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Symptom patterns of advanced cancer patients in a palliative care unit

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This study involved longitudinal evaluations of symptom severity and describes the symptom patterns of 77 terminal cancer patients (median age: 62 years; 61% female), selected from 537 consecutive patients admitted to the Palliative Care Unit of the National Taiwan University Hospital. The most common primary cancer sites in these patients were lung (23.4%), liver (15.6%), and stomach (13%). Nineteen physical and psychological symptoms were assessed using different scales. The median number of symptoms was 11 (range: 1–18) on admission, among which weakness, fatigue, anorexia, pain, and depression were the most common. A comparison of the initial symptom severity scores with those at one week after admission and two days before death suggested six symptom change patterns: A: continuous static (restless/heat, abdominal fullness, constipation, dizziness, and insomnia); B: static-increase (fatigue, weakness, nausea/vomiting, taste alteration, dysphagia, diarrhea, dry mouth, and night sweats); C: decrease-static (pain and depression); D: decrease-increase (anorexia and dyspnea); E: static-decrease (aggression); and F: gradually decrease (anxiety). These six symptom patterns can be divided into two categories on the basis of the relative severity of symptoms between one week after admission and two days before death. The first category included patterns A, C, E and F, and the symptoms improved with palliative care. However, the symptoms in the second category (patterns B and D), which were associated with the anorexia-cachexia syndrome and dyspnea, did not show improvement. As symptom management is an essential component of palliative care, holistic care, which encompasses physical, psychosocial and spiritual aspects, represents a rational approach for the relief of these incurable symptoms at the end stage of life for these patients. *Palliative Medicine* 2006; **20**: 617–622

Key words: advanced cancer; palliative care; symptom patterns

Introduction

Terminally ill cancer patients suffer from many physical and psychological symptoms as a result of multiple organ failures, and one of their main wishes is to be comfortable and symptom-free at the end stage of their lives.¹ Consequently, the initial and essential component of palliative cancer care is to provide advanced cancer patients with symptom relief in lieu of disease treatment.^{2,3} However, in the literature, information concerning longitudinal assessments of care outcomes at the end stage of life is scarce.

A comprehensive study, conducted in the Palliative Medicine Program of the Cleveland Clinic, indicated that

the median number of symptoms per patient upon initial referral was 11 (range: 1–27), and that the 10 most prevalent symptoms were pain, fatigue, weakness, anorexia, lack of energy, dry mouth, constipation, early satiety, dyspnea, and weight loss. Among these terminal patients, the symptom prevalence differed with age, gender, and performance status.⁴ Another study conducted in the Netherlands indicates that the functional status of end-of-life patients deteriorated from the time of their admission to palliative care units to one week before passing, but most symptoms did not worsen in the last three weeks of their lives. These patients exhibited decreases in pain, anxiety, and nausea, and patients who died between two and four weeks after admission appeared to have more favorable symptom change patterns than those who died within two weeks.⁵ Another longitudinal study of palliative care showed high initial symptom intensity and significant improvements

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over time were observed in those suffering from pain, lack of appetite, nausea/vomiting, sleeplessness and constipation.¹⁶

As cancer represents the leading cause of mortality in Taiwan, hospice and palliative care services have expanded rapidly over the last decade.⁶ A previous study conducted in our palliative care unit showed that patients averaged 9.1 symptoms at the time of admission. Although the majority of symptoms improved one week after admission, many symptoms actually worsened before death,⁷ suggesting inadequacy in symptom management. In an effort to provide optimal symptom relief for advanced cancer patients, a better understanding of the limitation and outcome of our symptom management program is required. Therefore, the aim of this study was to conduct longitudinal evaluations of symptom management and define the symptom patterns of advanced cancer patients in the Palliative Care Unit of the National Taiwan University Hospital.

Methods

Patients and palliative care setting

Participants in this prospective study were selected from consecutive patients with advanced cancer who consented and were admitted to the Palliative Care Unit of the National Taiwan University Hospital during the period from October 2002 through December 2003. Two criteria were used for selection. First, the individual's level of consciousness was sufficient (alert or lethargic consciousness) to report symptoms during admission. Second, the individual's survival time (from admission to the time of death) was expected to be longer than 12 days.

