**Table 1.** Characteristics of the study subjects according to the highest and lowest of the neuroticism (EPQ-R), helplessness/hopelessness (MACS), and depression (HADS) subscales ($n = 1178$).

| Score | Neuroticism (EPQ-R) | | Helplessness/hopelessness (MACS) | | Depression (HADS) | |
|---|---|---|---|---|---|---|
| | Q1 (lowest) ≤3 | Q4 (highest) 8≤ | Q1 (lowest) ≤7 | Q4 (highest) 14≤ | Q1 (lowest) ≤2 | Q4 (highest) 9≤ |
| Number of subjects | 356 | 307 | 261 | 282 | 311 | 261 |
| Mean (SD) age at the diagnosis | 64 (9) | 63 (10) | 62 (10) | 65 (9) | 63 (6) | 64 (9) |
| Women (%) | 27 | 29 | 32 | 28 | 29 | 30 |
| Histologic type (%) | | | | | | |
| Adenocarcinoma | 57 | 62 | 62 | 52 | 61 | 56 |
| Squamous cell carcinoma | 18 | 18 | 15 | 25 | 18 | 23 |
| Small cell carcinoma | 14 | 11 | 12 | 15 | 9 | 12 |
| Large cell carcinoma | 9 | 7 | 8 | 6 | 9 | 7 |
| Other | 2 | 3 | 3 | 2 | 2 | 2 |
| Educational level (%) | | | | | | |
| High school or less | 78 | 76 | 70 | 85 | 73 | 78 |
| College/University or higher | 22 | 24 | 30 | 15 | 27 | 22 |
| Marital status (%) | | | | | | |
| Married | 89 | 83 | 89 | 79 | 87 | 85 |
| Unmarried | 11 | 17 | 11 | 21 | 13 | 15 |
| Cohabitation (%) | | | | | | |
| Living alone | 6 | 10 | 7 | 10 | 4 | 8 |
| Living with another person | 94 | 90 | 93 | 90 | 96 | 92 |
| Smoking status (%) | | | | | | |
| Never smokers | 24 | 22 | 26 | 18 | 26 | 19 |
| Ex-smokers | 22 | 24 | 25 | 23 | 22 | 23 |
| Current smokers | | | | | | |
| 1–19 cigarettes/day | 11 | 10 | 9 | 13 | 11 | 11 |
| 20 or more cigarettes/day | 43 | 43 | 40 | 45 | 41 | 46 |
| Clinical stage[a] (%) | | | | | | |
| IA–IIB | 45 | 44 | 54 | 34 | 57 | 30 |
| IIIA–IIIB | 29 | 30 | 24 | 37 | 22 | 36 |
| IV | 25 | 26 | 22 | 29 | 21 | 34 |
| Performance status[b] (%) | | | | | | |
| 0 | 45 | 39 | 47 | 31 | 56 | 26 |
| 1≤ | 55 | 61 | 53 | 69 | 44 | 74 |
| Self-reported pain (%) | | | | | | |
| None to mild | 90 | 86 | 91 | 81 | 93 | 78 |
| Moderate to very severe | 10 | 14 | 9 | 19 | 7 | 22 |
| Self-reported dyspnea (%) | | | | | | |
| None to mild | 87 | 79 | 87 | 72 | 90 | 71 |
| Moderate to very severe | 12 | 21 | 13 | 28 | 10 | 29 |

[a] Clinical stages were defined by TNM classification: International Union Against Cancer.
[b] Performance status was defined by Eastern Cooperative Oncology Group (ECOG).

1.2 (95% confidence interval [95% CI], 0.9–1.4; $p$ for trend = 0.13). We also conducted analyses by separately adjusting for the socioeconomic variables ($p$ for trend = 0.10) and the smoking status ($p$ for trend = 0.12) using this model, and the results remained unchanged. Moreover, even after adjustment for each clinical state variable (model 2 or model 3), we found no significant association between neuroticism and the risk of mortality (Table 2).

### Helplessness/hopelessness

For model 1, in which the estimated HR was adjusted for socioeconomic variables and the smoking status, we found a significant, linear and positive association between helplessness/hopelessness and the risk of mortality. The HR for the highest level of helplessness/hopelessness vs that for the lowest level was 1.4 (95% CI, 1.1–1.8; $p$ for trend < 0.001). We also conducted analyses by separately adjusting for the socioeconomic variables ($p$ for trend < 0.001) and the smoking status ($p$ for trend < 0.001) using this model, and the results remained unchanged. However, after adjustment for the clinical state variables (model 2 or model 3), the point estimate for the highest level was 1.1 or 1.0 as compared with that for the lowest level, and no significant association was observed ($p$ for trend = 0.17 or 0.41, respectively) (Table 2).

**Table 2.** Hazard ratio (HR) for death from all causes among lung cancer patients according to the neuroticism (EPQ-R), helplessness/hopelessness (MACS), and depression (HADS) subscales ($n = 1178$)

| | Q1 (lowest) | Q2 | Q3 | Q4 (highest) | p for trend |
|---|---|---|---|---|---|
| Neuroticism (EPQ-R) | ⩽3 | 4–5 | 6–7 | 8⩽ | |
| Number of deaths/total subjects | 199/356 | 179/294 | 122/222 | 186/307 | |
| Median survival in months (range) | 24 (1–68) | 21 (1–67) | 24 (1–67) | 22 (1–67) | |
| Multivariate model 1, HR (95% CI) | 1.0 (referent) | 1.1 (0.9–1.3) | 1.1 (0.8–1.3) | 1.2 (0.9–1.4) | 0.13 |
| Multivariate model 2, HR (95% CI) | 1.0 (referent) | 1.1 (0.9–1.3) | 1.2 (0.9–1.5) | 1.2 (1.0–1.5) | 0.16 |
| Multivariate model 3, HR (95% CI) | 1.0 (referent) | 1.1 (0.9–1.3) | 1.1 (0.9–1.4) | 1.2 (0.9–1.4) | 0.48 |
| Helplessness/hopelessness (MACS) | ⩽7 | 8–10 | 11–13 | 14⩽ | |
| Number of deaths/total subjects | 137/261 | 196/349 | 165/286 | 188/282 | |
| Median survival in months (range) | 25 (1–68) | 25 (1–67) | 23 (1–67) | 19 (1–67) | |
| Multivariate model 1, HR (95% CI) | 1.0 (referent) | 1.0 (0.8–1.3) | 1.2 (0.9–1.5) | 1.4 (1.1–1.8) | <0.001 |
| Multivariate model 2, HR (95% CI) | 1.0 (referent) | 0.9 (0.7–1.1) | 1.0 (0.8–1.2) | 1.1 (0.9–1.4) | 0.17 |
| Multivariate model 3, HR (95% CI) | 1.0 (referent) | 0.9 (0.7–1.1) | 0.9 (0.7–1.2) | 1.0 (0.8–1.3) | 0.41 |
| Depression (HADS) | ⩽2 | 3–5 | 6–8 | 9⩽ | |
| Number of deaths/total subjects | 151/311 | 190/330 | 165/276 | 180/261 | |
| Median survival in months (range) | 27 (1–68) | 23 (1–67) | 21 (1–67) | 17 (1–67) | |
| Multivariate model 1, HR (95% CI) | 1.0 (referent) | 1.3 (1.0–1.6) | 1.4 (1.1–1.7) | 1.8 (1.5–2.3) | <0.001 |
| Multivariate model 2, HR (95% CI) | 1.0 (referent) | 1.0 (0.8–1.2) | 1.0 (0.8–1.3) | 1.3 (1.0–1.6) | 0.040 |
| Multivariate model 3, HR (95% CI) | 1.0 (referent) | 1.0 (0.8–1.2) | 1.0 (0.8–1.3) | 1.2 (0.9–1.4) | 0.26 |

Multivariate model 1 was adjusted for age at diagnosis, sex, histologic type, educational level (high school or lower or higher), marital status (married or unmarried), cohabitation (live alone or live with someone), and smoking (never smokers, ex-smokers, current smokers of 1–19 cigarettes per day, or current smokers of 20 or more cigarettes per day). Multivariate model 2 was adjusted for age at diagnosis, sex, histologic type, clinical stage (IA–IIB, IIIA–IIIB, or IV), and PS (0 or 1⩽). Multivariate model 3 was adjusted for the severity of self-reported pain and dyspnea (none to mild, moderate to very severe) in addition to the factors adjusted for in multivariate model 2. All hazard ratios (HRs) are given with 95% confidence intervals (CIs) in parentheses.

