

In palliative cancer care symptoms mean everything
Symptoms & symptom management in palliative care for cancer patients

Saskia Teunissen

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Teunissen, Saskia

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Symptoms & symptom management in palliative care for cancer patients

In de palliatieve fase van kanker zijn symptomen alles bepalend
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht
op gezag van de rector magnificus, prof. dr. W.H. Gispen,
ingevolge het besluit van het college voor promoties
in het openbaar te verdedigen op
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Saskia Cornelia Constantia Maria Teunissen
geboren op 21 februari 1963 te Mook

Promotores: Prof. Dr. E.E.Voest
Prof. Dr. J.C.J.M de Haes
Co-promotor: Dr.A. de Graeff

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*After the first death,
there is no other*
(Dylan Thomas)

*Aan Rolstoel Tonnie, mijn vader (†1984)
Aan de spirituele huisarts, Sjef Martin (†2003)
Voor mijn liefsten*

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In palliative cancer care symptoms mean everything

Chapter I

General introduction and outline of the thesis

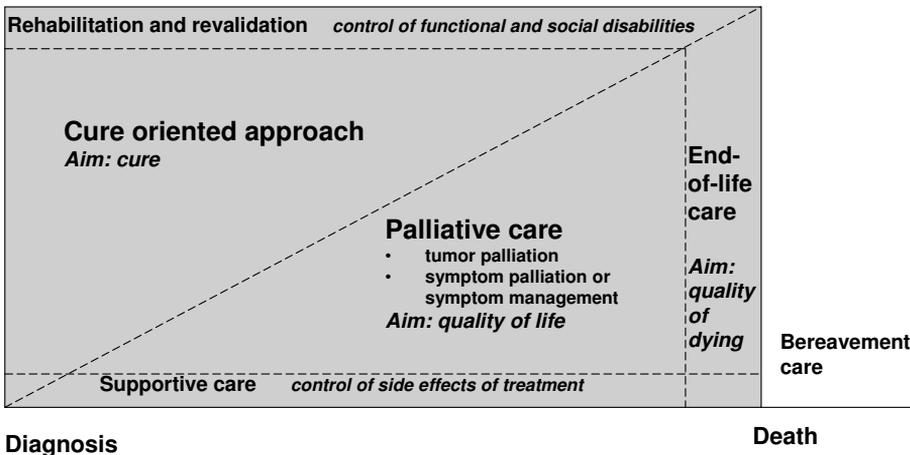


In palliative cancer care symptoms mean everything

Introduction

This thesis relates to symptoms and symptom management for patients with advanced cancer. The palliative phase starts at the moment that cure is not or no longer possible. The terminal phase is the last part of the palliative phase and refers to the point at which it becomes clear that the patient is in a progressive state of decline and that death is imminent. The transition point in the continuum of cancer care is the moment that treatment with curative intent must give way to treatment restricted to improvement or maintenance of quality of life; for this purpose, a distinction must be made between symptom-oriented palliative therapy and tumor-directed palliation (i.e. palliative chemotherapy, radiotherapy or surgery) (Figure 1)¹.

Figure 1: The continuum of cancer care



This shift in focus is an essential event and the beginning of a process with different dynamics in every patient. Physical symptoms, functional deficits and feelings of loss of control become the focus of patients' needs². A gap between patients' expectations and the reality of their situation may result in a low quality of life^{3,4}. This change of focal points is complicated, not only for cancer patients, their family and friends, but also for doctors and nurses.

Aims and principles of palliative care

The term palliative care is used in many ways: first, it may relate to treatment during the palliative phase of the disease (cancer or other), secondly, to treatment directed at symptom control only, and third, to end-of-life care. It may thus cover a wide range of care related activities over a long period of time. Different models of pal-

liative care have been discussed over the last 35 years and there is still no agreed definition of 'palliation' or a standard approach to its measurement. The definitions of palliative care as reported in the literature vary enormously⁵⁻¹². Over the past years, three definitions were given by the World Health Organization¹³, the British National Council for Hospice and Specialist Palliative Care Services¹⁴ and the European School for Oncology⁹, respectively.

- The World Health Organization defines palliative care as 'an approach to care which improves quality of life of patients and their families facing life threatening illness through the prevention and relief of suffering by means of identification and impeccable assessment of pain and other problems, physical, psychosocial and spiritual'¹³. Palliative care:
 - provides relief from pain and other symptoms
 - affirms life and regards dying as a normal process
 - intends neither to hasten nor postpone death
 - integrates the psychological and spiritual aspects of patient care
 - offers a support system to help patients live as actively as possible until death
 - offers a support system to help the family cope during the patient's illness and in their own bereavement.
- The British National Council for Hospice and Specialist Palliative Care Services¹⁴ states that palliative care includes treatment of both the disease and its symptoms in a multidimensional and multidisciplinary way. Supportive care is a continuous prerequisite for the management of treatment related side-effects. Attention for aspects of rehabilitation and revalidation regarding functional deficits and role functioning is needed during the whole palliative phase. Optimal interdisciplinary collaboration is required for disease management, symptom control and psychosocial care. A distinction must be made between general palliative care (low to moderate complexity of problems), specialist palliative care (moderate to high complexity of problems), supportive care (that which the patient and his/her family helps to cope with cancer and its treatment), hospice care (philosophy of multidimensional and multidisciplinary care in or outside hospice organizations) and terminal care (management of patients during the last days or weeks of life).
- The European School of Oncology⁹ introduced a 'new international framework' as formulated by an international working group. They define palliative care as person-centered care addressing symptoms, psychological, social and existential distress in patients with a limited prognosis, in order to optimize the quality of life of patients and their families or close friends. Based on their definition they

propose three further types of palliative care. *Basic palliative care* is the standard of palliative care that should be provided by all healthcare professionals, in primary and secondary care within their normal duties to patients with life-limiting diseases. *Specialized palliative care* is a higher standard of palliative care provided at expert level, by a trained multi-professional team, who must continually update their skills and knowledge, in order to manage persisting and more complex problems and to provide specialized educational and practical resources to other non-specialized members of the primary or secondary team. Specialized palliative care services should also contain, or be linked to, a center for research and education in palliative care developments. *End-of-life care* is the specific application of palliative care interventions and services in the last hours, days or weeks of life.

Doyle pleads in an editorial of *Palliative Medicine*²⁰⁰³ to avoid further discussion about the definition of palliative care. He states that “the definition of the WHO describes adequately what we do, why we do it, for whom it is appropriate, and what it can achieve and that it carries the authority of the WHO. Palliative care will not impress by changing definitions over and over again, but through the quality of the clinical work, the research and the teaching. Palliative care includes clinical palliative care, education, and research that focus on the quality of life of patients with advanced disease and their families”.

A group of Dutch researchers¹⁰ felt the need to clarify the term ‘palliative’ in clinical oncology because of the crucial importance of making a distinction between curative and palliative oncological treatments in relation to the treatment decision-making process. Clarification about the treatment goal may also be of great importance for communication with other professionals. Based on qualitative interviews with patients and physicians, differences between palliative care as defined by the WHO, and palliative (tumor directed) treatment in oncology (which simply reflects non-curative treatment) in oncology, were summarized as follows.

Palliative care as defined by WHO 2006	Palliative treatment in clinical oncology
Care directed to:	Treatments directed to:
1. persons with non-curable life-threatening disease	1. incurable patients (in all stages of the disease)
2. relief of symptoms	2. tumor and symptoms
3. quality of life, recognized by patients	3. quality of life, not always recognized by patients
4. neither hastening nor postponing death	4. life-prolonging

Kleffens and colleagues concluded that we should not use various definitions of the

term 'palliative'. Therefore they propose reserving the term 'palliative care' for care that is directed towards symptoms and symptom therapy.

We assume that patients in the palliative phase would benefit most from care that includes a combination of life-prolonging treatment when possible and appropriate as related to the patients' valuation of his quality of life, palliation of symptoms, rehabilitation, and support for caregivers. In this thesis we focus on symptoms and symptom management. Consequently, we use the term 'palliative care' (including end-of-life care in the terminal phase) to describe the care that the advanced cancer patients we studied received in response to their need for symptom control.

Symptoms and symptom management

Symptoms

Knowledge of the symptoms of advanced cancer, of the factors influencing those symptoms, of the prognostic meaning of symptoms and of the principles of symptom management is essential to improve palliative care. As symptoms and symptom management are the focus of this thesis, we elaborate on several aspects in order to gain insight into what has already been done.

Symptoms have been defined as "physical or mental phenomena, circumstances or changes of condition arising from and accompanying a disorder and constituting evidence for it"¹⁵. Symptoms are inherently subjective. Symptoms change over time. Symptoms may manifest rapidly and unexpectedly^{16,17,18}. Three symptom dimensions are distinguished by Bruera and his group (figure 2)¹⁶: production, perception and expression. The expression of the symptom by the patient, verbally or non-verbally, is the only dimension of the symptom that may be observed by others.

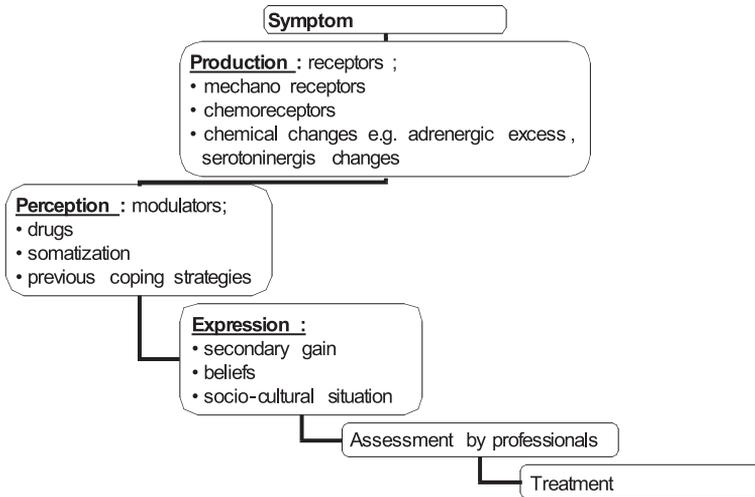
Symptoms cause symptom burden and vary from one individual to another. We describe symptom burden as the symptom related distress that results from several dimensions of the symptom: physical, emotional (e.g. anxiety, depression), cognitive (referring to the meaning and perspective of the symptom) and existential. These dimensions are influenced by psychological, social (interaction with significant others), cultural and environmental (e.g. admission in hospital) factors relevant to the individual. Symptoms have been shown to impact greatly on functional status and general well being and quality of life.

Prevalence of symptoms

A large number of studies have shown a high prevalence of debilitating symptoms in patients with advanced disease^{19,20-29}. During the last 10 years several groups reported a top ten of the most prevalent symptoms; many variations have been

Figure 2: Symptom production, perception and expression

Production , perception , and expression of symptoms
 Dalal , Fabbro , Bruera 2006



found¹⁷⁻³⁰. Diversity in prevalence figures may be based on differences between methods, populations (type of neoplasm, therapy, diagnostic criteria), location of care, measures used and time of measurement. The majority of studies used cross-sectional designs that provide information on prevalence but not on trends or clusters over the palliative trajectory.

Symptom clusters

A clear understanding of how symptoms ‘occur simultaneously’ is lacking³¹ When three or more concurrent symptoms (e.g. pain, fatigue and sleep disturbances, or nausea, vomiting and poor appetite) are related to each other, they are called a symptom cluster³¹⁻³². The symptoms within a cluster do not necessarily share the same etiology; for instance, pain may be caused by cancer, fatigue by cancer and its treatment and sleep disturbances by selected types of chemotherapy agents or anxiety. Symptom clusters may have an adverse effect on patient outcomes and may have a synergistic effect as a predictor of patient morbidity and mortality.

Symptoms as predictor for survival

Estimating life expectancy of advanced cancer patients has proven to be difficult.

The complexity of the process of estimating survival is reflected in the frequently reported overestimation of expected survival by medical doctors and sometimes in the underestimation thereof³³⁻⁴¹. A small number of specific symptoms such as shortness of breath in rest, dysphagia, dry mouth, appetite loss, anorexia and weight loss, fatigue/asthenia and cognitive impairment were recognized as independent predictors of survival in different populations. Reuben et al identified the 'terminal cancer syndrome', including functional status (KPS <50), dry mouth, shortness of breath, problems with eating, recent weight loss and troubles with swallowing³⁰.

Symptom management

Under-treatment of symptoms has been associated with under-reporting by patients. In addition, competence, knowledge and clinical expertise of the physician have been found to play a major role in symptom management⁴².

Assessment is essential to the prevention and management of common symptoms of advanced cancer patients. But, even though a variety of assessment instruments have been developed, during almost 40 years of palliative care there is still no gold standard. Optimal monitoring of symptoms should be carried out paying attention to severity, distress (influencing factors), treatment requests and treatment effect. Rapid and efficient numerical scales are needed to assess for the presence of multiple standardized symptoms, with a possibility to add volunteered symptoms.

Symptom control should be the outcome of effective symptom management and is the most essential step in the realization of the aim of palliative care: achieving or maintaining the best possible level of quality of life.

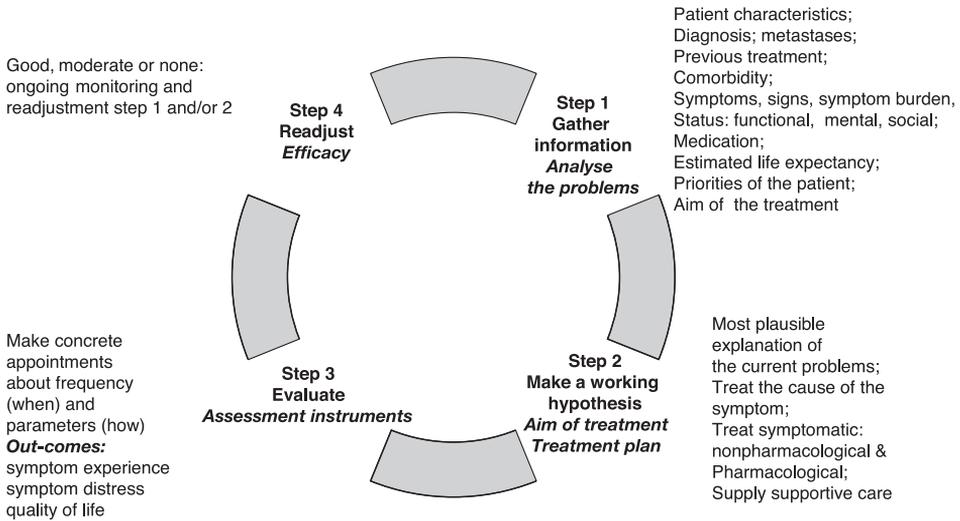
According to Twycross, symptom management falls into three categories: 'correct the correctable', non-drug treatments and drug treatment⁷. We believe that symptom management refers to a process: starting with the first observation of the symptoms (as expressed by the patient), followed by assessment, then multidimensional analysis (e.g., interaction with other symptoms and needs), treatment (including non-pharmacological and pharmacological interventions, depending the consequences of interventions for other symptoms), and, finally, by evaluation (e.g. by continuous monitoring) and re-assessment as a logical step of revision¹. Achievable goals should be identified and agreed on with the patient. Therefore, emphasis needs to be placed on coordination, cooperation, collaboration, possibilities for consultation and communication.

A comprehensive and structured way of thinking, based on the work of Twycross and Ajemian, which we have labeled as 'palliative reasoning', should form the framework for symptom management^{1,7}.

Communication in palliative care

Given the fundamentals of symptoms and symptom management discussed above, it is evident that communication is an important element of palliative care. Adequate communication is essential in the management of advanced cancer patients and may present a problem for patients, their families and professionals. The quality of communication with patients, kin and team members is regarded as fundamental by medical specialists with regard to the quality of care for the dying⁴³. We agree with Twycross, who claims that an explanation by the doctor prior to treatment of a symptom will do much to reduce the psychological impact of the symptom on the sufferer⁷.

Figure 3: Decision-making model of palliative reasoning



Effective communication skills are requisite in palliative care^{11,44}. These include effective sharing of information, active listening, determination of goals and preferences, assistance with medical decision-making and effective communication with all involved. On the other hand, ineffective communication was found to be one of the major barriers to optimal end-of-life care at the health care provider level^{45,46}. Relationship building, information exchange, decision-making, giving advice, and handling emotions are currently used as a framework to distinguish different communicative goals in oncology⁴⁷.

Consultation for symptom management

It has been argued that cancer patients may suffer unnecessarily due to insufficient knowledge of doctors and nurses caused by lack of training during the medical study and lack of experience in daily practice^{42,48-50}. Consultation of experts in palliative care is considered to have a major impact on the quality and direction of patient care⁵¹⁻⁵². For that reason, the possibility for consultation for palliative care patients is increasingly available, both in the Netherlands and in other countries, despite the fact that randomized trials show only a small benefit^{49,53-57}.

In the region of Utrecht, the Netherlands, several hospitals have started a palliative care team for bed-side consultation in the hospital (e.g. University Medical Center Utrecht 1998). In addition, a palliative care telephone consultation service for professionals in the whole region was initiated in 1999 by the Comprehensive Cancer Center Middle Netherlands.

Aim and overview of the thesis

In this thesis, we focus on symptoms and symptom management in palliative care, as we believe that deeper insight into symptoms will create more opportunities for adequate decision-making in order to attain symptom control. Moreover, we consider communication and consultation essential in order to apply and spread knowledge in the process of symptom management. Therefore, the thesis is divided in two parts: part I addresses issues about symptoms and symptom management and part II reports on communication and consultation.

The following issues have been studied in part I:

- ***What are the major symptoms of patients with incurable cancer?***

This question is addressed in chapter 2. The main aim was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic.

- ***What is the influence of age on symptoms?***

In chapter 3 we prospectively explored the differences in the prevalence of symptoms, palliative care problems and needs between three age groups of hospitalized advanced cancer patients by means of a standardized patient interview.

- ***Are symptoms related to mood disorders and fatigue and vice versa?***

Chapter 4 addresses the hypothesis that anxiety and depression are related to the presence and intensity of physical symptoms in hospitalized advanced cancer patients. In chapter 5, fatigue is conceptualized as a multidimensional construct and the correlates of fatigue are prospectively studied.

- ***Do symptoms have a prognostic significance for survival?***

In chapter 6 we assess the prognostic value of symptoms in the same sample of hospitalized advanced cancer patients as in chapter 3 and 5.

Next, in part II, the following issues about communication and consultation were studied:

- ***What is the meaning of communication in palliative care?***

Chapter 7 provides a review of the literature regarding the role of communication in palliative cancer care as published in 2004.

- ***Which professionals make use of a palliative care service and what questions do they have?***

Chapter 8 evaluates 5 years of experience of a regional palliative care telephone consultation service for professionals.

Chapter 9 provides a summary of the major findings of this thesis. Finally, the main conclusions and implications for clinical practice are discussed and recommendations for future research in symptom management are given.

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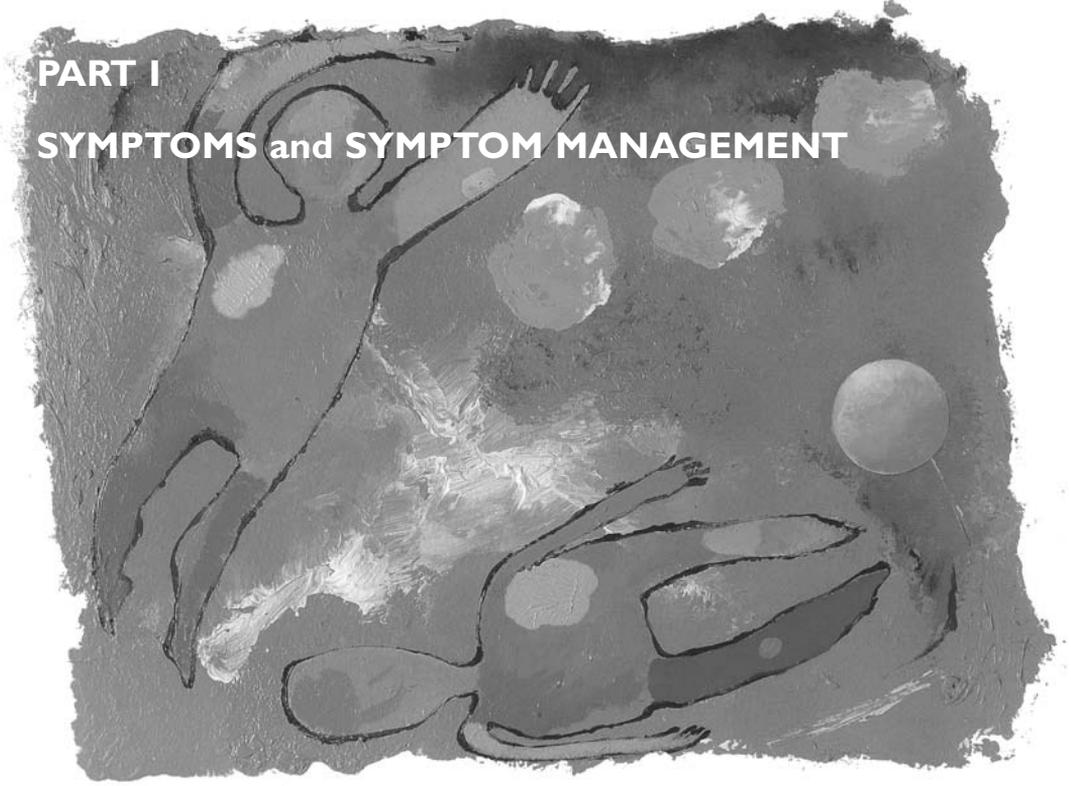
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In palliative cancer care symptoms mean everything

PART I

SYMPTOMS and SYMPTOM MANAGEMENT



In palliative cancer care symptoms mean everything

Chapter 2

Symptom prevalence in patients with incurable cancer: a systematic review

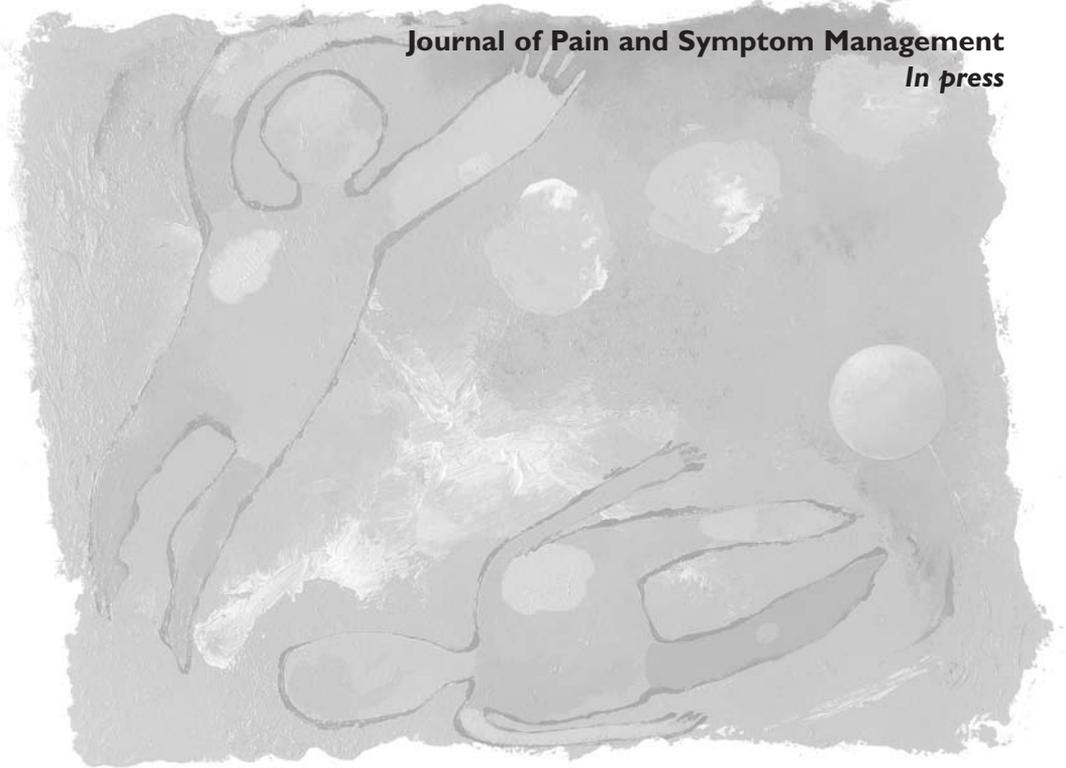
Saskia Teunissen¹
Wendy Wesker¹
Cas Kruitwagen²
Hanneke de Haes³
Emile Voest¹
Alexander de Graeff¹

¹ Department of Medical Oncology, University Medical Center Utrecht, Utrecht

² Center for Biostatistics, University of Utrecht, Utrecht

³ Department of Medical Psychology, Academic Medical Center, Amsterdam

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In press



In palliative cancer care symptoms mean everything

Abstract

Purpose

The suffering of patients with incurable cancer is determined to a large degree by the presence and intensity of the symptoms of their disease. Knowledge of symptom prevalence is important for clinical practice. The main aim of this study was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic.

