Original Article

Dyspnea and Its Correlates in Taiwanese Patients with Terminal Cancer

Tai-Yuan Chiu, MD, MHSci, Wen-Yu Hu, RN, PhD, Bee-Horng Lue, MD, Chien-An Yao, MD, MPH, Ching-Yu Chen, MD, and Susumu Wakai, MD, PhD
Hospice and Palliative Care Unit, Departments of Family Medicine (T.-Y.C., C.-A.Y, C.-Y.C.), School of Nursing Science (W.-Y.H.), and Department of Social Medicine (B.-H.L.), College of Medicine and Hospital, National Taiwan University, Taipei, Taiwan, and Department of International Community Health (T.-Y.C., S.W.), Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Abstract
This study prospectively assessed dyspnea and related bio-psycho-social-spiritual factors—including severity, cause, psychological distress, and fear of death—that were possibly related to dyspnea in 125 terminal cancer patients at admission and two days before their death. At admission, 74 patients had dyspnea, which improved but later worsened. Causes included cachexia, anemia, pleural effusion, and lymphangitis. Quality of life, anxiety, depression, and fear of death improved after admission; anxiety was correlated with dyspnea before death ($r = 0.211$, $P < 0.05$, *univariate analysis). Lung infection (odds ratio = 2.29, 95% confidence interval = 0.68–3.90; multiple regression), airway obstruction (2.27, 1.41–3.13), acidemia (1.82, 0.72—2.98), and pericardial effusion (1.38, 0.44–2.32) were independent correlates of dyspnea severity at admission (42.8% of explained variance). Before death, airway obstruction, esophageal cancer, pericardial effusion, lung infection, and mediastinal mass were independent correlates of severity (42.7% of explained variance). Comprehensive care, including improved psychospiritual status, can help in controlling dyspnea and enhancing patients' quality of life.* J Pain Symptom Manage 2004;28:123–132.

Key Words
Dyspnea, terminal cancer, severity, correlated factors

Introduction

Dyspnea is a common and distressing symptom in patients with terminal cancer. It may be difficult to control. Previous studies have shown that as many as 50%–70% of terminal cancer patients experience dyspnea during the last 6 weeks of life and that the symptom is aggravated with the progression of disease. Moreover, dyspnea is often accompanied by anxiety and fear, which severely diminish the patient's quality of life.[1–8] Thus, dyspnea usually persists, it can be uncontrollable, and it may be aggravated. This problem greatly challenges the goal of easing the patient's death and also deeply affects family members and medical professionals. Therefore, the comprehensive management of dyspnea,

Address reprint requests to: Tai-Yuan Chiu, MD, MHSci, No. 7 Chung-Shan South Road, Taipei, Taiwan.
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especially in the late terminal stage, has become one of the most important issues in palliative care.

To improve therapeutic success, the correlates of dyspnea in patients with terminal cancer must be understood. Bruera et al.[6] found that anxiety, maximal inspiratory pressure, and the presence of cancer in the lungs are correlates of the intensity of dyspnea in patients with advanced cancer. Dudgeon et al.[9] conducted a study in a general cancer population and found that some baseline data, such as a history of smoking, asthma, and chronic obstructive pulmonary disease, are significantly related to the presence of dyspnea. They also found in another study that only anxiety remained significant in a multivariate model based on data from 75 outpatients of a general oncology clinic.[10] In a third study, patients had a median of five different abnormalities that could have contributed to their shortness of breath, but only anxiety, a history of smoking, and pCO2 levels were statistically significantly correlated with shortness of breath in 100 terminally ill cancer patients.[11] Reuben and Mor[3] found that 75% of patients with lung involvement reported dyspnea at some point, but patients with lung or pleural involvement constituted only 39% of these terminally ill patients reporting shortness of breath. Heyse-Moore et al.[12] found in a study of 150 advanced cancer patients that correlation between dyspnea scores and spirometry was low.

The issue of dyspnea and its correlated factors in cancer patients also has drawn attention in Japan. Tanaka et al.[13] reported that psychological distress and the presence of organic causes, coughing, and pain are significantly correlated with dyspnea in patients with advanced lung cancer. Their results confirmed that dyspnea is multifactorial and that a beneficial therapeutic strategy might include intervention for psychological distress and pain.