### Depression

For model 1, in which the estimated HR was adjusted for socioeconomic variables and the smoking status, there was a significant, linear and positive association between depression and the risk of mortality. The HR for the highest level of depression vs that for the lowest was 1.8 (95% CI, 1.5–2.3; $p$ for trend $< 0.001$). We also conducted analyses by separately adjusting for the socioeconomic variables ($p$ for trend $< 0.001$) and the smoking status ($p$ for trend $< 0.001$) using this model, and the results remained unchanged. After adjustment for the clinical state variables of clinical stage and PS (model 2), we still found significant linear positive association between depression and the risk of mortality ($p$ for trend $= 0.040$). However, after adjustment for the clinical state variables of clinical stage, PS, and the self-reported pain and dyspnea (model 3), the point estimate for the highest level was 1.2 as compared with that for the lowest level, and no significant association was observed ($p$ for trend $= 0.26$) (Table 2).

### Association between clinical state variables and depression

We conducted a multivariate logistic regression analysis using a cross-sectional design to test the association between the clinical state variables and depression in the study patients (Table 3). Depression was defined based on a score of 9 or higher. The results indicated that more advanced clinical stage and a poorer PS were significantly associated with a higher prevalence of depression. The multivariate odds ratios (ORs) with reference to stage IA to IIB (95% confidence interval [CI]) were 1.6 (1.1–2.3) and 1.5 (1.0–2.3) in patients with stage IIIA–IIIB and IV, respectively. The multivariate OR with reference to PS0 (95% CI) was 1.8 (1.2–2.5) in patients with PS⩾1. Higher severity of pain and dyspnea was significantly associated with a higher prevalence of depression, independent of the clinical stage or PS. The multivariate OR with reference to none to mild self-reported pain (95% CI) was 1.6 (1.1–2.3) in patients with moderate to very severe self-reported pain. The multivariate OR with reference to none to mild self-reported dyspnea (95% CI) was 1.6 (1.1–2.3) in patients with moderate to very severe self-reported dyspnea.

## Discussion

Earlier studies suggested that negative psychological aspects may increase the risk of mortality among cancer patients [8–14]. Our results clearly do not support the above hypothesis. We found that the association between negative psychological aspects and the mortality risk among lung cancer patients no longer remained significant after adjustments for the clinical state variables (clinical stage, PS, and self-reported pain and dyspnea). Our results endorsed the hypothesis that the associations were largely confounded by the clinical state variables.

Among the five prospective studies conducted to date [11–13,33,34], three reported a statistically

**Table 3.** Odds ratio (OR) from a multivariate logistic regression model for the clinical states and depression among lung cancer patients ($n = 1178$)

| | Number of subjects | Number of depressed subjects (HADS score ≥ 9) | OR (95% CI) | p Value (vs each referent category) |
|---|---|---|---|---|
| Clinical stage[a] | | | | |
| IA–IIB | 513 | 78 | 1.0 (referent) | — |
| IIIA–IIIB | 348 | 93 | 1.6 (1.1–2.3) | 0.021 |
| IV | 317 | 90 | 1.5 (1.0–2.3) | 0.053 |
| Performance status[b] | | | | |
| 0 | 487 | 68 | 1.0 (referent) | — |
| 1 ≤ | 691 | 193 | 1.8 (1.2–2.5) | 0.003 |
| Self-reported pain | | | | |
| None to mild | 1018 | 204 | 1.0 (referent) | — |
| Moderate to very severe | 160 | 57 | 1.6 (1.1–2.3) | 0.021 |
| Self-reported dyspnea | | | | |
| None to mild | 957 | 185 | 1.0 (referent) | — |
| Moderate to very severe | 220 | 76 | 1.6 (1.1–2.3) | 0.007 |

This model was adjusted for age at diagnosis, sex, histologic type, clinical stage (IA–IIB, IIIA–IIIB, or IV), PS (0 or 1 ≤), or the severity of self-reported pain and dyspnea (none to mild, moderate to very severe). All odds ratios (ORs) are given with 95% confidence intervals (CIs) in parentheses.

[a] Clinical stages were defined by TNM classification: International Union Against Cancer.

[b] Performance status was defined by Eastern Cooperative Oncology Group (ECOG).

significant positive association between depression and the risk of mortality among lung cancer patients [11–13]. Faller *et al.* [11] followed up 103 patients with stage I–IV lung cancer for 7–8 years and documented 92 deaths; they found a significant linear positive association between depression and the risk of mortality in the cancer patients (after inclusion of tumor stage, PS, and emotional distress level as covariates). Faller *et al.* [12] also followed up another series of 59 patients with advanced lung cancer (stage III or IV) for about 5 years and documented 54 deaths; they again reported a significant linear positive association between depression and the risk of mortality in the patients (after inclusion of age, sex, tumor stage, histologic type, and PS as covariates). Buccheri [13] followed up 133 patients with stage I–IV lung cancer for about 2 years and documented 44 deaths; subjects with higher scores for depressive symptoms exhibited a significantly higher risk of death as compared with subjects with lower scores (after inclusion of sex and tumor stage as covariates). All of these three studies had methodological limitations, that is, they included only a small number of subjects and failed to control sufficiently for potential confounding variables such as clinical symptoms, socioeconomic variables, and smoking status. In our study, adjustment for the effect of socioeconomic variables and smoking status (model 1) and for the effect of the clinical stage and PS as clinical state variables (model 2) did not alter the significant positive association between depression and mortality. However, when self-reported pain and dyspnea were included in the multivariate model (model 3), the association became non-significant ($p$ for trend = 0.26) (Table 2). The severity of self-reported clinical symptoms, such as pain and dyspnea, was correlated with the tumor stage and/or PS among lung cancer patients [22,35]. However, the severity of self-reported pain and dyspnea was also described as an important independent prognostic factor in a population of lung cancer patients [22,23]. Therefore, when the association between the psychological state and cancer survival was examined, it was necessary to consider not only the tumor stage and the PS but also the severity of symptoms such as pain and dyspnea. Earlier studies were inadequate, even though the clinical stage and PS had been considered. As indicated in Table 3, the severities of self-reported pain and dyspnea were significantly associated with depression, independent of the clinical stage or PS. The severity of clinical symptoms reflected the severity of depressive symptoms among lung cancer patients. Thus, the association between depression and the risk of mortality was largely confounded by the clinical symptoms.

In the helplessness/hopelessness subscale, after adjustment for the effect of socioeconomic variables and smoking status (model 1), there was a significant, linear and positive association between helplessness/hopelessness and the risk of mortality. However, after inclusion of the clinical stage and PS (model 2) and the severity of self-reported pain and dyspnea in the multivariate model (model 3), the association became non-significant ($p$ for trend = 0.17 and 0.41, respectively). For the association between the clinical state variables and the score in the helplessness/hopelessness subscale in the cross-sectional design, the results were similar to the results for depression (data not shown). Thus, the association between the score in the helplessness/hopelessness subscale and the risk of mortality was largely confounded by the clinical

state variables. On the other hand, no association was noted between the score for neuroticism and the risk of mortality, regardless of adjustment for any variables.

Our study had several methodological advantages as compared with previous studies. Firstly, our sample size was the largest (1178 eligible subjects and 686 deaths). Secondly, our study controlled extensively for potential confounding variables, including clinical state and socioeconomic variables and the smoking status.

However, our study also had several limitations. First, the study dealt with patients who were treated at one institution, a teaching cancer hospital in Japan; therefore, the external validity of the finding has to be tested. Second, we considered the negative psychological aspects in the patients before the start of treatment. The effect of the negative psychological aspects after the start of treatment upon the mortality should also have been tested. Third, the study subjects consisted entirely of lung cancer patients. Since patients with cancers at other sites were not examined in this study, it remains unclear whether the results can be extrapolated to patients with cancers at other sites. Fourth, we focused on the all-cause mortality, because we did not have information on the cause of death. Therefore, the association with the risk of death from lung cancer is unknown. Finally, because the follow-up period in this study was short and the number of patients with early-stage cancer was small, long-term follow-up of early-stage patients may also be warranted in the future.