Patients and methods

We included 44 studies (including 25074 patients) on overall symptom prevalence (Group 1) and 6 studies (including 2219 patients) on symptom prevalence during the last 1-2 weeks of life (Group 2). In these studies symptom prevalence was assessed by a questionnaire, a standardized interview or the medical record.

Results

We identified 37 symptoms assessed in at least 5 studies. Almost all symptoms occurred in >10% of the patients. Five symptoms, fatigue, pain, lack of energy, weakness and appetite loss, occurred in more than 50% of the patients of Group 1. Weight loss occurred significantly more often in Group 2 compared to Group 1, and pain, nausea and urinary symptoms significantly less often. Generally, symptom prevalence was highest if assessed by a questionnaire.

Conclusion

The results of this study should be used to guide doctors and nurses in symptom management. Proper attention to symptom burden and suffering should be the basis for individually tailored treatment aimed at improving or maintaining quality of life of patients in their last period of life.

Introduction

Palliation implies a shift from cure and control of the disease to improvement or maintenance of quality of life. This shift in focus is an essential event for cancer patients and their loved ones, but also for doctors and nurses. Physical symptoms, functional deficits and feelings of loss of control become the focus of care^{1,2}.

The World Health Organization has defined palliative care as 'an approach to care which improves quality of life of patients and their families facing life threatening illness through the prevention and relief of suffering by means of identification and impeccable assessment of pain and other problems, physical, psychosocial and spiritual'³. The palliative phase has different dynamics in every patient. However, the suffering of these patients is determined to a large degree by the presence and intensity of the symptoms of their disease. Knowledge of symptom prevalence is important for clinical practice as it enables doctors and nurses to focus on the more prevalent symptoms and may help to anticipate problems and plan care for patients, to educate clinical staff, to direct assessments of health care need and for planning services⁴.

Many studies have addressed this issue in patients with incurable diseases, most often in those with cancer. However, these studies are heterogeneous with regard to patients and assessment method and the numbers of patients included are often relatively low.

The main aim of this study was to obtain a reliable estimation of symptom prevalence in patients with incurable cancer by performing a systematic review of studies assessing this topic. Secondary aims were 1) to study differences in symptom prevalence during the last 1-2 weeks of life and 2) to assess the influence of assessment method, gender and age on symptom prevalence.

Methods

Literature review

We performed a systematic literature review using the following databases: MEDLINE, EMBASE and CINAHL. When papers were found, they were hand searched for cross-references. In order to avoid problems concerning the meaning and categorization of symptoms, we included only papers in the English language. The data were primarily extracted by one of the authors (W.W.) and checked by two other authors (ST and AdG). These 3 authors decided how to categorize the symptoms (see Results). Papers were excluded if they:

- were not describing original studies
- focused on only one specific symptom (e.g. fatigue, depression) without prevalence data on other symptoms
- assessed symptoms by proxy

- gave only data on symptom intensity (without specifying the number or percentage of patients with or without the symptom)
 - included more than 10% of patients without cancer and did not supply data on symptom prevalence by diagnosis
 - included patients with cancer before, during or after curative treatment.
- Symptoms were included in the analysis only if they were assessed in at least 10% of the studies.

Analysis

We separated studies assessing symptom prevalence in the last 1-2 weeks of life (Group 2) from other studies (Group 1). If symptoms were assessed at different time points in the same study, only the baseline data were used for Group 1. If the last assessment was done in the last 1-2 weeks of life, these data were also used for Group 2.

Obviously, the prevalence of a symptom could be determined only for those studies assessing that specific symptom. Each prevalence was first transformed to log odds to better conform to a normal distribution. The Q test was used to determine whether there was heterogeneity in the log odds of the various studies. Pooled log odds were then estimated using the random effects model⁵, and consequently back transformed, resulting in pooled prevalence estimates with 95% confidence intervals. Non-parametric tests (Mann-Whitney, Kruskal-Wallis) were used to detect differences in mean percentages between groups.

For statistical analysis, the Statistical Package for the Social Sciences, version 12.0 (SPSS Inc., Chicago, IL) was used, and the statistical package R (R version 2.2.0, The R Development Core Team) with library "meta". Statistical significance was assumed if $p < 0.05$.

Results

We identified 46 studies that met the inclusion criteria,⁶⁻⁵⁵ including a total of 26223 patients. Some papers referred to the same patient population⁶, and ^{7,20} and ^{21,32} and ^{33,43} and ⁴⁴. Data of 40 of these studies⁶⁻⁵³ were included for Group 1, data of 4 studies were included for both groups,^{26,32} and ^{33,34,46} and data of 2 studies were included for Group 2 only^{54,55}. Patient characteristics are summarized in Table 1.

Group 1 included 25074 patients and Group 2 2219 patients. Ten studies gave data on median or mean survival, which varied from 3 to 12 weeks^{16,23,31,32,33,35,37,41,43,44,48,52}. As to be expected, symptoms were labeled differently in different studies. We categorized these symptoms (in order of decreasing prevalence) as follows: fatigue (including tiredness), pain, lack of energy, weakness (asthenia), appetite loss (anorexia), nervousness, weight loss, dry mouth (xerostomia), depressed mood (depression, mood changes, feeling low, miserable or sad), constipation, worrying, insomnia

Table 1. Patient characteristics

	<u>Group 1</u>	<u>Group 2</u>
Number of patients	25074	2219
Mean age	65 years	64 years
Gender:		
- Male	28%	53%
- Female	25%	47%
- Unspecified	47%	
Setting:		
- Hospice inpatient	45%	51%
- Hospital inpatient	25%	19%
- Outpatient	16%	8%
- Home	4%	14%
- Unspecified	10%	8%
Tumor type:		
- Brain	1%	2%
- Head and neck	5%	6%
- Lung	13%	25%
- Breast	9%	11%
- Gastro-intestinal	17%	26%
- Gynecological	4%	4%
- Prostate	3%	3%
- Other genito-urinary	5%	9%
- Skin/melanoma/sarcoma	1%	1%
- Hematological	2%	2%
- Other types of cancer	10%	11%
- Unspecified cancer	29%	-
No cancer	1%	-

(inability to sleep, difficulty or problems sleeping, sleeping problems or disturbances, sleeplessness, poor sleeping), dyspnea (breathlessness, shortness of breath, trouble with breathing), nausea, anxiety (fearfulness), irritability, bloating, cough, cognitive symptoms (memory or concentrating problems, difficulty concentrating), early satiety, taste changes (unpleasant taste), sore mouth/stomatitis (mouth sores or lesions, oral candida, oral or mouth discomfort, mucositis), vomiting (emesis), drowsiness (sleepiness, sedation), edema (swollen limb, lymph edema), urinary symptoms (dysuria, incontinence, problems with urination, loss of bladder control, bladder disturbances), dizziness, dysphagia (difficulty swallowing), confusion (disorientation), bleeding (haemorrhage), neurological symptoms (hemiplegia, paralysis, paresis, numbing/tingling, paresthesias), hoarseness, dyspepsia (gastric discomfort), skin symptoms (pressure, wound or bed sores, dermatological problems), diarrhea (loose stool), pruritis (itching) and hiccup.

For both groups, virtually all Q tests for statistical heterogeneity were (very) significant, indicating a very high level of heterogeneity of the studies included in this review.

Symptom prevalence in Group 1 (Table 2 and Appendix 1)

In total, we identified 37 symptoms which were assessed in at least 5 (>10%) studies (range: 5-40) for Group 1. Almost all symptoms occurred in >10% of the patients.

For Group 1, seventeen studies used a questionnaire (the Memorial Symptom

Table 2. Sympton prevalence in Group I

	Number of studies	Number of patients	Pooled prevalence %	95% confidence interval %
N.		25,074		
Fatigue	17	6727	74%	(63% ; 83%)
Pain	37	21917	71%	(67% ; 74%)
Lack of energy	6	1827	69%	(57% ; 79%)
Weakness	18	14910	60%	(51% ; 68%)
Appetite loss	37	23112	53%	(48% ; 59%)
Nervousness	5	727	48%	(39% ; 57%)
Weight loss	17	13167	46%	(34% ; 59%)
Dry mouth	20	6359	40%	(29% ; 52%)
Depressed mood	19	8678	39%	(33% ; 45%)
Constipation	34	22437	37%	(33% ; 40%)
Worrying	6	1378	36%	(21% ; 55%)
Insomnia	28	18597	36%	(30% ; 43%)
Dyspnea	40	24490	35%	(30% ; 39%)
Nausea	39	24263	31%	(27% ; 35%)
Anxiety	12	7270	30%	(17% ; 46%)
Irritability	6	1009	30%	(22% ; 40%)
Bloating	5	626	29%	(20% ; 40%)
Cough	24	11939	28%	(23% ; 35%)
Cognitive symptoms	9	1696	28%	(20% ; 38%)
Early satiety	5	1639	23%	(8% ; 52%)
Taste changes	11	3045	22%	(15% ; 31%)
Sore mouth/ stomatitis	8	2172	20%	(8% ; 39%)
Vomiting	24	9598	20%	(17% ; 22%)
Drowsiness	16	11634	20%	(12% ; 32%)
Edema	13	3486	19%	(15% ; 24%)
Urinary symptoms	15	12011	18%	(15% ; 21%)
Dizziness	12	3322	17%	(11% ; 25%)
Dysphagia	25	16161	17%	(14% ; 20%)
Confusion	17	11728	16%	(12% ; 21%)
Bleeding	5	8883	15%	(11% ; 20%)
Neurological symptoms	11	10004	15%	(10% ; 23%)
Hoarseness	5	1410	14%	(7% ; 26%)
Dyspepsia	7	3028	12%	(9% ; 15%)
Skin symptoms	7	9177	11%	(6% ; 20%)
Diarrhea	22	16592	11%	(7% ; 16%)
Pruritis	14	6676	10%	(7% ; 15%)
Hiccup	7	3991	7%	(3% ; 15%)

Assessment Scale,^{7,13,18,20,21,24} Edmonton Symptom Assessment Scale^{6,19} Support Team Assessment Schedule,^{10,15} Patient Disease Symptom/Sign Assessment Scale,⁸

Appendix I. Symptom prevalence of the individual studies (Group I)

Reference	6,7	8	9	10	11	12	13	14	15	16	17	18	19	20,21	22	23	24	25	26	27	28	29	
Assessment	Questionnaire																					Standardized interview	
N.	240	121	50	352	1635	146	192	480	133	278	60	178	162	243	151	100	66	952	176	125	254	39	
Fatigue		40				83		79	52	100	81		88			89							46
Pain	59	62	46	59		61	88	53	50	83		83	67	64		77	78			52	72		82
Lack of energy	62											89		74			83						
Weakness			82													86				77			41
Appetite loss		47	58	73	48	49			20	75	65	57	70	44	38	64	61	68	68	50			64
Nervousness	37							56				45				61							
Weight loss	33															27							51
Dry mouth	54		68									78		54		80	82			61		41	54
Depressed mood	40		52	40	31			51				42	71	65			55			53			39
Constipation			36	36	33	27	48	33	18	54					25	40	48	59	49	33	41	41	
Worrying	40							27				44		71			61						
Insomnia	45	67	46		59	36		49	10	64		37		52		50	55			35	40		54
Dyspnea	50	14	30	32	24	47		45	32	77	73	70	47	24	29		38	43	40	21			21
Nausea	27	24	42	24	27	29	32	23	11	66		38	29	44	42	30	61	78	26	28	39	41	
Anxiety	63				9								74							51			
Irritability	28						40					35				47							
Bloating												39				37							23
Cough	33		28			38			24		75	57		29	34		52	42	28				18
Cognitive symptoms							45	49				34		41			50						
Early satiety																							62
Taste changes							28	50						35			50					46	23
Sore mouth/ Stomatitis				59														68					
Vomiting			32	13	20	9			7			21		21	20	24	41			19	17	27	31
Drowsiness	44		4		2							44	79	60			74	23					
Edema		8	46						11								32						21
Urinary symptoms				14				25				21		17	22			26	8				
Dizziness			2									37		24		39	29						21
Dysphagia				22			16	6			23			11			24			28		24	3
Confusion			30													50		18		30			
Bleeding																							16
Neurological sympt				10								39		37									21
Hoarseness																							26
Dyspepsia			2		11																		36
Skin symptoms		17		3																			
Diarrhea			4	6	25		17	3	44			18		24			24			9			15
Pruritis			8	6		8						30		27	27		24						15
Hiccup															10	28							15

Symptom Monitor,¹² Symptoms and Concerns checklist,¹⁴ EORTC Core Questionnaire,¹⁶ Lung Cancer Symptom Scale,¹⁷ Symptom Distress Scale,²² Therapy Impact Questionnaire²³ or other questionnaires^{9,11}). Eighteen studies used a self-developed standardized interview by the doctor or nurse,²⁵⁻⁴⁴ 8 studies used the medical record⁴⁵⁻⁵² and in one study the method was unclear⁵³.

Five symptoms, fatigue, pain, lack of energy, weakness and appetite loss, occurred in more than 50% of the patients of Group I. Large 95% confidence intervals (>20%) were seen for lack of energy, weight loss, dry mouth, worrying, anxiety, early satiety and sore mouth/stomatitis.

30	31	32,33	34	35	36	37	38	39	40	41	42	43,44	45	46	47	48	49	50	51	52	53	
Standardized interview												Medical record				Unknown						
100	530	211	593	150	108	1592	312	78	100	166	1840	1000	1103	90	105	547	38	3030	400	171	6677	
52							98					67		58	85			84	23	43		
86	76	80		65	72	62	90	71	64	88	57	82	73	54		42	79	69	64	92	71	
38												59										
47		63			70				62	60	51	64		43	79	40		83	32	31	47	
68	64		37	57	44	79	53	42	48	56	30	64	31	8	76			57	34	36	67	
39						75	93	23	56	17	39	60			73		79			18	6	77
40	29	14	7	25		74			13	23		55								16	2	
34									7	27		40		8					48	16	32	
52		25	27	33	21	54	42	27	33	39	23	51		4		37		46	32	24	47	
																					3	
43			31		26		69		20	36	9	47		7					43	12	5	29
70	34	16	21	33	29	53	27	17	27	30	19	51	27	17	43	21			35	31	19	51
24		11	27	29	36	44	21		13	38	21	36	19	12		19		30	29	35	40	
27									3	58		23		21				60	13	11		
														6								
10																						
47			5	29	13			6	18			37		6			66		15	7	50	
6									6	14											29	
46									3			50								4		
32									3			28								2	1	
5				7						17							47				2	
15			16				11	49	12	24		23						16	16	16		
5		9	5						10	27				24						11	10	
16				27	8				23			28		4						12		
			14	23	10			24	21					3					14		23	
16			10				38		6					1							10	
9	24	10	21		16	43		12	7	12		18	22	3			74		7	4	23	
13		6	2			12		15	3	17	8	20	33	24		15		21				
						13																
				23	10				14	14							47		6		14	
																			8	6	8	
33									6			24									1	
13		8	12																		8	
								9	12	12										14		19
		4	5	7		25		6	3	16								9	10	7	4	
			7	3				6	4									8		2		
12																		4	2	1		

Symptom prevalence in Group 2 (Table 3 and Appendix 2)

One study used a questionnaire,⁵⁴ four studies used a standardized interview^{26,32,33,34,55} and one study used the medical record⁴⁶.

Twenty-six of the 37 symptoms from Group 1 were assessed in at least one study for Group 2 (range 1-6). Four symptoms, fatigue, weight loss, weakness, and appetite loss, occurred in >50% of patients. Large 95% confidence intervals (>20%) were seen for most of the symptoms.

Weight loss occurred significantly more often in Group 2 compared to Group 1, and pain, nausea and urinary symptoms significantly less often.

Table 3. Symptom prevalence in Group 2: patients in the last 1-2 weeks of life

	Number of studies	Number of patients	Pooled prevalence %	95% confidence interval %	p ¹
N		2219			
Fatigue	2	120	88%	(12% ; 100%)	.506
Weight loss	2	1149	86%	(77% ; 92%)	.023
Weakness	3	477	74%	(50% ; 89%)	.262
Appetite loss	5	2008	56%	(13% ; 92%)	.460
Pain	5	1626	45%	(32% ; 59%)	.004
Dyspnea	6	2219	39%	(20% ; 62%)	.695
Drowsiness	3	894	38%	(14% ; 70%)	.303
Dry mouth	4	1010	34%	(10% ; 70%)	.794
Neurological symptoms	1	176	32%	(26% ; 40%)	.500
Anxiety	2	266	30%	(11% ; 62%)	.923
Constipation	6	2219	29%	(16% ; 48%)	.747
Confusion	4	1070	24%	(6% ; 61%)	.410
Depressed mood	3	859	19%	(9% ; 36%)	.104
Nausea	6	2219	17%	(8% ; 31%)	.047
Skin symptoms	1	593	16%	(14% ; 20%)	.750
Dysphagia	4	1070	16%	(6% ; 37%)	.825
Insomnia	4	889	14%	(3% ; 44%)	.094
Cough	4	889	14%	(3% ; 43%)	.291
Vomiting	3	799	13%	(9% ; 18%)	.313
Bleeding	1	176	12%	(8% ; 18%)	.667
Edema	1	90	8%	(4% ; 16%)	.286
Dizziness	2	683	7%	(5% ; 9%)	.264
Irritability	1	90	7%	(3% ; 14%)	.571
Diarrhea	5	2129	6%	(2% ; 19%)	.258
Urinary symptoms	3	859	6%	(5% ; 8%)	.017
Dyspepsia	2	804	2%	(1% ; 4%)	.111

¹ Comparison of median percentages, Group 2 versus Group 1, Mann-Whitney test

Symptom prevalence by assessment method, gender, age and diagnosis

For 26 symptoms, different assessment methods could be compared (Table 4). Significant differences in mean percentages were found for dry mouth, insomnia, depressed mood, taste changes, confusion and pruritis. For all these symptoms, the highest mean percentages were found if the symptom was assessed by means of a questionnaire.

Six studies looked at gender differences in symptom prevalence^{9,11,14,15,30,44}. Only one study corrected for diagnosis⁴⁴. A clear indication for gender differences, occurring in most or all studies looking at that particular symptom, was found for dysphagia and insomnia (both more prevalent in men) and for nausea and vomiting

Appendix 2. Symptom prevalence of the individual studies (Group 2)

Reference	26	46	32,33	34	54	55
N	176	90	211	593	30	1119
Fatigue		52			100	
Weight loss					93	84
Weakness	82	49	85			
Appetite loss	80	6		12	93	90
Pain	30	34	47		57	60
Dyspnea	47	28	23	17	70	64
Drowsiness		57	51	15		
Dry mouth	70		10	16	60	
Neurological symptoms	32					
Anxiety	46	18				
Constipation	55	7	18	18	47	52
Confusion	68	28	29	3		
Depressed mood	39	4		21		
Nausea	13	13	4	20	23	44
Skin symptoms				16		
Dysphagia	46	7	14	10		
Insomnia	28	6		3	47	
Cough	18	7		3	60	
Vomiting	10			12	23	
Bleeding	12					
Edema		8				
Dizziness		6		7		
Irritability		7				
Diarrhea	7		1	4	3	27
Urinary symptoms	7	6		6		
Dyspepsia			1	3		

(more prevalent in women).

The relation between age and symptom prevalence was investigated in 4 studies^{11,16,44,45}. No study corrected for diagnosis. An indication for age differences, occurring in at least two of the studies, was found for pain and dysphagia, both decreasing with age.

Discussion

Many studies have addressed symptom prevalence in advanced cancer patients. However, almost all studies are heavily biased due to patient selection. Moreover, several studies included relatively low numbers of patients. This is the first systema-

Table 4. Symptom prevalence by assessment method

Assessment method	Questionnaire			Standardized interview			Medical record			p ¹
	No. of studies	Median %	Mean %	No. of studies	Median %	Mean %	No. of studies	Median %	Mean %	
N	4587			8326			5484			
Total number of studies	17			18			8			
Fatigue	8	83	77	4	60	66	5	58	59	.510
Pain	14	63	66	15	72	73	7	69	68	.370
Weakness	2	84	84	9	62	59	6	42	51	.084
Appetite loss	14	58	55	16	57	56	6	35	40	.236
Weight loss	3	29	30	9	51	50	4	46	44	.518
Dry mouth	6	73	69	12	35	36	2	9	9	.008
Depressed mood	9	51	50	6	37	33	4	24	26	.044
Constipation	11	36	36	17	39	38	5	32	29	.442
Insomnia	12	50	48	11	36	37	4	10	17	.018
Dyspnea	15	38	42	17	29	32	7	27	28	.124
Nausea	16	30	34	16	29	32	6	24	24	.294
Anxiety	3	63	49	4	25	26	4	17	26	.591
Cough	9	34	41	10	23	24	4	11	24	.095
Taste changes	4	43	41	5	28	26	2	2	2	.043
Sore mouth/stomatitis	2	36	36	4	12	24	2	25	25	.717
Vomiting	10	21	21	11	19	22	3	16	16	.574
Drowsiness	7	44	44	6	10	13	2	18	18	.327
Edema	4	19	23	7	23	22	2	8	8	.272
Urinary symptoms	5	21	20	7	21	18	2	9	9	.243
Dizziness	5	29	26	5	16	18	2	6	6	.192
Dysphagia	6	19	17	13	16	18	5	7	22	.692
Confusion	2	40	40	11	13	13	4	23	23	.023
Neurological symptoms	3	37	29	5	14	16	2	7	7	.084
Diarrhea	9	18	18	9	7	10	3	9	9	.383
Pruritis	7	24	19	5	6	7	2	5	5	.035
Hiccups	2	19	19	2	14	14	3	2	2	.105

¹ Comparison of mean percentages, Kruskal-Wallis test

tic review on symptom prevalence in patients with incurable cancer. As 46 different studies and 26223 patients were included, the estimations of symptom prevalence are likely to be as reliable as possible as the influence of sample size and selection bias is reduced as much as possible. Contrary to many systematic reviews on other topics, publication bias is unlikely to have influenced the results. There is no reason to presume that studies on symptom prevalence have not been published because of uninteresting or 'negative' results.

Thirty-seven symptoms (assessed in at least 5 studies) were identified, almost always occurring in >10% of patients. Overall, fatigue, pain, lack of energy, weakness and appetite loss were the most frequent symptoms, occurring in >50% of patients. During the last 1-2 weeks of life, fatigue, weight loss, weakness and appetite loss occurred in more than 50% of patients.

Several aspects of this study deserve further discussion.

The 95% confidence intervals of the symptom prevalence are quite large due to the heterogeneity of the studies included and probably also due to different interpretations of these symptoms in different studies. When combining the results from dif-

ferent studies, we had to make choices for categorizing symptoms which were labeled differently. Although most of these choices were relatively straightforward, one may argue about some of them, in particular: differences between fatigue, lack of energy and weakness; the various terms included for anxiety and depressed mood, respectively; grouping of symptoms as in mouth pain/stomatitis, cognitive, voiding, skin and neurological symptoms. Obviously, this has an impact on the symptom prevalence figures detected in our review.

Another factor that may influence symptom prevalence (and may also explain the large 95% confidence intervals) is the assessment method. We found clear differences in the prevalence of several symptoms between studies using different methods. Although this is an indirect comparison (no study compared different methods directly) and differences are probably partly due to patient selection, there seem to be patterns in prevalence differences for certain symptoms due to the assessment method used. For many symptoms, the lowest prevalence was seen in studies using the medical record. This finding emphasizes the importance of standardized comprehensive assessment of symptoms in palliative care^{56,57}. However, this was not (clearly) the case for all symptoms, e.g. for pain, dyspnoea, nausea and vomiting, constipation and skin problems. This probably reflects the fact that these symptoms are usually spontaneously mentioned by patients and/or are explicitly and routinely addressed by doctors and nurses. For other symptoms, studies using a questionnaire showed higher prevalence figures than studies using a standardized interview. Apparently, when completing a questionnaire, patients have more time and/or feel freer to indicate the presence of some symptoms that are less often mentioned during a standardized interview. Questionnaires may pick up symptoms that are not considered to be important and/or treatable by patients, doctors and nurses and thus are not addressed by standardized interviews or a routine history^{56,57}.