The participants were under the care of a multi-disciplinary team, consisting of physicians, nurses, psychologists, social workers, Buddhist chaplains and volunteers. The measurements of patients' symptoms were recorded daily by the same staff members, who assessed and recorded the presence or absence of symptoms and their severity according to patients' report. Team meetings were held once a week, and data for this study consisted of routine records, including patients' demographic data (age, gender, primary site of cancer, and survival days), and 'Symptom Reporting Forms' at the time of admission, one week after admission and two days before death. The study was approved by the ethical committee at the National Taiwan University Hospital.

Instruments

The assessment tool was a Symptom Reporting Form, modified from our previous study,⁷ designed by experienced specialists, which assessed both physical and psychological symptoms by different scale systems. Physical symptoms included fatigue, weakness, and pain

scores on a scale of 0–10 (0 = none, 10 = extreme); anorexia, nausea/vomiting, taste alteration, dysphagia, restless/heat, abdominal fullness, constipation, diarrhea, dry mouth, dizziness, dyspnea, insomnia and night sweats on a scale of 0–3 (0 = none; 1 = mild; 2 = moderate; 3 = severe). Psychological symptoms included depression, anxiety, and aggression on a scale of 1–5 (1 = almost none; 2 = mild; 3 = moderate; 4 = severe; 5 = extreme). The conscious levels of patients were divided into six categories: alertness, lethargy, obtundation, delirium, stupor and coma.

Statistical analysis

All data were analysed using SPSS 11.0 statistical software. Descriptive statistics were summarized as frequencies and percentages for categorical variables, median and range for number of symptoms, and mean and standard deviation for other continuous variables. Paired *t*-tests were used to delineate the changing patterns of symptom severity at three time points (on admission, one week after admission, and two days before death). *P* < 0.05 was considered significant.

Results

There were 537 consecutive patients admitted to our palliative care unit during the study period. Based on the two selection criteria, only 77 patients were enrolled in this study, for which the demographic and diagnostic data are summarized in Table 1. The median age was 62 years (range: 16–86), and male and female patients accounted for 39 and 61%, respectively. Two-thirds of these patients had an Eastern Co-operative Oncology Group (ECOG) performance status of 3 or 4. The leading primary cancer sites were lung (23.4%), liver (15.6%), and stomach (13.0%). The median number of symptoms of each patient in this series on admission, one week after admission and two days before death were 11 (range: 1–18), 11 (range: 2–19) and 12 (range: 1–18), respectively.

Table 2 summarizes the prevalence rate and average severity scores of the 19 symptoms recorded at three different times. Weakness (98.7%), fatigue (97.4%), anorexia (96.0%), pain (88.3%) and depression (81.9%) were the five most common symptoms on admission. Prevalence of constipation significantly increased and exceeded that of depression during the latter two recording times.

The severity of individual symptoms at the three time points were analysed by paired *t*-tests (Table 3). Six different patterns of changes in symptom severity scores (A–F) were identified throughout the course of data recording (Figure 1).

Pattern A, a continuous static pattern, included the symptoms of restless/heat, abdominal fullness, constipa-

Table 1 Demographics and diagnosis of included patients

Variable	Statistic ^a
Gender	
Male	30 (39%)
Female	47 (61%)
Age (year)	62 (16–86)
Survival time after admission (day)	26 (12–212)
ECOG	
1	9 (11.7%)
2	16 (20.8%)
3	29 (37.7%)
4	23 (29.9%)
Number of symptoms	
On admission	11 (1–18)
One week after admission	11 (2–19)
Two days before death	12 (1–18)
Primary cancer sites	
Lung	18 (23.4%)
Liver	12 (15.6%)
Stomach	10 (13.0%)
Colorectal	6 (7.8%)
Pancreas	6 (7.8%)
Head and neck	5 (6.5%)
Ovary	5 (6.5%)
Breast	3 (3.9%)
Cervical/uterus	3 (3.9%)
Others	9 (11.7%)

^a*n* (%) for categorical variables and median (range) for continuous variables.

tion, dizziness, and insomnia. These symptoms showed no significant changes in severity from admission through to two days before death.