In conclusion, negative psychological aspects such as neuroticism, helplessness/hopelessness, and depression were no longer associated with the risk of mortality among lung cancer patients after adjustment for the clinical state variables. Our data support the hypothesis that the association between helplessness/hopelessness and depression and the risk of mortality among lung cancer patients was largely confounded by the clinical state variables, including the clinical stage, PS, and severity of clinical symptoms. This hypothesis was proven, and it would reassure the cancer patients because poor psychological states in cancer patients were merely a consequence of illness but not a determinant of poor prognosis.

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*Original Article*

# Factors Correlated with Fatigue in Terminally Ill Cancer Patients: A Longitudinal Study

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***Abstract***

*Fatigue is among the most distressing symptoms experienced by terminally ill cancer patients. It is necessary to clarify factors correlated with fatigue to develop effective management strategies. A consecutive sample of cancer patients newly registered in the Palliative Care Unit (PCU) was assessed on three occasions: at the second visit to the outpatient clinic of the PCU (Time 1), three weeks after the Time 1 session over the telephone (Time 2), and at admission to the PCU (Time 3). The patients' fatigue and a broad range of biopsychosocial factors were assessed using the validated questionnaires, structured interviews, and medical record reviews at Time 1 and Time 3. Fatigue was the only factor assessed at Time 2. Two hundred patients participated in the Time 1 session, and 129 and 73 were followed at Time 2 and Time 3, respectively. Greater fatigue at Time 1 was significantly correlated with psychological distress, lower Karnofsky Performance Status score, dyspnea, and appetite loss (adjusted coefficients of determination [$R^2$] = 0.49). Greater fatigue at Time 2 was significantly correlated with psychological distress, lower Karnofsky Performance Status and fatigue at Time 1 (adjusted $R^2 = 0.51$). Greater fatigue at Time 3 was significantly correlated with changes for the worse in psychological distress, Karnofsky Performance Status, and dyspnea severity during the period between Time 1 and Time 3, after adjusting for Time 1 fatigue (adjusted $R^2 = 0.54$). The results indicate that fatigue in terminally ill cancer patients is determined by both physical and psychological factors. It may be important to include psychological intervention in the multidimensional management of fatigue in this population, in addition to physical and nursing interventions.* J Pain Symptom Manage 2008;35:515–523. © *2008 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

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*Key Words*
*Fatigue, depression, terminal, palliative care, quality of life, symptom management, psycho-oncology, psychiatry, end of life*

## *Introduction*

Fatigue is a critical problem among terminally ill cancer patients. Previous studies have shown the prevalence of fatigue in this population to be between 52% and 81%.[1–3] Symptom management to improve the quality of life of patients with incurable cancer is the primary task of medicine. However, there are no established strategies for the management of fatigue.[4] The general strategy for symptom management is to correct the cause of the symptom. Therefore, the factors that are correlated with fatigue in cancer patients must be clarified before management strategies can be developed.[5]

Fatigue is thought to be associated with various factors. Physical factors include anticancer treatment;[6] other symptoms such as pain and dyspnea;[3,7,8] and anemia.[9] Among the psychological factors contributing to fatigue, the role of depressive mood has been most discussed. Our previous study and some other studies in cancer patients have confirmed this association,[7,10–12] but other studies have failed to find one.[3,13] Although the relative contribution of each factor is thought to vary over the course of the illness, few studies have applied a longitudinal design, or have been conducted in terminally ill cancer patients.

Only one previous study has investigated the factors associated with fatigue in terminally ill cancer patients.[3] A convenience sample of 95 cancer patients who were inpatients at a palliative care unit were compared with 98 healthy individuals. The results of a cross-sectional analysis revealed that pain and dyspnea were the only factors that were significantly correlated with fatigue in the patient group, whereas depression and anxiety were found to be significant in the control group. The study could not clarify any longitudinal associations between fatigue and these factors.

Taking this information into consideration, we assessed a broad range of psychosocial factors in a longitudinal study to clarify the factors correlated with fatigue in terminally ill cancer patients.

## *Patients and Methods*

Consecutive outpatients with cancer, who had been seen at the Palliative Care Unit (PCU) of the National Cancer Center Hospital East, Japan, were asked to participate in the study. The eligibility criteria were (a) newly registered in the PCU, (b) not currently undergoing curative anticancer treatment, (c) informed of their cancer diagnosis, (d) well enough to complete the questionnaires and participate in at least a half-hour interview, and (e) not suffering from cognitive disorders, defined as a score of 24 or less on the Mini Mental State examination.[14] The Mini Mental State examination is a brief screening battery for detecting cognitive disturbances, and the Japanese version of the Mini Mental State examination has been validated.[15]

This study was approved by the Institutional Review Board and the Ethics Committee of the National Cancer Center, Japan. Written consent was obtained from each of the patients after they had been fully informed of the purpose and intent of the study.

Three sessions were held: at the time of the patient's second visit to the outpatient clinic of the PCU (Time 1); three weeks later over the telephone (Time 2); and at the time just after being hospitalized to the PCU (Time 3).

### *Measurements Performed at the Time 1 and Time 3 Sessions*

*Fatigue.* Fatigue was assessed using the Cancer Fatigue Scale (CFS), a 15-item self-rating scale for assessing fatigue in cancer patients.[16] The scale consists of three subscales (physical, affective, and cognitive) that address the multidimensional nature of fatigue. Each item has a five-point Likert scale (from 1 [not at all] to 5 [very much]), and the total fatigue score can range from 0 to 60, with higher scores

indicating greater fatigue. Separately from the CFS, a five-point Likert scale was also used at the same time to briefly assess fatigue (from 1 [not fatigued at all] to 5 [fatigued very much]).

*Psychological Factors.* The Hospital Anxiety and Depression Scale was used to evaluate the patients' psychological distress in the preceding week.[17] The Hospital Anxiety and Depression Scale consists of a seven-item anxiety subscale and a seven-item depression subscale but does not include questions about physical symptoms to avoid contaminating the mood assessments. Each item has a four-point Likert scale, and the total score can range from 0 to 42, with higher scores indicating greater distress. We previously established the reliability and validity of the Japanese version of this questionnaire in cancer patients.[18] The total score was used in the analyses because our interest was in the contribution of psychological distress to the manifestation of fatigue.

*Physical (Including Medical) Factors.* Medical information on each patient was obtained from their medical records. The Karnofsky Performance Status scale is a brief objective measure of a patient's functional status.[19] The score ranges from 100 (normal, no complaints) to 0 (dead). Independently, the attending physicians also clinically assessed the patients' Performance Status (PS), as defined by the Eastern Cooperative Oncology Group (ECOG). Patients were asked to express their severity of pain, dyspnea and constipation by selecting one score on a panel of from 1 (not at all) to 5 (very much). Appetite loss and insomnia were assessed in the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (revised) (SCID).[20] An investigator structurally questioned the patients regarding the severity of these symptoms and rated the patients as 1 (not at all), 2 (sub-threshold: present but does not reach the over-threshold criterion), 3 (over threshold: lasts more than two weeks and/or interferes with the patient's daily life). A physical examination, including measurements of height, body weight, body temperature and heart rate, was also performed for each patient. The body mass index (BMI) was calculated as the body weight / height$^2$.

*Social and Demographic Factors.* Sociodemographic data were obtained during a structured interview. The patients' use of confidants was used as an indicator of social support.[21] Patients were asked whether they had confided in anyone regarding their cancer, and if so, the type and number of confidants and their level of satisfaction with them. Changes in family and other relationships since their cancer diagnosis were also assessed using a 7-point Likert scale (1 [worsened considerably] to 7 [improved considerably]).

### *Measurements Performed at the Time 2 Session*

Data were obtained during a structured telephone interview. Fatigue was assessed using the CFS at Time 2 also. The validity of the usage of the CFS over the telephone has been established.[16]

### *Statistical Analysis*

Three models were analyzed using multiple regression analyses.

*Model 1: Cross-Sectional Analysis at Time 1.* This model used a cross-sectional design to clarify the factors correlated with fatigue. Fatigue at Time 1 was entered as a dependent variable. The possible independent variables were the factors investigated at Time 1.