As there is some evidence of a final common clinical pathway in patients nearing death,⁵⁵ we looked separately at symptom prevalence in patients during the last 1-2 weeks of life. As only 6 such studies were included and these studies varied greatly with regard to the number of patients included and symptoms assessed, the estimations are less reliable and comparison with the overall population of incurable cancer patients is difficult. A significant increase was found for weight loss and a significant decrease for pain, nausea and urinary symptoms. Longitudinal studies are needed to test the hypothesis that symptoms change and are less dependent on diagnosis as the end approaches.

A limitation of our study is the lack of availability of individual patient data. Therefore, we were unable to assess reliably the influence of gender and age on symptom prevalence. In the limited amount of studies addressing those issues, there

seemed to be limited relations between gender and age on the one hand and symptoms on the other hand. No definite conclusions about the presence or absence of these relationships can be drawn and more study is necessary in this area.

In conclusion, we performed a systematic review giving the most reliable estimates possible of symptom prevalence in patients with incurable cancer. Focus on the more prevalent symptoms in these patients should guide symptom management by doctors and nurses. However, it must be emphasized that treatment should be based on symptom intensity, symptom burden and the impact of symptoms on quality of life. This should be the subject of further studies, in order to help doctors and nurses to provide individually tailored treatment aimed at improving or maintaining quality of life of cancer patients in their last period of their life.

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In palliative cancer care symptoms mean everything

Chapter 3

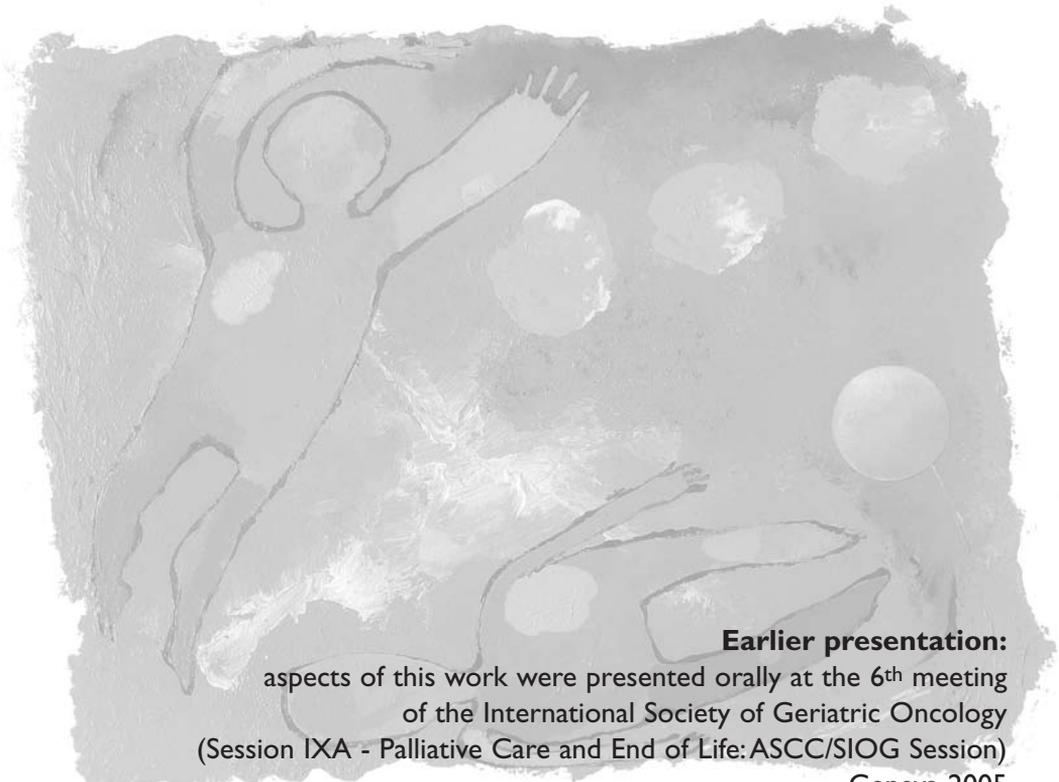
Does age matter in palliative care?

Saskia Teunissen¹,
Hanneke de Haes²
Emile Voest¹
Alexander de Graeff¹

¹Department of Medical Oncology, University Medical Center Utrecht, Utrecht

²Department of Medical Psychology, Academic Medical Center, Amsterdam

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In palliative cancer care symptoms mean everything

Abstract

Purpose

To assess whether age has an impact on symptoms, problems and needs of hospitalized advanced cancer patients.

Patients and methods

A prospective analysis of 181 patients referred to a Palliative Care Team was done using a standardized list of symptoms, problems and needs. Differences between 3 age groups (<60; 60-70; ≥70) were analyzed.

Results

Patients ≥70 years had a significantly different prevalence of depressed mood (48% vs 13% of patients 60-70 years and 24% of patients <60 years, $p=0.002$), urinary tract problems (20% vs 3% vs 8%, $p=0.024$) and drowsiness (18% vs 42% vs 25%, $p=0.039$). They expressed more problems with a shortage of informal caregivers (45% vs 42% vs 17%, $p<0.001$) and less need for support in coping (40% vs 61% vs 63%, $p=0.043$), relational support (3% vs 8% vs 14%, $p=0.019$) and support in communication (0% vs 8% vs 11%, $p=0.013$).

Conclusion

Fewer differences than expected were found. Elderly cancer patients admitted to a hospital have more or less the same symptoms, problems and needs as their younger counterparts. Despite these findings, age-specific assessment of symptoms, problems and needs ought to be part of optimal symptom management.

Introduction

There is considerable evidence showing underassessment and undertreatment of symptoms of older people and lack of access to specialized palliative care¹⁻⁶. Therefore, it is important to determine whether palliative treatment strategies should be adjusted according to the age of the patient.

Older patients with advanced cancer may be expected to have different symptoms, problems and support needs⁷. Specific age-related problems are conceptualized as 'difficulties of ageing'⁷. Physical and pharmacokinetic changes, comorbidity, loss of mobility, psychological alterations and changing social circumstances of elderly patients may add to the suffering from terminal disease. Comorbidity and functional status are important and independent predictors of outcome of treatment of elderly patients with cancer⁸. The concept of 'frailty', characterized by high susceptibility, low functional reserve and unstable homeostasis, is an important issue in geriatric medicine^{9,10}. Frailty is considered to be the result of a decline in the reserve of multiple organ systems and places the person at risk for disability or death from minor stress. The question is whether elderly advanced cancer patients must be automatically categorized as 'frail'.

The most commonly recorded symptoms in elderly patients with advanced disease are pain, anorexia, nausea, constipation, dyspnea, fatigue, insomnia, anxiety, depression and delirium^{7,11-23}. A significant decrease with age is reported for pain^{12,18,19,22,23}, dysphagia^{7,11,12,16,18}, nausea and vomiting^{11,19}, dyspnea and coughing^{7,11,18,19,23}, insomnia^{11,18-20,22}, anxiety^{11,19} and depression^{11,19}. A significant increase with age is found for urinary problems^{7,11,16,17,18}, confusion^{7,12,18}, and for delirium^{12,16}. Contradictory results (a decrease or an increase) are found for anorexia^{16,18} and constipation^{11,12,16,19}. Higher age is also associated with better emotional, role and social functioning^{22,23}.

Remarkably little is known of the psychosocial and functional consequences of advanced disease of elderly palliative care cancer patients. The problem of a shortage of informal caregivers, the need for adequate information and for comprehensive assessment are stressed by many authors^{1,2,5,14,19}. The knowledge about consequent problems of advanced cancer in the elderly and specific palliative care needs for these patients is limited due to a lack of systematic research in this field. Several of the studies looking at age differences were retrospective^{7,11,12,18} and/or by proxy^{7,11,18}. Most of the other studies assessed outpatients^{16,17,19}. No prospective patient-assessed studies have been performed in hospitalized patients. Therefore, we prospectively explored the differences in the prevalence of symptoms and in the expressed palliative care problems and the needs for support between three age groups of hospitalized advanced cancer patients by means of a standardized patient interview.

Patients and methods

Patients

A prospective analysis was carried out of patients with advanced cancer admitted to the University Medical Center Utrecht, who were referred to the Palliative Care Team (PCT) of the Department of Medical Oncology because of suboptimal symptom control. The PCT consists of a medical oncologist, an anesthesiologist, a psychiatrist and two clinical nurse specialists.

Between October 1998 and March 2004 203 patients were referred to the PCT. For 22 patients the assessment was incomplete because of cognitive impairment, mental or physical exhaustion, or inability to understand the Dutch language, leaving 181 patients with a full assessment. Based on previous research²⁴⁻²⁶, the cohort was divided into three age groups: <60 (younger group), ≥ 60 <70 (middle-aged group) and ≥ 70 (elderly).

Measures

Socio-demographic and medical data were obtained from the medical and nursing files. Functional status was measured by the WHO performance scale.

Symptoms, problems and needs were assessed as dichotomous variables (absent or present) by means of an interview with the patient by the clinical nurse specialist of the PCT using a standardized list developed by a multidisciplinary group of Dutch researchers²⁷ based on previous prevalence studies.

Palliative care problems were defined as emotional, social, spiritual and functional issues requiring professional assistance. Actual wishes to receive professional support in the emotional, social, spiritual and functional domains were labeled as palliative care needs.

Statistical analysis

Differences between the three age groups were assessed by using chi-squared tests on the respective contingency tables. When the validity of a standard chi-squared test was doubtful because of low frequencies, Fischer's exact alternative for this test was used. Length of survival was defined as the period between the date of consultation by the PCT and the date of the patient's death (event) or the last follow-up (censored) for those who were still alive at the time of data analysis (August 2004). The survival status and the date of death were obtained from the hospital registry or, if unavailable, by telephone calls to general practitioners. Differences in survival were assessed using the log-rank test. Statistical significance was considered if $p < 0.05$. All data analyses were generated using the Statistical Package for the Social Sciences version 12.0 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

Patient characteristics are depicted in Table I. Fifty-six percent of the patients were <60 years old, 21% 60-70 years old and 23% ≥70 years. Six patients (3%) were >85 years.

There were no significant differences between the three age groups with regard to gender, performance scale, primary cancer site and site of metastases. Patients ≥ 70 less often had a living partner (p=0.003).

Patients <60 had significantly less comorbidity (p=0.007), in particular a second cancer (p=0.043), COPD (p=0.007), heart failure (p<0.001) and diabetes (p=0.004)

Table I. Patient characteristics (n=181)

	Patients (%) < 60	Patients (%) ≥ 60 - <70	Patients (%) ≥ 70	p-value (χ^2 exact)
	(n=103)	(n=38)	(n=40)	
Gender				
Male	43 (42%)	21 (26%)	16 (20%)	ns
Age (years)				
Median (range)	47 (18-59)	65 (60-69)	77 (70-91)	-
Marital status				
Living partner	77 (75%)	26 (68%)	18 (45%)	0.003
Primary cancer site				
Breast	15 (15%)	5 (13%)	5 (13%)	ns
Gynecological	12 (12%)	3 (8%)	6 (15%)	ns
Gastrointestinal	14 (14%)	11 (29%)	10 (25%)	ns
Head- and neck	13 (13%)	3 (8%)	5 (13%)	ns
Lung	12 (12%)	6 (16%)	2 (5%)	ns
Prostate	3 (3%)	3 (8%)	7 (18%)	ns
Others	34 (33%)	7 (18%)	5 (13%)	ns
Local relapse	53 (51%)	14 (37%)	16 (40%)	ns
Site of metastases				
Bone	45 (44%)	18 (47%)	18 (45%)	ns
Lymph node	32 (32%)	12 (32%)	12 (30%)	ns
Lung	19 (18%)	8 (21%)	8 (20%)	ns
Liver	19 (18%)	9 (24%)	8 (20%)	ns
Brain	16 (16%)	3 (8%)	1 (2%)	ns
Viscera	11 (11%)	3 (8%)	1 (2%)	ns
Other	13 (13%)	3 (8%)	1 (2%)	ns
Co-morbidity				
any	47 (46%)	27 (71%)	24 (60%)	0.007
other cancer site	8 (8%)	9 (24%)	5 (13%)	0.043
neurological	5 (5%)	3 (8%)	1 (2%)	ns
COPD	1 (<1%)	2 (5%)	5 (13%)	0.007
heart failure	-	7 (18%)	12 (30%)	<0.001
diabetes	5 (5%)	3 (8%)	9 (23%)	0.004
other	38 (37%)	18 (47%)	22 (55%)	ns
Chemo- and/or radiotherapy				
≤3 months before consultation	26 (25%)	4 (10%)	3 (7%)	0.016
WHO Performance Status				ns
1	2 (2%)	2 (5%)	2 (4%)	-
2	26 (25%)	11 (29%)	13 (33%)	-
3	50 (49%)	20 (53%)	18 (45%)	-
4	25 (24%)	5 (13%)	7 (18%)	-
Median survival; days (range)	69 (1-1035)	39 (2-695)	42 (1-759)	0.037

Younger patients had received palliative chemotherapy and/or radiotherapy more often in the three months prior to consultation ($p=0.016$).

The median survival was 42 days for patients ≥ 70 , 39 days for patients between 60 - 70 and 69 days for patients < 60 ($p=0.037$).

Differences in symptom prevalence

We recorded 25 symptoms occurring in $>10\%$ in at least one of the three age groups (Table 2). Pain, excretory problems, anorexia, constipation, fatigue and anxiety were the most frequent symptoms in patients ≥ 70 , occurring in $\geq 50\%$ of

Table 2. Prevalence of symptoms occurring in $>10\%$ of at least one of the age groups

Symptoms	Patients (%) < 60	Patients (%) ≥ 60 - <70	Patients (%) ≥ 70	p-value (χ^2 exact)
Pain	93 (90%)	31 (82%)	36 (90%)	ns
Excretory problems	59 (57%)	20 (53%)	31 (78%)	ns
Anorexia	50 (49%)	27 (71%)	24 (60%)	0.049
Constipation	34 (33%)	14 (37%)	22 (55%)	ns
Fatigue	61 (59%)	26 (68%)	21 (53%)	ns
Anxiety	57 (55%)	19 (50%)	20 (50%)	ns
Depressed mood ^a	25 (24%)	5 (13%)	19 (48%)	0.002
Loss of mobility	45 (44%)	19 (50%)	17 (43%)	ns
Nausea	37 (36%)	14 (37%)	17 (43%)	ns
Sleeplessness	38 (37%)	15 (39%)	12 (30%)	ns
Dry mouth	24 (23%)	8 (21%)	10 (25%)	ns
Confusion ^b	14 (14%)	6 (16%)	10 (25%)	ns
Dyspnea in rest	33 (32%)	12 (32%)	9 (23%)	ns
Vomiting	27 (26%)	8 (21%)	9 (23%)	ns
Diarrhea	15 (15%)	5 (13%)	8 (20%)	ns
Urinary tract problems	8 (8%)	1 (3%)	8 (20%)	0.024
Drowsiness	26 (25%)	16 (42%)	7 (18%)	0.039
Sore mouth	19 (18%)	4 (11%)	7 (18%)	ns
Weight loss $>10\%$	15 (15%)	9 (24%)	7 (18%)	ns
Dysphagia	11 (11%)	4 (11%)	6 (15%)	ns
Cognitive impairment	14 (14%)	6 (16%)	6 (15%)	ns
Restlessness	8 (8%)	1 (3%)	4 (10%)	ns
Bedsores	13 (13%)	4 (11%)	4 (10%)	ns
Delirium	2 (2%)	1 (3%)	4 (10%)	ns
Coughing	13 (13%)	2 (5%)	1 (3%)	ns
Median number of symptoms (range)	6	6	7	ns

a answer to the question "are you depressed?"

b single symptom, without other signs of the delirium syndrome at the time of assessment

the patients. Significant age differences were found for anorexia, urinary tract problems, drowsiness and depressed mood. Patients ≥ 70 had a clearly higher prevalence of urinary tract problems and depressed mood and a clearly lower prevalence of drowsiness than the two other two age groups; for anorexia the trend was less clear. Sub-analysis of the small subgroup of 6 patients ≥ 85 did not disclose another trend.

There were no significant differences in the median number of symptoms between the age groups. A significant difference was found in the prevalence of patients having >3 physical complaints at the moment of assessment: 76% of the elderly patients versus 61% of the middle-aged group versus 58% of the younger patients ($p=0.038$). Overall, 12% of the patients reported ≥ 4 of the symptoms defined in the literature as 'difficulties of ageing'; of the patients ≥ 70 thirteen percent expressed 4 or more of these symptoms.

Differences in prevalence of palliative care problems and need for support

The median number of palliative care problems as expressed in the interview was 3 in each age group (range 0-7) and the median number of needs for support was 2 for the three age groups (range 0-5). In total 9 palliative care problems and 8 unmet support needs occurred in $>10\%$ in at least one of the age groups (Table 3). With regard to palliative care problems, there were no significant age differences, with the exception of the problem of a shortage of informal caregivers ($p < 0.001$), which occurred less frequently in younger patients.

The main support needs for all the age groups were the need for functional support, in particular in the middle-aged group, and support in coping, predominantly in the younger and middle-aged group. We found significantly less need of relational support and support in communication with advancing age.

Discussion

Our study is one of the first to assess prospectively symptoms, palliative care problems and expressed needs for support of different age groups of patients admitted to the hospital for symptom control. It shows that, despite a (moderately) shorter survival for patients ≥ 60 , there is a remarkable similarity with regard to the prevalence of symptoms, palliative care problems and needs for support between the different age groups. With advancing age, there were clear trends only for an increased prevalence of depressed mood and urinary tract problems; a decreased prevalence of drowsiness; more problems with a shortage of informal caregivers and less expressed need of support in coping, relational support and support in communication.

Table 3. Prevalence of palliative care problems and unmet support needs occurring in $\geq 10\%$ of at least one of the age groups

	Patients (%) < 60	Patients (%) ≥ 60 - <70	Patients (%) ≥ 70	p-value (exact test χ^2)
Palliative care problems				
Decreased ADL	46 (45%)	17 (45%)	19 (48%)	ns
Shortage of informal caregivers	17 (17%)	16 (42%)	18 (45%)	<0.001
Decreased mobility	45 (44%)	19 (50%)	17 (43%)	ns
Uncertainty about the future	37 (36%)	14 (37%)	12 (30%)	ns
Lack of control	34 (33%)	11 (30%)	9 (23%)	ns
Lack of autonomy	13 (13%)	8 (21%)	5 (13%)	ns
Disturbances in distress	16 (16%)	7 (18%)	5 (13%)	ns
Consequences of cognitive failure	9 (9%)	7 (18%)	5 (13%)	ns
Disturbances in symptom experience	11 (11%)	3 (8%)	3 (8%)	ns
<i>Median number of problems</i>	3	3	3	ns
Support needs				
Functional support	60 (58%)	29 (76%)	24 (60%)	0.021
Support in coping	65 (63%)	23 (61%)	16 (40%)	0.043
Emotional support	35 (34%)	11 (29%)	14 (35%)	ns
Support of informal caregivers	40 (39%)	11 (29%)	11 (28%)	ns
Spiritual support	8 (8%)	1 (3%)	5 (13%)	ns
Co-ordination of care	6 (6%)	8 (21%)	4 (10%)	ns
Relational support	14 (14%)	3 (8%)	1 (3%)	0.019
Support in communication	11 (11%)	3 (8%)	0 (0%)	0.013
<i>Median number of needs</i>	2	2	2	ns

An increased prevalence of the clusters of specific symptoms described in the literature and defined as 'difficulties of ageing' have not been found for the elderly group in our study population, not even in the small subgroup of 6 patients ≥ 85 . Several reasons may be given.

First, in progressive far-advanced disease age-related differences in symptom prevalence between patients may disappear supporting the known concept of the common final clinical pathway in patients with advanced cancer²⁸.

Second, elderly patients may not have been referred to the hospital as an expression of the barriers to the equity of access for older people to palliative care services as described before¹⁻⁶. Alternatively, this could be an expression of the preference of very old patients to stay at home as long as possible in the last phase of life or of the preferential referral to a hospice.

Third, once admitted to the hospital, elderly patients may not have been referred

to the PCT. Elderly inpatients are less likely to be referred to palliative care units²⁹ and it is possible that problems specifically associated with old age do not get recognized by health care professionals within the hospital as suitable for referral to PCTs. As we do not have data on the number of potential patients who would have been candidates for referral, we have no way of estimating the magnitude of such a referral bias.

The finding that elderly patients experience equal or even less need for support, despite the reduced availability of informal caregivers, is somewhat unexpected. A possible explanation could be a better emotional, role and social functioning of elderly patients as reported in the literature^{22,23}. Younger patients have more tasks with regard to partner, family and work and may therefore have more need for support.

The increase of depressed mood with age we found is in contrast with the reported decrease of this symptom some years ago in a palliative care population in the United States²⁰. The contradictory finding could possibly be explained by the differences in population: far-advanced hospitalized cancer patients in our study versus a population of palliative care patients referred to a transmural Palliative Care Program.

In conclusion, despite a shorter survival and higher rates of comorbidity of elderly patients, there were few significant differences between the three age groups with regard to symptom prevalence, palliative care problems and support needs. The clinical importance of the few statistically significant differences we found is limited. The results of our research indicate that elderly hospitalized advanced cancer patients do not seem to be more vulnerable or frail than their younger counterparts. This is a clinically relevant finding as it makes us realize that we may be prejudiced and, erroneously, expect elderly patients to have more problems and other expectations regarding symptom control, while actually they may be more satisfied with life and be less dependent than we assume.

Despite these findings, elderly cancer patients are different from their younger counterparts and an age-specific assessment of symptoms, problems and needs (i.e. based on the Comprehensive Geriatric Assessment^{30,31}) ought to be part of optimal symptom management. Such an assessment, particularly when consciously and systematically applied using an easy-to-fill-in daily instrument, have the potential of improving the quality of palliative care for elderly patients through timely recognition of symptoms and unmet needs for support.

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Does age matter in palliative care?

In palliative cancer care symptoms mean everything

Chapter 4

Are anxiety and depression related to physical symptom burden?

Saskia Teunissen¹
Alexander de Graeff¹
Emile Voest¹
Hanneke de Haes²

¹ Department of Medical Oncology, University Medical Center Utrecht, Utrecht

² Department of Medical Psychology, Academic Medical Center, Amsterdam

Submitted



In palliative cancer care symptoms mean everything

Abstract

Purpose

Anxiety and depression are common symptoms in hospitalized advanced cancer patients. It is often presumed that anxiety and depression affect the occurrence and experience of physical symptoms. To analyze the relation between anxiety, depression and the presence and intensity of physical symptoms.

Patients and methods

Anxiety and depression were assessed in a hospitalized advanced cancer population (n=79) primarily by the Hospital Anxiety and Depression Scale (HADS), and also by a single-item question "Are you anxious and /or depressed?" and by the Edmonton Symptom Assessment System (ESAS). Physical symptoms were assessed by a semi-structured interview and by the ESAS.

Results

Thirty-four percent of the patients reported anxiety, 56% depression and 29% both, as assessed by the HADS. The correlations between HADS, the single-item question and the ESAS were low. No association was found between anxiety or depression and the presence of physical symptoms. Patients who were anxious or depressed had higher ESAS scores for insomnia and drowsiness; scores for pain, anorexia, asthenia, nausea and dyspnea were independent of anxiety and/or depression.

Conclusion

The relationship between anxiety, depression and the presence and intensity of physical symptoms in hospitalized advanced cancer patients is very limited.

Introduction

Anxiety and depression are frequently reported in advanced cancer patients. The prevalence of anxiety^{1,2} and depression³⁻⁵ varies considerably in different studies due to differences in patient selection and, most importantly, differences in criteria and assessment methods; overall, anxiety occurs in 23-38% and depressed mood in 40-41% of patients with incurable cancer⁶. Anxiety occurs more frequently in the first stage of cancer, while depression is more common in advanced disease^{1,7}. Significant psychological distress, sometimes experienced and/or expressed as depression or anxiety, is typical for all stages of cancer. There is a lack of good data on anxiety and depression in advanced cancer patients. Anxiety has hardly been studied in these patients and the quality of the available research on depression is low due to small samples and high nonparticipation rates.³

To date, a variety of measuring instruments for screening and diagnosing anxiety or depression in cancer patients are used. The Hospital Anxiety and Depression Scale (HADS) and a single-item question for depression are the most widely used instruments^{3,8-11}.