Pattern B, a static-increase pattern, included the symptoms of fatigue, weakness, nausea/vomiting, taste

alteration, dysphagia, diarrhea, dry mouth, and night sweats. The severity scores of these symptoms showed no difference between the day of admission and one week after admission, but rose significantly at two days before death.

Pattern C, a decrease-static pattern, included the symptoms of pain and depression. These symptoms were improved one week after admission, and remained static through to two days before death.

Pattern D, a static-increase pattern, included the symptoms of anorexia and dyspnea. Although these symptoms showed initial improvement at the first week of admission, they deteriorated, to a greater extent, two days before death.

Pattern E, a static-decrease pattern, included the symptom of aggression. The severity score showed no improvement at one week after admission, but decreased significantly two days before death, indicating a significant relief at the end stage.

Pattern F, a gradually decreasing pattern, included the pattern of anxiety. The severity score showed a modest decrease, though not statistically significant, with time.

Discussion

Although a similar study was already conducted in our palliative care unit, the biostatistical methods used might have limitations in demonstrating the symptom change patterns.⁷ The study described here is aimed at improving the quality of symptom management by assessing the

Table 2 Prevalence and severity of symptoms during admission

Symptoms (range of severity)	On admission			One week after admission			Two days before death		
	<i>n</i>	% ^a	Mean ± SD	<i>n</i>	% ^a	Mean ± SD	<i>n</i>	% ^a	Mean ± SD
Fatigue (0–10)	75	97.4	5.8 ± 2.3	68	95.8	5.3 ± 2.6	74	97.4	7.2 ± 2.5
Weakness (0–10)	76	98.7	5.9 ± 2.3	69	97.2	5.4 ± 2.4	74	97.4	7.3 ± 2.3
Pain (0–10)	68	88.3	4.6 ± 2.8	60	84.5	2.8 ± 2.0	56	73.7	2.5 ± 2.3
Anorexia (0–3)	72	96.0	1.7 ± 0.8	59	84.3	1.4 ± 0.9	69	92.0	2.2 ± 1.0
Nausea/vomiting (0–3)	40	53.3	0.9 ± 1.1	38	53.5	0.8 ± 0.9	41	53.9	0.9 ± 1.0
Taste alteration (0–3)	27	37.0	0.5 ± 0.7	22	31.4	0.4 ± 0.7	32	43.8	0.7 ± 0.9
Dysphagia (0–3)	36	47.4	0.7 ± 0.8	30	42.3	0.6 ± 0.9	47	61.8	1.1 ± 1.1
Restless/heat (0–3)	22	29.0	0.3 ± 0.6	16	22.5	0.3 ± 0.6	33	44.0	0.6 ± 0.8
Abdominal fullness (0–3)	48	63.2	1.1 ± 1.1	43	60.6	1.0 ± 1.0	46	60.5	1.1 ± 1.1
Constipation (0–3)	52	69.3	1.2 ± 1.0	54	76.1	1.2 ± 1.0	60	78.9	1.4 ± 1.0
Diarrhea (0–3)	3	3.9	0.1 ± 0.3	6	8.5	0.1 ± 0.3	1	1.3	0.0 ± 0.1
Dry mouth (0–3)	41	53.9	0.7 ± 0.8	41	57.7	0.8 ± 0.8	53	69.7	1.1 ± 0.9
Dizziness (0–3)	38	50.0	0.7 ± 0.7	34	47.9	0.7 ± 0.9	38	50.0	0.7 ± 0.8
Dyspnea (0–3)	37	48.7	0.8 ± 0.9	30	42.3	0.5 ± 0.7	51	67.1	1.0 ± 0.9
Insomnia (0–3)	50	65.8	0.9 ± 0.8	39	54.9	0.8 ± 0.8	45	59.2	0.8 ± 0.8
Night sweats (0–3)	12	15.8	0.2 ± 0.5	10	14.1	0.2 ± 0.4	19	25.0	0.4 ± 0.7
Anxiety (1–5)	51	72.1	2.2 ± 0.9	50	73.5	2.1 ± 0.8	46	64.8	2.0 ± 0.9
Depression (1–5)	59	81.9	2.3 ± 0.9	48	69.6	2.0 ± 0.9	45	63.4	1.9 ± 0.9
Aggression (1–5)	32	45.1	1.7 ± 1.0	25	37.3	1.6 ± 0.9	14	19.7	1.3 ± 0.7

^aPercentage of patients who had reported that they had the symptom at the time.