*Model 2: Longitudinal Analysis 1.* This model was designed prospectively to clarify the temporal relationships between fatigue at Time 2 and the factors extracted in Model 1. Fatigue at Time 2 was entered as a dependent variable. The independent variables were all factors retained from the final Model 1. Time 1 fatigue and the interval between Time 1 and Time 2 sessions were entered to adjust the results.

*Model 3: Longitudinal Analysis 2.* This model was used to clarify the factors involved in change in fatigue severity. Fatigue at Time 3 was entered as a dependent variable. The possible independent variables were changes in the investigated factors between Time 1 and Time 3. The change in each value was calculated by subtracting the Time 1 value from the Time 3 value. Unchangeable variables, such as the cancer site and demographic data, were not included in this model. Also, Time 1 fatigue and the interval between Time 1 and Time 3 sessions were entered to adjust the results.

To determine the potential factors, univariate analyses between each dependent variable

and the possible independent variables were performed using Pearson's correlations, Spearman's rank correlations and unpaired Student's t-tests, where appropriate, in Model 1. Since we recognized the scores from Likert scales as ordinal variables, we used the Spearman's rank correlations when assessing the correlations between fatigue and the scores obtained by using Likert scales. For descriptive purposes, however, we tabulated the means and standard deviations for these variables. Partial correlations controlling for Time 1 fatigue and the interval between Time 1 and Time 3 sessions were performed in Model 3. Significantly correlated factors ($P < 0.05$) were retained. Multicollinearity diagnostics were calculated and examined. In Model 1, we conducted each of the three systematic variable selection procedures (backward, forward, and stepwise) and checked the consistency of the three models. Consistent results were expected. If differences were found, one model was selected based on clinical plausibility. In Models 2 and 3, forced-enter multiple regression analyses were conducted.

Median survival was calculated using the Kaplan-Meier product limit method. The level of significance was set at $P < 0.05$ in all of the statistical analyses. All reported $P$ values are 2-tailed. All statistical procedures were conducted using SPSS 10.0 J version software for Windows (SPSS Inc., 1999).

## Results

*Patients*

Detailed subject recruitment and retention are described in Fig. 1. The sociodemographic and clinical characteristics of the participants at Time 1 are shown in Table 1. There was a significant difference in ECOG PS between the participants ($n = 200$) and the non-participants ($n = 228$) at Time 1 (1.5 vs. 2.3, $P < 0.001$, Mann-Whitney U test). However, no significant differences in age, gender, cancer site or clinical stage were seen. The median survival times at the Time 1 and Time 3 sessions were 95 and 45 days, respectively. The median intervals between the Time 1–Time 2 and Time 1–Time 3 sessions were 20 (mean ± SD: 23 ± 6 days) and 64 days (92 ± 102 days), respectively.

*Prevalence of Fatigue*

The prevalence of fatigue (a score of 2 or greater on a 5-point Likert scale) was 64.0, 65.9 and 82.2% at Time 1, Time 2, and Time 3, respectively.

*Model 1: Cross-Sectional Analysis at Time 1.* The patients' mean total CFS score was 21.7 (± 9.5), significantly greater than the reference data obtained in disease-free breast cancer patients in our previous study (16.4 ± 7.9) ($t = 5.44$, $P < 0.001$, t-test).[7] Tables 2 and 3 show the results of the univariate analysis. The three multiple regression models using stepwise, forward, and backward variable selection procedures consistently showed that psychological distress, a lower Performance Status score and appetite loss were significantly correlated with Time 1 fatigue. Dyspnea was significantly correlated only in the backward model. Since a previous study reported an association between fatigue and dyspnea in advanced cancer patients,[3] we chose the results of this backward model. The final results of the model are shown in Table 4.

*Model 2: Longitudinal Analysis 1.* Fatigue decreased significantly between Time 1 and Time 2 (20.7 [SD = 9.2] and 18.2 [SD = 10.4], respectively, $t = 3.48$, $P = 0.001$, paired t-test). Psychological distress and Performance Status at Time 1 significantly predicted Time 2 fatigue, after adjusting for Time 1 fatigue (Table 4).

*Model 3: Longitudinal Analysis 2.* Fatigue increased significantly between Time 1 and Time 3 (21.9 [SD = 8.7] and 26.4 [SD = 9.7], respectively, $t = -4.62$, $P < 0.001$, paired t-test). Partial correlations showed that only changes in psychological distress level, Performance Status and dyspnea severity were significantly correlated with fatigue at Time 3 (Table 3). These results were almost consistent with the results of Model 1. Thus, we decided to use the same variable set of independent variables as that used in Model 1. A multiple regression analysis revealed that changes in psychological distress, Performance Status, dyspnea, and fatigue at Time 1 were significantly correlated with changes in fatigue (Table 4). Associations with changes in medication could not be

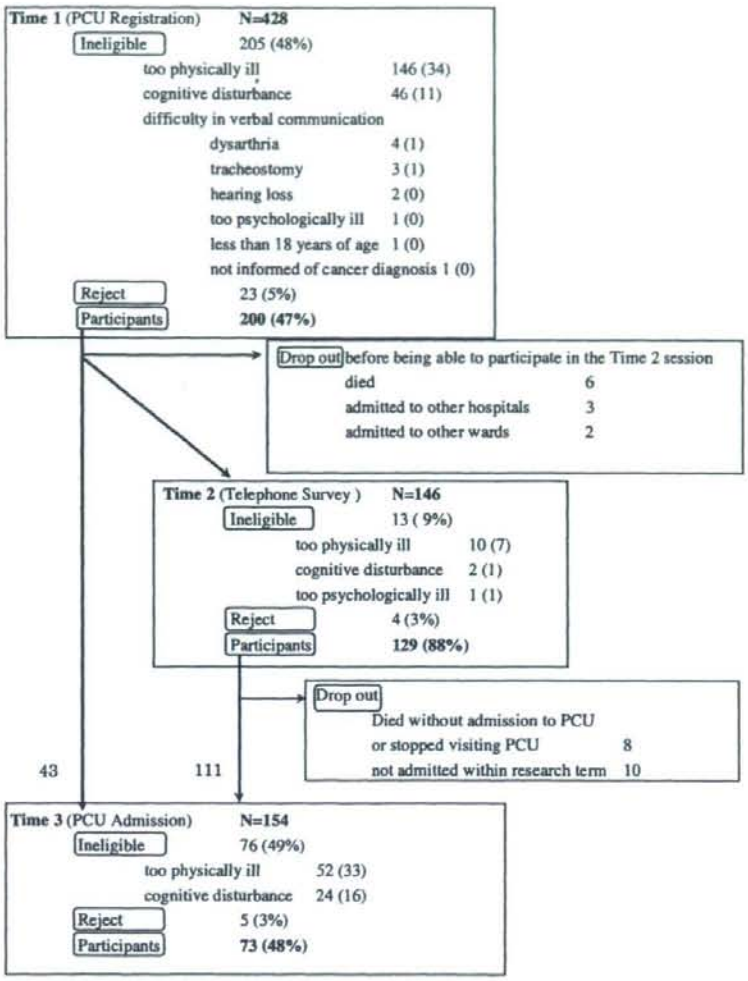


Fig. 1. Participant sampling. The participant sampling is summarized. Fifty-four patients dropped out or were admitted to the PCU before participating in the Time 2 session. PCU: Palliative Care Unit.

analyzed because the number of relevant patients was too small.

### *Association Between Physical Component of Fatigue and Psychological Distress*

Since we were interested whether the physical component of fatigue itself associated with psychological distress, we additionally investigated the correlates of the physical subscale of the CFS in the same manner. The results were consistent: a significant correlation was observed between the physical component of fatigue and psychological distress in all three models (multiple $R^2$ for psychological distress was 0.20, 0.11, and 0.08 in Models 1, 2, and 3, respectively).