The relation between physical symptoms and mood disorders in cancer patients is complex. Physical symptoms are used in the diagnosis and classification of mood disorders; in cancer patients such diagnostic criteria may be unreliable and of low specificity^{1,12}. In clinical practice, it is often assumed that anxiety and depression affect the presence and intensity of physical symptoms and distress^{7,13,14}. On the other hand, physical symptoms may lead to being depressed and/or anxious.

The main aim of this study is to analyze the relation between anxiety, depression and the presence and intensity of physical symptoms in hospitalized advanced cancer patients. To answer this research question, we first assessed anxiety and depression in this population, secondly, we compared different methods to measure anxiety and depression, and thirdly, we analyzed the influence of anxiety and depression on symptom presence and intensity.

Patients and methods

Patients

An analysis was performed of hospitalized patients with advanced cancer, who were referred to the Palliative Care Team (PCT) of the Department of Medical Oncology for symptom control from several departments of the University Medical Center Utrecht, The Netherlands. All patients had a thorough clinical assessment by one of the two clinical nurse specialists of the PCT.

Between October 1998 and March 2004, 203 patients were referred to the PCT. For 22 patients the assessment was incomplete because of cognitive impairment, mental

or physical exhaustion, or inability to understand the Dutch language. Of the remaining 181 patients, the score for the Hospital Anxiety and Depression Scale was available for 79 patients (44%). These patients represent the sample for the present analysis.

Measures

Sociodemographic and medical data were obtained from the medical and nursing files. Functional status was measured by the Karnofsky Performance Status (KPS)¹⁵. Symptoms were primarily assessed as a dichotomous variable (absent or present) during a semi-structured interview by the clinical nurse specialist, using a checklist¹⁶ based on a study by the Dutch Centers for Development of Palliative Care¹⁷. The list includes 49 of the most frequently occurring standardized symptoms of previous prevalence studies¹⁸⁻²².

Anxiety and depression were primarily assessed by means of the Hospital Anxiety and Depression Scale (HADS)⁸; the Dutch translation has been validated²³. The HADS is a simple, sensitive, and specific screening tool for psychiatric disorders in hospitalized patients avoiding the inclusion of somatic symptoms. It consists of two scales, one for anxiety and one for depression, each including 7 items with 4 response categories. The scales of the HADS are transformed to separate scores for anxiety and depression, ranging from 0 to 20. Anxiety and depression were also assessed by means of a single-item screening question (“Are you anxious/depressed: yes or no?”)^{9,10} and by the Edmonton Symptom Assessment System (ESAS)^{24,25}. The single-item question has been used for screening for depression in hospitalized patients. The question is related to the last week before the assessment. The original version of the ESAS uses visual analogue scales; we used a later version using a numeric scale (0-10; 0=none, 10=worst).

Patients were considered to be at risk for a mood disorder if they:

- had a score >11 on the HADS for the anxiety and/or depression scale,
- answered ‘yes’ to the single-item question, and/or
- had a score on the ESAS >5 or >2 for the anxiety and/or depression item. The cut-off of 5 on the ESAS was chosen as scores >5 on any numerical symptom scale from 0-10 are usually regarded as significant and indicate the need for treatment. A recent publication²⁶ indicated a cut-off value of 2 for anxiety and depression as a better predictor; we therefore used both cut-off values.

The intensity of some other symptoms (pain, nausea, drowsiness, anorexia, dyspnea, asthenia and insomnia) was also measured by means of the ESAS.

Analysis

Of the symptoms assessed by the checklist we analyzed only those occurring in

10% or more of the patients. The relation between anxiety, depression and the presence of physical symptoms was assessed by using chi-squared tests on the respective contingency tables. Three-dimensional contingency tables were applied to assess differences between patients who were anxious and depressed at the same time (with anxiety and depression as explanatory variables and symptoms as response variables). Statistics were calculated with 95% confidence intervals for proportions. If the validity of a standard chi-squared test was doubtful because of low frequencies, the Fischer's exact alternative for this test was used.

The Mann-Whitney test was used to compare the intensity of symptoms measured by the ESAS (pain, nausea, drowsiness, anorexia, dyspnea, asthenia and insomnia) for patients with or without anxiety and/or depression

Statistical significance was assumed if $p < .05$. Statistical analysis was done using the Statistical Package for the Social Sciences version 12.0 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

Patient characteristics are summarized in Table 1. No significant differences with regard to gender, age, primary cancer site, performance status and presence of symptoms were found between the 79 patients for whom the HADS data were available and the other patients of the total sample of 181 (data not shown).

At the moment of analysis, all except five patients had died, with a median survival of 41 days (range 1-1035). Twenty-six percent of the patients died within 1 month, 57% lived for 1-6 months and 17% of the patients lived longer than 6 months after the initial consultation.

The median number of physical symptoms per patient was 4 (range 1-8). We recorded 16 physical symptoms occurring in >10% of the patients (Table 2).

Presence of anxiety and depression

Based on the HADS, anxiety occurred in 34% of the patients and depression in 56% (Table 3). When assessed by the single question, the percentages for anxiety and depression were 58% and 37%, respectively; when assessed by the ESAS, the percentages for anxiety and depression were 49% and 44%, respectively, when the cut-off of 5 was used, and 67% and 73%, respectively, with a cut-off of 2. Both anxiety and depression as measured by the HADS, single question or ESAS (with cut-off values of 5 and 2) were present simultaneously in 29%, 22%, 34% and 60% of the patients, respectively.

Table 1. Patient characteristics (n=79)

	n (%)
Gender	
Female	45 (57%)
Age (years)	
Median (range)	57 years (21-85)
Primary cancer site	
Breast	13 (16%)
Gynecological	10 (13%)
Gastrointestinal	15 (19%)
Head- and neck	8 (10%)
Lung	8 (10%)
Prostate	6 (8%)
Others	19 (24%)
Metastases	
Bone	34 (43%)
Lymph node	34 (43%)
Lung	16 (20%)
Liver	18 (22%)
Brain	5 (6%)
Karnofsky Performance Score	
30-40	33 (42%)
50-60	33 (42%)
70-80	10 (14%)
90-100	3 (4%)

Table 2. Physical symptoms present in >10% of patients

Symptom	Patients (%)
Pain	75 (95%)
Anorexia	50 (63%)
Asthenia	47 (60%)
Constipation	35 (44%)
Insomnia	35 (44%)
Nausea	29 (37%)
Vomiting	22 (28%)
Dyspnea	19 (24%)
Drowsiness	19 (24%)
Dry mouth	19 (24%)
Sore mouth	18 (23%)
Weight loss >10%	13 (17%)
Diarrhea	12 (15%)
Confusion	11 (14%)
Paralysis	11 (14%)
Pressure ulcers	8 (10%)

Comparison of the measuring instruments

As the HADS is the only validated instrument to screen for anxiety and depression

Table 3. Presence of anxiety and depression by the three measuring instruments

Anxiety	
HADS ≥ 11	34%
Yes ¹	58%
ESAS ≥ 5	49%
ESAS ≥ 2	67%
Depression	
HADS ≥ 11	56%
Yes ²	37%
ESAS ≥ 5	44%
ESAS ≥ 2	73%
Anxiety and Depression	
HADS ≥ 11	29%
Yes ^{1,2}	22%
ESAS ≥ 5	34%
ESAS ≥ 2	60%

¹ "Are you anxious?" asked by the consulting nurse
² "Are you depressed?" asked by the consulting nurse

Table 4. Comparison of the instruments

HADS	Anxiety		Depression	
	<11	≥ 11	<11	≥ 11
Single item				
No	27	6	32	17
Yes	25	21	2	27
ESAS				
<5	26	2	19	11
≥ 5	8	19	7	17
ESAS				
<2	17	1	13	2
≥ 2	17	20	13	26

in physically ill patients, we considered it as the standard against which the other two instruments were compared (Table 4).

With regard to anxiety, the positive predictive value of the single-item question was 21/46 (46%) and the negative predictive value 27/33 (82%). For the ESAS (with a cut-off value of 5) the values were 19/27 (70%) and 26/28 (93%), respectively; when a cut-off value of 2 was used for the ESAS²⁶ the positive predictive value for anxiety was 20/37 (54%) and the negative predictive value 17/18 (94%).

Concerning depression, the positive predictive value of the single question was 27/29 (93%) and the negative predictive value 32/49 (65%). For the ESAS (with a

cut-off value of 5) the values were 17/24 (71%) and 19/30 (63%), respectively; when a cut-off of 2 was used for the ESAS26 the positive predictive value for depression was 26/39 (67%) and the negative predictive value 13/15 (87%).

Relation between anxiety, depression and symptom presence and intensity

Generally, the presence of anxiety or depression was not found to be related to symptom presence, irrespective of the assessment method used. The only exception was for the relation between anxiety (as assessed by the single question) and pain. The prevalence of pain was 96% for patients who were anxious as opposed to 80% for patients who were not anxious, based on the yes/no question (p=.001); differences were not significant if anxiety was assessed by the ESAS (p=.362) or the HADS (p=.493).

If patients with both anxiety and depression were compared with patients without either, no significant differences were found in symptom presence, except, again, for pain as assessed by the single question (p=.017).

With regard to symptom intensity, we found that patients with anxiety or depression assessed by the HADS had significantly higher ESAS-scores for insomnia and drowsiness (Table 5). There was no relationship between anxiety or depression and the ESAS-scores for pain, anorexia, asthenia, nausea and dyspnea. Results were similar when patients with both anxiety and depression were compared to patients without either (data not shown).

Table 5. Anxiety, depression and symptom intensity¹

	Anxiety ²			Depression ¹		
	Yes	No	p ³	Yes	No	p ³
Pain	5.8	6.0	.766	5.6	6.1	.410
Nausea	3.1	2.2	.159	3.0	2.0	.108
Drowsiness	4.7	3.1	.039	4.6	2.6	.009
Anorexia	6.0	6.4	.469	6.4	5.9	.737
Dyspnea	2.5	2.0	.243	2.5	1.8	.152
Asthenia	7.4	5.8	.069	7.2	5.6	.085
Insomnia	5.3	3.5	.035	4.8	3.2	.047

¹ Mean of ESAS-scores

² As measured with the HADS (Yes, if score ≥11; No, if score <11)

³ Mann-Whitney test

Discussion

In a sample of hospitalized patients with far advanced cancer, we found high levels of anxiety (34%) and particularly of depression (56%), based on the scores of the HADS. These levels were high compared to the literature^{2,3,5,26,27} and probably reflect the severely ill inpatient population included in our study, as demonstrated

by the high level of symptoms and the short median survival of 41 days.

We found virtually no relationship between anxiety or depression and symptom presence and only a limited relationship with symptom intensity. Therefore, symptom presence and intensity do not seem to be a reliable indicator of anxiety or depression in these patients. Conversely, anxiety and depression appear to have very limited influence on symptom presence and intensity. The lack of these relationships is contrary to what is usually assumed in clinical practice. For example, one often assumes that the presence of a symptom (e.g. pain) may induce or aggravate depression and that conversely, depression may influence the experience and intensity of that symptom.

There are several studies which look at the relation between depression and physical symptoms^{2,27-31}. In contrast, studies of the relation between anxiety and physical symptoms are largely lacking.

Our study design is remarkably similar to the study of Chen et al²⁷ but the results are quite different. They found an increased prevalence of insomnia, pain, anorexia, fatigue and pressure sores in depressed patients (as assessed by the HADS) compared to non-depressed patients. These differences in results may be explained by patient selection; the patients in the study of Chen were mostly admitted for chemotherapy and had a mean Karnofsky score of 81%, whereas our patients were admitted for symptom control and had a mean performance score of 51%. Cultural differences (Chinese versus Dutch patients) may also have played a role. In another study, a verbal rating scale for mood was correlated with verbal rating scores for pain and fatigue²⁹. However, when DSM-criteria were applied, no significant differences in symptom rating between depressed and non-depressed patients were found. Another study looked at the relation between both depression and anxiety (assessed by the HADS) and physical symptoms in patients with advanced cancer². The median Karnofsky score in this study was 60%. Multiple regression analysis showed significant associations between depression and fatigue and between anxiety and fatigue and nausea after correction for pain and illness severity.

Our data do not support the findings from these and other studies. There are some possible explanations for this discrepancy.

First, the screening instrument used may explain the results. We have used the HADS, which focuses on anhedonia and does not use any of the physical symptoms that are part of the DSM-criteria. In patients with cancer, the latter may confound diagnosis as these symptoms can result from cancer and are not indicative of depression. However, some of the studies among cancer patients have used instruments using such symptoms for diagnosing depression³² and may thus have over diagnosed depression.

Secondly, and probably more importantly, an existing association between a symptom and depression may disappear during the course of the illness, mood having progressively decreasing influence on symptom presence and intensity as death approaches. Many studies have been performed in earlier stages of disease and in outpatient settings, while our study focused on terminally ill inpatients.

Our results showed a striking difference in prevalence of anxiety and depression depending on the instruments used. The 37% prevalence of depression resulting from the question "Are you depressed?" is lower than the 56% prevalence as assessed by the HADS and slightly higher than the 20-28% prevalence found in other studies using the same question^{4,7,10,29}. Again, this may be due to patient selection. If the HADS is considered as the standard, the positive predictive value of the question (93%) is excellent, but the negative predictive value (65%) is inadequate. In other words, a patient answering 'Yes' to the question 'Are you depressed' is likely to have a high score with regard to prevalence. Lowering the on the HADS, but an answer of 'No' does not in any way exclude a high score on the HADS. For anxiety, the reverse was found. The 58% prevalence found with the single-item question was higher than the 34% prevalence based on the HADS. As far as we are aware, there are no data in the literature to compare this with. The positive predictive value (46%) of the question is inadequate, while the negative predictive value (82%) is acceptable.

Both for anxiety and depression, the ESAS items took an intermediate position cut-off value decreased the positive predictive value for anxiety, while the negative predictive value remained about the same. For depression, the positive predictive value remained the same, while the negative predictive value increased. Comparing these results to the study of Vignaroli²⁶ it should be noted that we used a cut-off of 5 instead of 4, which resulted in much higher positive predictive values. The optimal cut-off value remains to be determined.

In conclusion, in a sample of terminally ill hospitalized cancer patients we found high levels of anxiety and depression (as screened by means of the HADS) but no relationship with the presence of physical symptoms and only a limited relationship with symptom intensity. It is likely that such a relationship exists in earlier stages of disease, but disappears in the course of the illness supporting the concept of a common final clinical pathway in patients with advanced cancer²¹. Systematic screening for anxiety and depression is clinically relevant in advanced cancer patients admitted for symptom control. What the best screening instrument is, remains to be established³³.

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In palliative cancer care symptoms mean everything

Chapter 5

Multidimensional fatigue and its correlates in hospitalized advanced cancer patients

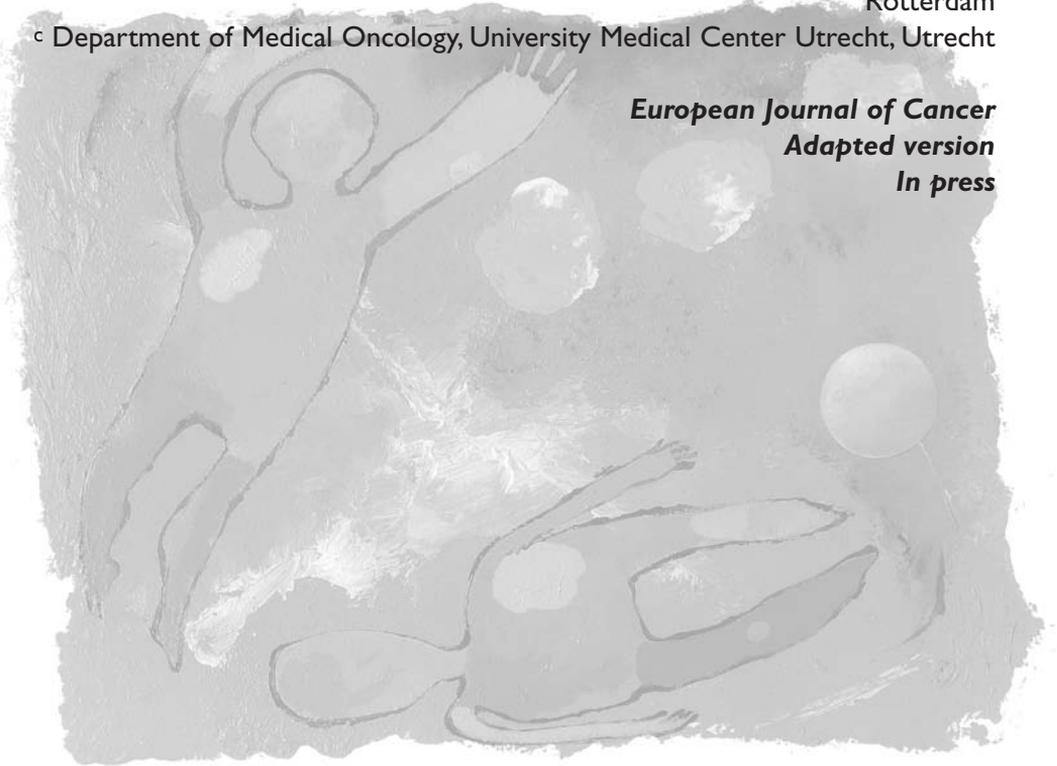
Michael Echteld^{a,b}
Saskia Teunissen^c
Jan Passchier^b
Susanne Claessena,
Ronald de Wita
Karin van der Rijta

^a Department of Medical Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam

^b Department of Medical Psychology and Psychotherapy, Erasmus Medical Center, Rotterdam

^c Department of Medical Oncology, University Medical Center Utrecht, Utrecht

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In palliative cancer care symptoms mean everything

Abstract

Purpose

Because multidimensional fatigue is seldom investigated in hospitalized advanced cancer patients, we determined fatigue levels and correlates with relevant medical and psychological variables within different fatigue dimensions. It was hypothesized that different fatigue dimensions have different levels and correlates.

Patients and Methods

100 advanced cancer patients admitted for symptom control were included. General Fatigue (GF), Physical Fatigue (PF), Reduced Activity (RA), Reduced Motivation (RM), and Mental Fatigue (MF) were measured with the Multidimensional Fatigue Inventory. Investigated correlates were tumor load, prior anti tumor treatment, medication use, hemoglobin levels, serum biochemical variables, physical symptoms (measured with the Organization for Research and Treatment of Cancer QLQ C-30), and mood (measured with the Hospital Anxiety and Depression Scale).

Results

Median GF, PF and RA scores were close to the maximum score of the scales. Median RM and MF scores were moderate and differed significantly from the GF, PF and RA scores. Multiple regression analyses showed that symptoms and mood correlated with all fatigue dimensions. Opioid and anticonvulsant use, ALAT and hemoglobin levels, and previous immunotherapy were other correlates of fatigue dimensions. The correlates differed across fatigue dimensions. Percentages explained variance were no greater than moderate to fair.

Conclusion

Hospitalized advanced cancer patients differ in fatigue levels depending on the fatigue dimension and each fatigue dimension has different correlates. Symptoms not often identified as correlates of fatigue are important correlates of fatigue, such as lack of appetite, nausea, and vomiting. The results confirm the advantages of multidimensional fatigue conceptualization.

Introduction

Levels of five fatigue dimensions and a prospective analysis of correlates of fatigue in hospitalized advanced cancer patients are presented. Knowledge of potential determinants of fatigue may help physicians make informed treatment decisions. Management of fatigue in advanced cancer patients is important because fatigue is an essential determinant of quality of life, health status, and symptom burden¹⁻⁵. Fatigue is named by the patients as the most important factor influencing daily functioning⁶. The importance of fatigue is further underlined by its high prevalence: fatigue in excess of the 95th percentile of a healthy control group was present in 78 percent of cancer patients receiving specialist inpatient palliative care³. Multidimensional conceptualization of fatigue is widely accepted⁷⁻⁹; fatigue manifests itself in multiple, reasonably independent¹⁰ dimensions, e.g. physical, cognitive, motivational, or in terms of reduced activities. Nevertheless, fatigue is seldom investigated as a multidimensional construct in hospitalized advanced cancer patients.

In this prospective study, fatigue is conceptualized as a multidimensional construct. Differences in levels and distributions of fatigue dimensions were determined, and relationships between a broad range of likely medical and psychological correlates and the fatigue dimensions were explored. It was hypothesized that due to their relative independence, the different fatigue dimensions have different levels and correlates.

Patients and Methods

Patient Population

One hundred patients with advanced cancer admitted to the palliative care unit (PCU) of the Erasmus MC Daniel den Hoed Cancer Center were included. All patients were admitted for symptom control. Of the 263 patients who were asked to participate in the study, 100 did not fulfill the inclusion criteria: 62 patients appeared to have received immunotherapy, or chemotherapy within 4 weeks prior to PCU admission, 34 patients could not be interviewed due to cognitive impairment, 4 patients had life expectancies of less than 14 days, and 2 patients had insufficient command of the Dutch language. Of the remaining patients, 33 patients refused participation, and 28 patients could not be included due to other reasons.

Data Collection

Data were collected within 48 hours after admission by trained oncology nurses. Socio-demographic data and data on anti-tumor therapies and medication use were collected from the medical records. All other data were obtained by interview using the instruments listed below.

The Multidimensional Fatigue Inventory (MFI) was used¹⁰ for the measurement of multidimensional fatigue. The MFI consists of 20 statements to which patients are requested to indicate agreement on a five-point scale. The MFI measures five dimensions of fatigue: General Fatigue (GF), Physical Fatigue (PF), Reduced Activity (RA), Reduced Motivation (RM), and Mental Fatigue (MF). Scores range from 4-20 (higher values indicate more fatigue). The Hospital Anxiety and Depression Scale¹¹ (HADS), a 14-item questionnaire with four-point rating scales, was used to measure anxiety and depressed mood. Scores range from 0-20 (higher scores denote more distress). Physical symptoms were measured with the symptom subscale of the European Organization for Research and Treatment of Cancer QLQ C-30¹². Patients indicate on four-point rating scales to what extent they suffer from dyspnea, pain, sleeping difficulties, lack of appetite, nausea, vomiting, and diarrhea (range 1-4; higher values indicate higher symptom levels). Fatigue-related items (need for rest, weakness, fatigue) were not used in the analyses. Data on itch and hiccups were additionally collected. Functional status was measured with the Palliative Performance Scale (PPS¹³) with which staff members assigned a performance percentage score (higher percentages indicate better performance). Tumor load was defined as the number of organs involved. Prior anti-tumor treatment variables were the number of chemotherapy lines, one or more instances of prior radiotherapy, and one or more instances of prior immunotherapy. Hemoglobin levels and serum biochemical variables were obtained through blood samples.

Statistical Analysis

Differences between fatigue dimensions were tested with Friedman's Chi-square test. Initial bivariate relationships were tested with Pearson correlations, One-way analyses of variance and Student's t-tests. When the p-values of these relationships with the fatigue dimensions were $\leq .10$, the correlates were entered into multiple regression analyses. The backward elimination method for entering correlates into the regression equation (probability of $F \geq .10$) was used. P-values of the regression analyses' t statistics of $\leq .05$ were considered significant. Analyses were performed using SPSS for Windows version 13.0.

Results

Patient inclusion

Patient characteristics, survival, and prior anti-tumor treatment are presented in Table I. The median number of symptoms was high, and more than half of the patients had considerable functional limitations.

