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ORIGINAL ARTICLE

Potential benefits of palliative care for polysymptomatic patients with late-stage nonmalignant disease in Taiwan

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Background/Purpose: Taiwan is only now beginning to offer palliative care to patients who do not have cancer. This study aimed to document the polysymptomatic presentation of illness in Taiwanese patients with late-stage nonmalignant disease and to evaluate the potential benefits of palliative care for these patients. The results may help to educate healthcare personnel regarding the need for and importance of palliative treatment as comprehensive, appropriate end-of-life care for patients with nonmalignant disease.
Methods: We retrospectively analyzed 115 patients without cancer hospitalized in a community hospital in Taiwan: 61 had organic brain disease, 31 had chronic obstructive pulmonary disease, 17 had chronic renal failure, 14 had congestive heart failure, 12 had liver cirrhosis, and 20 had multiple illnesses. The median age was 81 years (interquartile range 69—86 years), and 51% of patients were enrolled from intensive care. Symptoms and their severity were

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analyzed. Patients' and their families' understanding of the diagnosis and prognosis and "Do Not Resuscitate" (DNR) consent were evaluated pre- and post-palliative care.

Results: The four leading symptoms were fatigue (96%), fever (86%), cough (81%), and dyspnea (79%). No significant differences in symptom prevalence were found between different sexes, ages, performance statuses, ward locations, or underlying diseases, except for fewer episodes of dizziness, more frequent episodes of cough in patients older than 80 years, and more episodes of jaundice in ward service subjects. Only the presence of abdominal distension differed significantly between surviving and deceased patients (22.9% vs. 40.3%; $p = 0.004$). After the start of palliative care, patients' DNR consent increased (105/115 before, 114/115 after). Patients' recognition of the diagnosis and prognosis increased from 13 to 64, respectively, with a simultaneous increase in family members' recognition (66 before, 114 after).

Conclusion: Hospice care with good symptom control is warranted for patients with late-stage nonmalignant disease who need appropriate end-of-life care. Medical personnel need education in the importance of palliative care and the identification of patients who could benefit from it. In addition, patients should be informed of its availability.

Introduction

Given the aging of the human population worldwide, since the early 2000s, more people have died annually of chronic disease than of cancer, and they require symptom and pain management as they approach the end of life. Palliative care requirements for patients with cancer and nonmalignant diseases are similar.[1,2] Palliative care may have an important role in treating patients with congestive heart failure, chronic obstructive pulmonary disease, and chronic renal failure.[3–5] In the United States, for example, the majority of patients receiving palliative care have nonmalignant disease.[6]

Palliative care became popular in Taiwan after it was introduced in 1990, but at that time it was applied primarily to cancer patients.[7] Patients with nonmalignant diseases were rarely candidates for palliative care, in part because of lack of insurance coverage, until September 2009, when the national health insurance regulations changed and coverage was finally provided for palliative care for noncancer patients.

Knowledge of the prevalence of common end-of-life symptoms is necessary to identify patients' needs for symptom control and planning of palliative care. Weakness, pain, anorexia, and cachexia are the most common symptoms in terminal cancer patients in Taiwan.[8] However, although studies in other countries have reported characteristic symptoms for end-stage nonmalignant chronic disease, similar studies demonstrating these symptoms are lacking in Taiwan. Nevertheless, it is recognized that in both cancer patients and noncancer patients, most symptoms become increasingly difficult to control and progressively worsen closer to death. Early identification of the most prevalent end-of-life symptoms is necessary for early intervention and treatment planning, including possible referral to palliative care. Data regarding the patterns and prevalence of distressing end-of-life symptoms in patients with nonmalignant disease are not yet available in Taiwan; therefore, the present study is intended as an initial contribution to the collection of such data.

Knowledge of the prevalence of common late-stage symptoms, along with a greater awareness of the palliative care concept on the part of medical personnel, patients, and their families, may help to identify patients with nonmalignant disease who could benefit from palliative care. We retrospectively analyzed the prevalence of common symptoms in patients with life-threatening nonmalignant disease receiving palliative care in a community hospital in Taiwan that is the first institution in the country to provide such care on a nonprofit basis for this patient group. Our aim was to document the polysymptomatic presentation of illness in Taiwanese patients with late-stage nonmalignant disease and to evaluate the potential benefits of palliative care for these patients. The results may be useful in educating healthcare personnel regarding the capabilities and availability of palliative treatment for patients without cancer who need comprehensive and appropriate end-of-life care.

Methods

Patient selection

The 115 patients in this study were selected consecutively from those admitted to Saint Paul's Hospital who received care from the hospital's palliative care team from September 2007 through December 2009. Saint Paul's Hospital is an acute-care general hospital with 550 beds; it provides specialist palliative care service for 5–12 patients on a daily basis. There was no underlying assumption regarding the size of the sample.

Criteria for inclusion were related to diagnosis, referral source, and agreement with the care plan. Patients were required to be diagnosed with one (or more) of five chronic diseases—organic brain disease (OBD), defined as cerebrovascular accident with sequelae, hypoxemic encephalopathy, cerebral palsy, parkinsonism, or dementia; chronic obstructive pulmonary disease (COPD); congestive heart failure (CHF); decompensated cirrhosis of the liver (DLC); and chronic renal failure in uremic stage (CRF)—or multiple diseases, defined as a co-occurrence of at least two of the five chronic diseases, along with admission to the hospital because of an acute exacerbation of the underlying chronic

illness or an acute episode of infection, gastrointestinal bleeding, or shock. End-stage disease was defined as a combination of a long-term history of one of the five chronic diseases and the presence of distressing uncontrolled symptoms recognized clinically as leading to the terminal common pathway.

