members <sup>a</sup> $3.30 \pm 1.26$ (2–6)	46 (100)	$r=0.06$	0.694	$r=0.262$	0.078
Children younger than 18 years <sup>b</sup>					
No	30 (65)	32.7 (7.8)		36.8 (7.8)	
Yes	16 (35)	31.8 (5.8)	0.871	35.6 (6.9)	0.480
<b>Psycho-social factors</b>					
TAS-20 total score <sup>a</sup>					
Husbands $49.9 \pm 8.3$ (32.0–68.0)	46 (100)	$r=0.546$	$<0.001$	$r=0.203$	0.181
Patients $49.6 \pm 9.6$ (29.0–72.0)	46 (100)	$r=0.244$	0.102	$r=0.210$	0.161
<b>FAD</b>					
Husbands					
Problem solving <sup>a</sup> $1.92 \pm 0.55$ (1.00–3.50)	46 (100)	$r=0.043$	0.776	$r=0.095$	0.532
Communication <sup>a</sup> $1.99 \pm 0.42$ (1.11–2.89)	46 (100)	$r=0.237$	0.112	$r=0.207$	0.168
Roles <sup>a</sup> $1.84 \pm 0.40$ (1.00–2.73)	46 (100)	$r=0.127$	0.399	$r=0.376$	0.010
Affective responsiveness <sup>a</sup> $2.10 \pm 0.52$ (1.00–3.50)	46 (100)	$r=0.216$	0.150	$r=0.191$	0.202
Affective involvement <sup>a</sup> $1.95 \pm 0.41$ (1.14–3.14)	46 (100)	$r=0.433$	0.003	$r=0.273$	0.066
Behavior control <sup>a</sup> $1.97 \pm 0.42$ (1.00–2.56)	46 (100)	$r=0.229$	0.126	$r=0.255$	0.087
General functioning <sup>a</sup> $1.82 \pm 0.40$ (1.00–2.58)	46 (100)	$r=0.095$	0.529	$r=0.226$	0.131
Patients					
Problem solving <sup>a</sup> $2.07 \pm 0.45$ (1.17–3.17)	46 (100)	$r=0.178$	0.236	$r=0.004$	0.981
Communication <sup>a</sup> $2.04 \pm 0.47$ (1.00–3.00)	46 (100)	$r=0.029$	0.848	$r=-0.023$	0.881
Roles <sup>a</sup> $1.92 \pm 0.35$ (1.18–2.55)	46 (100)	$r=0.186$	0.216	$r=0.104$	0.494
Affective responsiveness <sup>a</sup> $2.21 \pm 0.53$ (1.33–3.50)	46 (100)	$r=0.055$	0.715	$r=0.087$	0.566
Affective involvement <sup>a</sup> $2.15 \pm 0.41$ (1.29–3.14)	46 (100)	$r=0.032$	0.835	$r=0.127$	0.399
Behavior control <sup>a</sup> $2.11 \pm 0.38$ (1.00–2.89)	46 (100)	$r=0.233$	0.119	$r=0.203$	0.176
General functioning <sup>a</sup> $1.89 \pm 0.52$ (1.00–3.50)	46 (100)	$r=0.079$	0.600	$r=-0.012$	0.936
SAS (patients) <sup>a</sup> $31.7 \pm 5.6$ (20–44)	46 (100)	$r=0.169$	0.260	$r=0.042$	0.783
SDS (patients) <sup>a</sup> $37.9 \pm 7.2$ (25–55)	46 (100)	$r=0.235$	0.115	$r=0.260$	0.081
<b>Medical factors</b>					
Months elapsed after surgery <sup>a</sup> $18.3 \pm 11.7$ months (3–47 months)	46 (100)	$r=0.044$	0.772	$r=0.228$	0.128
Pain <sup>b,c</sup>					
0	14 (30)	32.0 (6.2)		36.6 (8.1)	
1,2,3	32 (70)	32.5 (7.6)	0.981	36.3 (7.2)	0.719
Type of surgery <sup>b</sup>					
Mastectomy	24 (57)	33.5 (8.7)		36.9 (7.8)	
Lumpectomy	18 (43)	31.1 (4.9)	0.684	35.9 (7.8)	0.721
Adjuvant therapy (radiation, chemotherapy, or hormone therapy) <sup>b</sup>					
None	6 (13)	31.6 (6.1)		36.7 (8.1)	
One or more	40 (87)	32.5 (7.4)	0.911	36.3 (7.4)	0.909
Past history of psychiatric treatment					
No	45(98)	32.2 (7.1)		36.1 (7.2)	
Yes	1 (2)	40.0	0.141	49.0	0.087

<sup>a</sup> Univariate analysis was performed on Spearman's rank correlation coefficient

<sup>b</sup> Univariate analysis was performed on the Mann-Whitney *U*-test

<sup>c</sup> Coded as 0 = not at all, 1 = mild, 2 = moderate, 3 = very severe

**Table 3** Multiple regression analysis of predictors of SAS in patients

Variable	Coefficient	Standardized coefficient	<i>t</i>	<i>P</i>
TAS-20	0.204	0.355	2.313	0.026

Multiple  $R=0.355$ ; multiple  $R^2=0.126$ , adjusted  $R^2=0.103$

characteristics of the women in this sample were typical for other breast cancer patients in this culture and in this clinical setting and were also typical for their healthy peers.

#### Factors correlated with anxiety and depression in patients

Table 1 summarizes the results of the univariate analysis of the factors associated with patient SAS and SDS scores. Among the investigated variables, high patient total score on the TAS-20 and high patient scores on the communication and affective responsiveness subscales of the FAD were significantly associated with high patient SAS score. Meanwhile, high patient total score on the TAS-20, high patient scores on the communication, affective responsiveness, behavior control, and general functioning subscale scores of the FAD, and the presence of pain were significantly associated with high patient SDS scores. The results of the multiple regression analysis of factors correlated with patient SAS score are shown in Table 3. The only factor correlated with high patient SAS score was high patient TAS-20 total score. This indicated that a high degree of patient alexithymia correlated with a high degree of patient anxiety. This model revealed that the selected independent variable accounted for 12.6% of the variance in patient SAS scores. The results of the multiple regression analysis of factors correlated with patient SDS score are shown in Table 4. The only factor correlated with high patient SDS score was a high score on the affective responsiveness subscale of the FAD. This means that patient perceptions of inappropriate affective responsiveness among family members correlated with their high degree of depression. This model revealed that the selected independent variable accounted for 34.5% of the variance in patient SDS scores.

**Table 4** Multiple regression analysis of predictors of SDS in patients

Variable	Coefficient	Standardized coefficient	<i>t</i>	<i>P</i>
FAD (patients) Affective Responsiveness	8.220	0.588	4.416	<0.001

Multiple  $R=0.588$ ; multiple  $R^2=0.345$ ; adjusted  $R^2=0.327$

**Table 5** Multiple regression analysis of predictors of SAS in husbands

Variable	Coefficient	Standardized coefficient	<i>t</i>	<i>P</i>
TAS-20	0.387	0.433	3.140	0.003
Education <sup>a</sup>	-6.183	-0.420	-2.924	0.006
Adjuvant therapy <sup>b</sup>	7.010	0.337	2.299	0.027

Multiple  $R=0.597$ ; multiple  $R^2=0.356$ ; adjusted  $R^2=0.304$

<sup>a</sup> Coded as 0 ≤ 12 years, 1 > 12 years

<sup>b</sup> Coded as 0 = none, 1 = one or more

#### Factors correlated with anxiety and depression in husbands

The results of the univariate analysis of the factors associated with husband SAS scores and SDS scores are summarized in Table 2. Among the investigated variables, high husband SAS score was significantly associated with low husband education level, high husband total score on the TAS-20, and high husband score on the affective involvement subscale of the FAD. Meanwhile, low husband education level and high husband score on the roles subscale of the FAD were significantly associated with high husband SDS score.

The results of the multiple regression analysis of factors correlated with the husband SAS score are shown in Table 5. The factors correlated with high husband SAS score were high husband TAS-20 total score, low husband education level, and the delivery of adjuvant therapy for patients. This finding indicated that a high degree of alexithymia among husbands, a low husband education level, and adjuvant therapy for patients was correlated with high degrees of anxiety among husbands. This model revealed that the selected independent variables accounted for 35.6% of the variance in the husband SAS scores.