Table 1. Patient characteristics, survival, prior anti-tumor treatment, and distributions of diagnoses, metastases, functional status, symptoms, and fatigue dimensions

	N	%	Median (range)
Age			57.5 (29-78)
<i>Gender</i>			
Male	46	46	63.0 (5-911)
Female	54	54	
Survival (days)			
<i>Treatment before inclusion</i>			
Chemotherapy	64	64	
Radiotherapy	72	72	
Immunotherapy	7	7	
<i>Primary cancer site</i>			
Breast	25	25	
Gastrointestinal	17	17	
Lung and mesothelioma	12	12	
Urogenital	12	12	
Head and neck	5	5	
Other	22	22	
<i>Tumor localizations</i>			
Bone	46	46	2.0 (1- 8)
Lymph nodes	43	43	
Lung	40	40	
Liver	25	25	
Pleura	15	15	
Intra-abdominal	8	8	
Brain	7	7	
Skin	7	7	
Other	15	15	
Total number of organs involved			
<i>Symptoms and functional status</i>			
Symptom count with intensity > 0*			8.0 (2-12)
Functional status (Palliative Performance Scale)			60.0 (30-90)
<i>Fatigue dimensions</i>			
General Fatigue (GF)			18.0 (6-20)
Physical Fatigue (PF)			19.0 (9-20)
Reduced Activity (RA)			18.0 (5-20)
Reduced Motivation (RM)			14.0 (4-20)
Mental Fatigue (MF)			12.0 (4-20)

*Dyspnea, pain, need for rest, sleeping difficulties, weakness, lack of appetite, nausea, vomiting, diarrhea, fatigue (from the EORTC QLQ C-30), itch, hiccups

Distributions and correlates of fatigue dimensions

Median scores for GF and PF and RA were high (Table 1); scores 19-20 were found in 43%, 59%, and 48% of the patients respectively. Median scores for RM and MF were moderate and differed significantly from the GF, PF and RA scores (Friedman Chi-square=157.3; p<.01). RM and MF scores varied widely between the lowest and the highest possible score (4-20).

Table 2. Standardized regression weights, t-values, F-values, percentages explained variance and contributing independent variables in the last step of stepwise regression analyses (backward elimination method), for each fatigue dimension

Fatigue dimensions	Independent variables	Standardized regression weights (β)	t	p _i	F	Percentage explained variance (R ²)
General Fatigue (GF)	Lack of appetite	.25	2.71	<.01	7.25**	.38
	Depressed mood	.23	2.36	.02		
	Dyspnea	.18	2.00	.05		
	Opioid use	-.22	-2.51	.01		
	Hemoglobin levels	.18	1.98	.05		
Variables not in the equation [†] (bivariate correlations with GF): Nausea (.26*); anxiety (.25*); vomiting (.24*); diarrhea (.32**); itch (.18 [‡]); hiccups (.24*); anti-emetic use (.20*); albumin levels (.23*); tumor load (.15 [‡])						
Physical Fatigue (PF)	Dyspnea	.30	3.27	<.01	7.84**	.31
	Nausea	.20	2.14	.04		
	Anticonvulsant use	-.25	-2.74	<.01		
	ALAT levels	-.34	-3.78	<.01		
Variables not in the equation [†] (bivariate correlations with PF): Depressed mood (.27**); appetite (.24*); hiccups (.19 [‡]); diarrhea (.17 [‡]); albumin levels (.25*); hemoglobin levels (.21*)						
Reduced Activity (RA)	Nausea	.49	3.14	<.01	7.05**	.19
	Depressed mood	.26	2.60	.01		
Variables not in the equation [†] (bivariate correlations with RA): Appetite (.20 [‡]); diarrhea (.18 [‡]); corticosteroids levels (-.29**); hemoglobin levels (.23*); albumin levels (.17 [‡]); ALAT levels (-.17 [‡])						
Reduced Motivation (RM)	Depressed mood	.51	6.08	<.01	17.75**	.45
	Vomiting	.23	2.76	<.01		
	Previous immunotherapy	-.26	-3.15	<.01		
Variables not in the equation [†] (bivariate correlations with RM): Appetite (.38**); anxiety (.32**); nausea (.32**); diarrhea (.21*); opioid use (-.17 [‡]); albumin levels (.26**)						
Mental Fatigue (MF)	Anxiety	.37	3.94	<.01	12.85**	.23
	Pain	.29	3.11	<.01		
Variables not in the equation [†] (correlations with MF): Depressed mood (.27**); dyspnea (-.21*); appetite (.21*); nausea (.21*); vomiting (.19 [‡]); hemoglobin levels (.22*); creatinin levels (-.17 [‡])						

[‡]p<.10; *p<.05; **p<.01 [†]Variable entered into the regression equation, but not selected (probability of F<.10)

Results of the multiple regression analyses are shown in Table 2. The results show that symptoms, including the psychosocial factors depressed mood and anxiety, correlated with all fatigue dimensions. Opioid and anticonvulsant use, ALAT and hemoglobin levels, and previous immunotherapy were other correlates of one of the fatigue dimensions. The sets of correlates were unique for each dimension, and the numbers of correlates differed. The amounts of explained variance varied from moderate to fair. In addition, a number of correlates were uniquely related to one fatigue dimension (lack of appetite, hemoglobin levels, ALAT levels, anticonvulsant use, previous immunotherapy, anxiety, pain). PF was the only dimension without psychological correlates. Three correlates either had strong relationships with fatigue dimensions and/or were present as correlates in two or three dimensions: depressed mood (3), dyspnea (2), and nausea (2).

Discussion

The patients in this study experienced severe fatigue as measured by the dimensions of GF, PF, and RA; RM and MF levels were lower. Symptoms were related to all fatigue dimensions; especially depressed mood, dyspnea, and nausea had strong correlations with many fatigue dimensions. The bivariate correlations showed that many factors were correlated with fatigue, but were not *independently* related to fatigue, as shown by the multiple regression analyses. As hypothesized, fatigue distributions and correlates were different for each fatigue dimension, which suggest that multidimensional conceptualization of fatigue is justified. An important observation is that GF does not seem to be a 'sum' of all fatigue dimensions – it had correlates (opioid use and hemoglobin level) that did not relate to other dimensions. It is also notable that percentages explained variance was no greater than moderate to fair (19-45%): in this study, fatigue seems to present itself as a quality partly independent from symptom and treatment characteristics. However, several tumor-related variables, e.g. cytokines, were not measured.

The results are congruent with other studies that identified psychological distress, pain, dyspnea, and hemoglobin level as correlates of fatigue^{3,14-16}. However, this study shows that these factors relate to different dimensions of fatigue. In addition, symptoms not often identified as correlates of fatigue in the literature may be important, such as lack of appetite, nausea, and vomiting. It is notable that sleeping difficulties are not correlated with any of the fatigue dimensions. Other not often identified correlates are ALAT levels and the treatment modalities anticonvulsant use, opioid use, and previous immunotherapy. All treatment modalities had negative relationships with fatigue, which means that the treatments were associated with less fatigue. With regard to ALAT and immuno therapy, the reverse relationships were expected. The relationships between opioid and anticonvulsant use and fatigue dimensions may be mediated by pain levels—their use in this population may be associated with better pain control, which in turn may lead to less fatigue. Only seven patients received previous immunotherapy, which means that the relationship should be interpreted with caution.

Generalization of the results to other advanced cancer populations may not be justified because patients admitted to the PCU, by definition, have high symptom loads. Not only the fatigue dimensions GF, PF and RA were skewed, but also many of the correlates, which indicate that other correlates may be present in different populations. Furthermore, this study does not allow for causal statements to be made, causal relationships can only be explored in longitudinal studies. Suggestions for future research include longitudinal studies in different advanced cancer populations in order to (a) investigate whether different correlates of multidimensional fati-

gue are present in different populations, and (b) to explore causal relationships between predictors and fatigue dimensions. Intervention studies on better symptom control with fatigue as an outcome should also give clues about causality. Lastly, it would be particularly relevant for palliative care research to investigate whether the different fatigue dimensions predict quality of life differently.

In conclusion, most patients experienced extreme physical fatigue, but motivation and mental functioning seemed to be less impaired. This suggests that these patients are relatively capable and willing to perform mentally taxing tasks, but unable to carry out physically demanding roles. The results thus clearly show the advantages of multidimensional fatigue conceptualization: patients may differ in fatigue levels depending on the fatigue dimension, and each fatigue dimension has different correlates. These findings are a new and important step in the process of understanding fatigue better in advanced cancer.

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In palliative cancer care symptoms mean everything

Chapter 6

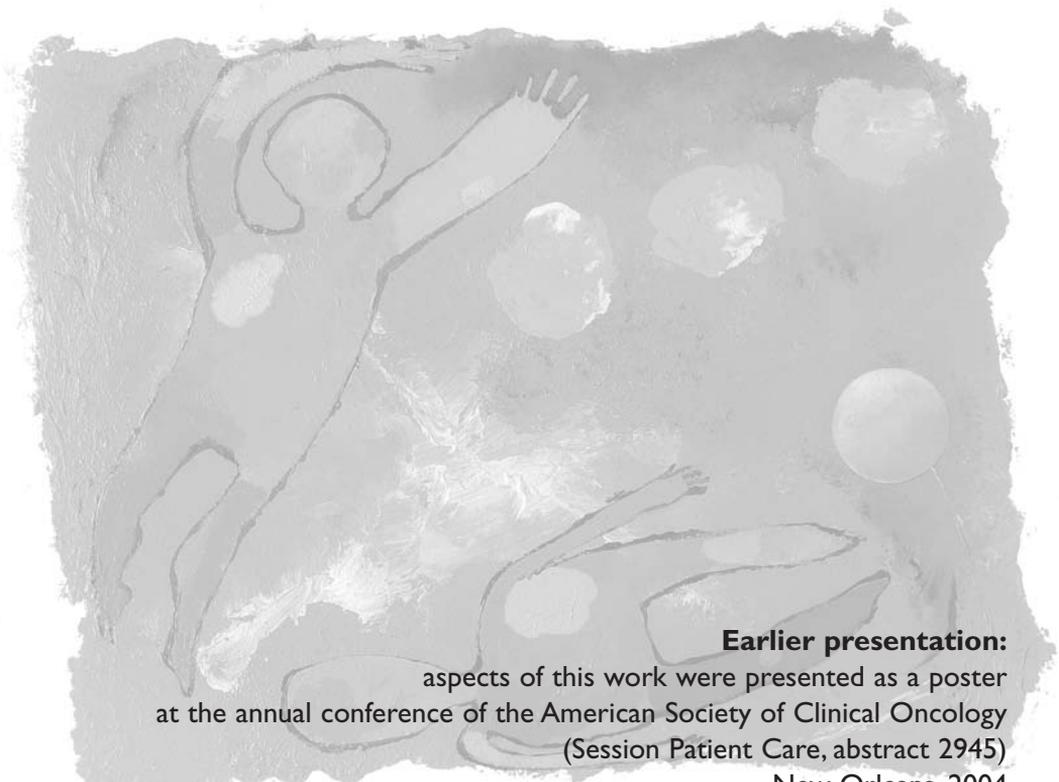
Prognostic significance of symptoms of hospitalized advanced cancer patients

Saskia Teunissen¹
Alexander de Graeff¹
Hanneke de Haes²
Emile Voest¹

¹ Department of Medical Oncology, University Medical Center Utrecht, Utrecht

² Department of Medical Psychology, Academic Medical Center, Amsterdam

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In palliative cancer care symptoms mean everything

Abstract

Purpose

To assess the prognostic value of symptoms in hospitalized advanced cancer patients.

Patients and methods

A prospective analysis was performed of 181 hospitalized patients referred to a Palliative Care Team. A comprehensive symptom questionnaire, functional status, estimated life expectancy and survival were assessed. Using a Cox regression model, a predictive survival model was built.

Results

Median survival: 53 days. Median number of symptoms: 4; 20 symptoms occurred in >10%. Multivariate analysis showed nausea, dysphagia, dyspnea, confusion and absence of depressed mood as independent prognostic factors for survival ($p < 0.05$) with relative risks of dying of 1.96, 1.81, 1.79, 2.35 and 1.79, respectively. Patients with 2, 3 or 4 of these factors at the same time had a relative risk of dying of 2.7, 2.1 and 9.0, respectively.

Conclusion

A cluster of factors comprising nausea, dysphagia, dyspnea, confusion and absence of depressed mood may be used to accurately predict survival in hospitalized advanced cancer patients.

Introduction

“How long do I still have?” is one of the most challenging questions that oncologists have to address when dealing with a patient with advanced cancer. In daily practice this question is answered by estimating the prognosis. Clinical predictions are traditionally based on performance status and symptom prevalence¹⁻³. The physician estimated prognosis also depends on the experience of the clinician who is confronted with the question⁴.

The accuracy of the estimated survival and actual survival has been studied by several groups^{5,6,7,8}. Between 1995 and 2005 four systematic reviews of physicians' survival predictions were published⁹⁻¹². The complexity of the process of estimating survival is reflected in the frequently reported overestimation of expected survival by medical doctors^{1-6,13,14,15} and sometimes in the underestimation^{3,11} thereof. Although performance status together with symptoms of the “the terminal cancer syndrome”¹⁶ are recommended to guide physicians in predicting survival of patients with advanced disease, the complexity of the disease in the final stages of life is illustrated by the variance of symptoms found to be indicative of survival.

A large number of studies have shown a high prevalence of debilitating symptoms in patients with advanced disease^{13,16-24}. To develop a symptom-based assessment of survival, functional status and frequently occurring symptoms were correlated with survival in several studies^{1,3,6-8,13-16,25-29}. Poor performance status (Karnofsky Performance Scale) was found to be the most significant clinical indicator in these studies^{1,6-8,13,14,16,25-27}. Furthermore, a small number of specific symptoms such as shortness of breath in rest^{7,14,16,27,28,30}, dysphagia^{13,16}, dry mouth¹⁶, appetite loss^{14,16,27}, anorexia and weight loss^{7,14,16,24,25,28,29}, fatigue/asthenia^{3,14} and cognitive impairment²⁵ were recognized as independent predictors of survival. Reuben et al¹⁶ identified the ‘terminal cancer syndrome’, including functional status (KPS <50), dry mouth, shortness of breath, problems with eating, recent weight loss and troubles with swallowing. Vigano et al¹⁰ confirmed the terminal cancer syndrome theory in their systematic review of survival prediction.

The studies that have addressed the relationship between symptoms and survival are mainly based on samples of patients in different care settings^{6,16,20,22,26} or in either a hospice or a home care setting^{3,7,8}. The population of patients admitted to the hospital for symptom management cannot be compared with patients admitted to a hospice. Hospitalized patients are a heterogeneous group, ranging from ambulatory and independent to moribund and bed-bound, with a variety of distressing symptoms^{13,17,18,20,21}. The prognostic significance of symptoms with regard to survival in the hospital population has not been systematically studied nor is there a predictive model for survival that has been validated in the setting of an inpatient oncology

ward. There is a clear need to gain additional insight into survival of patients with advanced cancer admitted for symptom management. Such insight may lead to i) better clinical estimation of survival during admission for symptom control, ii) prevention of unnecessary treatment, iii) timely initiation of specific logistic supportive care measures at home; iv) better use of specific resources such as hospice care. In the Netherlands, for example, only patients with an estimated survival of less than 3 months may be admitted to a hospice.

The aim of this study is to investigate whether the prognosis of hospitalized advanced cancer patients can be estimated correctly on the basis of their symptoms.

Patients and methods

Patients

A prospective analysis was performed on patients with advanced cancer admitted to several departments of the University Medical Centre Utrecht, who were referred to the Palliative Care Team (PCT) of the Department of Medical Oncology for symptom control. The PCT consists of a medical oncologist, an anaesthesiologist, a psychiatrist and two clinical nurse specialists. After a thorough clinical assessment the PCT gave advice to the treating clinician about symptom management.

Between October 1998 and March 2004 203 patients were referred to the PCT. Patients were interviewed by the clinical nurse specialist in order to get a comprehensive problem assessment. For 22 patients the assessment was incomplete because of cognitive impairment, mental or physical exhaustion, or inability to understand the Dutch language, leaving 181 patients with a full assessment.

Measures

Functional status was measured by the Karnofsky Performance Status (KPS)³². Socio-demographic and medical data were obtained from the medical and nursing files.

Symptoms were primarily assessed as a dichotomous variable (absent or present) during a semi-structured interview by the clinical nurse specialist, using a checklist³¹ derived from a nationally developed symptom registration instrument by the Dutch Centres for Development of Palliative Care¹⁸. The list included 49 of the most frequently occurring standardized symptoms of previous prevalence studies^{13,16,19,20,22}, with the possibility to add volunteered symptoms.

Analysis

Analysis of prediction of survival focused on two main questions: 1) the role of symptoms as an independent prognostic factor for death, and 2) clustering of pro-

ven prognostic symptoms in order to improve prognostication. Length of survival is defined as the duration between the date of the first consultation of the PCT and the date of the patient's death (event) or the last follow-up (censored) for those who were still alive at the time of data analysis (August 2004). The survival status and the date of death were obtained from the hospital registry or if unavailable by telephone calls to general practitioners.

Variables examined

We analyzed the relation between socio-demographic variables, diagnosis and performance status (KPS) on survival. Of the symptoms assessed we analyzed only those occurring in 10% or more of the cases (minimum of 18 events).

Statistical considerations

Survival and probabilities were determined using the Cox proportional hazard model; survival curves were drawn at the average of other co-variables instead of the one-to-one comparison of the Kaplan Meier technique. Differences between survival curves were assessed using the log-rank test. Statistical significance was considered if $p < 0.05$. After univariate analysis, all significant prognostic factors were entered into a multivariate Cox regression model to determine independent predictors of survival. The required validation of the prognostic factors was performed by a stepwise ('bootstrap') procedure: the same analysis was performed many times on a series of subsets from the same data set in order to evaluate the stability of the coefficients and the predictability of the model (based on the increment in the chi-square statistic)³³. Additional analysis with the log-rank test was done.

To study the effect of simultaneous symptoms on survival time, a multivariate regression model was fitted to the logarithms of the observed survival times. This was possible since nearly all of the patients had died at the time of the analysis and there were only three censored cases.

Statistical analysis was performed using Statistical Package for the Social Sciences version 12.0 (SPSS Inc., Chicago, IL).

Results

Patient characteristics

Patient characteristics and distribution of cancers by primary sites and metastases are summarized in Table I. Relatively few patients were treated with chemotherapy (19%) or radiotherapy (28%) during the last three months before their referral to the PCT. Only 12% of the patients had KPS scores of 70-80; almost half of the patients were severely disabled and bed bound (KPS <50).

Table 1. Patient characteristics (n=181)

	n (%)
Gender	
Male	80 (44%)
Age (years)	
Median (range)	58 years (18-91)
Primary cancer site	
Breast	25 (14%)
Gynaecological	21 (12%)
Gastrointestinal	35 (19%)
Head- and neck	21 (12%)
Lung	20 (11%)
Prostate	13 (7%)
Others	46 (25%)
Metastases	
Bone	81 (45%)
Lymph node	56 (31%)
Lung	35 (19%)
Liver	36 (20%)
Brain	20 (11%)
Viscera	29 (16%)
Other	27 (15%)
Unknown	5 (3%)
Karnofsky Performance Score	
10-20	8 (4%)
30-40	80 (44%)
50-60	72 (40%)
70-80	21 (12%)
90-100	-

At the moment of analysis, all except three patients were dead with a median survival of 53 days (range 1-1915). Most of the patients (43%) died within 1 month, 42% lived for 1-6 months and 15% of the patients lived longer than 6 months after the initial consultation.

Prognosis based on symptom prevalence

Symptom prevalence

The median number of symptoms per patient was 4 (range 1-8). We recorded 20 symptoms occurring in >10% of the patients (Table 2). Pain, asthenia, anorexia and anxiety were the most frequent symptoms, occurring in more than half of the patients. Almost all patients (88%) were in pain. Pain was differentiated into 11 sites of pain, with the highest incidence for backache (26%) and abdominal pain (22%). Forty-four percent of the patients had two or more different sites of pain at the moment of the initial visit with a maximum of 6 sites.

Table 2. Prevalence of symptoms occurring in >10% of patients

Symptom	Patients (%)
Pain ¹	160 (88%)
Asthenia	108 (60%)
Anorexia	101 (56%)
Anxiety	96 (53%)
Constipation	70 (39%)
Nausea	68 (38%)
Sleeplessness	65 (36%)
Dyspnea ²	54 (30%)
Depressed mood ³	49 (27%)
Drowsiness	49 (27%)
Vomiting	44 (24%)
Dry mouth	42 (23%)
Weight loss >10%	31 (17%)
Sore mouth	30 (17%)
Confusion ⁴	30 (17%)
Diarrhoea	28 (16%)
Paralysis	26 (14%)
Cognitive impairment	26 (14%)
Dysphagia	21 (12%)
Pressure ulcers	21 (12%)

* 20 symptoms out of a standardized list of 49

* median number of symptoms per patient 4 (range 1-8)

1. differentiation in 11 sites

2. in rest

3. answer to the question "are you depressed?"

4. single symptom, without other prodromes of the delirium syndrome at the moment of assessment

Table 3. Multivariate model: prognostic significance of symptoms, relative risk of dying

Symptom	Relative risk of dying	95% Confidence Interval	p-value
Nausea	1.960	1.328 – 2.892	0.001
Dysphagia	1.812	1.111 – 2.955	0.017
Dyspnea	1.795	1.274 – 2.531	0.001
Confusion	2.352	1.524 – 3.630	<0.001
Depressed mood	0.561	.385 - .817	0.003

Cox Regression coefficients with associated p-values and hazard rates

Cluster of five prognostic symptoms

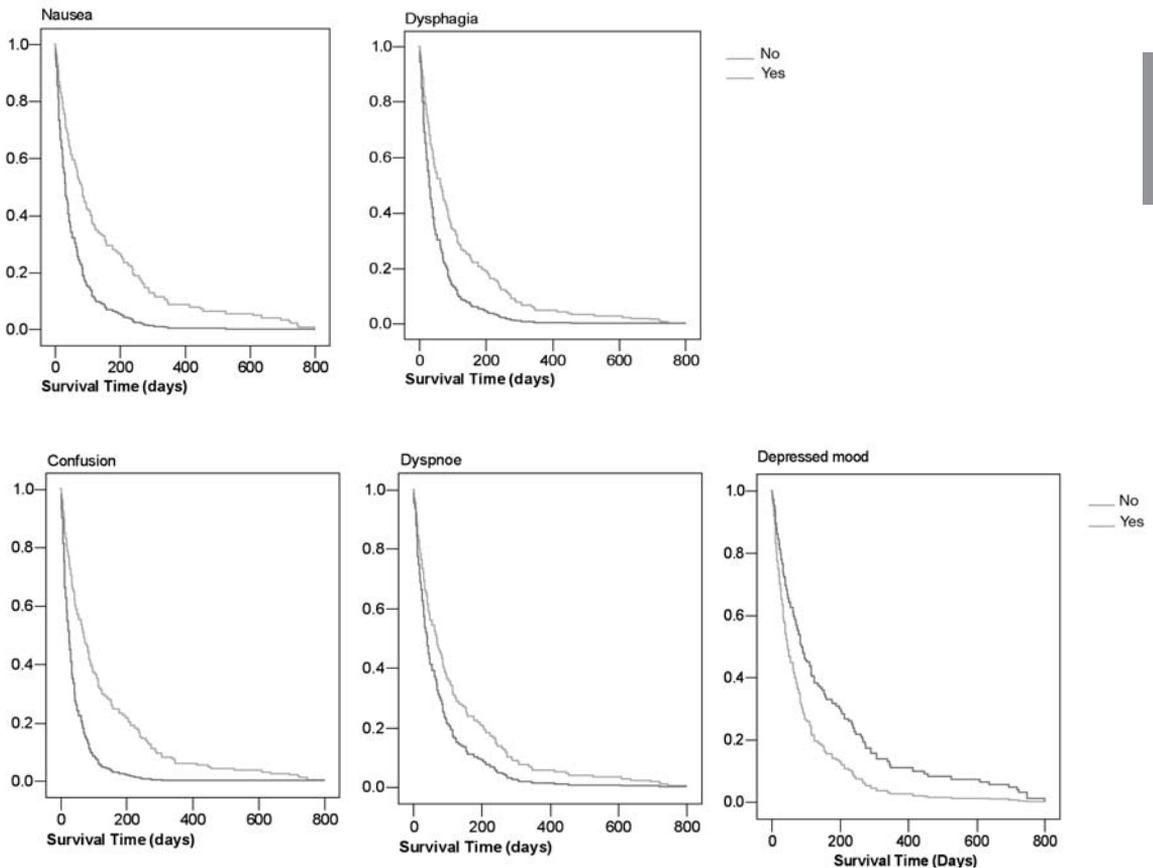
By univariate analysis 11 out of 49 symptoms were correlated with survival: headache, abdominal pain, anorexia, weight loss >10%, nausea, vomiting, dysphagia, dyspnea, drowsiness, confusion and depressed mood (p<0.05). In this analysis gastro-intestinal cancer was highly significant for poor survival (p<0.001); gender (p=0.114), age (p=0.076) and KPS (p=0.269) were not.