The five chronic illnesses were chosen based on the leading causes of death in Taiwan, excluding accidents, suicide, and acute illness. During the study period, a total of 464 patients died at Saint Paul's Hospital, 188 of whom had one or more of the five chronic illnesses, making the cover rate before death 55/188. Among the remaining patients with the five chronic illnesses, 133 patients were not referred to palliative care for several reasons, including: the primary physician determining it unnecessary or death being unanticipated ($n = 23$), the period enrolled in palliative care being less than 24 hours ($n = 21$; an exclusion criterion for this study); or the presence of concomitant malignant disease ($n = 20$; an exclusion criterion of this study). Another 13 patients refused combined care from their primary physician with the palliative care team.

With regard to the second criterion, patients were either referred by primary care physicians or actively recruited by the palliative care team if a "Do Not Resuscitate" (DNR) consent form had been signed after hospitalization. To meet the third criterion, patients and their family had to agree to combine care from the primary physician and the palliative care team. To ensure adequate time to assess patients' distressing symptoms, any patient with a lifespan of less than 24 hours after referral was excluded from the study. Patients diagnosed with malignancies were also excluded. We did not recruit a control group of patients who did not receive palliative care.

Hospice setting and data collection

The 115 participants were under the combined care of a primary care physician and a multidisciplinary palliative care team consisting of physicians, specialist nurses, social workers, Christian (Roman Catholic) chaplains, and volunteers. Team meetings were held every 1—2 weeks.

The study data consisted of patients' demographic data [age, gender, Eastern Cooperative Oncology Group (ECOG) performance statuses, underlying diseases, and survival times], and the patients' assessed distressing symptoms. Patients' symptoms were recorded immediately after the patients were referred to palliative care and were all recorded by the same specialist nurse using a formulated "Symptoms Record" form. Patients' symptoms were then recorded daily by the same specialist nurse who had initially evaluated them, who recorded the presence or absence of symptoms using a list of 29 common symptoms. These symptoms were chosen on the basis of our clinical experience and previously published studies involving patients with either cancer or terminal nonmalignant disease.[9—11]

Severity scores were determined for the different symptoms by the specialist nurse when the symptoms were being recorded. A five-stage scoring system was used in which 0 represented no symptoms; 1 represented mild symptoms presenting occasionally without causing discomfort; 2 represented moderate symptoms that might cause patient discomfort; 3 represented severe symptoms occurring frequently and limiting activities; and 4 represented extreme severity that persisted and could not be tolerated by the patient. The primary caregiver answered questions as far as possible when patients were unable to communicate.

All patients were followed until death or until the study conclusion—June 30, 2010. The study was approved by the ethics committee of Saint Paul's Hospital.

Statistical analysis

Statistical analyses were performed using SPSS 15.0 statistics software (SPSS Inc, Chicago, IL, USA). Basic demographic data were summarized as n (%) for categorical variables and median with interquartile range (IQR; Q1—Q3) for continuous variables. Furthermore, the prevalence of clinical symptoms was tabulated as n (%) by demographics, and compared using the Pearson chi-square test, or the Fisher's exact test if the number in any cell was less than 5. All statistical assessments were considered significant when $p < 0.05$.

Results

Data from 115 patients were analyzed in this study. Their basic demographic data are summarized in Table 1. There were 63 males (55%) and 52 females (45%), with a median age of 81 years (IQR 69—86 years). Half the patients (51%) were enrolled from the intensive care unit (ICU). The median time from admission date to referral was 8 days (IQR 3—15 days). Seventy-seven per cent had an ECOG performance status of Grade 4. The underlying diseases were observed as 61 (53%) cases of OBD, 31 (27%) of COPD, 17 (14.8%) of CRF, 14 (12.2%) of CHF, and 12 (10.4%) of DLC. In addition, 20 patients (17.4%) were diagnosed with multiple diseases. At the last follow-up, 48 (41.7%) of the 115 subjects had survived, and the median palliative care time was observed to be 19 days (IQR 5—93 days).

The number of symptoms and their prevalence are summarized in Table 2. The primary cause of fever in this study was infection due to acute exacerbation or complications of the underlying disease. The prevalence of pain in our palliative care patients was 20%. Seizures were present in 16% of patients. Patients who survived has a lower rate of abdominal distension (22.9%) compared with those who died (49.3%) ($p = 0.004$); these results are shown separately in Table 2 for surviving and deceased patients. However, no significant differences were found in other symptoms between survivors and those who died.

There was no difference in the prevalence of most symptoms when measured according to sex, performance status, age, and ward service. The overall prevalence of clinical symptoms greater than 50% was derived as 95.7% (110/115) with fatigue, 86.1% (99/115) with fever, 80.9% (93/115) with cough, 79.1% (91/19) with dyspnea, 61.7% (71/115) with edema, and 61.7% (71/115) with anemia. It was found that the prevalence of cough and dizziness were significantly different between patients younger than age 80 and 80 years or older. Furthermore, the prevalence of

Table 1 Subjects' basic demographic data (n = 115).