No formal studies of dyspnea and its correlated factors have been conducted in patients with terminal cancer in Taiwan, though dyspnea occurs in 56.6% of such patients.[8] The aim of our study was to investigate factors correlated with dyspnea—including a comprehensive range of medico-psycho-social-spiritual factors—in patients with terminal cancer. The findings may lead to the development of a model for managing dyspnea in terminal cancer patients in Taiwan.

Methods

Patients

All consecutive patients admitted to the hospice and palliative care unit of the National Taiwan University Hospital between February 2002 and January 2003 were enrolled in the study. Patients whose cancers were not responsive to curative treatment were identified in an initial assessment performed by members of the admissions committee. Patients who met the following inclusion criteria were considered eligible: 1) The patient was conscious and able to communicate, both at admission and in the 48 hours before his or her death, 2) the patient could provide informed consent or verbally agreed to participate, and 3) the patient was not so weak that answering the questions was a major burden. The patients' physicians and primary nurses determined their eligibility. The selection of patients and the design of this study were approved by both the Department of Health, Executive Yuan, Taiwan, and the ethical committee at the hospital. By the end of the study period, 125 of the 470 consecutive patients met the inclusion criteria and had completed the study.

Instruments

An assessment form was designed after the investigators carefully scrutinized the literature in this area and was used daily. On this form, we recorded the patients' demographic data, dyspnea scores (on a 0–10 scale), organic causes of dyspnea, psychological status (including anxious and depressed moods), family function, extent of any fear of death, and quality of life. A panel comprising 2 physicians, 2 nurses, 1 psychologist, and 1 chaplain tested the entire instrument for content validity. All members of the panel were experienced in the care of the terminally ill. Each item in the questionnaire was appraised on a scale of 1, "very inappropriate and not relevant," to 5, "very appropriate and relevant." A content validity index was used to determine the validity of the structured questionnaire; this instrument yielded an index of 0.96. In addition, a pilot study was conducted for 1 month in the same unit. The results of this pilot study further confirmed the instrument's content validity and ease of application.

Demographic and Medical Data. Demographic characteristics assessed included sex, age, education, primary tumor sites, metastasis sites, and survival. The organic causes of dyspnea were classified as follows: cancer (including pleural effusion, airway obstruction, pulmonary mass, mediastinal mass, pericardial effusion, lymphangitis, ascites, and cachexia); treatment-related causes (including lobectomy, irradiation, and chemotherapy); cancer-related causes (including anemia, pulmonary embolism, and infection); and co-morbidities (including chronic obstructive pulmonary disease and heart failure).

Modified Borg Scale of Dyspnea. The instrument for measuring dyspnea was modified from the Borg scale, which was introduced in 1982 as a category scale with ratio properties. Burdon et al.[14] adapted this scale to measure the intensity of the sensation of dyspnea. The self-reported scale consisted of a vertical scale labeled 0–10, with corresponding verbal expressions of progressively increasing sensation intensity, such as "nothing at all" to "maximal." This is the format most commonly used.[15–17] The modified Borg scale has been found to have good relation with visual analogue scale (VAS)[18] and currently is used frequently in Taiwan because it is easier for patients to understand and familiar to the local medical staff.

Psychological Distress Scale. The psychological distress scale consisted of the subscales for anxious mood and depressed mood. The reliability and validity of these subscales have been established in Taiwanese palliative care units.[19] The scale of anxious mood had 4 items: easily worrying too much, anticipating the most severe condition, fearing that something bad will happen, and easily displaying outbursts of temper. The scale of depressed mood comprised 5 items: feeling depressed, feeling sad, crying, having an attack of anger, and experiencing negative emotions in the morning. For each item, patients were asked to rate the extent of their anxious or depressed mood on a 0–3 Likert scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). An exploratory factor analysis was used to analyze the measure for construct validity. This process extracted 2 factors: anxiety (easily worrying too much, anticipating the most severe condition, and fearing that something bad will happen) and depression (easily displaying outbursts of temper, feeling depressed, feeling sad, crying, having an attack of anger, and experiencing negative emotions in the morning). The factor loading for all items was above 0.5. Cronbach alpha values for these 2 factors were 0.93 and 0.88, respectively. The alpha value for all 9 items was 0.92 for this study sample.