Multivariate analysis was performed after correcting for diagnosis, including all 20 symptoms occurring in more than 10% of the sample. After stepwise selection nau-

sea, dysphagia, dyspnoea, confusion and depressed mood were found to be independent prognostic factors for survival ($p < 0.05$) in the final proportional hazard regression model. The presence of nausea, dysphagia, dyspnea and confusion significantly increased the likelihood of dying with a relative risk of dying of 1.96, 1.81, 1.79 and 2.35 respectively (Table 3). In contrast, the presence of depressed mood significantly decreased the likelihood of dying with a relative risk of 0.56; in other words, the absence of a depressed mood was associated with a relative risk of dying of $1/0.56 = 1.79$. Figure 1 shows survival curves for patients with and without these symptoms. None of the patients in our study had more than 4 of these five prog-

Figure 1. Survival curves for each of the five significant symptoms

The survival curves for each of the symptoms are drawn at the mean values of the other symptoms. Since all symptoms are simultaneously used as covariates in the Cox regression model, the effects of these symptoms will differ from those tested for a symptom ignoring the influence of the other symptoms.



nostic factors (nausea, dysphagia, dyspnea, confusion and absence of depressed mood) at the same time; 34% reported only one of these factors.

From the multivariate regression model that was fitted to the logarithms of the observed survival, it appears that the survival time drastically decreases with increasing numbers of the above mentioned factors. All but one of the coefficients of this regression model are highly significant ($p < 0.01$). Patients with 2, 3 or 4 of these five factors simultaneously had an estimated risk of dying of respectively 2.7, 2.1 and 9.0 times higher than patients without any of these symptoms. Median survival was 122, 71, 36, 35 and 14 days for patients with 0, 1, 2, 3, and 4 of these factors respectively. The presence of 4 of the significant factors resulted in an 83% mortality rate at 1 month and a 100% mortality rate at 6 months, compared to a 1-month mortality of 20% and a 6-month mortality of 48% in patients without these factors. The Cox proportional hazard regression model fitted to the same data supports the above results (Table 4).

Table 4. Relative risk of dying based on the Cox proportional hazard model

Number of simultaneous factors*	Patients (%)	Regression Coefficients	Relative risk of dying	p-value
0	29 (15%)	-	1	-
1	62 (34%)	-0.388	1.47	0.111
2	54 (30%)	-1.002	2.73	< 0.001
3	32 (18%)	-0.752	2.12	0.006
4	6 (3%)	-2.202	9.01	< 0.001

*Nausea, dysphagia, dyspnea, confusion and absence of depressed mood.

Discussion

We conducted this prospective study to support physicians in predicting survival of hospitalized patients with advanced cancer on the basis of comprehensive symptom assessment. We have identified five symptoms which independently predicted survival in advanced cancer patients who were admitted to a university medical centre and referred to a palliative care team for symptom control. The predictive value of nausea, dysphagia, dyspnoea, confusion and absence of depressed mood could be enhanced by clustering these factors. The presence of several of these factors simultaneously indicated a significantly decreased survival.

The majority of studies have reported that some symptoms and performance status may have a predictive value^{1,6-14,16,25-27}. The prognostic value of nausea, dysphagia, dyspnea and confusion in hospitalized patients is consistent with the findings of others⁹⁻¹². Clustering of the five significant factors increased their prognostic value.

We fail to support the findings of others that have reported a correlation between gender, age, anorexia, weight loss, asthenia and survival⁹⁻¹². An explanation for this discrepancy may be the differences in i) patient population, e.g. home care versus hospice versus hospital; differences in stage of disease and life expectancy; ii) the way data were collected, for example different measures, prospective versus retrospective studies and convenience sampling versus selection based on difficulties in symptom management, iii) single center versus multicenter, data collection by one or two researchers versus several research teams and iv) statistical analysis. Criticism on previous studies included the validation process of the prognostic significance of factors. In order to evaluate the stability and predictive ability of our model we used the 'bootstrap' procedure in which the same analysis was performed many times on a series of subsets from the same data as suggested in the systematic review of Chow et al¹¹.

Our finding that confusion as a single factor without other clinical symptoms of delirium, and depressed mood have prognostic significance was not reported earlier in the hospital setting, although cognitive impairment has been recognised as a prognostic factor²⁵. We hypothesize that confusion may be interpreted as a prodrome for delirium which has been reported as an independent factor for survival in (elderly) patients^{27,34}.

Surprisingly, this study suggests that patients in a depressed mood have a lower risk of dying than patients not in a depressed mood (relative risk of dying 0.56). It is important to realize that this refers to the question "Are you depressed?"^{35,36} and does not reflect a psychiatric assessment of depression. It is intriguing to speculate on an explanation for this finding.

The majority of studies in this area show a relationship between depression or depressed mood and cancer progression³⁷. It should be noted that almost all studies used questionnaires to assess depression and that psychiatric (DSM-) criteria were almost never applied. These associations may merely reflect underlying physiologic processes mimicking symptoms of depression but that are markers for tumour burden or cancer progression. We assessed depressed mood by a simple question and did not take into account any symptoms for this diagnosis that have been caused by the disease. This may explain why we failed to find a decreased survival in patients with a depressed mood, but still does not explain their increased survival. There are some possible explanations. First, it might be possible that patients with depressed mood in an advanced disease stage are sooner referred to palliative care consultants. If so, earlier referral may lead to apparent longer survival (lead time bias). Secondly, earlier referral could also result in more adequate symptom management in particular of the prognostic symptoms we found in this

study. However it must be noted that there is no evidence that better symptom control results in prolonged survival. Thirdly, it might be argued that better psychosocial support (both professional and non-professional) of patients with depressed mood might result in better survival. However, the literature on the result of psychosocial treatment of depression on survival is highly controversial and intuitively, it does not seem very likely that any form of psychosocial support of intervention would have an effect on survival in this population with a very poor prognosis. Thus, the positive correlation between depressed mood and survival in this study remains largely unexplained.

Two limitations of this study deserve some comments. First, we assessed symptoms rather crudely as a dichotomous variable (absent or present). This has the practical advantage that it can readily be used in clinical practice. Whether the prognostic value of our symptom cluster can be improved by using questionnaires completed by the patient and by symptom intensity scores, should be a matter of further study. Second, the present findings are based on a single comprehensive symptom assessment at the first consultation of a PCT. The first consultation was defined by the clinician without subcategorizing the patient according to the stage of his advanced disease. In a certain way, our sample of hospitalized advanced cancer patients is heterogeneous as well. However, for each patient in our sample the consultation of the Palliative Care Team could be seen as the start of a new treatment cycle of comprehensive symptom management. Further study is needed to increase our insight into the development of the prognostic factors over time in subcategories, for example along functional status, during interventions and symptom management. Application of the symptom cluster might provide a new strategy for initial assessment, daily monitoring and clinical decision-making during the entire period of admission and specific information and advice to the general practitioner for affiliation afterwards at home.

In conclusion, the cluster of five factors we found in this study may contribute to a more accurate prediction of survival in advanced cancer patients admitted to the hospital. This will aid physicians to develop an individualized program for symptom control in order to prevent unnecessary treatment and transfers between settings of care. This could result in a realistic planning of professional and logistic support and improve the remaining time together for the patient and his nearest.

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In palliative cancer care symptoms mean everything

PART II

SYMPTOM MANAGEMENT in PRACTICE



In palliative cancer care symptoms mean everything

Chapter 7

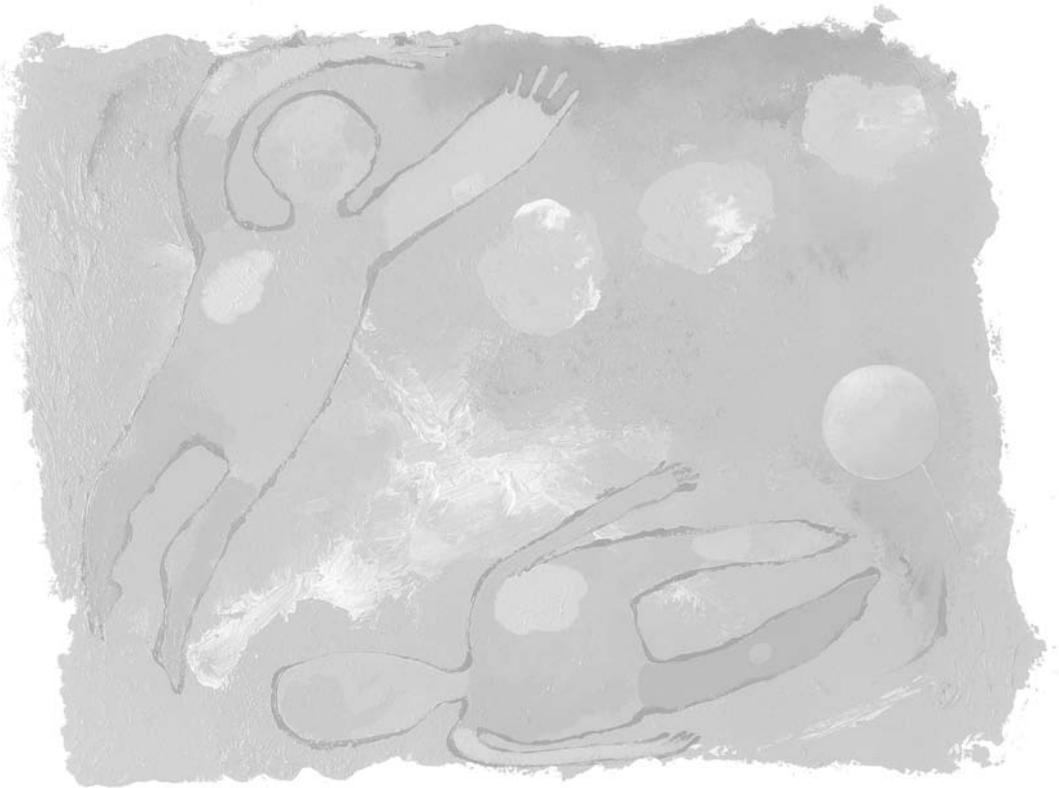
Communication in palliative care, a review of recent literature

Hanneke de Haes¹
Saskia Teunissen²

¹ Department of Medical Psychology, Academic Medical Center, Amsterdam

² Department of Medical Oncology, University Medical Center Utrecht, Utrecht

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In palliative cancer care symptoms mean everything

Abstract

Purpose

The quality of communication with patients, kin and team members, is an extremely important element in palliative cancer care. The current paper reviews the literature thereabout as published in 2004.

Results

1) Trust was found to be a major factor for relationship building. 2) Information gathered by patient self-report is the method of choice given improved insight into symptom prevalence, duration, frequency and interference. Cultural factors in information giving, the optimal process and content, and the difficulty of conveying hope were addressed. 3) Decision-making in palliative care requires a complex integration of conceptual knowledge, ethical and legal implications and communication skills. 4) Aspects of manageability were explored. 5) Though health care providers need to communicate about emotions, the existential distress of cancer patients and carers often goes overlooked in the last phases of life.

Conclusion

Other themes emerged: 1) education of health care providers is needed, 2) the need to care for carers is stressed, and 3) interdisciplinary communication gained some attention.

Little attention was given to the growing population of elderly patients. Also, observer based studies are unfortunately scarce making the actual practice of palliative communication unseen. Finally, few studies report the (cost-) effectiveness of palliative care interventions even though such studies may enhance palliative care and convince policy makers of the need to support such care. More empirical work is needed to further improve the level of quality needed to ensure a good remaining lifetime for those cancer patients who cannot be cured.

Introduction

The concept palliative care sometimes refers to all non-curative oncological treatments and sometimes to treatments addressing cancer patients' quality of life in later disease stages. It may therefore cause confusion¹. Still, one generally agrees that it covers cancer care that focuses on the relief of suffering rather than survival benefit². Palliative care may relate to, first, the phase of diagnosis of disease recurrence and life prolonging rather than curative treatment, second, the phase of treatment directed at symptom control only, and third, the terminal phase and end-of-life care. Thus it may cover a wide range of care related activities over a long period of time.

Besides symptom control, different elements of palliative care are currently distinguished, such as patient management, communication, multidisciplinary teamwork as well as support for the family^{3,4}. The encouragement of understanding of patients, the development of clear treatment goals, delivery of care consistent with patient and family goals as well as the promotion of quality of life have been defined as components of optimal end-of-life care^{5,6}. A prolonged process of nearing death faced by older patients was acknowledged in an alternative model for palliative care for the elderly: the TLC model⁷. The TLC model refers to a Timely, Team Oriented, Longitudinal, Collaborative and Comprehensive approach.

It is, given these descriptions, evident that communication is an important element in palliative care. The quality of communication with patients, kin and team members was indeed found to be fundamental to the quality of care for the dying by medical specialists⁸. At the same time, ineffective communication was found to be one of the major barriers to optimal end-of-life care at the health care provider level^{5,7}.

The current paper reviews the literature regarding the role of communication in palliative cancer care as published in 2004. Given this literature, ample attention is devoted to end-of-life care. We depart from the framework we currently hold to distinguish different communicative goals in medicine⁹. Such a framework is helpful in categorizing the relevant domains of communication. Also, reviewing from such a perspective automatically uncovers which areas have received little or no attention in the literature. Thus, in the present paper we will address the following elements of communication: relationship building, information exchange, decision-making, giving advice, and handling emotions. We will conclude by discussing some more general themes on the basis of the literature described.

Relationship building

A good patient-physician relationship is a prerequisite for effective communication. When patients have to provide and understand information, make complicated

decisions in accordance with their personal values and have to be able to accept advice, trust is a major factor¹⁰. Obviously, this is especially important in the palliative treatment phase when cure is no longer at stake and the patients' usual life conditions are continuously threatened.

Attention to trust was scarce in the palliative care literature reviewed but some findings can be mentioned. Positive relationships of clinicians with patients and families were found to be built on growing trust and produce concordant goals in patient care⁸. Hurwitz and colleagues¹¹ provide examples of how an honest dialogue can be pursued when facing the enormous challenges of caring for children with cancer at the end of life and their families. Being 'respectful, competent, reliable, and showing frankness' were the most important values in the relation with the treating physician for terminally ill patients at home¹².

Negative relationships, on the other hand, were found to be associated with distrust, confrontation, and 'power struggles'. Patients may feel abandoned and, in fact, 'raise the specter of litigation' against the doctor who provided care¹³. Family anger and hostility were also found to generate strong emotions in clinicians⁸.

Information exchange

Information gathering

Within the context of palliative care, the health care team needs to gather information about the patient: a) to establish the occurrence and severity of symptoms and distress and b) to understand what decision alternatives would be wise given the patient's condition and values and c) what advice could be manageable. Because these issues are largely subjective, patient self-reporting is the method of choice. For example, in a review about pain in lung cancer patients, it was indeed found that the prevalence was higher when lung cancer patients were asked systematically than when pain was reported in case notes¹⁴. Using patient completed measures, moreover, was found to yield extra information regarding symptom duration, frequency and interference¹⁴.

The development and validation of several instruments meant to enhance systematic assessment of symptoms and care needs were described, such as: the 'Palliative care quality of life instrument'⁶, the 'Problems and Needs in Palliative Care questionnaire'¹⁵ and a structured problem list¹⁶. Specific methods for the establishment of cognitive failure in palliative care were reviewed¹⁷ and the regular assessment of spiritual needs in supportive and palliative care was advocated¹⁸. For comprehensive assessment in elderly people in assisted living facilities, validated instruments drawn from palliative and geriatric care were combined⁷.

Information giving

Information is given to patients for several reasons: it is the basis for decision-making, it reduces uncertainty and it supports coping efforts. What information is to be conveyed has been studied extensively. Cultural factors turned out to play a role: Koreans, for example, were less likely to want to be informed. Such avoidant strategies may hinder understanding and the informed consent process, though¹⁹. Kirk and colleagues²⁰ investigated qualitatively the optimal process as well as content in information giving in palliative care. Process related suggestions include playing straight, being clear, showing one cares, giving time, pacing and not abandoning the patient. Essential content related areas include prognosis and the provision of hope.

The difficulty of conveying hope and, at the same time, being straight is addressed in several papers^{21,22,23}. Many clinicians may believe that communication a bad prognosis would destroy hope. Illusions may indeed contribute to the reshaping of information to one's own needs and may help to maintain cognitive and affective control²². Still, redirecting patients and family members towards other, achievable goals can be worthwhile in helping to seek realistic goals and pursue alternative methods of care²³. How to deliver bad news and still maintain hope and a good relationship involves a well thought-out process^{24,7}. It was suggested that open communication, attention to cues or symbols and to the basic life assumptions of patient and family as well as their prior understanding of the disease process should be involved²⁵.

Few studies have directly investigated the actual information giving process. When patients had to decide about palliative chemotherapy, medical oncologists were found to explain the absence of cure in most cases but the disease course, symptoms and prognosis in only 53-35 % of patients. The alternative, watchful waiting or supportive care, was explained in only a quart of the relevant consultations. Often clinicians would only say the alternative was to 'do nothing'²⁶. Retrospectively, patients and family were found to be distressed when physicians communicated about the ending of anticancer treatment and said they could 'do nothing'²¹.

The effectiveness of interventions was seldom investigated but Jack and colleagues²⁷ found that a hospital based palliative care team was indeed more effective than standard care in improving cancer patients' understanding of the disease and prognosis. The authors suggest this may be due to enhanced communication skill in the care team.

Decision-making

In the palliative treatment of cancer patients, decision-making is of utmost importance. First, making trade-offs is often at stake. Intrusive therapies are increasingly available. In such cases, uncertain gains in terms of survival, response or time to

progression, have to be weighed against the side effects of such symptom provoking treatment regimens and quality of life effects. Evidence suggests that physicians overuse technologically aggressive, life prolonging treatment and underuse communication skills that can assist patients in choosing from a wide range of treatment options²⁸.

Secondly, when patients unsuccessfully decline continued aggressive, life prolonging strategies, they may decide to hasten dying rather than accept a natural death²⁹. Thus, end-of-life decisions, such as requests for assistance in dying are common and have to be dealt with³⁰.

Thirdly, a choice for the preferred care setting may become relevant: whether the patient will be treated in the hospital, can stay at home and/or is referred to a hospice³¹. Physicians, together with patients and their families and other health care providers share the burden of decision making throughout the course of a terminal illness²⁸. Decision making in these situations requires a complex integration of relevant conceptual knowledge of ethical implications, the principles of surrogate decision-making, legal considerations and communication skills that address the highly charged emotional issues under discussion³².

Yet, interestingly, little empirical work investigating either decision-making preferences or decision-making practice was reported recently. Mostly, the articles reviewed cover reviews themselves, case reports^{33,28} or opinion papers. One paper explored the preferred role of gynecologists in end-of-life decision-making³⁴. Half of those interviewed believed that the gynecologist influences the way these decisions are made, even if they thought that patients should be allowed to make end-of-life choices.

Currently, shared decision making is advocated as the model of choice. Tailibert and colleagues² suggested a six step method: 1) to arrange an appropriate setting, 2) to assess current knowledge, 3) to assess the desire for knowledge, 4) to share information, 5) to respond empathically, and 6) to arrange follow up. Also, as stressed in the usual shared decision making models, the exploration of patients' and next of kin's values and preferences deserves pronounced attention for decisions to be made on a firm basis³⁵.

The complexity of these decisions based on medical facts as well as personal factors goes along with an enormous emotional burden for both the clinician and the patient. The oncologist may view death as a personal failure and the patient's psychological state may affect decision-making. Important aspects of decision-making then are to keep focusing around patients' goals and to remain timely and honest²⁸.

Giving advice

Giving advice is more than telling a patient what to do. Good advice implies taking

into account the patient's conditions, preferences and possibilities. Communication should involve exploring those conditions, preferences and possibilities for advice to be effective.

Little attention has been paid to advice giving, though a wide range of issues are at stake in the palliative treatment phase. What is the patient allowed or stimulated to do, given his/her physical functioning in terms of daily activities, physical exercise and work? Is the patient able to adhere to aggressive treatments or other medication regimens? For example, overall adherence rates for analgesics have turned out to range from 91% to as low as 22%³⁶. Can the patient continue social activities and, if so, how? What is the preferred care setting? There is consistent evidence that over 50% of patients would like to die at home³¹. Yet, if so, appropriate care needs to be organized. As an example, Pan and colleagues³⁷ wrote an impressive account of how difficult it was to arrange dying at home for an elderly lady.

In the context of palliative and end-of-life care, the family carers' role in advice giving becomes increasingly important. Increasingly, family care giving precedes death in the United States: informational support and lay medical care provided by family members partners and friends³⁸. Addressing the 'inconveniences of cancer' may seem strange at first, but over time families tend to find out how difficult it may be to plan their usual lives²⁴. This further complicates the communication of giving advice.

Milberg & Strang²⁵ explore the meaning of the concept manageability in the context of palliative care. They distinguish several relevant aspects: a) the physical, functional, psychological, social, economical and spiritual power; b) the support that can be generated; c) competence; and d) accessibility.

A common understanding should be reached and the parties involved should share in the development of recommendations that are practical and feasible. Though not referred to in the literature reviewed the principles of behavior change counseling or motivational interviewing might be useful in the palliative care setting. The principles involved are, first, to explore the patients', or carers' motivation to adhere to the advice given and, secondly, to establish whether the parties involved have indeed the efficacy or competence to bring the advice into practice³⁹. Effective communication of patient, family and the medical team was found to lead to satisfying management in end-of-life care. On the other hand, ineffective communication was found to be characterized by misunderstanding and conflict⁸.

Handling emotions

One of the goals of palliative care is the promotion of quality of life with practical, functional, emotional and spiritual support and minimization of distress^{5,7}. Patients may have difficulty confronting death, fear or unwillingness to accept the prognosis

and a desire to sustain life rather than accept a potentially terminal disease. Parents carry even deeper burdens when facing the prospect of losing a child with cancer. They are likely to experience sadness, guilt, anger, exhaustion and insomnia¹¹. Finally, the illness experience may also thoroughly affect adult family members' psychological health. Kristjanson⁴⁰ mentions 1) the basic intrusion in the person's orientation to living, 2) fears of losing a significant person, and 3) isolation when friends and other family members do not respond empathetically.

The expression and discussion of feelings of loss and grief can be very difficult for incurable patients and their families⁴¹. Still, health care providers are often confronted with these emotions and need to communicate about them. Moreover, an important physician skill is to distinguish clinically relevant levels of psychological distress, e.g., depression or anxiety disorders, from the normal grief and sadness associated with an incurable disease²⁸. Yet, the existential distress of cancer patients and their carers often is overlooked by services focusing on the last phases of life⁴².

As these last phases of life are laden with emotions and psychological distress for patients and their families, one would expect the literature regarding communicating about such distress to be extensive. However, few studies seem to have been performed recently regarding either the systematic screening for or communication about emotional distress, or the way such distress can be handled in palliative care. A few communicative interventions to relieve emotional distress of either patients or family members have been described though. Hurwitz and colleagues¹¹ give a well thought-out account of their approach of the child with cancer and the parents thereof, stressing that real and honest interactions in pediatric palliative care can hold the potential to mine rich personal and professional relationships. Chan and colleagues⁴³ report on the implementation of Family Focused Grief Therapy in which grief, family communication, cohesion and conflict are the major themes to be discussed.

Discussion and conclusion

Other themes emerging

Several related themes emerged from the literature.

First, if communication is to become effective, education of health care providers is needed. Three teaching courses for medical students were described and evaluated. One focused on a half-day workshop addressing 'end-of-life skills', such as breaking bad news and discussing advance directives⁴⁴. Evaluations of these reflected that respondents felt that the workshop enhanced their skills at 6-month follow up. A second course, developed to promote interdisciplinary exchange in palliative care, was found to be effective in increasing understanding when compared

to a control group⁴⁵. A third course, to enhance pain management by medical students turned out to improve communication skills as seen in a structured clinical examination⁴⁶. Postgraduate courses for nurses covering, among others, social-therapeutic and informal skills⁴⁷ and difficult telephone conversations⁴⁸ were successfully implemented. The educational needs of children's hospice doctors were also investigated⁴⁹. Interestingly, a disparity was found in this study between self report measures of educational needs and educational diaries: the first indicating there was little need to learn about communication whereas the latter method yielded results clearly indicating that interpersonal and communication skills were about the most important educational needs.

Secondly, the need to care for carers is stressed in the literature. Emotional support in preparing for the patients' death as well as coping with life after death was found to be available for many professional caregivers⁵⁰. On the other hand, it was suggested that in the US education and compensation should enhance physicians' opportunities to be of service to family caregivers⁵¹.