The results of the multiple regression analysis of factors correlated with the husband SDS scores are shown in Table 6. The factors correlated with high husband SDS score were high husband scores on the roles subscale of the FAD, low husband education level, and a large number of

**Table 6** Multiple regression analysis of predictors of SDS in husbands

Variable	Coefficient	Standardized coefficient	<i>t</i>	<i>P</i>
FAD (husbands) Roles	5.775	0.312	2.251	0.030
Education <sup>a</sup>	-5.174	-0.350	-2.514	0.016
Number of family members	1.733	0.306	2.188	0.035

Multiple  $R=0.543$ ; multiple  $R^2=0.295$ ; adjusted  $R^2=0.238$

<sup>a</sup> Coded as 0 ≤ 12 years, 1 > 12 years

family members. This meant that husband perceptions of inappropriate shares of roles among family members, low husband education level, and large number of family members correlated with the high degree of depression among husbands. This model revealed that the selected independent variable accounted for 29.5% of the variance in the husband SDS scores.

## Discussion

We found that alexithymia, family functioning, and other factors might be related to psychological distress in women with breast cancer and in their husbands. We also found that there are important differences in related factors between anxiety and depression, or between patients and husbands.

### Alexithymia and anxiety among patients and husbands

High degrees of alexithymia among patients and husbands was correlated with high degrees of anxiety in both. Alexithymia has been found to exist at high rates in patients with anxiety disorders such as panic disorder and PTSD [58]. The salient feature of alexithymia is difficulty identifying and describing subjective feelings [37]. That is, high anxiety in alexithymic people may be related to a deficit in emotional regulation that reflects both deficits in the cognitive-experiential component of emotion response systems (i.e., deficits in the top-down regulation from the higher-order brain regions, such as language areas to the limbic structure) and deficits at the level of interpersonal regulation of emotion (i.e., an inability to express their emotions and to get support from others) [57]. But family functioning (an important factor in social support) and alexithymia in spouses were not correlated with anxiety in patients or husbands. These results could indicate the possibility that anxiety in patients and husbands is related to deficits in the internal regulation of emotion rather than to deficits in interpersonal regulation of emotion. So, to decrease the anxiety of patients and husbands, it may be insufficient to encourage emotional expression and to get support from others, as in the emotion suppression model, but it may be useful to facilitate the internal control of emotion (e.g., biofeedback or relaxation training) or to treat symptoms directly by medication.

Moreover, we would like to refer to the issue of whether alexithymia, as observed in this study, had trait or state characteristics. Theoretically, alexithymia has been considered as a developmental deficit [56, 58]. Several longitudinal studies have indicated alexithymia as a stable personality trait [51, 53, 55]. From the point of view of anxiety, Berthoz et al. [6] has suggested that alexithymia was correlated with both state anxiety and trait anxiety, although partial

correlations revealed a tight link between trait anxiety and alexithymia. So, we consider that alexithymia observed in this study also has trait characteristics. However, some researchers have indicated that “secondary (reactive) alexithymia” existed in kidney transplantation patients and in hemodialysis patients [15, 17], and these secondary alexithymia were considered as a defensive reaction to stressful events. Because cancer causes many stressful events, alexithymia in this study also may, at least in part, have reactive characteristics. However, as this study was conducted by a cross-sectional design, we cannot conclude with certainty that alexithymia has either trait or state characteristics. Further longitudinal study will be needed to clarify this issue.

### Family functioning and depression in patients and husbands

Family functioning was related to depression in both patients and husbands. Family functioning has been reported to be related to depression in major depression patients without cancer [25, 26]. The present study indicated that family functioning is related to depression in cancer patients and their husbands as well as in people without cancer. But the subtypes of family functioning that correlated with depression differed between patients and husbands. Patient depression was correlated with patient perceptions of inappropriate affective responsiveness among family members in the FAD, while husband perceptions of inappropriate roles among family members in the FAD was correlated with depression in husbands. According to its definition in the FAD, affective responsiveness refers to the ability of family members to respond with appropriate qualities and quantities of feelings to a wide range of stimuli [26]. The importance of emotional support of cancer patients by family members is well known [4, 5, 27, 30, 31, 38]. Some researchers have discussed the importance of the quality of communication among patients and family members, especially the importance of empathy [32, 48]. The results of the present study also could be considered to indicate that family members’ emotional responsiveness to distress could greatly influence the patient’s mental state, particularly pertaining to depression. In other words, we speculate that patient depression worsens if the patient cannot get an empathic response from family during times of distress.

Meanwhile, one factor related to husband depression was the role of the FAD. According to the definition in the FAD, roles are recurrent patterns of behavior necessary to fulfill the instrumental and affective needs of family members [26]. Many breast cancer patients have central roles in caring for family members, such as housework, childcare, and communication with neighbors or relatives. Husbands must play not only their own occupational roles



but also the roles that their wives have ever played, including tending to the needs of other family members. Furthermore, the husband must also care for his ill wife; patients and the total burden become very severe. The results of this study may indicate a great relationship between husband depression and husband frustration about their share of family roles after a decrease in patient function; in other words, frustration over the increase in their burden. The number of family members was also correlated with husband depression. This might also indicate the relation between husband depression and increasing burden because the larger the family, the more people the husband must care for. Thus, although family functioning was associated with depression in both breast cancer patients and husbands, the subscales of family functioning, which correlated with depression, differed between patients and husbands. So, different types of family intervention might be effective for breast cancer patients and their husbands. Intervention to accelerate empathic communication among family members might be effective for breast cancer patients, while intervention to decrease the burden on husbands, such as promoting the sharing of roles among family members or giving information about resources for patient care, might be effective for husbands.

#### Differences among risk factors for anxiety and depression

As mentioned above, different factors were correlated with anxiety and depression in breast cancer patients and their husbands. Previous studies have demonstrated some differences among risk factors for anxiety and depression in psychiatric populations or in general populations. Newman et al. [39] found that life events were more strongly correlated with major depressive episodes than with general anxiety disorder. Murphy et al. [36] suggested that although the prevalence of depression was significantly higher in a population having low socioeconomic status than in populations of other socioeconomic statuses, the relationship between anxiety and socioeconomic status remained unclear. These studies suggest that depression may be affected more by environmental factors than by anxiety. Interestingly, this study also seems to support these previous findings because family functioning as an environmental factor was correlated with depression, while alexithymia, as an individual personality characteristic, was correlated with anxiety. In cancer populations, the importance of social support has been indicated repeatedly, as mentioned above. But the influences of personality characteristics on anxiety and depression remain unclear, as few previous studies have investigated related factors, including personality characteristics, simultaneously for anxiety and depression, in cancer patients or in their relatives. In future studies of psychological distress in cancer patients and their

relatives, personality characteristics such as alexithymia and other factors should be considered.

#### Other related factors

##### *Education level*

Low education level in husbands was correlated with both anxiety and depression in husbands. A study of healthy subjects found that a low education level was associated with a high degree of anxiety and depression [24, 47]. Low education level has been reported as a risk factor for major depressive disorder [8, 20, 33]. These results are consistent with those of the present study. We speculate that because husbands with low education levels might not collect or analyze useful information and might fail to adjust to the changed situations after spouses get cancer, they might have high degrees of anxiety and depression. Interventions to give adequate information that meet husbands' needs against their increased burden and to support their problem solving may be useful.

##### *Adjuvant therapy*

Husbands of patients receiving adjuvant therapy were more anxious than husbands of patients not receiving it. As far as we know, distress in the spouses of cancer patients has never been studied in relation to adjuvant therapy. Several researchers have reported on breast cancer patients' distress during adjuvant therapy, but their results have been controversial. Cathcart et al. [10] reported a high prevalence of depression during adjuvant tamoxifen therapy in breast cancer patients. On the other hand, Cassileth et al. [9] and Montgomery et al. [35] reported no difference in distress levels during adjuvant therapy compared with control groups (an observation group and a healthy control group, respectively). In the present study, patient anxiety and depression were not correlated with husband anxiety and depression. So, we consider that adjuvant therapy does not influence husband anxiety through patient anxiety and depression. One possible explanation for the association between adjuvant therapy and husband anxiety is that when the patient receives adjuvant therapy, the husband might recognize that his wife's condition is not curable, and his anxiety about his wife relapsing might increase. Further study is needed to confirm this interpretation, as we did not investigate the contents of anxiety in this study.