Family Function. Family function was assessed by using a family adaptability, partnership, growth, affection, and resolve (APGAR) index, which contained 5 structured questions about family interactions. The scores were as follows: 0 = seldom, 1 = sometimes, and 2 = always, where a higher score indicated higher quality of family support.[20] The alpha value for all 5 items was 0.912 for this study sample.

Extent of the Fear of Death. We evaluated the extent of the patients' fear of death with one item scored on a 1–5 Likert scale (1 = not at all, 2 = a little bit, 3 = moderately, 4 = quite a bit, 5 = extremely). A spiritual care team designed this measure for use in Taiwanese patients with terminal disease and used it to assess spirituality in Taiwanese patients in palliative care units.[21] The chaplains in the study unit used this measure to evaluate each patient.

Single-Item Scale for Quality of Life. Cohen et al. originally designed the single-item scale (SIS) in 1997.[22] It is a self-reported scale related to the patient's overall quality of life from his or her perspective: The SIS "considers all parts of my life: physical, emotional, social, spiritual, and financial—my quality of life in the past two days was…very bad (0)/excellent (10)." The SIS score is assumed to be the best available indicator of quality of life as perceived by the patient and its Taiwanese version has been initially validated.[23]

Procedure

Staff members asked patients about the severity of dyspnea and recorded the results on a daily basis in the normal process of caring for them. Otherwise, the staff members evaluated and discussed the causes of dyspnea according to the patient's history of disease, physical examination findings, imaging studies (chest radiography, computed tomography, magnetic

resonance imaging), and hemoglobin level. The collected data were analyzed at the time of admission, at 1 week after admission, and in the 48 hours prior to the patient's death (usually retrospectively) in weekly team meetings.

Statistical Analysis

Data management and statistical analysis was performed by using SPSS 11.0 statistical software (SPSS, Chicago, IL). A frequency distribution was used to describe the demographic data and the distribution of each variable. Means and standard deviations (SD) were used to analyze the intensity of dyspnea and psychosocial-spiritual scores. A paired *t* test was used to compare the differences in the scores for these items at different times. Univariate analysis, including the Chi-square test, Fisher's exact method, independent *t* test, and Pearson correlation coefficient analysis, was performed between the possible correlates (demographic data, anxious and depressed mood, family function, extent of the fear of death, quality of life) and the intensity of dyspnea to identify significant differences. Afterward, backward stepwise multiple regression analysis was used to investigate significant predictors of dyspnea. A probability value of less than 0.05 was considered to indicate a statistically significant difference.

Table 1
Characteristics of Patients (n = 125)

Variable	*n*	%
Sex		
Men	74	59.2
Women	51	40.8
Age (years)		
≤18	1	0.8
19–35	7	5.6
36–50	27	21.6
51–64	23	18.4
≥65	67	53.6
Mean ± SD	62.06 ± 16.45	NA
Primary site of tumor		
Lung	23	18.4
Liver	19	15.2
Stomach	13	10.4
Ear, nose, throat	12	9.6
Colon and rectum	11	8.8
Cervix/uterus	9	7.2
Uncertain	8	6.4
Breast	6	4.8
Pancreas	5	4.0
Esophagus	3	2.4
Skin	3	2.4
Leukemia	2	1.6
Bladder	2	1.6
Brain	1	0.8
Prostate	1	0.8
Other	7	5.6
Metastasis		
Bone	42	33.6
Liver	35	28.0
Lung	33	26.4
Brain	12	9.6
Skin	5	4.0
Other	39	31.2
Survival (days)		
≤3	14	11.2
4–6	27	21.6
7–13	35	28.0
≥14	49	39.2
Mean ± SD	17.29 ± 20.41	NA

NA indicates not applicable.