Thirdly, interdisciplinary communication in palliative care gained some, though limited attention. In a Japanese context, the nursing staff had difficulty with the treatment oriented attitude of doctors and their limited communication skills whereas for doctors the main perceived barriers were lack of alternatives to the medical approach and legal concerns⁵². Therefore, improving doctor/nurse communication was advocated.

Some considerations

When looking at the literature of the year 2004 some thoughts come up that may deserve further attention.

First, it is surprising that some themes are addressed less frequently than others. For example, children with cancer at the end of life gain relatively much attention as compared to the elderly. Obviously, these children's situation is extremely distressing, but the prevalence of disease is also very low. The growing population of elderly patients, moreover, may have specific needs because of increasing frailty and fewer informal caregivers, and may thus be in more need of professional help.

Secondly, it is also striking that few studies seem to focus on what actually happens in the communication in palliative care. Observer based studies²⁶ are scarce. This is unfortunate not only because the actual practice of palliative communication thus remains unseen but also because the mechanisms behind what happens in real life are more difficult to study.

Thirdly, it is amazing that very few studies reporting the (cost-) effectiveness of palliative care interventions were described. A comprehensive care intervention as

described by Rabow³⁸ including, among others, psychosocial support and family caregiver training turned out to lead to decreased symptom experience and health care use. Such studies may enhance palliative care and also convince policy makers of the need to support high quality palliative care.

Finally, all in all it is interesting to see how much attention was paid to communication in palliative care in 2004 and how, unanimously, this field was considered to be of great importance. More empirical work will further enhance such care and yield the level of quality that is needed to ensure a good remaining lifetime for those cancer patients who cannot be cured. Interdisciplinary communication and collaboration will help to ensure progress to be made in the methodological, ethical and practical issues inherent in research in palliative care.

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In palliative cancer care symptoms mean everything

Chapter 8

Telephone consultation in palliative care for cancer patients: 5 years of experience in the Netherlands

Saskia Teunissen¹
Sicco Verhagen²
Mirjan Brink²
Barbara van der Linden³,
Emile Voest¹
Alexander de Graeff¹

¹ Department of Medical Oncology, University Medical Center Utrecht, Utrecht

² Comprehensive Cancer Center Middle Netherlands, Utrecht

³ ZonMw, The Hague

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In palliative cancer care symptoms mean everything

Abstract

Purpose

To analyze cancer patient-related consultations of a Telephone Helpdesk (TH) for palliative care, over a period of 5 years in the region of Utrecht, the Netherlands.

Patients and methods

A descriptive analysis was performed of consultations over a period of 5 years (2001-2006). Discipline and location of requesting professionals, patient characteristics, reasons for calling, symptoms, palliative care problems and needs for support were registered.

Results

1794 consultations were analyzed. There were an increasing number of consultations during the study period. Fifty-one percent of the patients were male and their median age was 65 (range 0-104). Eighty-four percent were treated at home by their general practitioner. Two thirds of the patients had a life expectancy <4 weeks. Most questions referred to pain (49%), delirium (20%), nausea & vomiting (16%) and dyspnea (12%). The median number of symptoms was 1 (0-6). Fifty-four percent of the questions were related to pharmacological problems, 19% to psychological problems and 21% to the organization of care. Seventeen percent of the requesting professionals asked for support for themselves. Fourteen percent of the consultations were related to end-of-life issues: palliative sedation (11%) and euthanasia (3%).

Conclusion

After more than five years the 24-hour telephone consultation service fulfils a need for general practitioners dealing with daily dilemmas in palliative care treatment for cancer patients at home during the last period of their life.

Introduction

Since 1998 (the start of a National Program for the Development of Palliative Care funded by the Dutch government) consultation in palliative care has developed increasingly in The Netherlands. In the region of Utrecht, a central region covering more than 1.6 million inhabitants, health care is provided by 750 general practitioners, 1 university hospital, 8 general hospitals and 4 home care organizations. To optimize palliative care, two types of consultation service were developed under the flag of the Center for Development of Palliative Care Utrecht. The goal was to create an integrated regional system of palliative care based on previously existing but independently operating general practice, home care, specialist care, nursing home and hospice services¹². In order to provide the possibility of consultation for palliative care patients, the University Medical Center Utrecht developed a hospital based palliative care team in 1998 and in collaboration with the Comprehensive Cancer Center Middle Netherlands (CCCMN) a regional telephone consulting service was conceived in 1999.

In this paper we focus on the telephone consultation service, 'the telephone helpdesk' (TH), of the CCCMN. The consulting team of the TH is accessible for all professionals involved in palliative care in the region of the CCCMN on a 24-hour basis, seven days a week. The purpose of this service is to provide specialized palliative care expertise for the benefit of all professionals in the region.

During the first two years of the TH (May 1999- April 2001) there was a growing number of consultations (192 consultations in the first year and 287 in the second year), mainly from general practitioners (72%) and mainly about physical symptoms (75%)¹³. Almost 25% of the consultations took place outside office hours. Consultations required a mean of 85 minutes (range 20 minutes- 6.5 hours) including time spent on the telephone with the caller, consultation with others, writing notes, looking up references, writing advice and sending reports. In 40% of the cases consultation of other team members or professional experts outside the TH took place. The nurse consultant conferred often with his or her medical colleagues, as specified by standard procedure. Based on these results the service was developed further: enlargement of the team, more specification of the working methods, development of written guidelines on symptom management⁵ and improvement of the registration procedure.

A national database for registration of all consultations of the participating services in the Dutch National Program was started in 2001. Kuin et al. analyzed the data of the first year (March 2001- March 2002) of 19 Dutch palliative care consultation teams (including ours) offering a variety of services (e.g. telephone, bedside, mono- and multidisciplinary)¹². The majority of the 2,040 consultations were

requested by doctors (66%) and nurses (22%), most of them working in primary care (61%); 60% of the consultations were by telephone. The mean age of the patients, who were the subject of the consultation, was 64; 50% were male; 90% had cancer and most were treated at home (77%) Their functional status was low to very low (87% ECOG performance status³⁻⁴) and life expectancy as estimated by the requesting professional was maximally one week for 35% of patients, one week tot one month for 32% and more than one month for 33%. The consultations referred to physical, pharmacological, psychological and organizational problems in 77%, 34%, 33%, and 36% of the cases, respectively. General palliative care questions (unrelated to a specific patient) were registered in 8% of the consultations. In two other Dutch studies, results of a 2-year registration were analyzed^{6,18}. Similar outcomes in terms of patient and professional characteristics were found.

These three studies were heterogeneous with regard to the type of consultation and covered only the first 1-2 years of the services. Studies of palliative care services from other countries also often covered the first year(s) after the set up of a service, and are seldom restricted to a telephone service for professionals^{7,9,11}. Results of an analysis of one type of consultation over a longer period after the first 1-2 years have not been published. Therefore, we aimed to provide a descriptive analysis of the patient-related consultations of our TH over a period of five years (January 2001 to January 2006) following the first 2 years. As the great majority of the consultations referred to cancer patients and their symptoms and problems are likely to be different from those of patients with non-malignant disease, we restricted our analysis to cancer patients. We will address the following questions:

1) which professionals consult the TC?; 2) what kind of patients are the subject of the consultation?; and 3) which symptoms and palliative care problems are discussed during consultation?

Patients and methods

Working methods of the telephone helpdesk

During the study period the TH team increased in size. In 2001 the team consisted of 1 general practitioner, 1 nursing home physician, 2 medical specialists (a medical oncologist and an anaesthesiologist/pain specialist) and 3 clinical nurse specialists in palliative care. During the years more general practitioners and nurse specialists were added to the team; in 2005 the team consisted of 3 general practitioners, 1 nursing home physician, 1 hospice physician, a medical oncologist, an anaesthesiologist/ pain specialist and 5 clinical nurse specialists. Each con-

sultant has at least several years experience in palliative care. All team members are practicing and continue their primary activities in addition to their work for the TH. The team members rotate in daily shifts. The consultant on call is available 24 hours a day through a central telephone number.

All professionals in the region can contact the TH on a 24-hour basis, seven days a week, with questions concerning palliative care. Questions can be patient-based, pertaining to a specific individual case, or general questions, concerning palliative care treatment and palliative care services.

The consultant interviews the requesting professional to clarify the problem. If possible, the consultant gives his advice immediately. Alternatively, if consultation of other team members, other professionals or literature is necessary, the consultant proposes a follow-up contact within a few hours. All consultants are considered to be able to give advice independently, regardless of their discipline. For nurse-consultants there is the possibility of conferring with a medical team member.

All advice given is based on the Palliative Care Guidelines of the CCCM5 and on a systematic and multidimensional way of problem analysis. Eighteen guidelines for symptom control (anorexia/weight loss, ascites, constipation, dehydration, delirium, depression, diarrhea, dyspnea, genito-urinary symptoms, hiccups, hypercalcaemia, intestinal obstruction, lymph edema, mouth symptoms, nausea/vomiting, pain, pruritis and oncological ulcers) and three guidelines for other issues in symptom management (complementary medicine, palliative sedation and euthanasia) had been developed by team members and other palliative care experts in the region between 1992 and 2001 and were issued as a book in January 2002.

After the telephone contact the requesting professional receives a written summary (in standardized format) of the consultation by fax or e-mail. For each consultation, the consultant completes a standardized registration form. Registration forms and procedures changed three times due to the collaboration in the National Program.

Professionals are invited to call again for any remaining or newly arising problems. Each case is reported and discussed in a bi-weekly team meeting.

Analysis

A descriptive analysis was performed of the following issues as registered in the registration form:

- discipline and location of the requesting professional
- patient characteristics (gender, age, place of care, diagnosis, comorbidity and life expectancy)

- the primary reason for calling
- symptoms, palliative care problems and needs for support (absent or present) using a checklist derived from a nationally developed symptom registration instrument by the Dutch Centers for Development of Palliative Care¹². The nine most frequently occurring symptoms are registered routinely: pain, nausea & vomiting, constipation, delirium, dyspnea, mouth symptoms, skin symptoms, fatigue and appetite loss. There is a possibility of adding volunteered symptoms.

Data were entered into 4 different databases. Files could not be clustered because during the years of development of the service a) different aspects of registration were required and b) different institutes were responsible for the registration and used different databases. Therefore only frequencies were computed with the statistical software package SPSS (version 14.0).

Results

Between January 1st 2001 and January 1st 2006 2089 consultations were registered by the TH team; 1997 were patient-related questions and 1794 (90%) concerned cancer patients. These consultations are the subject of the present analysis. During the study period, there was an increase in the number of patient-related consultations from 319 in 2001 to 452 in 2005. About 25% of the consultations took place during out-of-office-hours.

Consulting professionals (Table 1)

The TH was mainly consulted by medical doctors (94%) of whom 86% were general practitioners (GP's). There was an average of 3 consultations per GP per year. Only 5% of the requesting professionals were nurses.

Table 1. Consulting professionals (n=1794)

Medical doctors*	1665 (93%)
GP	1548 (86%)
MO	39 (2%)
NH	-
Other	-
Unknown	78 (5%)
Pharmacologists	10 (<1%)
Nurses	93 (5%)
Other	11 (<1%)
Unknown	15 (<1%)

* GP=general practitioner; MO=medical oncologist; NH=nursing home doctor

Patient characteristics (Table 2)

Fifty-one percent of the patients were male and the median age was 65 (range 0-104). The majority (84%) of these patients was at home at the time of consultation. Two thirds of the patients had a life expectancy (as estimated by the requesting professional) of less than 4 weeks. Over the period of 5 years there was no trend toward changes in patient characteristics (data not shown).

Table 2. Patient characteristics (n = 1794)

Gender		
	Male	917 (51%)
Age (years)		
	Median (range)	64 (0-104)
Physician estimated life expectancy*		
	< 1 week	606 (34%)
	1-4 weeks	567 (32%)
	1-6 months	281 (16%)
	> 6 months	14 (<1%)
	unknown	326 (18%)
Place of care		
	Home	1502 (84%)
	Hospital	106 (6%)
	Nursing or elderly home	69 (4%)
	Hospice	88 (5%)
	Unknown	29 (2%)

* by the requesting professional

Content of the consultations

Physical symptoms (Table 3)

Most questions with regard to physical symptoms referred to pain (49%), delirium (20%), nausea & vomiting (16%) and dyspnea (12%). Only 2% concerned fatigue and appetite loss. The median number of symptoms per consultation was 1 (0-6).

Table 3. Symptoms referred to during consultations (n=1794)

Pain	877 (49%)
Delirium	354 (20%)
Nausea & vomiting	288 (16%)
Dyspnea	213 (12%)
Constipation	164 (9%)
Mouth symptoms	69 (4%)
Skin symptoms	33 (2%)
Fatigue	31 (2%)
Appetite loss	36 (2%)
Other symptoms	233 (13%)
Median number of symptoms (range) per consult	1 (0-6)

* More symptoms per patient possible in 1 consultation

Other palliative care problems (Tables 4 and 5)

Fifty-four percent of the questions were related to pharmacological problems and 19% to psychological problems. Spiritual problems were not registered during this study. In 21% of the consultations advice was requested for the organization of care and 17% of the requesting professionals asked for support for themselves. Fourteen percent of the consultations were related to issues concerning end-of-life decision making: palliative sedation (11%) and euthanasia (3%).

Table 4. Palliative care problems referred to during the consultation process (physical symptoms excluded) in 1794 consultations

Pharmacological problems	969 (54%)
Organization of care	381 (21%)
Psychological problems	333 (19%)
Support professional caregivers	308 (17%)
Social problems	117 (7%)
Support informal caregivers	155 (9 %)
Problems in daily functioning	112 (6%)
Other	141 (8%)
Median number of problems (range) per consultation	1 (0-5)

* More problems per patient possible in 1 consultation

Table 5. Questions for support in end-of-life decision making

End-of-life decision making	2003	2004	2005	Total
Palliative sedation	25 (8%)	76 (20%)	100 (22%)	201 (11%)
Euthanasia	4 (1%)	20 (5%)	35 (8%)	59 (3%)
Total	29 (8%)	96 (23%)	135 (27%)	260 (14%)

No systematic registration in 2001-2002

Discussion

Five years of experience of the Telephone Helpdesk (TH) shows an obvious need for support of general practitioners in the management of physical symptoms, pharmacological issues and end-of-life decision-making of patients with advanced and terminal cancer treated at home. In line with previous studies in the Netherlands^{6,12,18} and other European countries^{1,4,8}, we found that most questions related to patients treated at home with a (very) short life expectancy. After a period of more than 5 years the TH receives a still increasing number of questions; this 5 year 'survival' of a consultation service is seen as crucial for success³.

Few other doctors than GP's and few community nurses consulted the TH. The lack

of requests for consultation from doctors from nursing homes and hospitals may be explained by the availability of institution based protocols, internal possibilities for consultation and ongoing collaboration between medical and other disciplines. Nurses working in community care should encounter serious problems in palliative care. The lack of consultations on their part may be explained by the availability of a network of advanced nurse practitioners and clinical nurse specialists and/or reluctance in seeking advice without involvement of the GP.

In the Netherlands the general practitioner is considered to be the coordinator of palliative care for cancer patients¹⁹. It has been argued that cancer patients may suffer unnecessarily due to insufficient knowledge of doctors caused by lack of training during the medical study and lack of experience in daily practice^{2,19}. Schuit and colleagues studied the efficacy of an educational intervention on symptom control for GPs^{19,20}. The effects were significant, but small.

Considering the low number of psychosocial issues discussed during the consultations and the absence of questions about spiritual issues, it seems that requesting GPs focus on symptom control and the organization of care. This could reflect the long relationship GPs have with their patients, support not being necessary because of the familiarity with the patients' coping mechanisms and their social network. In addition, GPs could assume that the consultants of the TH have more expertise on physical than on psychological, social and spiritual issues. It may also be assumed that consultation by telephone is not suitable to address psychosocial and spiritual issues and that bedside consultation is necessary for a more comprehensive approach.

The possibility of a bedside consultation is available for the majority of other palliative care services. Before the start of the TH in 1999 the needs for consultation of professionals in the region were explored by a questionnaire and interviews. The outcome clearly showed that there was no need for bedside consultation. During the following years, after completion of each consultation, an evaluation questionnaire was sent to the requesting professional. One of the questions referred to the possibility for bedside consultation; only a minority of the respondents would appreciate a bedside visit by the TH consultant. However, analysis of the differences between telephone and bedside consultation by Schrijnemaekers and colleagues showed that most 'telephone patients' were at home (most questions came from GPs), and most 'bedside patients' were treated in hospital (most questions came from nurses and medical specialists)^{ref}. Several hospitals in de the region of the CCCMN have the disposal of a palliative care team for bedside consultation within the hospital. Until now, the TH remains reluctant to extend their service, but does not preclude the possibility for bedside consultation in the future.

Palliative sedation is used frequently in the Netherlands¹⁵. Approximately 48% of all

GP's in the Netherlands has used palliative sedation at least once. In the guidelines used by the TH5 this topic is also addressed. During the study period a national guideline was developed¹⁷. During the first two years of our study questions concerning this topic were not registered separately, but included in the category 'other questions'. Over the last three years of the TC registered an increasing number of consultations about palliative sedation. With regard to euthanasia, the TH has never given advice. For this purpose, the (compulsory) consultation may be provided by a nationwide project 'Support and consultation on euthanasia in the Netherlands (SCEN)'¹⁰. The consultation of the TH regarding euthanasia dealt usually with the question whether patients requesting euthanasia had received optimal palliative care.

As there is no standardized follow-up contact with requesting professionals or patients, the effectiveness of the consultations on a patient level could not be assessed. Therefore, the question of the impact of the consultations on patient well-being remains to be addressed. Proving the efficacy of palliative care has been recognized as an ethically and methodologically trying theme world-wide^{1,14,16}. How to include some indicators of success based on patient parameters has been under debate for several years^{19,20}. Due to the working method of the consultation service, advices are given to the requesting professional without becoming a secondary attendant and without a request for report about the effect of the consultation. Thus, in this model, measuring patient outcomes would interfere with the working principles. For the future, we believe that assessment of the effectiveness of consultation, based on patient outcomes such as symptom intensity and quality of life, are still needed in evaluation studies of consultation services. Alternatively, competencies of professionals could be measured²⁰.

After more than five years our TH has not been able to reach all the professionals involved in palliative care for cancer patients in our region. Thus, the primary goal to realize an integrated system of palliative care has not been achieved. Despite this, the findings of this study clearly show that a 24-hour telephone consultation service fulfills a need for GP's for help with the daily dilemmas of palliative care treatment at home. In addition, members of the TH provide continuing education concerning symptom management to the regional palliative care networks, which have been established over the past years. It is our belief that both consultation and education will result in improvement of care for dying patients at home in our region.

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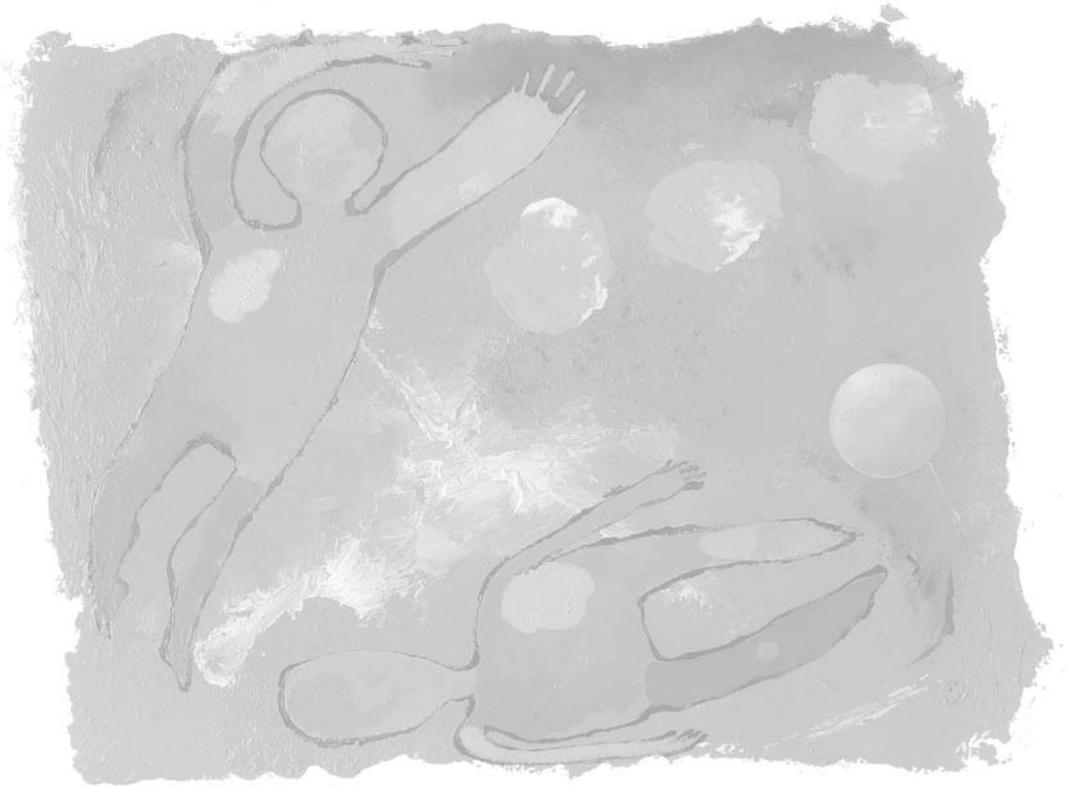
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In palliative cancer care symptoms mean everything

Chapter 9

Summary and general discussion



In palliative cancer care symptoms mean everything

This thesis aims to provide deeper insight into symptoms, in order to improve the adequacy of decision-making for optimizing symptom control in palliative care for cancer patients. Several aspects of symptoms and symptom management were investigated as were some aspects of communication and consultation, because we consider these essential for applying and spreading knowledge in the process of symptom management. The first part of the thesis focuses on symptoms; the second part addresses the other topics.

In this chapter, the principal results reported in chapters 2 to 8 are summarized and placed in perspective. A number of methodological issues are discussed; directions for future research are given and the clinical implications of the most important findings are outlined.

Summary of results

The introduction, **chapter 1**, gives insight into the purpose of the thesis. Attention is given to the debate on aims and principles of palliative care, to the concept of symptoms and symptom management, the role of communication and the function of consultation in the process of applying and spreading knowledge of palliative care. The following questions are studied:

- *What are the major symptoms of patients with incurable cancer?*
- *What is the influence of age on symptoms, problems and needs?*
- *Are symptoms related to mood disorders and fatigue and vice versa?*
- *Do symptoms have a prognostic significance for survival?*
- *What is the position of communication in palliative care?*
- *Which professionals use a palliative care service and what questions do they have?*

Chapter 2 aimed to obtain a reliable estimation of **symptom prevalence** in patients with incurable cancer by performing a systematic review of studies assessing this topic. Secondary aims were a) to study differences in symptom prevalence during the last 1-2 weeks of life and b) to evaluate the influence of assessment method, gender and age on symptom prevalence. We included 44 studies, comprising 25074 patients, on overall symptom prevalence (Group 1) and 6 studies, including 2219 patients, on symptom prevalence during the last 1-2 weeks of life (Group 2). In these studies symptom prevalence was assessed by a questionnaire, a standardized interview or the medical record. We identified 37 symptoms assessed in at least 5 studies. Almost all symptoms occurred in >10% of the patients. Five symptoms, fatigue, pain, lack of energy, weakness and appetite loss, occurred in more than 50% of the patients of Group 1. Weight loss occurred significantly more often in Group 2 than in Group 1; pain, nausea and urinary symptoms occurred signifi-

cantly less often. Generally, symptom prevalence was highest if assessed by a questionnaire. In the limited number of studies addressing those issues, there seemed to be limited relations between gender and age on the one hand and symptoms on the other hand. No definite conclusions about the presence or absence of these relationships could be drawn. The results of this should be used to guide doctors and nurses in symptom management. Proper attention to symptom burden and suffering should be the basis for individually tailored treatment aimed at improving or maintaining quality of life of patients in their last period of life.