There are several limitations to this study. First, because the sample size was small, so other important factors related to couples' anxiety and depression may have been overlooked. For example, patient pain and a history of psychiatric treatment in husbands each was significantly related to, or tended to be correlated with, anxiety and

depression among couples in univariate analysis but not in multiple regression analysis. Second, the proportion of related factors to couple anxiety and depression is relatively small in this study, and other factors not assessed in this study might be correlated with anxiety and depression (e.g., other personality characteristics or social support issues other than those related to family). Finally, because this study was performed using a cross-sectional design, no causal relationships could be determined. To investigate such relationships, further study, including a prospective study, is needed.

In conclusion, the present study revealed that alexithymia and family functioning were associated with anxiety and depression, respectively, in both women with breast cancer and their husbands. Generally, it has been known that anxiety and depression often occur simultaneously and share many common symptoms [50], so it might be useful to take care in putting into perspective both individual traits, such as alexithymia, and family functioning when we intervene to treat anxiety and depression in breast cancer patients and their husbands. Moreover, the present results suggest we should pay attention to alexithymia especially in anxious (rather than depressive) patients and their husbands and to family functioning in depressive (rather than anxious) patients and husbands. As mentioned above, although this study has several limitations, its results are meaningful as a first report demonstrating a correlation between alexithymia and anxiety and between family functioning and depression simultaneously in women with breast cancer and in their husbands. In future studies, a detailed investigation of personality characteristics such as alexithymia and family functioning is needed to formulate strategies to decrease anxiety and depression in women with breast cancer and their husbands.

**Acknowledgments** The authors are grateful to all the patients and their husbands for so willingly giving their time. The authors would also like to acknowledge the collaborative support from the surgeons and from the nursing staff of the Mammary Gland Dispensary at Hiroshima University Hospital.

## References

- Akechi T, Fukue-Saeki M, Kugaya A (2000) Psychometric properties of the Japanese version of the Mental Adjustment to Cancer (MAC) scale. *Psycho-oncology* 9:395–401
- Bagby RM, Parker JDA, Taylor GJ (1994) The twenty-item Toronto alexithymia scale-I. Item selection and cross validation of the factor structure. *J Psychosom Res* 38:23–32
- Bagby RM, Taylor GJ, Parker JDA (1994) The twenty-item Toronto alexithymia scale-II. Convergent, discriminant, and concurrent validity. *J Psychosom Res* 38:33–40
- Baider L, DeNour A (1984) Couples' reactions and adjustment to mastectomy: a preliminary report. *Int J Psychiatry Med* 14:265–276
- Baider L, DeNour A (1988) Adjustment to cancer—who is the patient, the husband or the wife? *Isr J Med Sci* 24:631–636
- Berthoz S, Consoli S, Perez-Diaz F, Jouvent R (1999) Alexithymia and anxiety: compounded relationships? A psychometric study. *Eur Psychiatr* 14:372–378
- Bloom JR (1982) Social support, accommodation to stress, and adjustment to breast cancer. *Soc Sci Med* 16:1329–1338
- Bruce ML, Hoff RA (1994) Social and physical health risk factors for first-onset major depressive disorder in a community sample. *Soc Psychiatry Psychiatr Epidemiol* 29:165–171
- Cassileth BR, Knuiam MW, Abeloff MD, Falkson G, Ezdinli EZ, Mehta CR (1986) Anxiety levels in patients randomized to adjuvant therapy versus observation for early breast cancer. *J Clin Oncol* 4:972–974
- Cathcart CK, Jones SE, Pumroy CS, Peters GN, Knox SM, Cheek JH (1993) Clinical recognition and management of depression in node negative breast cancer patients treated with tamoxifen. *Breast Cancer Res Treat* 27:277–281
- Coyne JC, Bolger N (1990) Doing without social support as an explanatory concept. *J Soc Clin Psychol* 9:148–158
- Coyne JC, DeLongis A (1986) Going beyond social support: the role of social relationships in adaptation. *J Consult Clin Psychol* 54:454–460
- Derogatis LR, Morrow GR, Fetting J, Penman D, Piasetsky S, Schmale AM, Henrichs M, Carnicke CL Jr (1983) The prevalence of psychiatric disorders among cancer patients. *JAMA* 249:751–757
- Epstein NB, Bishop DS, Levin S (1978) The McMaster model of family functioning. *J Marriage Fam Counsel* 4:19–31
- Freyberger H (1977) Supportive psychotherapeutic techniques in primary and secondary alexithymia. *Psychother Psychosom* 28:337–342
- Fukuda K, Kobayashi S (1973) A study on a self-rating depression scale. *Seishin Shinkeigaku Zasshi* 75:673–679 (in Japanese)
- Fukunishi I (1992) The influence of defense mechanisms on secondary alexithymia in hemodialysis patients. *Psychother Psychosom* 57:50–56
- Fukunishi I, Nakagawa T, Nakamura H, Kikuchi M, Takubo M (1997) Is alexithymic construct a culture-bound? Validity and reliability of the Japanese version of the 20-item Toronto Alexithymia Scale (TAS-20) and modified Beth Israel Hospital Psychosomatic Questionnaire (BIQ). *Psychol Rep* 80:787–799
- Funch DP, Mettlin C (1982) The role of support in relation to recovery from breast surgery. *Soc Sci Med* 16:91–98
- Gallo JJ, Royall DR, Anthony JC (1993) Risk factors for the onset of major depression in middle age and late life. *Soc Psychiatry Psychiatr Epidemiol* 28:101–108
- Irvine D, Brown B, Crooks D, Rovers J, Browne G (1991) Psychological adjustment in women with breast cancer. *Cancer* 67:1097–1117
- Iwamitsu Y, Shimoda K, Abe H, Tani T, Okawa M, Buck R (2005) Anxiety, emotional suppression, and psychological distress before and after breast cancer diagnosis. *Psychosomatics* 46:19–24
- Jamison KR, Wellisch DK, Pasnau RO (1978) Psychosocial aspects of mastectomy: I. The woman's perspective. *Am J Psychiatr* 135:432–436
- Kaplan GA, Roberts RE, Camacho TC, Coyne JC (1987) Psychosocial predictors of depression. Prospective evidence from the human population laboratory studies. *Am J Epidemiol* 125:206–220
- Keitner GI, Miller IW (1990) Family functioning and major depression: an overview. *Am J Psychiatr* 147:1128–1137
- Keitner GI, Ryan CE, Miller IW, Kohn R, Bishop DS, Epstein NB (1995) Role of the family in recovery and major depression. *Am J Psychiatr* 152:1002–1008
- Kissane DW, Bloch S, Onghena P, McKenzie DP, Snyder RD, Dowe DL (1996) The Melbourne family grief study, II: psychosocial morbidity and grief in bereaved families. *Am J Psychiatr* 153:659–666