Variable	(n = 115)
Sex[a]	
Male	63 (54.8)
Female	52 (45.2)
Age (y)[b]	81 (69—86)
< 70 (n = 29)	55 (47.5—66.0)
70—79 (n = 19)	75 (72—76)
80—89 (n = 50)	84 (81.7—86.0)
> 90 (n = 17)	91 (90.5—95.0)
Patients' inpatient location[a]	
Ward	56 (48.7)
Intensive care unit	59 (51.3)
Enrollment condition	
Physician referral	10 (8.7)
Post-DNR status	105 (91.3)
ECOG performance status[a]	
Grade 1	1 (0.9)
Grade 2	2 (1.7)
Grade 3	23 (20.0)
Grade 4	89 (77.4)
Underlying disease[a]	
Organic brain lesion	47 (40.9)
Chronic obstructive pulmonary disease	24 (20.9)
Liver cirrhosis	10 (8.7)
Chronic renal failure	8 (7.0)
Congestive heart failure	6 (5.2)
Multiple diseases	20 (17.4)
Median from admission to referral[b] (d)	8 (3—15)
Number of survivors at last follow-up[a]	48 (41.7)
Median total palliative care[b] (d)	19 (5—93)

DNR = Do Not Resuscitate; ECOG = Eastern Cooperative Oncology Group.
[a] Data were summarized as n (%) for categorical data and median (interquartile range, Q1—Q3).
[b] Data were summarized as n (%) for continuous data.

with organic brain lesions may have a lower prevalence of clinical symptoms of edema, anemia, mental disturbance, abdominal distension, anorexia, pain, nausea, jaundice, insomnia, and ascites, whereas those with COPD may have a higher prevalence of cough, dyspnea, mental disturbance, anorexia, and insomnia. Patients with DLC may have a lower prevalence of cough, and dyspnea, but a higher prevalence of anemia, gastrointestinal bleeding, abdominal distension, pain, and nausea. Those with CRF may have a higher prevalence of edema and dyspnea, but a lower prevalence of pruritus. Fifty-five (47.8%) patients had death listed as the reason for discharge. The median survival time after referral to the palliative care team was 37 days (95% CI 0—86 days). The 6 months' survival rate was 37.6% (Fig. 1).

Palliative care was shown to benefit patients and their families (Table 5). The ratio of patients who signed DNR forms increased from before to after the start of palliative care, from 105/115 to 114/115, respectively. More patients were also able to recognize their diagnosis and prognosis. The number of patients increased from 13 to 64 for those understanding their diagnosis, and from 10 to 25 for those understanding their prognosis. A simultaneous increase was recorded in patients' family members recognizing diagnosis and prognosis (before 66, after 114). No patients received cardiopulmonary resuscitation, intubation, or cardiac massage after their enrollment in palliative care.

Discussion

The distribution of the diagnoses of nonmalignant disease in this study was similar to that of the leading noncancer causes of death in Taiwan in 2006.[12] This study confirmed that patients with late-stage nonmalignant disease are poly-symptomatic in the same manner as cancer patients. The prevalence of most symptoms closely resembled those of patients with terminal cancer published in previous reports.[8] No statistically significant differences were observed in the prevalence of most symptoms when sex, age, performance status, care setting, and underlying disease were compared. The terminal common pathways were similar between cancer and nonmalignant disease.[13,14]

Fatigue was the most frequent symptom in this study and is one of the most common symptoms reported in palliative care patients.[11] In our study, there was a 96% prevalence of fatigue for all patients, which is quite similar to published studies reporting an 84% prevalence in a study of 1000 patients with advanced cancer,[11] and a 99% prevalence in patients following radiotherapy or chemotherapy.[15] In nonmalignant conditions, fatigue was reported in 96% of patients with COPD[16] and in 82% of those with heart failure.[17] Some observers therefore maintain that fatigue in cancer patients as well as in patients with nonmalignant disease is underrecognized, underassessed, and undertreated.[18]

Fever was the second most common symptom in this study. Wachtel et al reported a 35% prevalence of fever in end-stage cancer patients.[13] Fever in cancer patients is generally associated with infection, treatment-related myelosuppression, and complications of a procedure or

jaundice was also found to differ significantly between ward patients versus those in the ICU.

The statistical analysis of the severity of symptoms at admission is shown in Table 3. Severity was determined for the different symptoms by the specialist nurse using a five-stage scoring system (0—5 as described in Methods). The symptoms are listed according to severity, with fatigue, fever, cough, and dyspnea at the top of the list as most severe and most frequent, followed by less severe and less frequent symptoms. Of all the symptoms, only abdominal distension is shown separately for surviving and deceased patients since this was the only symptom that showed significant differences between patients who survived and those who died during the study.

The prevalence and severity of symptoms in the various diseases is summarized in Table 4. Fatigue was a common symptom in all disease categories. Fever and cough were frequent in every disease except liver cirrhosis. A higher percentage of patients with DLC had anemia, gastrointestinal bleeding, abdominal discomfort, pain, jaundice, and ascites; however, this result was not statistically significant when compared with other disease entities. The subjects

Table 2 Prevalence of patients' clinical symptoms.