Results

Of 470 consecutive patients with terminal cancer, 125 were conscious and able to communicate 2 days before their death. Characteristics of these 125 evaluable patients are summarized in Table 1. Of them, 74 (59.2%) were men, and 51 (40.8%) were women. A total of 53.6% of the patients were older than 65 years, and only 1 patient was younger than 18 years. The primary sites of cancer were the lung (18.4%), liver (15.3%), stomach (10.4%), and head/neck (9.6%). Thirty-three patients (26.4%) whose primary sites of cancer were not the lung were found to have lung metastasis, as noted on imaging studies. The mean survival of these patients after admission was 17.29 ± 20.41 days.

Table 2 shows the prevalence and severity of dyspnea. At admission, 74 patients (59.2%) had dyspnea, which was rated mild in 25 patients (20.0%) and moderate or severe in 49 (39.2%). One week after admission, their dyspnea improved; 38 (52.8%) of 72 patients who survived longer than 1 week still had this symptom. The severity of dyspnea, compared with the severity at admission, improved; however, the change was not statistically significant (t = 0.065, P = 0.948). Seventy-five (60.0%) patients had dyspnea 2 days prior to their death; this symptom was moderate or severe in 41.6%. The mean dyspnea score again increased, but the score was still lower than that at admission, and the change was not statistically significant (t = 0.886, P = 0.377).

Table 2
Frequency and Severity of Dyspnea (n = 125)

Dyspnea[a]	At admission (%)	At 1 week (%)[b]	2 days before death (%)[c]
None	51 (40.8)	34 (47.2)	50 (40.0)
Mild (1–2)	25 (20.0)	15 (20.8)	23 (18.4)
Moderate (3–7)	39 (31.2)	20 (27.8)	46 (36.8)
Severe (8–10)	10 (8.0)	3 (4.2)	6 (4.8)
Total	125 (100.0)	72 (100.0)	125 (100.0)
Mean ± SD	2.31 ± 2.67	1.76 ± 2.24	2.16 ± 2.39

[a]Numbers in parentheses are scores.
[b]Admission vs. 1 week: $t = 0.065$; $P = 0.948$.
[c]Admission vs. 2 days before death: $t = 0.886$; $P = 0.377$.

The organic causes of dyspnea in the patients' last 48 hours of life are shown in Table 3. Causes of moderate or severe dyspnea included cachexia (86.5%), anemia (80.8%), pleural effusion (73.1%), lung mass (67.3%), airway obstruction (61.5%), and lymphangitis (59.6%). About 76% of patients without dyspnea also had anemia, 48.0% had ascites, 36.0% had lymphangitis, and 30.0% had a lung mass.

Table 4 shows possible psycho-social-spiritual factors related to the intensity of dyspnea. These included psychological status, family function, extent of the fear of death, and quality of life. The mean scores of the 2 subscales for anxiety and depressed mood at admission were 3.68 (range 0–12) and 5.58 (range 0–24), respectively. These scores significantly improved in the 48 hours before death (mean = 2.92, $P < 0.001$; mean = 4.52, $P < 0.01$, respectively). The total mean score for family function was 8.13 ± 2.43 (SD), range 0–10), indicating good family support for the study patients.

Regarding fear of death, the mean score declined from 2.45 at admission to 2.06 before death ($P < 0.001$), indicating the effects of spiritual care. As for the quality of life, the mean SIS score increased from 3.16 at admission to 3.74 before death ($P < 0.001$).

Tables 5 and 6 summarize the univariate correlations between the severity of dyspnea and significantly different variables at admission and in the 48 hours before death. At the time of admission, only organic causes (such as lung cancer, cervical cancer, lung metastases, pleural effusion, lung mass, and lung infection) were significantly correlated with the severity of dyspnea. Anxiety and fear of death did not show a significant correlation ($r = 0.122$ and $r = 0.127$, respectively) (Table 5).