28. Kissane DW, McKenzie M, McKenzie DP, Forbes A, O'Neill I, Bloch S (2003) Psychosocial morbidity associated with patterns of family functioning in palliative care: baseline data from the family focused grief therapy controlled trial. *Palliat Med* 17:527–537
29. Kornblith AB, Herr HW, Ofman US, Sher HI, Holland JC (1994) Quality of life of patients with prostate cancer and their spouses: the value of a database in clinical care. *Cancer* 73:2791–2802
30. Lederberg MS (1998) The family of the cancer patient. In: Holland JC (eds) *Handbook of psycho-oncology*. Oxford University Press, New York, pp 981–993
31. Lichtman RR, Taylor SE, Wood JV (1987) Social support and marital adjustment after breast cancer. *J Psychosoc Oncol* 5:47–74
32. Liu JE, Mok E, Wong T (2005) Perceptions of Chinese cancer patients of the favorable and unfavorable words conveyed by their social support providers. *Cancer Nurs* 28:348–354
33. McCall NT, Parks P, Smith K, Pope G, Griggs M (2002) The prevalence of major depression or dysthymia among aged medicare fee-for-service beneficiaries. *Int J Geriatr Psychiatry* 17:557–565
34. Miller IW, Epstein NB, Bishop DS, Keitner GI (1985) The McMaster family assessment device: reliability and validity. *J Marital Fam Ther* 11:345–356
35. Montgomery GH, McClary KA, Bovbjerg DH (1996) Adjuvant therapy for breast cancer and psychological distress. *Ann Oncol* 7:977–978
36. Murphy JM, Olivier DC, Monson RR (1991) Depression and anxiety in relation to social status. *Arch Gen Psychiatry* 48:223–229
37. Nemiah JC, Freyberger H, Sifneos PE (1976) Alexithymia: a view of the psychosomatic process. In: Hill OW (ed) *Modern trends in psychosomatic medicine*, vol.3. Butterworths, London, pp 430–439
38. Neuling SJ, Winefield HR (1988) Social support and recovery after surgery for breast cancer: frequency and correlates of supportive behaviours by family, friends and surgeon. *Soc Sci Med* 27:385–392
39. Newman SC, Bland RC (1994) Life events and the 1-year prevalence of major depressive episode, generalized anxiety disorder, and panic disorder in a community sample. *Compr Psychiatry* 35:76–82
40. Northouse LL (1988) Social support in patients' and husbands' adjustment to breast cancer. *Nurs Res* 37:91–95
41. Northouse L, Dorris G, Charron-Moore C (1995) Factors affecting couples' adjustment to recurrent breast cancer. *Soc Sci Med* 42:69–76
42. Northouse L, Swain MA (1987) Adjustment of patients and spouses to initial impact of breast cancer. *Nurs Res* 36:221–225
43. Okamura H, Yamasaki M, Sera H, Kawai K, Kouhata S, Yamawaki S (1991) A study on the reliability and validity of the self-rating anxiety scale. *Seishinka-shindangaku* 2:113–119 (in Japanese)
44. Omne-Ponten M, Holmberg L, Bergstrom R, Sjoden P, Burns T (1993) Psychosocial adjustment among husbands of women treated for breast cancer: mastectomy vs. breast-conserving surgery. *Eur J Cancer* 29A:1393–1397
45. Pennebaker JW (1997) *Opening up—the healing power of expressing emotions*. Guilford, New York
46. Peters-Golden H (1982) Breast cancer: varied perceptions of social support in the illness experience. *Soc Sci Med* 16:483–491
47. Pillay AL, Sargent CA (1999) Relationship of age and education with anxiety, depression, and hopelessness in a South African community sample. *Percept Mot Skills* 89:881–884
48. Pistrang N, Barker C (1995) The partner relationship in psychological response to breast cancer. *Soc Sci Med* 40:789–797
49. Pistrang N, Barker C, Rutter C (1997) Social support as conversation: analysing breast cancer patients' interactions with their partners. *Soc Sci Med* 45:773–782
50. Pollack MH (2005) Comorbid anxiety and depression. *J Clin Psychiatry* 66(Suppl 8):22–29
51. Porcelli P, Leoci C, Guerra V, Taylor GJ, Bagby RM (1996) A longitudinal study of alexithymia and psychological distress in inflammatory bowel disease. *J Psychosom Res* 41:569–573
52. Rime B (1999) Expressing emotion, physical health, and emotional relief: cognitive–social perspective. *Adv Mind Body Med* 15:175–179
53. Saarijarvi S, Salminen JK, Toikka TB (2001) Alexithymia and depression: a 1-year follow-up study in outpatients with major depression. *J Psychosom Res* 51:729–733
54. Saeki T, Asukai N, Miyake Y, Miguchi M, Yamawaki S (1997) Reliability and validity of the Japanese version of the Family Assessment Device. *Archives of Psychiatric Diagnostics and Clinical Evaluation* 8:181–192 (in Japanese with an English abstract)
55. Salminen JK, Saarijarvi S, Aarela E, Tamminen T (1994) Alexithymia—state or trait? One-year follow-up study of general hospital psychiatric consultation out-patients. *J Psychosom Res* 38:681–685
56. Sifneos PE (1996) Alexithymia: past and present. *Am J Psychiatry* 153:137–142
57. Taylor GJ (2000) Recent developments in alexithymia theory and research. *Can J Psychiatry* 45:134–142
58. Taylor GJ, Bagby RM, Parker JDA (1997) *Disorder of affect regulation alexithymia in medical and psychiatric illness*. Cambridge University Press, Cambridge
59. Watson M, Greer S, Rowden L, Gorman C, Robertson B, Bliss JM, Tunmore R (1991) Relationships between emotional control, adjustment to cancer and depression and anxiety in breast cancer patients. *Psychol Med* 21:51–57
60. Zung WWK (1965) A self-rating depression scale. *Arch Gen Psychiatry* 12:63–70
61. Zung WW (1971) A rating instrument for anxiety disorders. *Psychosomatics* 12:371–379

Shuichi Ozono  
Toshinari Saeki  
Tomoyuki Mantani  
Akiko Ogata  
Hitoshi Okamura  
Shigeto Yamawaki

## Factors related to posttraumatic stress in adolescent survivors of childhood cancer and their parents

Received: 2 May 2006  
Accepted: 19 July 2006  
Published online: 5 October 2006  
© Springer-Verlag 2006

S. Ozono  
Department of Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Japan

T. Saeki  
Department of General Medicine, Hiroshima University Hospital, Hiroshima, Japan

S. Ozono · T. Mantani · S. Yamawaki (✉)  
Division of Frontier Medical Science, Programs for Biomedical Sciences, Department of Psychiatry and Neurosciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima, 734-8551, Japan  
e-mail: yamawaki@hiroshima-u.ac.jp  
Tel.: +81-82-2575208  
Fax: +81-82-2575209

A. Ogata  
Graduate School of Education, Hiroshima University, Hiroshima, Japan

H. Okamura  
Graduate School of Health Science, Hiroshima University, Hiroshima, Japan

**Abstract** *Goals of work:* The purpose of this study was to investigate factors related to severe posttraumatic stress symptoms (PTSS) in adolescent survivors of childhood cancer and their parents. *Materials and methods:* Eighty-nine families (88 adolescent survivors of childhood cancer, 87 mothers, 72 fathers) completed a self-report questionnaire. Multivariate logistic regression analyses were performed using the following risk factors for severe PTSS: trait anxiety, family functioning, demographic and medical variables. *Main results:* Severe PTSS were reported by 10.9% ( $n=9$ ) of the survivors, 20.7% ( $n=18$ ) of the mothers, and 22.2% ( $n=16$ ) of the fathers. Preliminary analyses found significant correlations of PTSS between mother-survivor (Spearman's  $\gamma=0.377$ ,  $p<0.01$ ) and mother-father (Spearman's  $\gamma=0.483$ ,  $p<0.01$ ). The results of multivariate analyses indicated that higher trait anxiety [odds ratio (OR):1.16; 95% confidence interval (CI): 1.03–1.31;  $p<0.05$ ] and having medical sequelae (OR: 5.85; 95% CI:1.02–33.72;  $p<0.05$ ) were significant factors

related to PTSS for survivors. For mothers, the significant PTSS-related factors were: higher trait anxiety (OR:1.13; 95% CI:1.04–1.23;  $p<0.01$ ); 5- to 9-year interval from the first diagnosis to the present investigation, compared to more than a 10-year interval (OR: 6.45; 95% CI:1.67–24.89;  $p<0.01$ ); and a relatively lower rating on “roles” of family functioning (OR: 12.34; 95% CI:1.11–136.97;  $p<0.05$ ). For fathers, trait anxiety was a significant related factor (OR: 1.07; 95% CI:1.01–1.14;  $p<0.05$ ). *Conclusions:* Survivors and their parents suffered from PTSS after long interval from completion of treatment, and PTSS-related factors varied for each family member. Appropriate allocation of responsibility for family functioning may promote the ability to decrease PTSS, especially for mothers.

**Keywords** Psychology · Posttraumatic stress · Long-term survival · Quality of life · Parents

### Introduction

During the last three decades, the treatment of childhood cancer has dramatically improved, and the number of long-term survivors is increasing. A number of researchers have reported observing physical and psychological delayed adverse effects of treatment among survivors of childhood

cancer [24]. Recent perspectives on the psychological outcomes for cases of childhood cancer have been based on the assumption that both cancer and its treatment are fundamentally traumatic events. In fact, “being diagnosed with a life-threatening illness” is mentioned as an example of a traumatic event that is included among the diagnostic criteria for posttraumatic stress disorder (PTSD) listed in

the American Psychiatric Association's diagnostic manual [1]. A cluster of symptoms (e.g., reexperiencing the traumatic event, hyperarousal, and avoidance of event reminders) is characteristic of PTSD.

Previous research has revealed that the prevalence of clinically significant levels of PTSD and/or posttraumatic stress symptoms (PTSS) in survivors ranged from 2 to 20%, and young adult survivors tended to show higher levels of posttraumatic stress [27]. Cancer affects not only patients but also entire families. In cases of childhood cancer, 10–30% of parents of survivors showed symptoms of posttraumatic stress [27]. Several factors may predict PTSS, including the individual's general level of anxiety [9, 13], medical factors, posttreatment factors, maternal psychological vulnerability [17], family functioning, and social support [12, 21]. Most studies have noted that predictors for PTSS were different for each family member.