Symptoms	Total	Age		Sex		Inpatient location		ECOG status		Last follow-up outcome	
	(n = 115)	< 80 y	≥ 80 y	Males	Females	Ward	Intensive care unit	Grades 1—3	Grade 4	Dead	Survivors
		(n = 48)	(n = 67)	(n = 63)	(n=52)	(n = 56)	(n = 59)	(n = 26)	(n = 89)	(n = 67)	(n = 48)
Fatigue	110 (95.7)	46 (95.8)	64 (95.5)	61 (96.8)	49 (94.2)	55 (98.2)	55 (93.2)	25 (96.2)	85 (95.5)	65 (97.0)	45 (93.8)
Fever	99 (86.1)	44 (91.7)	55 (82.1)	55 (87.3)	44 (84.6)	46 (82.1)	53 (89.8)	23 (88.5)	76 (85.4)	55 (85.9)	41 (85.4)
Cough	93 (80.9)	34 (70.8)	59 (88.1)**	53 (84.1)	40 (76.9)	43 (76.8)	50 (84.7)	21 (80.8)	72 (80.9)	52 (77.6)	41 (85.4)
Dyspnea	91 (79.1)	35 (72.9)	56 (83.6)	52 (82.5)	39 (75.0)	41 (73.2)	50 (84.7)	19 (73.1)	72 (73.1)	52 (77.6)	39 (81.3)
Edema	71 (61.7)	26 (54.2)	45 (67.2)	38 (60.3)	33 (63.5)	33 (58.9)	38 (64.4)	14 (53.8)	57 (64.0)	43 (64.2)	28 (58.3)
Anemia	71 (61.7)	31 (64.6)	40 (59.7)	36 (57.1)	35 (67.3)	32 (57.1)	39 (66.1)	19 (73.1)	52 (58.4)	45 (67.2)	26 (54.2)
Constipation	53 (46.1)	22 (45.8)	31 (46.3)	28 (44.4)	25 (48.1)	25 (44.6)	28 (47.5)	14 (53.8)	39 (43.8)	31 (46.3)	22 (45.8)
Mental disturbance	49 (42.6)	17 (35.4)	32 (47.8)	32 (50.8)	17 (32.7)	27 (48.2)	22 (37.3)	12 (46.2)	37 (41.6)	30 (44.8)	19 (39.6)
Gastrointestinal bleeding	48 (41.7)	23 (47.9)	25 (37.3)	25 (39.7)	23 (44.2)	19 (33.9)	29 (49.2)	8 (30.8)	40 (44.9)	31 (46.3)	17 (35.4)
Abdominal distension	44 (38.3)	18 (37.5)	26 (38.8)	22 (34.9)	22 (42.3)	22 (39.3)	22 (37.3)	9 (34.6)	35 (39.3)	33 (49.3)	11 (22.9)**
Anorexia	45 (39.1)	19 (39.6)	26 (38.8)	25 (39.7)	20 (38.5)	26 (46.4)	19 (32.2)	12 (46.2)	33 (37.1)	28 (41.8)	17 (35.4)
Pressure sore	38 (33.0)	18 (37.5)	20 (29.9)	24 (38.1)	14 (26.9)	20 (35.7)	18 (30.5)	7 (26.9)	31 (34.8)	25 (37.3)	13 (27.1)
Diarrhea	29 (25.2)	13 (27.1)	16 (23.9)	16 (25.4)	13 (25.0)	14 (25.0)	15 (25.4)	6 (23.1)	23 (25.8)	17 (25.4)	12 (25.0)
Pain	23 (20.0)	10 (20.8)	13 (19.4)	11 (17.5)	12 (23.1)	13 (23.2)	10 (16.9)	6 (23.1)	17 (19.1)	17 (25.4)	6 (12.5)
Nausea	20 (17.4)	9 (18.8)	11 (16.4)	9 (14.3)	11 (21.2)	9 (16.1)	11 (18.6)	6 (23.1)	14 (15.7)	9 (13.4)	11 (22.9)
Seizure	18 (15.7)	11 (22.9)	7 (10.4)	11 (17.5)	7 (13.5)	9 (16.1)	9 (15.3)	4 (15.4)	14 (15.7)	9 (13.4)	9 (18.9)
Delirium	15 (13.0)	6 (12.5)	9 (13.4)	11 (17.5)	4 (7.7)	10 (17.9)	5 (8.5)	3 (11.5)	12 (13.5)	12 (17.9)	3 (6.3)
Wound	14 (12.2)	7 (14.6)	7 (10.4)	8 (12.7)	6 (11.5)	7 (12.5)	7 (11.9)	1 (3.8)	13 (14.6)	9 (13.4)	5 (10.4)
Urinary retention	11 (9.6)	3 (6.3)	8 (12.1)	5 (7.9)	6 (11.8)	8 (14.3)	3 (5.2)	2 (7.7)	9 (10.2)	8 (11.9)	3 (6.4)
Pruritus	11 (9.6)	5 (10.4)	6 (9.0)	7 (11.1)	4 (7.7)	4 (7.1)	7 (11.9)	2 (7.7)	9 (10.2)	6 (7.0)	5 (10.4)
Jaundice	10 (8.7)	6 (12.5)	4 (6.0)	6 (9.5)	4 (7.7)	8 (14.3)	2 (3.4)*	4 (15.4)	6 (6.7)	6 (9.0)	4 (8.3)
Insomnia	9 (7.8)	5 (10.4)	4 (6.0)	3 (4.8)	6 (11.5)	5 (8.9)	4 (6.8)	4 (15.4)	5 (5.6)	6 (9.0)	3 (6.3)
Ascites	9 (7.8)	6 (12.5)	3 (4.5)	7 (11.1)	2 (3.8)	6 (10.7)	3 (5.1)	4 (15.4)	5 (5.6)	6 (9.0)	3 (6.3)
Dizziness	8 (7.0)	7 (14.6)	1 (1.5)**	4 (6.3)	4 (7.7)	3 (5.4)	5 (8.5)	1 (3.8)	7 (7.9)	6 (9.0)	2 (4.2)
Oral ulcer	8 (7.0)	5 (10.4)	3 (4.5)	5 (7.9)	3 (5.8)	4 (7.1)	4 (6.8)	1 (3.8)	7 (7.9)	6 (9.0)	2 (4.2)
Hematuria	5 (4.3)	1 (2.1)	4 (6.0)	3 (4.8)	2 (3.8)	3 (5.4)	2 (3.4)	2 (7.7)	3 (3.4)	4 (6.0)	1 (2.1)
Dysphagia	4 (3.5)	2 (4.2)	2 (3.0)	2 (3.2)	2 (3.8)	3 (5.4)	1 (1.7)	1 (3.8)	3 (3.4)	1 (1.5)	3 (6.3)
Incontinence	2 (1.7)	0 (0)	2 (3.0)	2 (3.2)	0 (0)	2 (3.6)	0 (0)	0 (0)	2 (2.2)	1 (1.5)	1 (2.1)
Hiccups	1 (0.9)	0 (0)	1 (1.5)	1 (1.6)	0 (0)	1 (1.6)	0 (0)	1 (3.8)	0 (0)	1 (1.5)	0 (0)