## *Discussion*

This is the first longitudinal study to clarify that both physical and psychological factors

*Table 1*
**Demographic and Clinical Characteristics of the Patients at Time 1**

| Characteristics | *n* | % |
|---|---|---|
| Age (years), mean ± SD (median) | 61.0 ± 10.2 (61) | |
| Gender | | |
| Female | 69 | 35 |
| Education level | | |
| Junior high school or less | 58 | 29 |
| Marital status | | |
| Married | 74 | 87 |
| Household size | | |
| Lives alone | 10 | 5 |
| Cancer site | | |
| Lung | 79 | 40 |
| Colon | 24 | 12 |
| Head and neck | 15 | 8 |
| Stomach | 13 | 7 |
| Liver | 13 | 7 |
| Other | 56 | 28 |
| Clinical stage | | |
| Recurrence | 34 | 17 |
| Metastatis | | |
| Presence | 184 | 92 |
| History of anti-cancer therapy (multiple choice) | | |
| Surgery | 84 | 42 |
| Chemotherapy | 115 | 58 |
| Radiotherapy | 71 | 36 |
| Performance status[a] ≤60 | 55 | 28 |

[a]Defined by Karnofsky criteria.

*Table 2*
**Associations Between Potential Factors and Time 1 Fatigue ($n = 200$)[a]**

| | Association with Time 1 CFS Total Score | | | |
|---|---|---|---|---|
| Potential Factors | *n* | Mean | *t* | *P* |
| Education | | | | |
| Junior high school or less | 58 | 18.6 | −2.93 | 0.04 |
| Other | 142 | 22.9 | | |
| Current medication | | | | |
| Anxiolytics | | | | |
| Presence | 23 | 25.5 | −2.08 | 0.04 |
| Absence | 177 | 21.2 | | |
| Opioids | | | | |
| Presence | 54 | 24.4 | −2.57 | 0.01 |
| Absence | 146 | 20.6 | | |
| Antiemetics | | | | |
| Presence | 38 | 24.8 | −2.27 | 0.02 |
| Absence | 162 | 20.9 | | |
| Laxatives | | | | |
| Presence | 86 | 23.4 | −2.30 | 0.02 |
| Absence | 114 | 20.3 | | |

[a]Factors with $P < 0.05$ are shown.

independently play important roles in the development of fatigue in terminally ill cancer patients. Three factors were consistently found to be correlated with fatigue: psychological distress and the Karnofsky Performance Status in all three investigated models, and dyspnea in Models 1 and 3. This consistency indicates the stability of these results. Also, the high coefficients of determination in each model confirm the adequate validity of the results.

The effectiveness of psychological interventions for the amelioration of fatigue has been reported, although the goal was not to reduce patient fatigue and the subjects were not terminally ill cancer patients in most of those studies.[4] Among psychotropics, the usefulness of methylphenidate (a type of psychostimulant) in the amelioration of fatigue has been suggested from preliminary experiments in terminally ill cancer patients,[22] but a recent randomized controlled trial failed to find significant superiority over placebo.[23] Another study indicated that paroxetine (a selective serotonin reuptake inhibitor antidepressant) had no influence on fatigue in patients receiving chemotherapy.[24] Further research is required to confirm the effectiveness of psychological intervention strategies, including these approaches.

In contrast to our results, Stone et al. failed to find an association between fatigue and psychological distress in their study in a palliative care setting.[3] This discrepancy may be explained by the following three differences between the two studies. First, differences in the instruments applied to assess fatigue may account for the discrepancy; they used the Fatigue Severity Scale, which was developed for patients with collagen disease. Second, the patient characteristics differed. They used a convenience sample population and did not exclude patients with cognitive dysfunction using neuropsychometric tests. Third, other factors, such as cross-cultural differences in the perception and expression of fatigue, may also influence this phenomenon. However, there are no studies that confirm this assumption.

Karnofsky Performance Status was revealed to be significantly correlated with fatigue, in addition to psychological distress. Disability in cancer patients may arise from a number

*Table 3*
**Correlations Between Potential Factors and Time 1 ($n = 200$) or Time 3 ($n = 73$) Fatigue**

| Potential Factors | Descriptive Statistics (Mean ± SD, Median)[a] | | Correlation with Time 1 CFS Total Score | | Correlation Between Times 1–3 Change and Time 3 CFS Total Score | |
|---|---|---|---|---|---|---|
| | At Time 1 | At Time 3 | Correlation coefficient[b] | *P* | Correlation coefficient[c] | *P* |
| Physical factor | | | | | | |
| Performance status (Karnofsky Performance Status)[d] | 73.5 ± 14.6, 70 | 52.7 ± 16.6, 50 | −0.45* | <0.001 | −0.31 | <0.01 |
| Body Mass Iindex[e] | 20.7 ± 3.4, 20.7 | 20.1 ± 3.7, 19.6 | −0.21* | <0.01 | −0.14 | 0.31 |
| Pain[f] | 1.9 ± 0.9, 2 | 2.1 ± 1.2, 2 | 0.23 | 0.001 | 0.05 | 0.65 |
| Dyspnea[f] | 1.9 ± 1.0, 2 | 2.0 ± 1.0. 2 | 0.36 | <0.001 | 0.32 | <0.01 |
| Constipation[f] | 1.8 ± 1.1, 1 | 2.0 ± 1.3, 1 | 0.24 | 0.001 | −0.02 | 0.86 |
| Diarrhea[f] | 1.2 ± 0.5, 1 | 1.5 ± 1.0, 1 | <0.01 | 1.00 | 0.04 | 0.76 |
| Appetite loss[g] | 1.9 ± 0.9, 2 | 2.2 ± 0.8, 2 | 0.42 | <0.001 | 0.05 | 0.69 |
| Sleep disturbance[g] | 1.6 ± 0.7, 1 | 1.8 ± 0.8, 2 | 0.26 | <0.001 | 0.12 | 0.32 |
| Psychological factor | | | | | | |
| Total score of HADS | 11.6 ± 6.7, 11 | 14.8 ± 7.5, 15 | 0.62* | <0.001 | 0.46 | <0.001 |
| Social factor | | | | | | |
| Satisfaction with confidants[h,i] | 5.5 ± 1.4, 6 | 5.7 ± 1.5, 6 | −0.17 | 0.02 | −0.11 | 0.36 |

HADS=Hospital Anxiety and Depression Scale.
[a]Mean and SD of the ordinal variables were calculated also for descriptive purposes.
[b]All correlation coefficients are Spearman rho correlation coefficients, except for * Pearson *r* correlation coefficients.
[c]Partial correlation coefficient controlling for Time 1 CFS total score and interval between Times 1–3.
[d]Defined by Karnofsky criteria.
[e]Body Mass Index, calculated as body weight/height$^2$.
[f]Assessed using a five-point Likert scale (1 [not at all] to 5 [very much]).
[g]Assessed using a three-point objective rating (1 [not at all] to 3 [over threshold]).
[h]Assessed using a seven-point Likert scale(1 [not satisfied at all] to 7 [very much satisfied]) at Time 1.
[i]Assessed using a five-point Likert scale(1 [very much worse] to 7 [very much improved]) at Time 3.
HADS=Hospital Anxiety and Depression Scale.

of causes, including the direct effects of the cancer itself or of anticancer treatment, as well as indirect effects, such as cancer-related symptoms and deconditioning, which refers to the negative effect of prolonged bed rest and immobility upon various body systems.[25] The effectiveness of exercise for improving physical functions[26] and reducing fatigue[27] has been reported, although most of this evidence was not obtained in terminally ill cancer patients. Individualized, adequate interventions to maintain or gain physical activity, including exercises or a scheduled rest–activity pattern, may be beneficial for reconditioning body systems, even in terminally ill cancer patients.

The present results also suggested an association between dyspnea and fatigue, although the causality could not be determined. Interactions between multiple symptoms are an important area of symptom management research.[28] Most patients have multiple symptoms. Concurrent symptoms may share the same biological mechanisms, and an intervention to alleviate one symptom may also improve another symptom. Unfortunately, cancer-related dyspnea is not well understood.[29] Although the elucidation of a causal association remains to be made in future studies, the management of dyspnea should be attempted and may be helpful in ameliorating fatigue.