In addition to the factors related to PTSS for each family member, oncology clinicians need to view the family as a system. The family system framework, as well as consideration of individual differences, is important for supporting families of childhood cancer survivors. Cancer might impact on multiple family members, and it might be reasonable to agree on the level of PTSS within family members. Kazak et al. [14] reported that one-third of two-parent families had both parents fulfill criteria for the arousal symptom cluster, and 84% of families had both parents endorse symptoms of reexperiencing, and suggested the importance of evaluating all family members for PTSS. As for family functioning, Pelcovitz et al. [21] found that PTSD symptoms are associated with chaotic family functioning among adolescent survivors. Brown et al. [4] found a significant correlation between PTSD symptoms and family supportiveness, and a negative correlation between PTSD symptoms and family conflict among the mothers of survivors of childhood cancer. In general, however, the relationship between PTSS and family functioning or framework is not well understood because few researchers have focused on this issue.

The purpose of this study was to investigate the prevalence of severe PTSS in a sample of 12- to 20-year-old childhood cancer survivors and their parents. We examined the contributions to severe PTSS of family functioning, trait anxiety, medical factors, and posttreatment factors. We also explored PTSS within the family members and assessed the impact of cancer for family. We predicted that medical factors, elevated trait anxiety, and impaired family function would account for a significant amount of the variance in PTSS. In addition, the relative influence of these factors was expected to differ among family members.

## Materials and methods

### Study sample and recruitment

Japanese pediatric cancer survivors and their parents were recruited from three large hospitals in urban areas located in western Japan. Survivors who met the following criteria were identified from the tumor registry of each hospital during the 15-month period from July 2003 to September 2004: (1) age of 12–20 years at the time of the investigation; (2) first diagnosis at least 5 years before the interview and off treatment for a minimum of 1 year; (3) the cancer was in remission; (4) receiving regular medical follow-up treatment as an outpatient; (5) physical health was good enough for the patient to complete several questionnaires; (6) Eastern Cooperative Oncology Group performance status (PS) of 0–2; and (7) absence of cognitive impairment. Survivors of brain tumors were excluded.

The registries of Research on the Treatment of Specific Chronic Childhood Diseases identified 144 eligible patients at three sites as follows: 65 at Hiroshima University hospital, 57 at Kurume University hospital, and 22 at Hiroshima Red Cross-Atomic Bomb hospital. When a patient and his/her parent(s) visited an outpatient clinic, a pediatric oncologist provided the family with an outline describing the purposes and protocol of the current study. The interviewer was allowed to meet with the participants, provided that the parent(s) agreed to participate in the investigation. Survivors who visited the outpatient clinic alone were handed letters for their parents that explained the study and invited them to participate. Written consent was obtained after the participants had been fully informed about the study. Then questionnaires were handed or mailed to the participants after a brief interview. A 1,000-yen book coupon was given to families upon agreement of study participation. The participants completed the questionnaires at home and returned them by mail. A reminder card was mailed to those participants who did not return the questionnaires 1 month after they had been delivered. To maintain anonymity, the questionnaires were returned without names or any type of identification code on the envelope. The protocol was approved by the Institutional Review Board of each institution.

### Questionnaires completed by parents and children

The Impact of Event Scale-Revised (IES-R) is a 22-item self-report instrument that assesses three symptoms of PTSD: intrusion, avoidance, and hyperarousal [28]. Symptoms are rated on a five-point Likert scale for frequency of

occurrence during the previous week. High scores indicate a high frequency of symptoms of PTSD. Participants were asked to focus on the child's cancer experience as the stressful event. The Japanese version of the IES-R [2] has a high internal consistency (Cronbach  $\alpha=0.92-0.95$ ) and test-retest reliability (Pearson  $\gamma=0.86$ ). According to the standardization study, IES-R scores of 25 or more are indicative of severe posttraumatic stress.

The State-Trait Anxiety Inventory (STAI) is a 40-item self-report instrument that measures anxiety symptoms that are either current (state) or related to personality (trait) [25]. A higher score indicates a higher level of anxiety. The STAI has high internal consistency as well as adequate construct and discriminative validity across diverse samples. The Japanese version of the STAI has yielded satisfactory internal consistency [20]. Only trait anxiety was evaluated in this study because prior studies reported that trait anxiety predicts PTSS/PTSD for childhood cancer survivors and their parents [9, 12, 13].

The Family Assessment Device (FAD) [7] is a 60-item self-report scale that assesses seven dimensions of family functioning based on the McMaster Model of Family Functioning (MMFF) [6]. Seven of the scales on the FAD reflect the following dimensions of family functioning: (1) Problem solving: the ability to resolve problems to maintain effective family functioning. (2) Communication: how the family members exchange information. (3) Roles: the repetitive patterns of behavior by which the individuals fulfill family functions; role allocation and role accountability are elemental components. (4) Affective responsiveness: the ability to respond to a range of stimuli. (5) Affective involvement: the degree to which the family shows interest in and values the activities and interests of family members. (6) Behavior control: the pattern the family adopts for handling behavior. (7) General functioning. Low scores indicate good functioning and high scores indicate poor functioning. The English and Japanese versions of the FAD have been shown to have adequate validity and reliability [23].

Life events data were obtained from the Japanese version of Holmes-Rahe measure of social adjustment [11, 18]. If a responder had had one or more life event(s) listed on the measure since the first diagnosis, the responder was classified as positive (+) for life events.

#### Variables obtained from medical records

An intensity of therapy rating was based on medical record review. Each child's medical information was obtained from the medical chart and rated by a pediatric oncologist (M.K.). The intensity of therapy was classified as follows: I (mild; 12%)=less than 6 months of chemotherapy only and/or surgery; II (intermediate; 62%)=therapy for standard to high-risk cancers according to the protocol of children

cancer study groups in Japan; or III (severe; 25%)=stem cell transplantation, or extremely high-risk cancers. The medical sequelae were also assessed based on chart review by a pediatric oncologist (M.K.). Survivors were classified into two groups as follows: I (none; 64%)=survivors who needed no limitations of activity and no special medical attention; II (yes; 36%)=survivors who needed medical attention because of disease or the longer-term effects of treatment. Information about patients' diagnosis, age at first diagnosis, age at the investigation, interval from diagnosis to the investigation, treatment of cranial irradiation, and relapse were picked up from charts and assessed as medical factors.

#### Statistical analysis

All analyses were conducted with SPSS 11.5J for Windows (SPSS, Chicago, IL, USA), and two-tailed probabilities were reported. Analyses were separately undertaken on data sets from survivors, mothers, and fathers. First, Spearman's correlation coefficients were calculated to examine intercorrelations among family members using the IES-R total score as continuous variables. Second, the IES-R was used to categorize subjects as having severe PTSS (25 or greater), or a mild-to-no PTSS (24 or less) [2]. Preliminary statistical comparisons between the two groups used the Pearson chi-square (for categorical variables) and the non-parametric Mann-Whitney *U* test (for continuous variables). To identify the final association factors, variables with a *p* value of less than 0.05 in the bivariate analysis were entered into a multivariate logistic regression model as independent variables. The independent explanatory values of the characteristics were expressed in odds ratios (OR), with 95% confidence intervals (CI). Before the study initiation, the necessary sample size was determined to detect differences in bivariate groups. Response rates were expected to be about 70%. Based on the review by Taïeb et al. [27], a prevalence of severe PTSS (P) of 0.20 and an OR of 2.5 were assumed. It was estimated that a minimum of 77 of each category of participants would be needed to detect a minimum difference with a power of 0.80 and an  $\alpha$  level of 0.05 calculated by Whittemore's formula [29]. A *p* value of less than 0.05 was set as the level of significance for all the statistical analyses.

We adopted a stepwise forward selection for the logistic regression model because the purpose of this analysis was to identify which variables were the most relevant risk factors associated with severe PTSS. For the stepwise selection, a "provisional model" was first applied, including all potential explanatory variables, and then the non-significant variables were removed, or significant variables were added one at a time, until those remaining in the model were found to contribute significantly.

**Results**

**Characteristics of the study sample**

Among the 144 eligible families, 125 families visited the outpatient clinic during the study's entry period, and 103 families agreed to participate in the study. Finally, a total of 89 families (61.8%) returned the questionnaires. Characteristics of the study population and the reasons for non-participation are shown in Fig. 1. All participants were Japanese.