Table 3 Changes in the severity of symptoms between three time points

Symptoms (range of severity)	Admission to one week after admission			Admission to two days before death			One week after admission to two days before death		
	<i>n</i>	Mean differences	<i>t</i>	<i>n</i>	Mean differences	<i>t</i>	<i>n</i>	Mean differences	<i>t</i>
Fatigue (0–10)	71	0.45	1.78	76	–1.29	–4.61***	70	–1.73	–7.08***
Weakness (0–10)	71	0.38	1.56	76	–1.34	–5.11***	70	–1.79	–7.22***
Pain (0–10)	71	1.94	6.22***	76	2.13	6.05***	70	0.21	0.79
Anorexia (0–3)	69	0.23	2.34*	74	–0.47	–4.55***	69	–0.65	–6.34***
Nausea/vomiting (0–3)	69	0.1	0.93	74	0.07	0.58	70	–0.03	–0.34
Taste alteration (0–3)	68	0.03	0.70	72	–0.24	–2.32*	68	–0.28	–2.99**
Dysphagia (0–3)	70	0.01	0.24	75	–0.41	–3.73***	70	–0.44	–4.22***
Restless/heat (0–3)	70	0.01	0.24	74	–0.27	–2.79**	70	–0.29	–3.39**
Abdominal fullness (0–3)	70	0.10	1.10	75	0.03	0.27	70	–0.04	–0.52
Constipation (0–3)	69	0.01	0.13	74	–0.23	–1.92	70	–0.19	–1.69
Diarrhea (0–3)	70	–0.04	–0.90	75	0.04	1.14	70	0.09	1.93
Dry mouth (0–3)	70	–0.09	–1.35	75	–0.35	–3.77***	70	–0.27	–3.24**
Dizziness (0–3)	70	–0.01	–0.15	75	–0.01	–0.14	70	–0.01	–0.17
Dyspnea (0–3)	70	0.21	2.73**	75	–0.24	–2.17*	70	–0.53	–5.22***
Insomnia (0–3)	70	0.11	1.11	75	0.12	1.22	70	0.04	0.47
Night sweats (0–3)	70	0.04	0.83	75	–0.17	–2.19*	70	–0.20	–2.49*
Anxiety (0–5)	68	0.18	1.89	69	0.30	2.52*	66	0.15	1.49
Depression (0–5)	69	0.29	3.30**	69	0.39	3.29**	66	0.14	1.27
Aggression (0–5)	67	0.12	1.65	69	0.45	4.15***	65	0.34	3.52**

* $P < 0.05$.** $P < 0.01$.*** $P < 0.001$.

pattern of changes in physical and psychological symptoms of end-stage cancer patients.

This study identified six different changing patterns among 19 different symptoms, which might be of help in assessing symptom control in advanced cancer patients. It is noteworthy that a proportion of patients showed no

deterioration in symptom severity at the first week of admission, ie, the severity score remained the same or decreased. This lack of symptom deterioration might be, in part, attributable to the faith of patients in palliative care, the good rapport between patients and team members, and the total care provided by our palliative

Figure 1 Symptom patterns of advanced cancer patients. (a) Static: no significant difference in symptom severity between the two time points. (b) Increase: severity of the symptom at latter time point is significantly *higher* than that at the former time point. (c) Decrease: severity of the symptom at latter time point is significantly *lower* than that at the former time point. (d) Gradually decrease: the severity of the symptom at the time of 'on admission' is significantly higher than that at the time of 'two days before death'. However, there is no significant difference between the times of 'on admission/one week after admission' or 'one week after admission/two days before death'.

care team. At the National Taiwan University Hospital, the palliative care team consists of individuals with medical, psychological, and religious backgrounds, including physicians, nurses, clinical psychologists, Buddhist chaplains, and social workers. Once cancers become refractory to curative therapy, symptoms from multiple organ failures inevitably develop and deteriorate. At the end stage of cancer patients' lives, palliative care provides total care to modify the natural course of symptom progression, and the symptom relief enables advanced cancer patients to experience a peaceful death.