Table 3
Dyspnea and Organic Causes in the Last 48 Hours of Life (n = 125)

Cause	Dyspnea score ≥3 (%)	Dyspnea score <3 (%)	Dyspnea score 0 (%)	Total (%)
Cancer				
Pleural effusion	38 (73.1)	11 (47.8)	13 (26.0)	62 (49.6)
Airway obstruction	32 (61.5)	10 (43.5)	9 (18.0)	51 (40.8)
Pulmonary mass	35 (67.3)	13 (56.5)	15 (30.0)	63 (50.4)
Mediastinal mass	28 (53.8)	14 (60.9)	14 (28.0)	56 (44.8)
Pericardial effusion	9 (17.3)	2 (8.7)	1 (2.0)	12 (9.6)
Lymphangitis	31 (59.6)	15 (65.2)	18 (36.0)	64 (51.2)
Ascites	29 (55.8)	11 (47.8)	24 (48.0)	64 (51.2)
Cachexia	45 (86.5)	21 (91.3)	41 (82.0)	107 (85.6)
Treatment-related				
Lobectomy	1 (1.9)	0 (0.0)	0 (0.0)	1 (0.8)
Irradiation	9 (17.3)	6 (26.1)	5 (10.0)	20 (16.8)
Chemotherapy	14 (26.9)	10 (43.5)	12 (24.0)	36 (28.8)
Cancer-related				
Anemia	42 (80.8)	17 (73.9)	38 (76.0)	97 (77.6)
Pulmonary embolism	2 (3.8)	1 (4.3)	1 (2.0)	4 (3.2)
Infection	27 (51.9)	6 (26.1)	10 (20.0)	43 (34.4)
Co-morbidities				
COPD	15 (28.8)	5 (21.7)	5 (10.0)	25 (20.0)
Asthma	3 (5.8)	2 (8.7)	1 (2.0)	6 (4.8)
Heart failure	17 (32.7)	2 (8.7)	10 (20.0)	29 (23.2)
Acidemia	16 (30.8)	5 (21.7)	4 (8.0)	25 (20.0)
Total	52 (100.0)	23 (100.0)	50 (100.0)	125 (100.0)

COPD = Chronic obstructive pulmonary disease.

Table 4
Variables Potentially Related to the Severity of Dyspnea (n = 125)

Variable	At admission	2 days before death	Range	t Value
Psychological status	9.26 ± 6.938	7.43 ± 5.901	0–36	3.809[c]
Anxiety mood	3.68 ± 2.570	2.92 ± 2.171	0–12	4.419[c]
Easily worrying too much	1.20 ± 0.897	1.00 ± 0.791	0–4	2.884[b]
Anticipating the most severe condition	1.22 ± 0.953	0.97 ± 0.807	0–4	3.684[c]
Fear something bad will happen	1.25 ± 0.883	0.95 ± 0.767	0–4	4.310[c]
Depression mood	5.58 ± 4.790	4.52 ± 3.873	0–24	3.019[b]
Temper outbursts	0.78 ± 0.983	0.60 ± 0.799	0–4	2.405[a]
Feeling depressed	1.37 ± 1.044	1.09 ± 0.906	0–4	3.436[c]
Feeling sad	1.12 ± 1.031	0.90 ± 0.894	0–4	2.968[b]
Crying	0.73 ± 0.927	0.47 ± 0.700	0–4	3.295[c]
Negative emotion in morning	0.71 ± 0.862	0.59 ± 0.723	0–4	1.687
Anger attack	1.00 ± 1.034	0.84 ± 0.851	0–4	1.942
Family function	8.13 ± 2.426	NA	0–10	NA
Adaptability	1.69 ± 0.545	NA	0–2	NA
Partnership	1.54 ± 0.644	NA	0–2	NA
Growth	1.61 ± 0.582	NA	0–2	NA
Affection	1.57 ± 0.587	NA	0–2	NA
Resolve	1.72 ± 0.504	NA	0–2	NA
Fear of death	2.45 ± 0.687	2.06 ± 0.658	1–5	5.910[c]
Quality of life in the last 2 days	3.16 ± 0.820	3.74 ± 0.730	1–5	−8.295[c]

NA indicates not applicable.
[a] $P < 0.05$.
[b] $P < 0.01$.
[c] $P < 0.001$.