A comparison of participants and non-participants revealed no significant differences among survivors in terms of current age, age at diagnosis, gender, type of cancer, interval since the first diagnosis, interval since the end of treatment, treatment intensity, cranial irradiation, medical sequelae, and relapse.

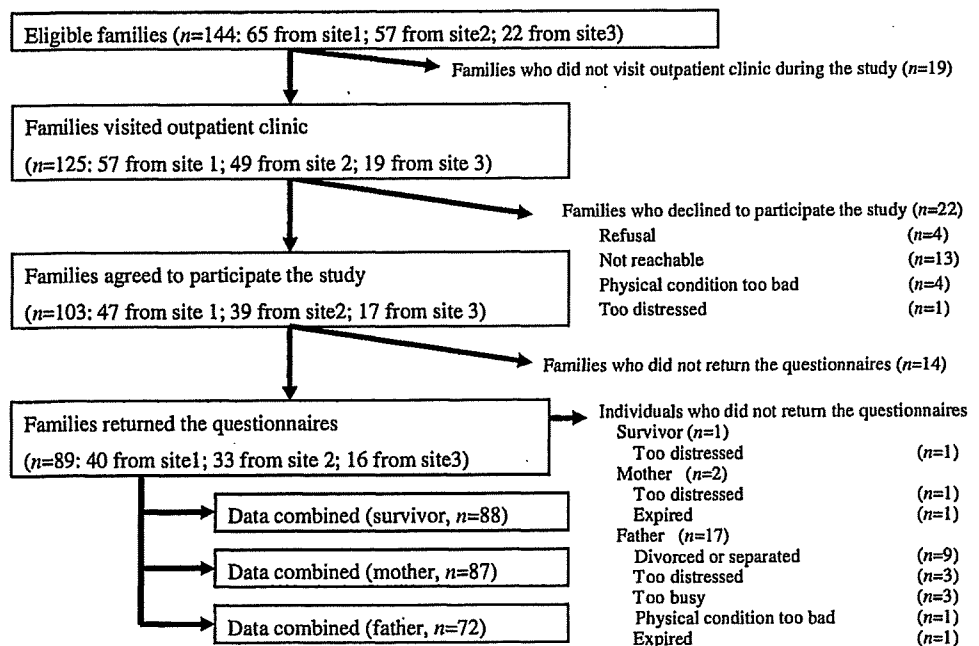
There were also no significant differences in terms of survivor's age, gender, medical sequelae, family size, socioeconomic status, parents' age, and history of psychological care between each institution. However, several differences were found among the three samples. The site 1 and site 2 samples contained a higher number of infant neuroblastoma and other solid tumor survivors than the site 3 sample [ $\chi^2(8, n=89)=23.478, p<0.01$ ]. The site 3 sample contained a higher number of survivors who received more intensive treatment [ $\chi^2(4, n=89)=29.185, p<0.01$ ] and cranial radiation [ $\chi^2(2, n=89)=10.938, p<0.01$ ]. The demographic and medical factors of survivors, which were combined, are shown in Table 1.

**Table 1** Demographic and medical characteristics of survivors (n=89)

	No. of survivors (%)	
Male gender	40	(45)
Age at investigation (mean±SD)	16.2±2.3	
Age at diagnosis (<6 years)	57	(64)
Time since diagnosis (<10 years)	39	(44)
Relapse ≥1	12	(14)
Diagnosis		
Acute lymphoblastic leukemia	46	(52)
Other leukemia	14	(16)
Malignant lymphoma	9	(10)
Infant neuroblastoma	11	(12)
Other solid tumor	9	(10)
Treatment intensity		
I (mild)	11	(12)
II (intermediate)	55	(62)
III (severe)	23	(25)
Medical sequelae		
I (None)	57	(64)
II (Yes)	32	(36)
Socioeconomic status		
I	2	(2)
II	17	(19)
III	57	(64)
IV	11	(13)
V	2	(2)

Socioeconomic status was calculated using Hollingshead and Redlich two-factor index of social position [10].

**Fig. 1** Flow chart showing the study population



### IES-R dimensional scores and intercorrelations of PTSS for each family member

The means and SDs for the IES-R dimensional scores are shown in Table 2. Compared to survivors, mothers and fathers showed relatively higher ratings on intrusion and avoidance, and mothers and fathers showed comparable scores on each dimension. Using 24/25 as the cutoff for the IES-R, severe PTSS were present in 9 of the 88 survivors (10.9%), 18 of the 87 mothers (20.7%), and 16 of the 72 fathers (22.2%). Spearman's intercorrelation coefficients for the total IES-R scores were significant for survivor-mother and father-mother pairs. The survivor-father correlations were not significant.

### Severe PTSS and related factors for survivors

Results of bivariate comparisons of demographic characteristics, medical variables, trait anxiety, and family functioning between those with either severe PTSS or not severe PTSS are shown in Table 3. The results indicated that subjects with severe PTSS had higher trait anxiety and exhibited a lower level of family functioning with respect to factors such as roles and affective responsiveness. Also, these subjects were more likely to have medical sequelae. As predicted, no significant differences were found with respect to the ratings for treatment intensity, time lapse from diagnosis to the study, history of relapse, and cranial radiation.

Table 4 shows the results from the multivariate logistic regression model in which severe PTSS was used as the bivariate outcome. Higher rating on trait anxiety and having medical sequelae were found to be significant factors related to severe PTSS, whereas family functioning was not found to be a significant PTSS-related factor.

**Table 2** Means(SD) of IES-R dimensional score and correlations of IES-R between family members

	Survivors (n=88) Mean (SD)	Mothers (n=87) Mean (SD)	Fathers (n=72) Mean (SD)
IES-R total	9.0 (10.4)	15.0 (12.4)	16.0 (14.3)
Intrusion	2.9 (3.9)	5.7 (4.7)	6.0 (5.3)
Avoidance	3.1 (4.8)	6.0 (5.4)	6.8 (6.0)
Hyperarousal	3.0 (3.3)	3.3 (3.8)	3.2 (4.1)
Correlations (IES-R total)			
1. IES-R survivors			
2. IES-R mothers	0.377**		
3. IES-R fathers	0.179	0.483**	

IES-R Impact of Event Scale-Revised; \*\* $p < 0.01$

### Severe PTSS and related factors for mothers of survivors

The results of the bivariate comparisons of variables between those with severe or not severe PTSS are shown in Table 3. The results indicate that subjects with severe PTSS had higher trait anxiety and lower levels of family functioning, as determined by the dimension of roles and general functioning. For mothers with severe PTSS, the child was diagnosed as having cancer at an older age, and the time interval since the first diagnosis to the present study was shorter. However, no other significant differences were found in terms of age of the mother and life events [ $\chi^2(1, n=87) 0.5, p=0.47$ ].

The results of the multivariate logistic regression model yielded three significant factors for severe PTSS: higher trait anxiety, a 5- to 9-year period since the first diagnosis to the present investigation as compared to an interval of more than 10 years, and a relatively lower rating on "roles" of family functioning (Table 4).

### Severe PTSS and related factors for fathers of survivors

The results of the bivariate comparisons of variables between those with severe or not severe PTSS are shown in Table 3. The results indicate that subjects with severe PTSS had higher trait anxiety scores. However, no other significant differences were found in terms of any family functioning, medical variables, child's age at diagnosis [ $\chi^2(1, n=72) 2.6, p=0.11$ ], time since disease onset ( $\chi^2(1, n=72) 1.4, p=0.24$ ), life events [ $\chi^2(1, n=72) 0.8, p=0.37$ ], and demographic factors. Higher rating on trait anxiety was found to be a significant factor related to severe PTSS in logistic regression model (Table 4).

## Discussion

The current study examined the prevalence of severe PTSS among long-term childhood cancer survivors and their parents. This study also investigated other factors, including family functioning, for each family member. The results indicate that some survivors and their parents suffered from symptoms of posttraumatic stress after a long interval from the completion of treatment. The prevalence of severe PTSS obtained for the survivors (10.9%) was comparable to that reported by Stuber et al. [26] (severe PTSS 12.5%), Erickson and Steiner [8] (current PTSD 10%), and Langeveld et al. [16] (severe PTSS 12.5%), although a higher prevalence of PTSD was reported by Hobbie et al. [9] (20.5%) and Meeske et al. [19] (22%).