Some methodological qualifications deserve mention. First, the heterogeneity of the study population needs to be discussed. The patients had cancers that were at different sites and stages, and had different metastatic lesions, courses, and prognoses. Second, we observed considerable patient attrition because of physical and cognitive deterioration, which hampered participation in the study. The condition of non-participants was more serious, as shown in the Results. Thus, the prevalence of fatigue may have been underestimated in this study. Also, it may not be possible to generalize our findings to all terminally ill cancer patients. However, in this type of research field, such limitations are unavoidable. In fact, the minimal attrition rate may indicate the appropriateness of our research methodology. We also noticed a high prevalence of

*Table 4*
**Multiple Regression Analyses—Factors Correlated with Fatigue**

| Model | Independent Variable | Coefficient | Standardized Coefficient | Multiple $R^2$ | $t$ | $P$ |
|---|---|---|---|---|---|---|
| Model 1 ($n=192$) | Psychological distress[a] | 0.69 | 0.48 | 0.30 | 8.23 | <0.001 |
| | Performance status[b] | −0.14 | −0.22 | 0.10 | −3.37 | <0.001 |
| | Dyspnea[c] | 1.09 | 0.11 | 0.03 | 2.03 | 0.04 |
| | Appetite loss[d] | 1.59 | 0.15 | 0.06 | 2.52 | 0.01 |
| Dependent variable: fatigue at Time 1, intercept = 19.30, multiple $R^2 = 0.50$, adjusted $R^2 = 0.49$ | | | | | | |
| Model 2 ($n=129$) | Psychological distress | 0.32 | −0.20 | 0.11 | 2.49 | 0.01 |
| | Performance status | −0.16 | −0.22 | 0.11 | −2.85 | <0.01 |
| | Dyspnea | 0.92 | 0.09 | 0.03 | 1.27 | 0.21 |
| | Appetite loss | 0.61 | 0.05 | 0.02 | 0.68 | 0.50 |
| | Fatigue at Time 1 | 0.45 | 0.40 | 0.26 | 4.56 | <0.001 |
| | Interval between Time 1 and Time 2 | 0.09 | 0.06 | 0.00 | 0.97 | 0.33 |
| Dependent variable: fatigue at Time 2, intercept = 13.13, multiple $R^2 = 0.53$, adjusted $R^2 = 0.51$ | | | | | | |
| Model 3 ($n=73$) | Change in psychological distress | 0.49 | 0.32 | 0.12 | 3.76 | <0.001 |
| | Change in performance status | −0.11 | −0.19 | 0.02 | −2.20 | 0.03 |
| | Change in dyspnea | 2.40 | 0.25 | 0.05 | 3.11 | <0.01 |
| | Change in appetite loss | −0.01 | 0.00 | 0.00 | −0.01 | 0.99 |
| | Fatigue at Time 1 | 0.70 | 0.63 | 0.37 | 7.53 | <0.001 |
| | Interval between Time 1–3 | −0.01 | −0.12 | 0.02 | −1.46 | 0.15 |
| Dependent variable: fatigue at Time 3, intercept = 8.58, multiple $R^2 = 0.57$, adjusted $R^2 = 0.54$ | | | | | | |

[a]Total score of HADS (Hospital Anxiety and Depression Scale).
[b]Defined by Karnofsky criteria.
[c]Assessed using a five-point Likert scale (1 = not at all to 5 = very much).
[d]Assessed using a three-point objective rating (1 = not at all to 3 = over threshold).

patients who suffered from cognitive dysfunction.[30] This problem should be considered in future studies of comparable populations. Another limitation was the use of invalid methods to assess symptoms other than fatigue. No comprehensive symptom inventories that were sufficiently brief and simple to use with severely exhausted patients were available at the time of protocol development.

In conclusion, this study revealed that fatigue in terminally ill cancer patients is closely correlated with both physical and psychological factors and that both of these factors may be closely related to the manifestations of fatigue. More attention to these factors could lead to a better understanding of fatigue in this population. Further research is required to examine whether the management of these factors may be effective for ameliorating fatigue. Also, patient suitability for the application of each mode of treatment should be clarified.

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# Cancer patients' reluctance to disclose their emotional distress to their physicians: a study of Japanese patients with lung cancer

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## Abstract

***Purpose*: To explore cancer patients' concerns about emotional disclosure (ED) to their physicians, and to investigate the factors associated with them.**

***Subjects and Methods*: Randomly selected ambulatory patients with lung cancer participated in this study. An 18-item questionnaire to assess patients' beliefs regarding ED to their physicians was developed for this study. Factor analysis was used to extract the underlying factors of this scale. Patients were asked to answer this questionnaire along with other self-administered questionnaires.**

***Results*: Complete data were available from 104 patients. Four factors were extracted by factor analysis: 'Hesitation to disturb the physicians by ED', 'No perceived need for ED', 'Negative attitude towards ED', and 'Fear of a negative impact of ED'. All factors reached standards of internal consistency. The prevalence of the above concerns, in that order, among the patients was 68, 67, 46, and 20%. Patients with high distress levels were significantly more likely to endorse 'Negative impact' ($p = 0.02$). Older patients were more likely to report 'Negative attitude' ($p = 0.06$), whereas male patients were more likely than females to report 'Hesitation' ($p = 0.05$).**

***Conclusion*: Knowledge of such patient-related barriers should better prepare physicians to build good communication channels with their cancer patients.**



**Keywords: cancer; oncology; communication; psycho-oncology; depression**

## Introduction

Cancer patients frequently have psychological distress. The prevalence of major depression and adjustment disorder among these patients have been reported to range from 5 to 35% [1]. Since depression is not only distressing and disturbs the patients' quality of life, but also kindles the desire for death, affects usage of health care and poses a burden for the family; intensive treatment of depression in these patients is essential [2].

Delivery of supportive and palliative care, including psychological support, is one of the primary tasks of oncologists. A global Core Curriculum in Medical Oncology, released by the American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO), includes 'Psychosocial aspects of cancer' as one of the topics [3]. The Japanese Society of Medical Oncology has also implemented this curriculum.

An accurate evaluation of the symptom severity is crucial to the provision of optimal symptom management. Emotional disclosure (ED) by patients themselves is a primal source of assessing the degree of psychological distress in the patients. However, patients often hesitate to share their emotional distress and/or concerns with their physicians [4,5], even though most consider their attending oncologist as an invaluable person with whom to discuss their emotional distress [6]. A survey of cancer patients' preferences for discussing their psychological problems showed that 67% of cancer patients were willing to discuss their problems with the physicians, but 26% were willing to do so only at the initiative of their doctor [4]. Furthermore, one study indicated that patients with higher degrees of distress were less likely to disclose their concerns [5].

Why are they reluctant to do so? To the best of our knowledge, few studies have been conducted to explore the concerns for patients who do not

discuss their emotional problems with their physicians in the cancer care setting. A study in the general practice setting in UK investigated the reasons for patients not discussing their emotional problems with their physicians [7], and identified the top two reasons as 'doctors do not have enough time' (48%), and 'there is nothing that the doctor can do' (39%). Another study conducted in the general practice setting in New Zealand revealed that patients believed that 'their general practitioner was not the best person to talk to' (34%), and 'mental problems should not be discussed at all' (28%) [8]. These may also be applicable in the cancer care setting [9,10].

The purpose of this study was to explore the cancer patients' concerns about ED to their physicians, and to investigate the factors associated with them.

## Subjects

The study subjects were ambulatory patients with lung cancer attending the outpatient clinic of the Respiratory Medicine Division of Tokai University Hospital, located in a suburban residential area, about 50 km from Tokyo, Japan. We chose this population as subjects since provision of better supportive care for them is urgently and highly required. In a study examining psychological distress and its relation to the site of cancer, Dugan *et al.* reported that primary lung cancer was strongly associated with psychological distress in cancer patients [11]. In addition, Zabora *et al.* and Carlson *et al.* have demonstrated that the highest prevalence of psychological distress was observed among patients with lung cancer [12,13]. The incidence of lung cancer in Japan is increasing, and it is the commonest cause for all cancer mortality in Japan and accounts for 18% of all cancer deaths. Furthermore, the prognosis of patients with lung cancer has been poor.

The eligibility criteria were (a) 18 years of age or older, (b) informed of the cancer diagnosis, (c) well enough to complete the questionnaire and participate in a brief interview, and (d) not suffering from severe mental or cognitive disorders. We selected participants at random using a visiting list and random number table only for logistic reasons (to control the number of patient enrolled per day).

This study was approved by the Institutional Review Board and Ethics Committee of Tokai University, Japan. Written consent was obtained from each patient after a thorough explanation of the purpose and method of the study.

## Methods

Patients were randomly sampled using a planned visiting list and a table of random numbers. After informed consent had been obtained, the patients were asked to complete the self-administered questionnaires described below at home and mail them the next day. In the case of inadequate answers, clarifications were sought over the telephone.