Among psychosocial demographic factors, only anxiety was significantly correlated with the severity of dyspnea ($r = 0.211$, $P < 0.05$) in the 48 hours before the patients' death. Organic causes, such as pleural effusion, airway obstruction, lung mass, pleural effusion, and lung infection, had strongly significant differences (all $P < 0.001$) (Table 6). In the study, patients had a median of four different abnormalities that could have contributed to the intensity of dyspnea at admission, and a median of three in the 48 hours before death.

Table 5
Univariate Analysis Between Dyspnea Scores and Potential Factors at Admission (n = 125)

Potential factor	Mean dyspnea score (no/yes)	t Value
Primary site of tumor		
Lung	2.07/3.39	−2.177[a]
Cervix/uterus	2.17/4.11	−2.127[a]
Lung metastasis	1.92/3.39	−2.785[a]
Cancer		
Pleural effusion	1.34/3.47	−4.837[c]
Airway obstruction	1.19/4.10	−6.270[c]
Pulmonary mass	1.27/3.33	−4.666[c]
Mediastinal mass	1.75/3.21	−2.870[b]
Pericardial effusion	2.05/6.13	−4.483[b]
Lymphangitis	1.63/3.03	−3.042[b]
Lobectomy	2.77/8.00	−2.170[a]
Cancer-related infection	1.77/3.88	−3.574[c]
Complications		
COPD	1.94/3.80	−3.230[b]
Asthma	2.18/4.57	−2.345[a]
Heart failure	2.04/3.46	−2.382[a]
Acidemia	1.99/4.22	–3.417[b]

COPD = Chronic obstructive pulmonary disease.
[a] $P < 0.05$
[b] $P < 0.01$
[c] $P < 0.001$.

Table 6
Univariate Analysis Between Dyspnea Score and Potential Factors at 2 Days Before Death (n = 125)

Potential factor	Mean dyspnea score (no/yes)	t Value
Primary site of tumor		
Stomach	2.31/0.85	3.144[a]
Esophagus	2.02/8.00	−4.628[b]
Lung metastasis	1.80/3.15	−2.860[a]
Cancer		
Pleural effusion	1.34/3.14	−4.521[b]
Airway obstruction	1.34/3.48	−4.975[b]
Pulmonary mass	1.32/2.98	−4.144[b]
Mediastinal mass	1.70/2.90	−2.647[a]
Pericardial effusion	1.95/5.25	−4.007[b]
Cancer-related infection	1.75/3.34	−3.386[b]
COPD	1.82/3.52	−2.796[a]
Level of consciousness		
Clear	1.33	−2.566[c]
Drowsy	1.82	

Anxious mood (0–9) had a correlation coefficient of 0.211.
COPD = Chronic obstructive pulmonary disease.
[a] $P < 0.01$.
[b] $P < 0.001$.
[c] $P < 0.05$.

Results of multiple regression analysis of the factors correlated with the dyspnea score are shown in Tables 7 and 8. Airway obstruction, pleural effusion, acidemia, and lung infection were independently correlated with the dyspnea score at admission (odds ratio [OR] = 2.27, 95% confidence interval [CI] = 1.41–3.13; OR = 1.38, 95% CI = 0.44–3.32; OR = 1.83, 95% CI = 0.72–2.98; OR = 2.29, 95% CI = 0.68–3.90, respectively). This model accounted for 42.8% (multiple R^2) of the variance in the dyspnea score (Table 7). Multivariate analysis in the patients with dyspnea in the 48 hours before death revealed that airway obstruction, esophageal cancer, pericardial effusion, lung infection, and mediastinal mass were independent correlates of the dyspnea score. The model of this multivariate analysis accounted for 42.7% of the variance in the dyspnea score. Psychosocial and demographic factors were not in the models of multivariate analysis, either at admission or at 2 days prior to death. This finding indicated that the organic causes were strong correlates of the dyspnea score in these terminal cancer patients.

Some studies found that the influence in quality of life due to a specific symptom appears to be detected within intensity values of ≥ 30% of maximum.[6,24,25] Thus the study also performed the multiple regression analysis for the moderate and severe intensity (≥ 3/10) of dyspnea. The results showed airway obstruction and lung infection were independent correlates of the dyspnea score ≥ 3/10 at admission (OR = 1.61, 95% CI = 0.40–2.90; OR = 1.38, 95% CI = 0.15–2.61). On the other hand, airway obstruction, sex and esophageal cancer were independent correlates of the dyspnea score ≥ 3/10 in the 48 hours before death (OR = 1.76, 95% CI = 0.92–2.61; OR = −1.12, 95% CI = −1.95–0.29; OR = 2.30, 95% CI = 0.57–4.02, respectively).