The prevalence of severe PTSS in the present study for mothers (20.7%) and fathers (22.2%) were somewhat higher than those reported by Barakat et al. [3] (10.1% of



**Table 3** Comparison of medical factors and psychological variables between survivors and their parents with severe PTSS and those with not severe PTSS

	No. with severity of PTSS (%)		Analysis	
	Severe PTSS	Not severe PTSS	Statistic	P
Survivors (n=88)	n=9	n=79		
Age; mean (SD)	16.1 (1.9)	16.2 (2.3)	T(df=86) 0.16	0.87
Male gender	5 (56)	34 (43)	$\chi^2(1, n=88)$ 0.5	0.47
Medical sequelae: I (none)	3 (33)	55 (70)	$\chi^2(2, n=88)$ 8.3	<0.01
Medical sequelae: II (yes)	6 (66)	24 (30)		
Trait anxiety; mean (SD)	56.2 (8.6)	43.2 (9.9)	112.5 <sup>a</sup>	<0.01
FAD-Roles; mean (SD)	2.3 (0.3)	2.1 (0.4)	193.0 <sup>a</sup>	0.03
FAD-Affective responsiveness; mean (SD)	2.5 (0.6)	2.1 (0.5)	208.5 <sup>a</sup>	0.04
Mothers (n=87)	n=18	n=69		
Age; mean (SD)	43.4 (5.0)	43.9 (4.8)	t(df=85) 0.44	0.69
Child's age at diagnosis (<6 years)	11 (61)	21 (30)	$\chi^2(1, n=87)$ 5.8	0.02
Time since disease onset (<10 years)	13 (72)	23 (33)	$\chi^2(1, n=87)$ 8.9	<0.01
Trait anxiety; mean (SD)	52.2 (10.2)	41.5 (9.9)	280.5 <sup>a</sup>	<0.01
FAD-Roles; mean (SD)	2.2 (0.3)	2.0 (0.4)	383.0 <sup>a</sup>	0.01
FAD-General functioning; mean (SD)	2.1 (0.4)	1.9 (0.5)	425.0 <sup>a</sup>	0.04
Fathers (n=72)	n=16	n=56		
Age; mean (SD)	47.1 (7.8)	47.4 (5.5)	t(df=70) 0.19	0.85
Trait anxiety; mean (SD)	46.5 (10.5)	39.4 (9.7)	266.5 <sup>a</sup>	0.01

PTSS Posttraumatic stress symptoms, SD standard deviation, FAD family assessment

<sup>a</sup>Mann-Whitney U test

mothers and 7.1% of fathers had severe PTSS) and Kazak et al. [12] (10.2% of mothers and 7.1% of fathers had severe PTSS), although they were lower than those reported by Stuber et al. [26] (39.7% of mothers and 33.3% of fathers had severe PTSS). Differences in the prevalence of PTSS among these samples may be affected by differences in sample size, sample age, psychological

instruments used, cultural background, and the state of disease among survivors. Generally, the results of the present study are consistent with previous studies, which found that the prevalence of severe PTSS/PTSD among parents was higher than that among patients.

The association of impaired "roles" of family functioning with posttraumatic stress in mothers suggests two important issues. First, when the assignment of responsibilities for family functions is not appropriately distributed, an excessive burden may fall on a specific family member. Second, as a result of impairment of the accountability for the responsibilities that are allocated to each family member, the effectiveness of the job being done would be diminished. This situation may place a specific member of a family at greater risk for poor adaptation to a traumatic stressor and, subsequently, to possible psychiatric disorder, including PTSD.

These findings are in accord with the findings of Brown et al. [4], who found that mothers' greater self-reported level of support within their families was predictive of fewer or less intense maternal PTSS, although no such association was found among survivors. Kazak et al. [13] reported similar findings that family functioning was associated with anxiety and posttraumatic stress in both mothers and fathers. One possible reason for this discrepancy is that the study of Kazak et al. [13] used the Family Adaptability and Cohesion Evaluation Scales—Version III A, which has only three dimensions as family system variables. A path analysis was then used, which might be

**Table 4** Factors related to severe PTSS in survivors (n=88), mothers (n=87), and fathers (n=72): logistic regression analysis of medical and psychological variables

	B	exp(B)
Survivors		
Step 1: trait anxiety	0.15*	1.16 (1.03–1.31)
Step 2: medical sequelae (Yes)	1.77*	5.85 (1.02–33.72)
Step 3: FAD-Affective responsiveness	1.00	5.20 (0.73–37.06)
FAD-roles	1.19	1.15 (0.11–11.76)
Mothers		
Step 1: trait anxiety	0.12**	1.13 (1.04–1.23)
Step 2: time since disease onset (<10 years)	1.86**	6.45 (1.67–24.89)
Step 3 FAD-Roles	2.51*	12.34 (1.11–136.97)
FAD-General functioning	-1.42	0.24 (0.03–1.78)
Fathers		
Step 1: trait anxiety	0.07*	1.07 (1.01–1.14)

FAD Family Assessment Device; \* $p < 0.05$ ; \*\* $p < 0.01$

more sensitive to identify an association of PTSS with family functioning.

Preliminary analyses found the moderate correlation of PTSS between mother and father. While speculative, this indicates that mothers and fathers share a similar perception about their child's state of disease. Interestingly, these findings contradict those reported in another paper by Kazak et al. [14] in which they report very low levels of concordance of PTSD within a family. Cultural difference might contribute to these contradictions. Our finding of a correlation between mothers and survivors indicates that survivors' PTSS are resonant with mothers but not fathers. It is not clear why a correlation was not found between survivors and fathers. One possible speculation is that most of the adolescent survivors spend much time attending school, participating in extracurricular activities, or in peer relationships. They may not spend much time with their fathers, who, in Japan, come home late in the evening because of work. These situations decrease communication with fathers more than with mothers.

The time elapsed after the first diagnosis of cancer was found to be a significant factor for mothers' PTSS. It is commonly reported that trauma-induced psychological symptoms decrease with time. Kessler et al. [15] reported in a general population study that about two-thirds of people with an episode of PTSD recovered over time, even without treatment. The results of our study are consistent with the finding of Phipps et al. [22] that parents of recently diagnosed patients showed higher levels of PTSS than parents of long-term survivors. Kazak et al. [13] reported similar findings that a mother's posttraumatic stress was indirectly related to the interval since the final treatment, as determined by the mother's appraisal of the degree of threat to the life of the child.

As regards the fathers of survivors, Kazak et al. [12] reported that the number of months off treatment was negatively related to variables of posttraumatic stress. However, it is not necessarily the case that a time lapse reduces PTSS. The present study did not establish the associations of time lapse with severe PTSS in survivors and their fathers. One possible reason for this discrepancy is that because our sample was families of long-term survivors with a mean follow up period 10.8 years (range 5–19), they might be affected by medical sequelae or other concurrent stressors rather than the past intensive cancer treatment. This pattern may be more appropriate for a diagnosis of adjustment disorder than PTSD, although several participants showed a clinical level of PTSD.

Our study also revealed that trait anxiety was an associated factor for PTSS for survivors and parents. It must be noted that caution is warranted in interpreting anxiety as a predictor for PTSS, as trait anxiety is well-known to coexist with PTSD-like symptoms. Moreover, it is important to distinguish symptoms of anxiety from PTSS because they are conceptually overlapping but not identical. PTSS is attributed to reexperiencing and avoidant

behavior based on the traumatic memories and is closely related to the general level of anxiety. Thus, clinicians should carefully rule out a primary anxiety disorder from the anxiety related to PTSS.

The existence of medical sequelae was a significant factor related to severe PTSS in survivors. Some of these survivors may have experienced physical symptoms at the time of the study and continued limitations of activities in daily life. Thus, it would not be surprising if they reported experiencing increased anxiety or if they perceived their life as currently threatened. This pattern is consistent with the findings from Langeveld et al. [16] that severe sequelae or health problems were associated with posttraumatic stress. However, these findings are not in accord with reports by Hobbie et al. [9], who did not find any association between medical sequelae and PTSS. Specifically, Hobbie et al. [9] reported that subjective factors related to cancer and its treatment (e.g., beliefs regarding a life threat and/or perceived treatment intensity) are more important than the objective medical data about cancer. While speculative, the reason for this discrepancy may be that the study of Hobbie et al. [9] contains a relatively larger proportion of survivors (about 65%) who had moderate to severe medical sequelae, while only 36% of the survivors in our study had medical sequelae, so it was more difficult to identify the relationship between PTSD and medical sequelae.