### Reluctance for emotional disclosure

The Reluctance for Emotional Disclosure Questionnaire (REDQ) was developed for this study to investigate the patients' beliefs which might affect their ED to physicians, as there was no appropriate instrument available previously for this purpose. First, we conducted a systematic review to collect and create items that could be useful. Papers focusing on stigma, under-recognition, under-treatment of depression [14,15] or other symptoms such as pain [16] and fatigue [17] in cancer and non-cancer populations, or medical staff–patient communication [7,9,10] were investigated. Then, we developed a draft of this scale based on the review, and asked 10 inpatients with lung cancer to complete them. In-depth discussions about the issue were also conducted with them. The items with small between-patient variability were deleted. Finally, an 18-item questionnaire was developed. Each item was to be rated on a 5-point Likert scale (1[not at all] to 5[very much agree]).

### Psychological distress

The Hospital Anxiety and Depression Scale (HADS) was used to evaluate the psychological distress level of the cancer patients. This questionnaire, developed by Zigmond *et al.* [18], is composed of a 7-item anxiety subscale and a 7-item depression subscale to assess the patients' condition over the preceding week. The characteristic of this scale was that questions about physical symptoms were not included in this scale. We have established the reliability and validity of the Japanese version of this questionnaire in cancer patients [19]. The optimal cutoff point for screening high distress (adjustment disorder or major depressive disorder) was $\frac{10}{11}$.

### Sociodemographic and biomedical factors

An *ad hoc* self-administered questionnaire was used to obtain information on the sociodemographic status, including marital status, level of education, and employment status. Performance status, as defined by the Eastern Cooperative Oncology Group (ECOG), was evaluated by the attending physicians. All other medical information (clinical stage and anti-cancer treatment) was obtained from the patients' charts.

## Statistical analysis

Factor analysis followed by Varimax rotation was conducted to extract the underlying factors of REDQ. The number of items was identified by Keiser's criterion (eigenvalue of 1.0 or greater). Items having factor loading scores of less than 0.50 on all factors were deleted from each subscale to clarify the meaning of each factor. We calculated the average of the constituent items for each subscale. The reliability of the scale was evaluated by calculating Cronbach's alpha coefficient, a measure of the internal consistency of the responses to a group of items.

To determine the correlated factors, univariate analyses between each factor and the independent variables were performed using unpaired Student's *t*-tests. A $p$ value of less than 0.05 was adopted as the significance level in all of the statistical analyses, and all $p$ values reported are two-tailed. All statistical procedures were conducted with the SPSS 13.0J version software for Windows.

## Results

### Patient characteristics (Table 1)

Data were available for 104 cancer patients. A pool of 123 potential lung cancer patients was identified for the study. Nineteen patients (16%) were excluded, including 5 (4%) who refused to participate, 5 with cognitive disturbances, 4 (3%) with serious illness, and 5 for other reasons. The patient characteristics are summarized in Table 1; of the total, 77% had advanced cancer (stage IIIb, IV, or recurrence). The mean HADS total score was $12.6 \pm 7.4$, and 58% scored above the validated cutoff of HADS for adjustment disorder and major depressive disorder (a score of 11 or more on a HADS total scale). Two physicians were enrolled in the study. Patients had been followed by the same physician and one physician had followed the majority of patients (87%).

### Reasons for reluctance for ED; extracted from REDQ (Table 2)

Four factors were identified by Keiser's criterion. The results of the factor analysis are shown in Table 2. The first four variables comprising 'No perceived need for ED' showed significant loading on Factor 1. Two items, including items related to 'Fear of negative impact of ED' loaded on Factor 2. Four items related to 'Negative attitude to ED' loaded on Factor 3, and three items representing 'Hesitation to disturb physicians with ED', showed high loading on Factor 4. After deleting six items having item loading $<0.50$ on any factors, we repeated factor analysis and found the same factor loading pattern. Factor 1 accounted for 21%, Factor 2 for 13%, Factor 3 for 14%, Factor 4 for 13% of the total variance in the data. Cronbach's alpha coefficients showing internal consistency reliability ranged from 0.72 to 0.86, indicating substantial consistency (Table 3). When we used a cutoff to determine reluctance in an expedient manner, the most frequently endorsed reason was 'Hesitation' (68%), followed by 'No perceived need' (67%). About 90% of the patients had one or more reasons. Even if we excluded 'No perceived need' from the analysis, 77% of the patients had at least one reason and 44% had two or more reasons.

### Factors correlated with each subscale of the REDQ (Table 4)

The results of univariate analyses are shown in Table 4. Patients with high distress levels were significantly more likely to endorse 'Negative impact' ($p = 0.02$), whereas patients with low distress levels were significantly more likely to endorse 'No perceived need'. 'Negative attitude' and 'Hesitation' were not correlated with the level of distress. With regard to demographic factors, older patients were more likely to report 'Negative attitude' ($p = 0.06$), whereas male patients were

**Table 1.** Demographical and clinical characteristics of patients ($N$= 104)

| Sample characteristic | | N | (%) |
|---|---|---|---|
| Age (year) | Mean: 65 (SD=10); median: 65 (range, 43–84) | | |
| Sex | Male | 82 | 78 |
| Spouse | Married | 81 | 22 |
| Job | Employed (full-time/part-time) | 27 | 26 |
| Clinical stage | Advanced (IIIb, IV, or recurrence) | 80 | 77 |
| ECOG performance status[a] | 0 | 21 | 20 |
| | 1 | 77 | 74 |
| | 2 or worse | 6 | 6 |
| History of anticancer treatment | Operation | 15 | 14 |
| | Chemotherapy | 95 | 91 |
| | Radiation therapy | 97 | 93 |
| Days after diagnosis | Mean: 358 (SD=502); median: 159 (range, 24–2413) | | |
| HADS total score | Mean: 12.6 (SD=7.4); median: 12 (range, 0–30) | | |

[a]ECOG: Eastern Cooperative Oncology Group.

**Table 2.** Factor loading pattern (followed by varimax rotation) of the Reluctance for Emotional Disclosure Questionnaire ($N$= 104)

| Items | Factor | | | |
|---|---|---|---|---|
| | No perceived need | Fear of negative impact | Negative attitude | Hesitation |
| No support is needed for my emotional distress, because it resolves spontaneously | **0.88** | −0.21 | 0.13 | 0.03 |
| No support is needed to deal with my emotional distress, because I can deal with it by myself | **0.85** | −0.04 | 0.18 | 0.05 |
| No support is needed for the emotional distress, because its occurrence is natural | **0.81** | 0.03 | 0.20 | 0.09 |
| My emotional distress is not as serious as my other problems | **0.51** | 0.08 | −0.02 | 0.11 |
| I would rather want my doctor to spend time in treating my cancer than spend time on reducing my emotional distress | 0.36 | 0.32 | 0.25 | 0.13 |
| My relation with my doctor will become poor if I discuss my emotional distress with them | 0.00 | **0.80** | 0.14 | 0.04 |
| If I describe my emotional distress to my doctor, they will conclude that I will not tolerate my cancer treatment | −0.05 | **0.74** | 0.17 | 0.05 |
| I have no intention of notifying my doctor about my emotional distress | −0.18 | 0.43 | 0.20 | 0.26 |
| My doctor is not interested in my emotional distress | −0.01 | 0.40 | 0.38 | 0.39 |
| It is not the role of my doctor to reduce my emotional distress level | 0.26 | 0.34 | 0.05 | 0.25 |
| In general, I do not like to speak about my emotions | 0.07 | 0.09 | **0.86** | 0.17 |
| I do not like to speak about my emotional distress with any medical staff | 0.09 | 0.40 | **0.61** | 0.16 |
| Talking about my emotions will not alter any radical treatment | 0.18 | 0.15 | **0.58** | 0.04 |
| I leave the matter of my psychological distress up to my doctor | 0.29 | 0.09 | 0.42 | 0.23 |
| My doctor doesn't have enough time to talk about my psychological distress | 0.05 | 0.07 | 0.16 | **0.79** |
| My doctor doesn't ask me about my emotional distress | 0.14 | 0.03 | 0.07 | **0.69** |
| I don't want to bother my doctor by bringing up my emotional distress | 0.17 | 0.42 | 0.12 | **0.51** |
| I try not to complain of my emotional distress to my doctor | 0.14 | 0.28 | 0.35 | 0.48 |

**Table 3.** Descriptive data and reliability of the Barriers Questionnaire ($N$= 104)

| Subscale | Number of items | Mean ± SD | Median | Cronbach's alpha coefficient | Percentage of patients endorsing[a] |
|---|---|---|---|---|---|
| No perceived need | 4 | 2.4 ± 1.1 | 2.3 | 0.86 | 67.3 |
| Fear of negative impact | 2 | 1.4 ± 0.7 | 1.0 | 0.81 | 20.2 |
| Negative attitude | 3 | 1.9 ± 0.9 | 1.9 | 0.76 | 46.2 |
| Hesitation | 3 | 2.6 ± 1.1 | 2.6 | 0.72 | 68.3 |
| Total scale | 12 | 8.3 ± 2.4 | 7.8 | 0.78 | — |

[a]Defines the cutoff of ⩾2 as indicating reluctance.

more likely than female patients to report 'Hesitation' ($p = 0.05$). However, these differences did not reach the conventional statistical significance level. The level of education and marital status were not associated with any of the factors.