Data were summarized as n (%) for each category, and compared using the Pearson chi-square test, or Fisher exact test if any number in the cell was lower than 5.
*$p < 0.05$; ** $p < 0.01$.
ECOG = Eastern Cooperative Oncology Group.

Table 3 Statistical analysis of severity of symptoms at admission.

Symptom		Severity			
		1	2	3	4
Fatigue	n = 110	29 (26.4)	50 (45.5)	25 (22.7)	6 (5.5)
Fever	n = 99	43 (43.4)	47 (47.5)	9 (9.1)	0 (0)
Cough	n = 93	21 (22.6)	57 (61.3)	15 (16.1)	0 (0)
Dyspnea	n = 91	2 (2.2)	23 (25.3)	41 (45.1)	25 (27.5)
Edema	n = 71	7 (9.9)	34 (47.9)	26 (36.6)	4 (5.6)
Constipation	n = 53	11 (20.8)	29 (54.7)	13 (24.5)	0 (0)
Mental disturbance	n = 49	2 (4.1)	19 (38.8)	21 (42.9)	7 (14.3)
Gastrointestinal bleeding	n = 48	7 (14.6)	33 (68.8)	8 (16.7)	0 (0)
Abdominal distension[a]	n = 44	0 (0)	22 (50)	20 (45.5)	2 (4.5)
Deceased	n = 33	0 (0)	17 (51.5)	16 (48.5)	0 (0)
Survivors	n = 11	0 (0)	5 (45.5)	4 (36.4)	2 (18.2)
Anorexia	n = 44	2 (4.5)	28 (63.6)	13 (29.5)	1 (2.3)
Pressure sore[b]	n = 27	6 (22.2)	17 (63.0)	4 (14.8)	0 (0)
Diarrhea	n = 29	4 (13.8)	22 (75.9)	3 (10.3)	0 (0)
Pain	n = 23	3.91 ± 1.31 (range 2−7)			
Nausea	n = 20	4 (20.0)	14 (70.0)	2 (10.0)	0 (0)
Seizure	n = 18	3 (16.7)	8 (44.4)	7 (38.9)	0 (0)
Delirium	n = 15	3 (20)	4 (26.7)	7 (46.7)	1 (6.7)
Wound	n = 14	6 (42.9)	7 (50.0)	1 (7.1)	0 (0)
Urinary retention	n = 11	7 (63.6)	4 (36.4)	0 (0)	0 (0)
Pruritus	n = 11	0 (0)	8 (72.7)	3 (27.3)	0 (0)
Insomnia	n = 9	1 (11.1)	4 (44.4)	3 (33.3)	1 (11.1)
Ascites	n = 9	0 (0)	1 (11.1)	5 (55.6)	3 (33.3)
Dizziness	n = 8	1 (12.5)	6 (75.0)	1 (12.5)	0 (0)
Oral ulcer	n = 8	1 (12.5)	6 (75.0)	1 (12.5)	0 (0)
Hematuria	n = 5	1 (20.0)	3 (60.0)	1 (20.0)	0 (0)
Dysphagia	n = 4	0 (0)	3 (75.0)	1 (25.0)	0 (0)
Incontinence	n = 2	0 (0)	2 (100)	0 (0)	0 (0)
Hiccups	n = 1	0 (0)	1 (100)	0 (0)	0 (0)

Data were summarized as n (%) for each specific symptom except for pain, which was scored as mean ± standard deviation (range = minimum to maximum).
 [a] Abdominal distension was only symptom showing a significant difference between those who were deceased and survivors in Table 2.
 [b] Eleven subjects had missing data on pressure sores; hence, severity was recorded for only 27 subjects.

the cancer itself.[19] The prevalence of fever in nonmalignant disease is, however, not well documented in the literature. The higher prevalence of fever in this study was mainly attributed to sepsis, with 96% of patients documented to have had at least one infection during hospitalization.