For better assessment, these six patterns could be divided into two categories according to the control trend. The first category, including patterns A, C, E, and F, commended good symptom controls by the current palliative care system, while the second category, including pattern B and D, did not. It is evident that those poorly-controlled symptoms were associated with the anorexia-cachexia syndrome and dyspnea.

The cancer anorexia-cachexia syndrome is an irreversible event, of which the clinical manifestations include muscle wasting and other metabolic disturbances.⁸ This syndrome is caused mainly by pro-inflammatory cytokines, such as TNF α , IL-1, IL-6, and prostaglandins secreted by both cancer and inflammatory cells.⁹ As these mediators could not be completely blocked by therapeutic agents, especially in the far advanced stage, the associated symptoms progress and distress patients with time. Dyspnea represents another challenge in the symptom management of advanced cancer patients. Dyspnea was reported as one of the most difficult symptoms to manage by hospice nurses in the US.¹⁰ Our previous study indicated a high prevalence of dyspnea on admission (59.2%), which was higher than the rate of the present study (48.7%).¹¹ Another of our studies showed that the symptom of dyspnea improved in the first week after admission, but worsened afterward.⁷ The correlated causes for dyspnea included cachexia, anemia, pleural effusion, and lymphangitis.¹¹ These intractable symptoms represent challenging issues for palliative care. In addition to investigating the underlying mechanisms in order to develop more effective therapeutic strategies, improving the nutritional status and psychospiritual support of patients is also crucial in establishing a comprehensive care model.

The other major symptoms belonging to pattern A, C, E, and F are abdominal fullness, constipation, pain, and psychospiritual distress-related symptoms, such as restlessness, insomnia, depression, aggression, and anxiety. In Taiwan, better pain control has been achieved following the introduction of educational programs on analgesia, which have been implemented since 1990.⁷ A common adverse effect of opioid analgesia is constipation, but we could use prokinetic and laxative agents to prevent it. In addition, integrated care from an inter-

disciplinary team in a palliative care unit might effectively alleviate psychosocial and existential suffering in terminally ill cancer patients.¹⁷ Therefore, these symptoms have favorable symptom change patterns.

Although we could not completely relieve all symptoms of patients with end stage cancer, there are several strategies to promote their quality of life. First, late referrals are often associated with a rapid deterioration in the patient's physical condition, and should be avoided.⁷ Second, pharmacological and non-pharmacological management for symptom relief should be reassessed frequently to reach optimal efficacy after admission.^{12,13} Third, psycho-social-spiritual care should be emphasized more, especially during the last few days of life.¹⁴ Fourth, good communication and rapport should be quickly established among patients, family, and health professionals.¹⁵ Fifth, family caregivers should share responsibility in implementing symptom management.¹⁰

Moreover, cognitive impairment and compromised consciousness are common problems in advanced cancer patients.⁷ Of the 537 consecutive patients in this study, only 96 were (alert or lethargic consciousness) were able to report symptoms during admission. For assessment of subjective symptoms, patients with cognitive impairment were excluded from this study. More attention should be paid to these patients and their families, especially in providing psycho-spiritual support. The mean length of hospitalization was 13.7 ± 11.5 days in the previous study conducted in our palliative care unit.⁷ Therefore, patients with <12 days life-span were excluded from this study. In fact, 19 were excluded from the 96 patients with alert or lethargic consciousness.

In conclusion, symptom management is an essential component of palliative care. The symptom patterns described in this study might be used as an audit of symptom management in palliative care units, and could be used as a basis for further clinical research.

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