#### Limitations

The current study has several limitations. First, only 62% (89 of 144 families) of the subjects could be included in the analysis, and the prevalence of severe PTSS in survivors was relatively lower than that of parents, so the current study may not have had optimal statistical power. As the present results suggest that only 10.9% of survivors showed severe PTSS, researchers would have to investigate twice as many families to get more valid results.

Second, the result relies on self-reported questionnaires only, which do not allow a proper diagnosis of clinically relevant disorder. Further study is needed to determine the true prevalence of current PTSD compared to "severe PTSS".

Third, the design of the study was cross-sectional, and this investigation lacked a matched control group, so no conclusions regarding causality can be drawn. It needs further consideration that family functioning from the mother's viewpoint is affected by the phase of adolescence, with ensuring conflicts, role changes, and developmental tasks. Comparison to families with healthy adolescents probably would yield further information.

Fourth, as this study was conducted at three sites, and the disease distribution differed among these sites, an institutional bias may have influenced the results.

Finally, the assessments of the treatment intensity and medical sequelae were conducted by an ad hoc method, and the validity and reliability of these measures was not well established, and they may have resulted in classification errors. Replication of the present study with a large, longitudinally followed sample and more optimal assessment tools is needed to provide a better description of factors related to PTSS in childhood cancer survivors and their families.

### Clinical implications

The present data give rise to several important clinical implications for families with childhood cancer survivors. Even when the treatment was successful, some survivors cannot avoid suffering from medical sequelae, so long-term follow up of physical and psychological functioning after treatment is clearly desirable. The Children's Oncology Group website [5] provides detailed guidelines and information about specific later-onset effects for long-term survivors. Moreover, as the risk factors for severe PTSS vary for each family member, health care professionals in pediatric oncology units should assess each member of families and provide suitable treatment. The regular use of "family conferencing" would enable clinicians to bring the dynamics of the family system into relief and focus on the specific individual issues as well. It

is important to specify the family functions, to ascertain whether the family has allocated the responsibilities for these functions appropriately, and whether there are suitable mechanisms built in for accountability.

Parents also may benefit from education about their child's and their own symptoms and how to manage them effectively. At the same time, clinicians should assess and treat the general level of anxiety of each family member. Cognitive-behavioral approach and educational information may provide structure and support when anxiety and avoidance discourage exploration. If the situation becomes complicated, referral to a social worker, psychologist, or consultation-liaison psychiatrist would be a good option. Further research is needed to develop intervention programs that are effective in improving family functioning, and that may reduce PTSS in families with childhood cancer survivors.

**Acknowledgements** The authors thank all the patients and their parents who so willingly give their time. The authors would also like to acknowledge the collaborative support given by the pediatrician, especially Masao Kobayashi M.D., Ph.D., Shinichiro Nishimura M.D., Ph.D., Takashi Sato M.D., Ph.D. in Hiroshima University Hospital, Kazuko Hamamoto M.D., Ph.D. in Hiroshima Red Cross-Atomic Bomb Hospital, and Toyojiro Matsuishi M.D., Ph.D., Hiroko Inada M.D., Ph.D., Takako Hattori in Kurume University Hospital. This research was supported in part by a Grant-in-Aid for Cancer Research (11-2) from the Japanese Ministry of Health, Labor and Welfare.

### References

1. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Association, Washington, DC
2. Asukai N, Kato H, Kawamura N, Kim Y, Yamamoto K, Kishimoto J, Miyake Y, Nishizono-Maher A (2002) Reliability and validity of the Japanese-language version of the impact of event scale-revised (IES-R-J): four studies of different traumatic events. *J Nerv Ment Dis* 190:175-182
3. Barakat LP, Kazak AE, Meadows AT, Casey R, Meeske K, Stuber ML (1997) Families surviving childhood cancer: a comparison of posttraumatic stress symptoms with families of healthy children. *J Pediatr Psychol* 22:843-859
4. Brown RT, Madan-Swain A, Lambert R (2003) Posttraumatic stress symptoms in adolescent survivors of childhood cancer and their mothers. *J Trauma Stress* 16:309-318
5. Children's Oncology Group (2004) The Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers; <http://www.survivorshipguideline.org/>
6. Epstein NB, Bishop DS, Levin S (1978) The McMaster model of family functioning. *J Marriage Fam Counsel* 4:19-31
7. Epstein NB, Baldwin LM, Bishop DS (1983) The McMaster family assessment device. *J Marital Fam Ther* 9:171-180
8. Erickson SJ, Steiner H (2000) Trauma spectrum adaptation: somatic symptoms in long-term pediatric cancer survivors. *Psychosomatics* 41:339-346
9. Hobbie WL, Stuber M, Meeske K, Wissler K, Rourke MT, Ruccione K, Hinkle A, Kazak AE (2000) Symptoms of posttraumatic stress in young adult survivors of childhood cancer. *J Clin Oncol* 18:4060-4066
10. Hollingshead AB (1957) Two factor index of social position. Yale University, Department of Sociology, New Haven, CT
11. Holmes TH, Rahe RH (1967) The social readjustment rating scale. *J Psychosom Res* 11:213-218
12. Kazak AE, Barakat LP, Meeske K, Christakis D, Meadows AT, Casey R, Penati B, Stuber ML (1997) Posttraumatic stress, family functioning, and social support in survivors of childhood leukemia and their mothers and fathers. *J Consult Clin Psychol* 65:120-129
13. Kazak AE, Stuber ML, Barakat LP, Meeske K, Guthrie D, Meadows AT (1998) Predicting posttraumatic stress symptoms in mothers and fathers of survivors of childhood cancers. *J Am Acad Child Adolesc Psych* 37:823-831
14. Kazak AE, Alderfer M, Rourke MT, Simms S, Streisand R, Grossman JR (2004) Posttraumatic stress disorder (PTSD) and posttraumatic stress symptoms (PTSS) in families of adolescent childhood cancer survivors. *J Pediatr Psychol* 29:211-219

15. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB (1995) Post-traumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* 52:1048-1060
16. Langeveld NE, Grootenhuis MA, Voute PA, de Haan RJ (2004) Posttraumatic stress symptoms in adult survivors of childhood cancer. *Pediatr Blood Cancer* 42:604-610
17. Manne S, DuHamel K, Redd WH (2000) Association of psychological vulnerability factors to post-traumatic stress symptomatology in mothers of pediatric cancer survivors. *Psychoonkologia* 9:372-384
18. Masuda M, Holmes TH (1967) The social readjustment rating scale: a cross-cultural study of Japanese and Americans. *J Psychosom Res* 11:227-237
19. Meeske KA, Ruccione K, Globe DR, Stuber ML (2001) Posttraumatic stress, quality of life, and psychological distress in young adult survivors of childhood cancer. *Oncol Nurs Forum* 28:481-489
20. Nakazato K, Mizuguchi T (1982) Development and validation of Japanese version of state-trait anxiety inventory—a study with female subjects. *Shinshin Igaku* 22:107-112
21. Pelcovitz D, Libov BG, Mandel F, Kaplan S, Weinblatt M, Septimus A (1998) Posttraumatic stress disorder and family functioning in adolescent cancer. *J Trauma Stress* 11:205-221
22. Phipps S, Long A, Hudson M, Rai SN (2005) Symptoms of post-traumatic stress in children with cancer and their parents: effects of informant and time from diagnosis. *Pediatr Blood Cancer* 45:952-959
23. Saeki T, Asukai N, Miyake Y, Minoguchi M, Yamawaki S (1997) Reliability and validity of the Japanese version of the Family Assessment Device (FAD). *Seishinka Shindangaku* 8:181-192
24. Schwartz CL (1999) Long-term survivors of childhood cancer: the late effects of therapy. *Oncologist* 4:45-54
25. Spielberger CD, Gorsuch RL, Lushene RE (1970) STAI manual. Consulting Psychologist, Palo Alto, CA
26. Stuber ML, Christakis DA, Houskamp B, Kazak AE (1996) Posttrauma symptoms in childhood leukemia survivors and their parents. *Psychosomatics* 37:254-261
27. Taieb O, Moro MR, Baubet T, Revah-Levy A, Flament MF (2003) Posttraumatic stress symptoms after childhood cancer. *Eur Child Adolesc Psychiatry* 12:255-264
28. Weiss DS, Marmar CR (1997) The impact of the event scale-revised. In: Wilson JP, Keane TM (eds) *Assessing psychological trauma and PTSD: a practitioner's handbook*. Guilford, New York, pp 399-411
29. Whittemore AS (1981) Sample size for logistic regression with small response probability. *J Am Stat Assoc* 76:27-32