Additionally, we investigated whether physicians' individual characteristics have an influence on the level of patients' reluctance by examining the differences in the severity between patients seen by one physician and those seen by the other physician, and only the level of 'No perceived need' was found to be significant.

## Discussion

It is often assumed that cancer patients may be reluctant to talk about their psychological distress to the medical staff [20]. This is the first study to intensively investigate cancer patients' concerns about ED to their physicians. Factor analysis allowed us to conceptualize four categories of concerns about ED; 'No perceived need for ED', 'Fear of negative impact of ED', 'Negative attitude to ED', and 'Hesitation to disturb physicians with ED'. The four-factor construct found in this study was statistically valid and reliable, and also meaningful from the clinical point of view. Understanding the patients' concerns about ED through these four aspects would allow us to deal with this issue more comprehensively.

'Hesitation to disturb physicians with ED' was the most prevalent reason in this population. This finding was consistent with that in the previous studies [7,8], in spite of the differences in the subjects' characteristics (e.g. cancer vs primary care), study methods (e.g. quantitative vs qualitative), or cultural background (e.g. oriental vs

**Table 4.** Factors correlating with each subscale ($N = 104$)

| Potential factors | | | Subscales | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | No perceived need | | Fear of negative impact | | Negative attitude | | Hesitation | |
| | | N | Mean | p | Mean | p | Mean | p | Mean | p |
| *Demographic factor* | | | | | | | | | | |
| Age | <64 | 51 | 2.3 | 0.64 | 1.4 | 0.71 | 1.8 | **0.06** | 2.4 | 0.15 |
| | ≥65 | 53 | 2.4 | | 1.4 | | 2.1 | | 2.7 | |
| Sex | Male | 82 | 2.5 | 0.17 | 1.4 | 0.35 | 1.9 | 0.91 | 2.7 | **0.05** |
| | Female | 22 | 2.1 | | 1.3 | | 1.9 | | 2.2 | |
| Education | >Junior high school | 73 | 2.3 | 0.30 | 1.4 | 0.48 | 1.9 | 0.38 | 2.5 | 0.46 |
| | ≤Junior high school | 31 | 2.6 | | 1.5 | | 2.0 | | 2.7 | |
| Spouse | Married | 81 | 2.4 | 0.44 | 1.4 | 0.49 | 1.9 | 0.78 | 2.6 | 0.58 |
| | Others | 23 | 2.2 | | 1.5 | | 1.9 | | 2.4 | |
| Job | Having full-time or part-time job | 27 | 2.2 | 0.37 | 1.5 | 0.44 | 1.8 | 0.44 | 2.9 | **0.10** |
| | Others | 77 | 2.5 | | 1.4 | | 2.0 | | 2.5 | |
| *Medical factor* | | | | | | | | | | |
| Performance status | 0 | 21 | 2.7 | 0.10 | 1.6 | 0.25 | 2.0 | 0.84 | 2.7 | 0.37 |
| | 1 or worse | 83 | 2.3 | | 1.4 | | 1.9 | | 2.5 | |
| Clinical stage | Advanced (IIIb, IV, recurrence) | 80 | 2.3 | 0.36 | 1.4 | 0.80 | 1.8 | **0.05** | 2.6 | 0.99 |
| | Non-advanced | 24 | 2.6 | | 1.4 | | 2.3 | | 2.6 | |
| *Psychological factor* | | | | | | | | | | |
| HADS total score | ≥11 | 60 | 2.2 | **0.02** | 1.5 | **0.02** | 1.9 | 0.74 | 2.6 | 0.47 |
| | <11 | 44 | 2.7 | | 1.2 | | 1.9 | | 2.5 | |

occidental culture) among these studies. Such hesitation must hamper effective communication and make it difficult to recognize patients' emotional concerns, and furthermore, may negatively influence other outcomes, such as symptom control [21]. Also this study found that this attitude was more prevalent in male than female patients, indicating gender differences in emotional expressiveness. Physicians should thus understand the patients' hesitation, and give them clear messages to let them know that they are indeed interested in their psychological problems.

About a half of the patients had a 'Negative attitude to ED'. The result that older patients were more likely to endorse this attitude may indicate some relation to Japanese traditions which place much value on being modest and reserved. Many other beliefs may underlie this attitude such as cultural background and stigma attached to psychological problems, and further research is needed on this issue. We did not consider the results to imply that it might be harmful to ask the patients about their emotional distress. Rather, physicians should make enquiries about their patients' psychological distress, as also about their preferences for dealing with the problems.

In clinical settings, reluctance about ED is the most problematic, especially in patients with high levels of distress. Thus, sufficient attention must be paid to 'Fear of negative impact of ED', although the prevalence was relatively low in this study population. The significant association of this factor with the HADS score suggested that this concern may arise from a pessimistic way of thinking influenced by depressive mood; alternatively, there may be common mediators, such as a personality trait of neuroticism. Patients having such concerns may also be at a high risk of underestimating their psychological distress.

The score of 'No perceived need for ED' was significantly lower in patients who had low levels of distress than in those with high levels of distress. This indicated that the patients' awareness regarding the need for psychological care may be reliable, we, however, should bear in mind that a subset of patients might be in a denial process [22], and as a result they might report a high level of 'No perceived need'. Physicians may acknowledge that emotional communication may not always be required by the patient, especially when denial works adaptively.

Considering the interactive nature of communication, each physician's attitude and atmosphere should influence whether patients feel safe to share their emotional experience or not. The physicians' cultural background may also affect their communication style. Including physicians' perspective in the future study may be fruitful, and may enhance the generalizability of the findings.

Several limitations of this study deserve mention. First, we had to use an *ad hoc* questionnaire to investigate the reluctance on the patients' part for ED. No validated questionnaire had been developed before for this purpose, therefore, we developed our own following the standard procedures for scale development and arrived at meaningful

subscales with adequate reliability. In addition, the possibility of biases originated from the questionnaire's characteristics, which focused entirely on the potential for a negative interaction as one of the limitations that should be stated. Second, the sample size was not sufficient for conducting factor analysis for an 18-item questionnaire, but deletion of six items did not influence the factor structure and we were able to arrive near the usually recommended item, that is, a patient ratio of 1:10. Third, this was a single-institution study and included Japanese patients with lung cancer. Adequate care must be given before generalizing the findings to other populations. Especially, the external validity of the REDQ has not yet been established. Further studies should be undertaken to utilize this questionnaire among patients with different characteristics.

Despite these limitations, we believe that the findings of this study would be meaningful for improving the emotional communication between patients and physicians. Removing barriers that prevent effective communication is the first step towards providing psychological care. Physicians should be aware of their patients' hesitation for ED, and clearly convey to them that they are indeed interested about the psychological problems of their patients, by regularly making enquires to determine their psychological status. They also need to keep in mind that each patient has different care needs. Patients should be given the opportunity to learn that their physician is a primal source of emotional support, and that they are ready to listen to the patients' stories. Further research is needed to examine whether the reluctance is actually associated with under-recognition of the distress by physicians, and how the reluctance for ED influences the patients' outcome, such as the severity of depression.

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