Cough and dyspnea were the third and fourth most common symptoms in this study. Published studies report a 52% prevalence of cough in cancer patients[10] and an 80%, 46%, and 44% prevalence in patients with COPD, CRF, and CHF, respectively.[16,17,20] The prevalence of dyspnea has been reported to range between 31% and 70% in cancer patients[11]; 94% and 98% in patients with COPD[16,21]; 11% and 82% in patients with CRF[20,22]; and 83% and 88% in patients with CHF.[17] Edema is reported to affect 73% of patients with CRF,[20] with a 43% prevalence evident for CHF.[23] The high prevalence of cough, dyspnea, and edema in this study is related to the underlying diseases.

The prevalence of pain is reported in the literature to be 52−84% for cancer patients[11] and 21−70% for patients with nonmalignant disease.[16,20,22] The prevalence of pain was 20% in this study, which is lower than figures reported in

previously published studies. There was a wide variation in the prevalence of pain in our patient group: 64% of patients with DLC had pain complaints, whereas only 4% of patients with OBD complained of pain. We believe that the difference is most likely due to the fact that many patients in our study were disoriented, 43% had confused consciousness, and 13% demonstrated delirium—it was very difficult to evaluate the subjective distress related to pain in disoriented patients. Warden et al reported a PAINAD scale as a tool for caregivers to evaluate pain in advanced dementia patients.[24] Palliative care staff, however, should recognize that pain in disoriented patients is both underestimated and undertreated.

Seizure has a prevalence of 24−29% in patients with primary or metastatic brain tumors.[25,26] The prevalence of seizure in late-stage nonmalignant disease is not known. Eighteen patients (16%) in this study had seizure episodes, which caused suffering to the patient and stress for the family. Early identification of high-risk patients and avoidance of precipitating factors are mandatory in the palliative care management of seizures.

Our patients' median survival after referral to palliative care was 37 days. Fifty-six per cent of patients died in the

Table 4 Prevalence of clinical symptoms according to disease diagnosis.