Table 7
Multiple Regression Analysis of Factors Independently Correlated With Dyspnea at Admission (n = 125)

Variable	Coefficient	Beta	t Value	95% CI
Airway obstruction	2.27	0.40	5.243[a]	1.41–3.13
Pericardial effusion	1.38	0.22	2.901[b]	0.44–2.32
Acidemia	1.82	0.24	3.248[b]	0.72–2.99
Lung infection	2.29	0.22	2.814[b]	0.68–3.90
Constant	0.76	NA	2.796[b]	0.22–1.29

Multiple R value = 0.670; multiple R^2 = 0.428.
CI indicates confidence interval; NA, not applicable.
[a] $P < 0.001$.
[b] $P < 0.01$.

Table 8
Multiple Regression Analysis of Factors Independently Correlated with Dyspnea at 2 Days Prior to Death (n = 125)

Variable	Coefficient	Beta	t Value	95% CI
Airway obstruction	2.23	0.44	4.831[a]	1.32–3.14
Esophageal cancer	4.97	0.32	4.420[a]	2.74–7.20
Pericardial effusion	1.96	0.25	3.220[b]	0.75–3.16
Lung infection	1.11	0.22	2.903[b]	0.35–1.87
Mediastinal mass	−0.95	−0.19	−2.036[c]	−1.87–0.02
Constant	1.01	NA	3.950[a]	0.50–1.52

Multiple R value = 0.673; Multiple R^2 = 0.427.
CI indicates confidence interval; NA, not applicable.
[a] $P < 0.001$.
[b] $P < 0.01$.
[c] $P < 0.05$.

Discussion

To our knowledge, this study is one of the first to prospectively reveal the correlates of dyspnea in terminal cancer patients, particularly in patients with a Confucian culture. Previous studies showed that organic causes are significantly associated with the presence and intensity of dyspnea.[6,9,13] However, Bruera et al.[6] found that lung involvement was not an independent correlate for the intensity of dyspnea in patients with moderate-to-severe dyspnea. They suggested that better characterization of the severity of lung involvement may be required. On the other hand, Tanaka et al.[13] reported that, despite the significant correlation of organic causes with dyspnea, these causes accounted for only a relatively small part of the total score in the cancer-related dyspnea scale (multiple R^2 = 0.098). They indicated the same need for better characterization of organic causes. Therefore, in our study, we characterized the organic causes related to the severity of dyspnea and grouped them into several categories, including cancer, treatment-related, cancer-related, and co-morbidities. This characterization can be helpful for the

evaluation and management of possible organic factors to improve the severity of dyspnea. Meanwhile, this characterization contributed to the multivariate model that accounted for 42.8% (at admission) and 42.7% (2 days before death) of the variation scores, which were higher than in previous studies.

In previous studies, psychological distress has been correlated with dyspnea.[6,9–11,13] However, we believed that the intensity of psychological distress in terminal cancer patients should be related to their cultural background. Hence, we used the psychological distress measure, the reliability and validity of which have been established in a Taiwanese palliative care unit.[19] This measure also demonstrated a good level of reliability and validity in this study sample. To evaluate the patient's spiritual status, we tried to use one item to measure the extent to which patients had a fear of death, which is believed to be an important index of spiritual status. Our spiritual care team developed this measure, which is commonly used to evaluate the spiritual status of terminal cancer patients in Taiwan.[21] Although the psychospiritual and sociodemographic factors were not in the final model in the study, a higher percentage was achieved in accounting for the variation in dyspnea scores. Future studies to investigate the comprehensive factors related to the sensation of dyspnea are still a worthwhile effort.