Symptom	Total (n = 115)	Organic brain lesion		Heart failure		Chronic obstructive pulmonary disease		Cirrhosis		Renal failure		Concurrent illness	
		No (n = 68)	Yes (n = 47)	No (n = 109)	Yes (n = 6)	No (n = 91)	Yes (n = 24)	No (n = 105)	Yes (n = 10)	No (n = 107)	Yes (n = 8)	No (n = 95)	Yes (n = 20)
Fatigue	110 (95.7)	66 (97.1)	44 (93.6)	104 (95.4)	6 (100)	88 (96.7)	22 (91.7)	100 (95.2)	10 (100)	102 (95.3)	8 (100)	90 (94.7)	20 (100)
Fever	99 (86.1)	56 (84.9)	40 (87.0)	93 (86.1)	3 (75)	75 (85.2)	21 (87.5)	90 (88.2)	6 (60.0)	88 (84.6)	8 (100)	81 (85.3)	18 (90.0)
Cough	93 (80.9)	56 (82.4)	37 (78.7)	89 (81.7)	4 (66.7)	69 (75.8)	24 (100)*	90 (85.7)	3 (30.0)**	86 (80.4)	7 (87.5)	75 (78.9)	18 (90.0)
Dyspnea	91 (79.1)	58 (85.3)	33 (70.2)	85 (78.0)	6 (100)	68 (74.7)	23 (95.8)**	87 (82.9)	4 (40.0)*	85 (79.4)	6 (75.0)	72 (75.8)	19 (95.0)
Edema	71 (61.7)	50 (73.5)	21 (44.7)*	66 (60.6)	5 (83.3)	55 (60.4)	16 (66.7)	66 (62.9)	5 (50)	63 (58.9)	8 (100)*	55 (57.9)	16 (80.0)
Anemia	71 (61.7)	48 (70.6)	23 (48.9)*	67 (61.5)	4 (66.7)	55 (60.4)	16 (66.7)	61 (58.1)	10 (100)*	63 (58.9)	18 (100)*	61 (64.2)	10 (50.0)
Constipation	53 (46.1)	32 (47.1)	21 (44.7)	51 (46.8)	2 (33.3)	40 (44.0)	13 (54.2)	49 (46.7)	4 (40.0)	51 (47.7)	2 (25.0)	42 (44.2)	11 (55.0)
Mental disturbance	49 (42.6)	37 (54.4))	12 (25.5)**	45 (41.3)	4 (66.7)	32 (35.2)	17 (70.8)**	42 (40.0)	7 (70.0)	47 (43.9)	2 (25.0)	42 (44.2)	7 (35.0)
Gastrointestinal bleeding	48 (41.7)	31 (45.6)	17 (36.2)	47 (43.1)	1 (16.7)	39 (42.9)	9 (37.5)	39 (37.1)	9 (90.0)**	44 (41.1)	4 (50.0)	40 (42.1)	8 (40.0)
Abdominal distension	44 (38.3)	35 (51.5)	9 (19.2)**	43 (39.5)	1 (16.7)	32 (35.2)	12 (50.0)	35 (33.3)	9 (90.0)**	39 (36.5)	5 (62.5)	36 (37.9)	8 (40.0)
Anorexia	45 (39.1)	36 (52.9)	9 (19.2)**	44 (40.4)	1 (16.7)	30 (33.0)	15 (62.5)**	41 (39.1)	4 (40.0)	40 (37.4)	5 (62.5)	34 (35.8)	11 (55.0)
Pressure sore	38 (33.0)	20 (29.4)	18 (38.3)	36 (33.0)	2 (33.3)	32 (35.2)	6 (25.0)	36 (34.3)	2 (20.0)	34 (31.8)	4 (50.0)	32 (33.7)	6 (30.0)
Diarrhea	29 (25.2)	19 (27.9)	10 (21.3)	27 (24.8)	2 (33.3)	23 (25.3)	6 (25.0)	25 (23.8)	4 (40.0)	26 (24.3)	3 (37.5)	25 (26.3)	4 (20.0)
Pain	23 (20.0)	20 (29.4)	3 (6.4)**	23 (21.1)	0 (0)	16 (17.6)	7 (29.2)	17 (16.2)	6 (60.0)**	19 (17.8)	4 (50.0)	20 (21.1)	3 (15.0)
Nausea	20 (17.4)	16 (23.5)	4 (8.5)*	20 (18.4)	0 (0)	17 (18.7)	3 (12.5)	16 (15.2)	4 (40.0)	19 (17.8)	4 (50.0)*	15 (15.8)	5 (25.0)
Seizure	18 (15.7)	11 (16.2)	7 (14.9)	16 (14.7)	2 (33.3)	12 (13.2)	6 (25.0)	17 (16.2)	1 (10.0)	16 (15.0)	2 (25.0)	18 (18.9)	0 (0)*
Delirium	15 (13.0)	9 (13.2)	6 (12.8)	14 (12.8)	1 (16.7)	14 (15.4)	1 (4.2)	11 (10.5)	4 (40.0)	14 (13.1)	1 (12.5)	13 (13.7)	2 (10.0)
Wound	14 (12.2)	8 (11.8)	6 (12.8)	13 (11.9)	1 (16.7)	12 (13.2)	2 (8.3)	14 (13.3)	0 (0)	13 (12.2)	1 (12.5)	10 (10.5)	4 (20.0)
Urinary retention	11 (9.6)	7 (10.5)	4 (8.5)	11 (10.1)	0 (0)	7 (7.8)	4 (16.7)	9 (8.6)	2 (20.0)	11 (10.4)	0 (0)	10 (10.5)	1 (5.3)
Pruritus	11 (9.6)	9 (13.2)	2 (4.3)	11 (10.1)	0 (0)	9 (9.9)	2 (8.3)	9 (8.6)	2 (20.0)	8 (7.5)	3 (37.5)*	9 (9.5)	2 (10.0)
Jaundice	10 (8.7)	9 (13.2)	1 (2.1)*	10 (9.2)	0 (0)	10 (11.0)	0 (0)	2 (1.9)	8 (80.0)**	10 (9.4)	0 (0)	9 (9.5)	1 (5.0)
Insomnia	9 (7.8)	9 (13.2)	0 (0)*	9 (8.3)	0 (0)	3 (3.3)	6 (25.0)**	7 (6.7)	2 (2.0)	9 (8.4)	0 (0)	8 (8.4)	1 (5.0)
Ascites	9 (7.8)	8 (11.8)	1 (2.1)*	9 (8.3)	0 (0)	9 (9.9)	0 (0)	1 (1.0)	8 (80.0)**	9 (8.4)	0 (0)	9 (9.5)	0 (0)
Dizziness	8 (7.0)	4 (5.9)	4 (8.5)	8 (7.3)	1 (7.1)	6 (6.6)	2 (8.3)	7 (6.7)	1 (10.0)	8 (7.5)	0 (0)	7 (7.4)	1 (5.0)
Oral ulcer	8 (7.0)	4 (5.9)	4 (8.5)	8 (7.3)	0 (0)	7 (7.7)	1 (4.2)	7 (6.7)	1 (10.0)	8 (7.5)	0 (0)	6 (6.3)	2 (10.0)
Hematuria	5 (4.3)	4 (5.9)	1 (2.1)	5 (4.6)	0 (0)	2 (2.2)	3 (12.5)	5 (4.8)	0 (0)	5 (4.7)	0 (0)	4 (4.2)	1 (5.0)
Dysphagia	4 (3.5)	1 (1.5)	3 (6.4)	4 (3.7)	0 (0)	3 (3.3)	1 (4.2)	4 (3.8)	0 (0)	4 (3.7)	0 (0)	4 (4.2)	0 (0)
Incontinence	2 (1.7)	1 (1.5)	1 (2.3)	2 (1.8)	0 (0)	1 (1.1)	1 (4.2)	2 (1.9)	0 (0)	2 (1.9)	0 (0)	2 (2.1)	0 (0)
Hiccups	1 (0.9)	1 (1.5)	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (4.2)	1 (1.0)	0 (0)	1 (0.9)	0 (0)	1 (1.1)	0 (0)