Dyspnea is one of the most common symptoms in patients with terminal cancer. After admission, the frequency of dyspnea decreased and the severity of dyspnea improved in our patients. Nevertheless, the prevalence of dyspnea increased (60%) again in the late terminal stage. These findings, which were compatible with those of a previous study,[8] revealed the difficulties in managing dyspnea in the late terminal stage.

The organic causes that were significantly correlated with the intensity of dyspnea in the multivariate analysis included airway obstruction, pleural effusion, and lung infection. In the hospice, the medical staff carefully calculates all of the medical benefits and risks/burdens for possible treatments (such as palliative radiotherapy, pleurocentesis, and antimicrobial therapy) to relieve dyspnea. Any medical procedure can be offered with the patient's consent (if possible). Medications, including bronchodilators, corticosteroids, and anxiolytics, and supportive care, such as nebulizer therapy, breathing exercises, and emotional support, are also provided. In our hospice, invasive treatments (such as pleurocentesis and palliative radiotherapy) are usually withheld because of the deteriorating condition of patients with terminal cancer and because of their short survival.

Some patients without dyspnea had lung lesions or other possible organic causes of dyspnea. The results in this study also showed a significant correlation between anxiety and the severity of dyspnea in the 2 days prior to death, as demonstrated in the univariate analysis. These findings might be partially explained by the compression of tumors at different locations, but they also allow for the possibility of a nonpharmacologic approach to control dyspnea. Clinically, we try to provide a warm, caring environment and give full support to terminally ill patients in our hospice. Instead of using benzodiazepines to control dyspnea,[26] we try to communicate with our patients about their concerns and ensure their continuous care. In addition, we explain that our medical team is able to give comprehensive care for any distress, including dyspnea.

In Asian countries, some breathing methods are believed to be useful for the management of dyspnea. The Queisee method is a kind of religious breathing exercise practiced in Taoism. This technique helps people to breathe calmly and to use the least amount of oxygen to maintain survival. Most Taiwanese people are familiar with this breathing method, which can help patients relieve their anxiety and effectively control their breathing. In addition to introducing the Queisee breathing method, we also explain to our patients that the residual volume in their lungs should be adequate to maintain their body's real need for oxygen. We usually measure the hemoglobin oxygen saturation (which had no significant correlation with dyspnea in previous studies), and we show normal data from the pulse oximeter to patients and their families to decrease their worries. These interventions seem to be useful for controlling dyspnea in the study patients. It is worthwhile to further investigate the effects of these methods.

Dyspnea near the late terminal stage often becomes severe and difficult to control.[1–11] In addition to medical treatment, we often teach patients in the active dying process to

strengthen their religious faith by means of prayer with Buddhist Sanskrit (A-Mi-Tou-Fo). Since more than 80% of people in Taiwan have their faith in the Buddhist philosophy, they believe that prayer with Buddhist words in the stage of imminent death is helpful in their death and afterlife. Prayer involving patients and their families may help distract them from the dyspnea and is useful for releasing anxiety in patients, their families, and staff.

After patients are provided with active total care for dyspnea, the severity could be improved after their admission and controlled to the extent possible during the dying process. In this study, several organic causes were independently correlated with the dyspnea score, both at admission and prior to death. Although reversing these causes is difficult in patients with terminal illness, comprehensive care could still decrease the severity of their dyspnea.

Lung infection was strongly correlated with the severity of dyspnea, both at admission and prior to death. Although the use of antimicrobial agents in terminal patients is controversial because the benefits and burdens are unclear,[27,28] our findings suggest that controlling lung infections may have an important role in relieving dyspnea.

Certain caveats should be mentioned in relation to our study. First, we attempted to research the correlates of dyspnea in patients with terminal cancer, but respiratory function tests were not performed. Results of these test have previously been found to be predictors of the intensity of dyspnea. However, these tests may not be a practical tool in patients with terminal cancer because almost all of them are unable to complete these tests. Second, the participants were in a unit for only palliative care, and with a 3-week mean survival, the generalizability of the findings is a concern.

In conclusion, the severity of dyspnea in patients with terminal cancer could be improved with active total care, despite the fact that organic causes may irreversibly progress and despite their strong correlation with the intensity of dyspnea. More studies are required to identify other psychosocial-spiritual factors and the sensitivity of these measures.

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