Data were summarized as n (%) for each category and compared using the Pearson chi-square test, or Fisher exact test if any number in the cell was lower than 5.
* $p < 0.05$; ** $p < 0.01$.
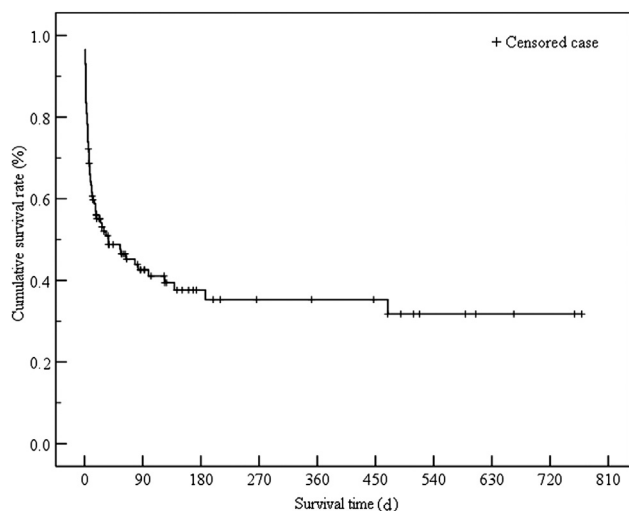
Figure 1 Cumulative survival rate of the 115 subjects who received palliative care. The curve was observed to approximate to the Kaplan—Meier survival curve. The estimated median survival time was 37 days (95% confidence interval 0—86.7 days)

hospital. The overall 6-month survival rate for all patients was 37.6%, the short survival time reflecting late referral to palliative care. The course of disease varied between patients with cancer and nonmalignant disease. Patients with nonmalignant disease had a longer natural course of illness because the underlying disease progressed more slowly. These patients were older and had multiple co-morbidities. The main causes of death in these patients were either repeated acute exacerbations of the underlying disease or acute complications such as infections or other acute illness.[27] We did not observe any significant differences in symptoms between those who survived and those who died, but patients who died had a higher rate of abdominal distension (49.3%) than surviving patients (22.9%).

Accurate prediction of a 6-month survival time—the standard window of time for referral to hospice care—in patients with nonmalignant disease is difficult, and leads patients and families to hesitate about requesting such care.[1,28] This may be a missed opportunity for patients to receive proper evaluation of their symptoms and be referred to a hospice for comprehensive, appropriate end-of-life care, which is an important reason behind having a better understanding of the symptoms prevalent in polysymptomatic late-stage nonmalignant patients in Taiwan.

Another major barrier to promoting palliative care in nonmalignant disease occurs because medical staff and families do not consider chronic illness to be a terminal

disease.[29] Only 10% of patients in this study were referred to palliative care by their primary physician. A recent study of the willingness of junior physicians in Taiwan to provide palliative care indicates that educational intervention regarding end-of-life care is highly needed among health-care personnel in our country.[30]

Because of prognostic uncertainty, we agree that palliative care referral should depend on the patient's needs rather than the estimated survival time.[14] The short survival times after referral in this study reflect late enrollment in palliative care and indicate a significant opportunity to improve access to palliative care for patients with nonmalignant disease in Taiwan. We believe that palliative care can help more patients and their family members to calmly face and be clearly aware of the diagnosis and prognosis of their late-stage disease. Besides identifying characteristic end-of-life symptoms in patients with nonmalignant disease in order to help identify candidates for palliative care, the benefits of palliative care have been demonstrated in two important ways in this study: we observed an increase in the number of patients who signed DNR consent forms and an increase in patients' and relatives' understanding of their diagnosis and prognosis.

The opportunity to provide hospice services or palliative care rather than more aggressive end-of-life care is important and should not be missed for patients who would benefit. Services for a cohort of 242,530 cancer patients who died between 2000 and 2006 were evaluated and were found to have become increasingly aggressive in the patients' last month of life; however, cardiopulmonary resuscitation, mechanical ventilation, and intubation decreased, while use of hospice services increased.[7] The authors concluded that the quality of end-of-life care in Taiwan was inferior to that recommended as a benchmark for not providing overly aggressive care in the last days of life.

In the present study, we observed that no patient received cardiopulmonary resuscitation, intubation, or cardiac massage after being enrolled in hospice care, which points to a need for higher awareness on the part of medical personnel, patients, and their families of the palliative care concept, which could be applied at the appropriate time when characteristic symptoms leading to the terminal common pathway became apparent. Knowledge of the prevalence of common symptoms is necessary to identify the patients who are in need of and could benefit from palliative care.

Study limitations

Our study had several limitations. First, we did not recruit a control group of patients who did not receive palliative care. Second, we did not analyze the results of a survey of

Table 5 Awareness of disease and prognosis of patients/family before and after palliative care.

	Before palliative care	After the start of palliative care
Patients who signed a "Do Not Resuscitate" order	105	114
Awareness of disease diagnosis on the part of patients	13	64
Awareness of disease prognosis on the part of patients	10	25
Awareness of disease and prognosis on the part of family members	66	114

patients' and families' satisfaction with hospice care. Third, we did not compare our results with those of other palliative care facilities in other hospitals in Taiwan or elsewhere in eastern Asia. Future prospective studies are necessary to address these limitations. In addition, future research is needed to determine when patients with nonmalignant disease approaching the end of life should seek palliative care.

Conclusions

Patients with life-threatening nonmalignant disease are polysymptomatic at the end of life, and this characteristic should be taken into account in providing appropriate end-of-life care in the same way as it is for cancer patients. The four leading symptoms in our patient sample were fatigue, fever, cough, and dyspnea, indicating their presence across the five late-stage disease entities. Early identification of these distressing symptoms is necessary to assist medical staff in the selection of candidates for palliative care and to provide early management and appropriate symptom control for this patient population. Hospice care with good symptom control is warranted for patients with late-stage nonmalignant disease who need appropriate end-of-life care. Education of medical personnel in the availability and capabilities of palliative care, and in identifying patients who may benefit, is warranted, as is the production and distribution of patient education materials regarding the benefits and availability of palliative care.

Author disclosure statement

Acknowledgments

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