Chapter 3 assessed **whether age has an impact on symptoms**, palliative care problems and needs for support of hospitalized advanced cancer patients. A prospective analysis of 181 patients referred to a Palliative Care Team was done using a standardized list of symptoms, problems and needs. Differences between 3 age groups (<60; 60-70; ≥70 years) were analyzed. Patients >70 years had a significantly different prevalence of depressed mood (48% vs 13% of patients 60-70 years and 24% of patients <60 years, $p=0.002$), urinary tract problems (20% vs 3% vs 8%, $p=0.024$) and drowsiness (18% vs 42% vs 25%, $p=0.039$). They expressed more problems with a shortage of informal caregivers (45% vs 42% vs 17%, $p<0.001$) and less need for support in coping (40% vs 61% vs 63%, $p=0.043$), relational support (3% vs 8% vs 14%, $p=0.019$) and support in communication (0% vs 8% vs 11%, $p=0.013$). No other age differences with regard to symptoms and palliative care problems and needs were found. Fewer differences than expected were found. Elderly cancer patients admitted to a hospital for symptom control have more or less the same symptoms, problems and needs as their younger counterparts. This may be due to the fact that in progressive far-advanced disease previously existing age-related differences in symptom prevalence between patients may disappear supporting the known concept of the final clinical pathway in patients with advanced cancer. Alternatively, it could be due to patient selection, elderly patients with terminal disease not being admitted to the hospital and/or referred to the palliative care team. Despite these findings, age-specific assessment of symptoms, problems and needs ought to be part of optimal symptom management in palliative care.

In **chapter 4** the **relation between anxiety, depression and the presence and the intensity of physical symptoms**, was analyzed in 79 hospitalized advanced cancer patients. Anxiety and depression were assessed by 1) the Hospital Anxiety and Depression Scale (HADS), 2) by a single-item question "Are you anxious and /or depressed?" and 3) by the Edmonton Symptom Assessment System (ESAS). Physical symptoms were assessed by a semi-structured interview and by the

ESAS. Anxiety was reported by 34% of the patients, depression by 56% and a combination of the two by 29% as assessed by the HADS. The correlations between HADS, the single-item question and the ESAS were low. No association was found between anxiety and/or depression and the presence of physical symptoms. Patients who were anxious or depressed had higher ESAS scores for insomnia and drowsiness. Scores for pain, anorexia, asthenia, nausea and dyspnea were independent of anxiety and/or depression. Thus, the relationship between anxiety, depression and the presence and intensity of physical symptoms in hospitalized advanced cancer patients is very limited. Therefore, symptom presence and intensity do not seem to be a reliable indicator of anxiety or depression in these patients. Conversely, anxiety and depression appear to have very limited influence on symptom presence and intensity. The lack of these relationships is contrary to what is usually assumed in clinical practice and what is found in some other studies on this topic. The most likely explanation is that an existing association between a symptom and depression may disappear during the course of illness, mood having a progressively decreasing influence on symptom presence and intensity as death approaches. Many studies have been performed in earlier stages of disease and in outpatient settings, while our study focused on terminally ill patients.

Chapter 5 investigated fatigue in another sample of hospitalized advanced cancer patients. In a multidimensional model, fatigue levels and correlates with relevant medical and psychological variables were determined within different fatigue dimensions. It was hypothesized that different fatigue dimensions have different levels and correlates. One hundred advanced cancer patients admitted for symptom control were included. General Fatigue (GF), Physical Fatigue (PF), Reduced Activity (RA), Reduced Motivation (RM), and Mental Fatigue (MF) were measured by the Multidimensional Fatigue Inventory. Investigated correlates were physical symptoms (measured by the EORTC QLQ C-30), mood (measured by the Hospital Anxiety and Depression Scale), tumor load, hemoglobin levels, serum biochemical variables, prior antitumor treatment and medication use. Median GF, PF and RA scores were close to the maximum score of the scales. Median RM and MF scores were moderate, and differed significantly from the GF, PF and RA scores. Multiple regression analyses showed that appetite loss and depressed mood correlated with all fatigue dimensions. Nausea, dyspnea, anxiety, ALAT and hemoglobin levels, previous immunotherapy and opioid and anticonvulsant use were other correlates of fatigue dimensions. Sleeping difficulties were not correlated. The correlates differed across fatigue dimensions. Percentages explained variance was no greater than moderate to fair. The results gave insight into the difference of fatigue levels of hospitalized

advanced cancer patients, depending on the fatigue dimension whereby each fatigue dimension has different correlates. Symptoms not often identified as correlates of fatigue such as lack of appetite, nausea and vomiting, turned out to be important correlates of fatigue, The results confirm the necessity of multidimensional fatigue conceptualization.

In **chapter 6** the **prognostic value of symptoms** in hospitalized advanced cancer patients was assessed. A prospective analysis was performed of 181 hospitalized patients referred to a palliative care team for symptom control. Symptom prevalence and survival were assessed. Using a Cox regression model, a predictive survival model was built. Median survival was 53 days. The median number of symptoms was 4; twenty symptoms occurred in >10%. Multivariate analysis showed nausea, dysphagia, dyspnea, confusion and absence of depressed mood as independent prognostic factors for survival ($p < 0.05$) with relative risks of dying of 1.96, 1.81, 1.79, 2.35 and 1.79, respectively. Patients with 2, 3 or 4 of these factors at the same time had a relative risk of dying of 2.7, 2.1 and 9.0, respectively. A cluster of factors comprising nausea, dysphagia, dyspnea, confusion and absence of depressed mood may be used to accurately predict survival in hospitalized advanced cancer patients. This will aid physicians to develop an individualized program for symptom control in order to prevent unnecessary treatment and transfers between settings of care. This could result in a realistic planning of professional and logistic support and improve the remaining time together for the patient and his nearest.

Chapter 7 reviewed **the literature** as published in 2004 about the quality of communication with patients, kin and team members in palliative cancer care. The following conclusions were drawn:

- Trust was found to be a major factor for building relationships.
- Information gathered by patient self-report is the method of choice given improved insight into symptom prevalence, duration, frequency and interference.
- Decision-making in palliative care requires a complex integration of conceptual knowledge, ethical and legal implications and communication skills.
- Though health care providers need to communicate about emotions, the existential distress of cancer patients and carers is often overlooked in the last phases of life.

In addition to the above themes, the necessity for education of health care providers and the need to care for carers was stressed. Interdisciplinary communication was given more attention.

Little attention was given to the growing population of elderly patients. Also, obser-

ver based studies are unfortunately scarce, making the actual practice of palliative communication invisible. More empirical work is needed to further improve the level of quality needed to ensure a good remaining lifetime for those cancer patients who cannot be cured.

In **chapter 8** cancer patient-related **consultations of a Telephone Helpdesk (TH)** for palliative care in the region of Utrecht, The Netherlands, over a period of 5 years (2001-2006) were analyzed. An increasing number of consultations during the study period were registered. Seventeen hundred and ninety-four consultations were analyzed. Fifty-one percent of the patients were male and their median age was 65 (range 0-104), 84% were treated at home by their general practitioner and two thirds of the patients had a life expectancy <4 weeks. Most questions referred to pain (49%), delirium (20%), nausea & vomiting (16%) and dyspnea (12%). The median number of symptoms was 1 (0-6). Fifty-four percent of the questions were related to pharmacological problems, 19% to psychological problems and 21% to the organization of care. Seventeen percent of the requesting professionals asked for support for themselves. End-of-life issues were addressed in 14% of the consultations: palliative sedation (11%) and euthanasia (3%).

After more than five years the 24-hour telephone consultation service fulfils a need for general practitioners dealing with daily dilemmas in palliative care treatment for cancer patients at home during the last period of their life. The lack of requests for consultation from doctors of nursing homes and hospitals may be explained by the availability of institution based protocols, internal possibilities for consultation and ongoing collaboration between medical and other disciplines.

General discussion

In this thesis several aspects of symptoms and symptom management are reported. It is evident from the results that advanced cancer patients suffer from a variety of symptoms and that a lot of challenges remain to improve symptom management. Palliative care for cancer patients is recognized as a field that needs attention at all settings (home, hospital, nursing home, hospice) where the patient could be treated. However, research in this field is limited by the (inter)national debate about a lot of factors: the definition of the domain and populations, the research paradigm, the methodology and ethical dilemma's, the assessment instruments, low survival rates and constraints in participation rates of patients in studies due to progressive disease and debilitating symptoms¹⁻⁸.

Overall this thesis has highlighted a number of symptoms and aspects of symptom management to focus on in clinical practice as well as in further research. We will

focus on these aspects, but first we will reflect on the methodology of the presented studies.

Methodological reflections

Study design

This thesis includes several prospective studies, most with an observational, explorative or descriptive design. No intervention study could be presented; however, this study generated hypotheses for intervention research.

A limitation of the reported studies may be that most findings are based on a single measurement. It would have given more insight if we had monitored the symptoms during a longer period or preferably, the whole admission. This requires for implementation of symptom assessment with variable instruments for a whole ward-staff. Permanent education and training in communication issues related to the application of the more intensive measurements is recommended.

Instruments used to assess symptoms

To assess the presence and intensity of symptoms, we chose instruments that have been widely used in the hospitalized advanced cancer population.^{3,9-15} All instruments were validated and translated into Dutch.

- 1 The single item question (absence/presence) to assess any symptom presence
- 2 The 9-item numerical Edmonton Symptom Assessment Scale (ESAS) to assess presence and intensity (including mood disorders)
- 3 The Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire with four-point rating scales, to screen for anxiety and depression
- 4 The Multidimensional Fatigue Inventory (MFI), a 20-item questionnaire with five-point agreement scale, to assess five dimensions of fatigue.

The single item question (symptom present yes or no) is frequently discussed and used in palliative care research because it is easy to apply. We applied a standardized checklist of symptoms confirmed by a Dutch group of researchers¹⁶. The ESAS was relatively easy to apply in seriously ill patients, although the meaning of the described symptoms was not always clear for the patient. Therefore, the measurement sometimes took too much of the patient's time and energy. It is recommended, for both the single item question and the ESAS, to come to a sort of description of symptoms before the measurement starts. Fatigue, weakness and depressed mood were especially difficult items to determine. The screening instrument HADS was more complicated to complete, because of the concentration required. Besides, some items initiated a train of thoughts and emotions about the patient's own situation. Emotional support after the first measurement with the HADS is warranted, as well as communication with the family about the aim, contents and results of the assessment.

Generalizability

All patients included in the studies reported in this thesis were treated in a university medical center, most of them by medical oncologists. Moreover, patients were referred to a palliative care team or palliative care unit for symptom control by their initial doctor. It is not known how these patients compare to the total population of advanced cancer patients. However, our samples are heterogeneous as well since all patients were referred by different medical specialists. These patients by definition have high symptom loads. It is most likely that referred patients have more distressing symptoms and other palliative care problems than patients who are not or could not be referred. Considering the complexity of their situation, hospitalized advanced cancer patients admitted for symptom control form a very interesting population for further intervention research.

Final conclusions, implications for clinical practice and future research

Fatigue, pain, lack of energy, weakness/asthenia and appetite loss/anorexia turned out to be the most frequent symptoms, occurring in >50% of the total group of palliative care patients (all places of care). Most of these symptoms have a meaning in the hospital based studies we performed. With advancing age, we found only significant differences between age groups for increased prevalence of depressed mood and urinary tract problems, and a decreased prevalence of drowsiness. Fatigue, as measured by a multidimensional instrument, was related to dyspnea, nausea and depressed mood in all dimensions. Nevertheless, depression and anxiety do not seem to be indicated by symptom presence and intensity; nearly no relationship was found between anxiety or depression and symptom presence. What was striking was the finding that, after correction for diagnosis, the absence of depressed mood independently predicted an increase of the survival-time, whereas the presence of nausea, dysphagia, dyspnea and/or confusion predicted a significantly decreased survival. These findings together suggest that symptoms change, but are less dependent on diagnosis and age in progressive, far-advanced disease than we might believe.

Suggestions for future research

To begin, we think that our review of symptom prevalence in palliative care, is the most reliable estimation until now; therefore, in the coming years, symptom prevalence studies will no longer be needed in samples of advanced cancer patients. On the other hand, work has to be done in defining the labels of symptoms used in assessment instruments. In addition, it would be interesting to apply the same systematic approach to other populations such as patients with advanced cardiovascular disease, COPD and/or ALS.

Moreover, longitudinal studies are needed to test the hypothesis that symptoms change and are less dependent on diagnoses, within the advanced cancer population and/or between other populations, as the end approaches. The concept of a common final clinical pathway in patients with advanced cancer¹⁷ could be invigorated by studies like that, in order to create a paradigm for further research concerning patients in the last weeks of life.

Systematic individualized symptom assessment (including the most frequent symptoms as described in this thesis) could be applied as an intervention in itself, with symptom experience, symptom distress and quality of life as outcome variables.

Screening for anxiety and depression remains a major challenge in palliative care because of the impact these symptoms have for patients, family and professionals. What the best screening instrument is needs to be established in the next few years. Studies of the relation between anxiety and physical symptoms are largely lacking and should be performed especially in hospitalized advanced cancer patients because of the high levels of anxiety we found in our sample of admitted palliative care patients.

Fatigue was the most prevalent symptom in all studies, although GP's seldom requested the Telephone Helpdesk for advice on fatigue. Hence, causal relationships between predictors and fatigue dimensions need to be further explored. Particularly relevant is the question of whether different fatigue dimensions predict quality of life differently.

The prognostic significance of a cluster of symptoms is probably the most challenging finding of this thesis. This finding is limited by the single measurement. Therefore, we suggest applying the model of the prognostic factors over time in subcategories, for example along functional status and physician estimated survival, during intervention and symptom management. It could be useful to stratify for different age groups, with special attention to the patients >85 years of age. In addition it would be interesting to apply the model in another setting of care, for instance a hospice.

As consultation services are more and more integrated in the health care system, assessment of the effectiveness of consultation, based on patient outcomes such as symptom intensity and quality of life, are needed in evaluation studies. Alternatively, competencies of professionals could be measured¹⁸.

Focus on what actually happens in the communication in palliative care should be another goal for research. Along the framework of communicative goals in oncology¹⁹ (relationship building, information exchange, decision-making, giving advice, and handling emotions) observer based studies are highly recommended. Evaluation of decision-making is of the utmost importance, because those processes reflect

the interdisciplinary communication and collaboration, and the methodological, ethical and practical issues inherent in research in palliative care.

All in all, we think that more research in the specific population of hospitalized advanced cancer patients is extremely desirable to develop possibilities for intervention studies in this highly distressed group of patients. Intervention studies concerning symptom treatment are seriously needed in the domain of palliative care with regard to the emancipation process of the discipline. We would like to emphasize that the outcome of (experimental) treatment should be based on symptom intensity, symptom burden and the impact of symptoms on quality of life.

Implications for general practice

Focus on the more prevalent symptoms in advanced cancer patients admitted for symptom control should guide symptom management by doctors and nurses. However, it must be emphasized that treatment should be based on symptom intensity, symptom burden and the impact of symptoms on quality of life.

The studies in this thesis add appealing findings of symptoms of hospitalized advanced cancer patients concerning prevalence figures, differences by age, relation with mood disorders and fatigue and the prognostic significance.

To optimize symptom management in daily practice we suggest the following.

- 1 Implementation of systematic individualized symptom assessment, including anxiety and depression, is needed for all patients (including the elderly) admitted for symptom control. It is recommended to use a quick and easy to fill in numerical scale with space for volunteered symptoms. Ensure that the most prevalent symptoms and the prognostic symptoms will be included and define the symptom labels with the patient before the first measurement.
- 2 Guidance in the application of available knowledge and guidelines is required; interdisciplinary collaboration is a precondition.
- 3 Decision-making needs a framework to ensure the interpretation of the outcomes of symptom assessment and to guide the further process in a comprehensive and structured way of thinking. We suggest the model of 'palliative reasoning'²⁰ because it is assumed to be easy to implement by all disciplines in all settings of care.
- 4 Consultation services could fulfill an easy to apply additional service. Besides telephone services, possibilities for bedside consultation should be further explored to develop a more comprehensive approach.
- 5 If communication in palliative care is to become effective, more and structural education and multidisciplinary training of doctors and nurses is needed and care for the carers should be provided.

In palliative cancer care symptoms mean everything

In palliative care symptoms mean everything. We believe, that in palliative care, control of symptoms is a prerequisite to allow patients to address the other dimensions of their lives.

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In palliative cancer care symptoms mean everything

Nederlandse samenvatting



In palliative cancer care symptoms mean everything

Palliatieve zorg en onderzoek

Dit proefschrift gaat over symptomen van mensen met kanker in de palliatieve fase van hun ziekte en behandeling. De palliatieve fase is de fase waarin genezing niet langer mogelijk is. Palliatieve zorg is de integrale zorg voor mensen met een levensbedreigende ziekte die niet meer kunnen genezen. Het vakgebied is slechts een veertigtal jaren oud en krijgt in Nederland sinds een aantal jaren toenemende aandacht. De palliatieve fase maakt deel uit van het continuüm van de kankerzorg. De overgang van een adjuvante of een in opzet curatieve behandeling naar de palliatieve fase is daarom ook nooit een absolute. Er is sprake van een transitie, een proces waarin voort schrijdende ziekte leidt tot tumor palliatie en vervolgens overgaat in symptoom palliatie tot de dood volgt. De palliatieve fase kan enkele weken tot enkele jaren duren en is daarmee een aandachtsgebied voor professionals op alle locaties van zorg waar de patiënt verblijft: thuis, in een verzorgings- of verpleeghuis, een ziekenhuis of een hospice. In dit proefschrift wordt vooral aandacht besteed aan patiënten opgenomen in het ziekenhuis.

Onderzoek in de palliatieve fase heeft een nog kortere traditie dan de zorg als zodanig. Het is een zich ontwikkelend onderzoeksgebied zonder helder paradigma dat kampt met problemen die zeer divers van aard zijn, o.a. door onuitgemaakte definitie kwesties, heterogeniteit van populaties en verblijfplaatsen, beperkte infrastructuur, ethische dilemma's rondom interventie onderzoek, beperkingen in meetinstrumenten en effectmaten, korte overlevingsduur van patiënten, een beperkte groep geïnteresseerde, bekwame en gerenommeerde onderzoekers en zeer beperkte financieringsmogelijkheden. Tegelijkertijd biedt dit alles veel ruimte voor verbetering en creativiteit. Onderzoek is noodzakelijk om experience meer body te geven en evidence op te bouwen in vele facetten van de palliatieve behandeling en zorg.

Het onderzoek dat is weer gegeven in dit boekje is gericht op het verkrijgen van meer inzicht in klachten en symptomen, om daardoor in de eerste plaats de besluitvorming rondom de bestrijding van symptomen te verbeteren. Vervolgens kan die betere besluitvorming leiden tot een optimalisering van medisch en zorgbeleid welke uiteindelijk ruimte creëren voor behoud van de eigenheid van de mens in zijn laatste levensfase. Leven volgens onze eigen waarden en drijfveren, met onze geliefden, is immers een primaire en universele levensbehoefte van iedere mens, ook of juist wanneer de resterende tijd van leven nog maar beperkt is.

Symptomen zijn alle klachten die de patiënt uit als gevolg van de voortschrijdende ziekte of de behandeling ervan. Symptomen zijn lichamelijk, functioneel, psychisch, emotioneel, sociaal en/of spiritueel van aard. Symptoom management is in dit proefschrift gedefinieerd als een proces vanaf het observeren van de klachten, het meten en behandelen ervan tot en met het evalueren van het effect van de behandeling. Symptoom

management maakt integraal onderdeel uit van het palliatieve zorg beleid. Additioneel is aandacht uit gegaan naar communicatie en consultatie als essentiële instrumenten voor de toepassing en verspreiding van kennis met betrekking tot symptoom management. Het eerste deel van het proefschrift concentreert zich op de symptomen en enkele onderdelen van symptoom management, namelijk observatie, monitoring en betekenis voor besluitvorming in beleid. In het tweede deel gaat de aandacht uit naar evaluatie van de toepassing in communicatie en consultatie.

De volgende onderzoeksvragen zijn bestudeerd:

- Wat zijn de belangrijkste symptomen van mensen met ongeneeslijke kanker?
- Wat is de invloed van leeftijd op symptomen, problemen en behoeften?
- Is er een relatie tussen symptomen, angst, depressie en vermoeidheid en vice versa?
- Hebben symptomen een voorspellende waarde voor de resterende overlevings-tijd?
- Hoeveel aandacht krijgt communicatie in palliatieve zorg?
- Welke professionals maken gebruik van de mogelijkheden voor consultatie en welke vragen hebben zij?

Samenvatting van de resultaten

Vanwege de vele verschillende data over symptoom prevalentie in de palliatieve fase en het daardoor ontbreken van goed inzicht in symptoom prevalentie is besloten tot een **systematische beschouwing van alle literatuur over de mate van voorkomen van symptomen**. Het systematische review is weer gegeven in **Hoofdstuk 2** Doelstelling is daarmee te komen tot een optimaal inzicht in symptomen in de palliatieve fase bij kanker. Daarnaast zijn de verschillen in symptoom voorkomen bij alle patiënten in de ‘totale’ palliatieve fase (groep 1) en specifiek bij patiënten in de laatste 2 weken voor overlijden (groep 2) in kaart gebracht. Ook is er gekeken naar de invloed van geslacht en leeftijd en is de invloed van de instrumenten waarmee gemeten is geëvalueerd. Groep 1 bevat 44 studies met totaal 25074 patiënten, groep 2 omvat 6 studies met totaal 2219 patiënten. In deze studies is de prevalentie van symptomen geregistreerd met behulp van een vragenlijst, een gestandaardiseerd interview of het medische dossier. Er zijn 37 verschillende symptomen geïdentificeerd die in tenminste 5 studies voor kwamen. Bijna alle symptomen presenteerden zich in >10% van de patiënten. Vijf symptomen, vermoeidheid, pijn, gebrek aan energie, gevoel van zwakte en verlies van eetlust, deden zich voor bij meer dan 50% van de totale groep patiënten. Gewichtsverlies deed zich significant vaker voor in de laatste 2 weken voor overlijden dan in de periode

daarvoor; pijn, misselijkheid en urinewegproblematiek kwam significant minder vaak voor. In het algemeen was de prevalentie van symptomen het grootst indien er werd geregistreerd met behulp van een vragenlijst. In een beperkt aantal studies werd enige relatie gevonden tussen geslacht, leeftijd en symptomen en vice versa; conclusies kunnen er niet aan worden verbonden. Wel kunnen de bevindingen uit dit systematische literatuuronderzoek worden gebruikt als 'gids' voor artsen en verpleegkundigen in symptoom management, meer concreet: als uitgangspunt voor het observeren, meten en registreren van symptomen als basis voor adequaat symptoom management..

De toenemende aandacht voor de vergrijzing en daarmee de oudere patiënt binnen de oncologie is aanleiding geweest voor het onderzoek dat is beschreven in **hoofdstuk 3**. Centraal stond de vraag wat **de invloed is van leeftijd op symptomen, op palliatieve zorg problemen en de behoefte aan ondersteuning** van mensen met gemetastaseerde kanker opgenomen voor symptoombestrijding. Aan de hand van een gestandaardiseerde lijst van symptomen, behoeften en wensen werd een prospectieve analyse van 181 patiënten die verwezen waren naar een palliatieteam (UMC Utrecht) uitgevoerd. Er werd een analyse van 3 leeftijdsgroepen gemaakt: <60 jaar, 60-70jaar en ≥ 70 jaar. Bij patiënten van 70 jaar of ouder was sprake van een significant andere prevalentie van somberheid (48% vs 13% van de 60-70 jarigen en 24% van de groep <60 jaar, $p=0.002$), urinewegproblemen (20% vs 3% vs 8%, $p=0.024$) en sufheid (18% vs 42% vs 25%, $p=0.039$). Ook was er binnen die oudste groep sprake van een groter tekort aan informele mantelzorgers (45% vs 42% vs 17%, $p<0.001$) en werd er significant minder behoefte geuit aan ondersteuning in probleemhantering (40% vs 61% vs 63%, $p=0.043$), relatie (3% vs 8% vs 14%, $p=0.019$) en communicatie (0 vs 8% vs 11%, $p=0.013$). Verder werden er geen verschillen gevonden tussen de leeftijdsgroepen, symptomen, problemen en behoeften. Dit was buiten verwachting: oudere patiënten hebben dus min of meer dezelfde symptomen, problemen en wensen als hun jongere lotgenoten. Deze bevindingen kunnen mogelijk verklaard worden door een verdwijnend onderscheid van leeftijdsgebonden verschil ten gevolge van de progressieve ziekte. Dit ondersteunt het bekende concept van de 'final common pathway' dat aangeeft dat patiënten in de terminale fase meer op elkaar gaan 'lijken'. Een andere mogelijkheid is dat de patiëntenselectie verantwoordelijk is voor de beperkt gevonden verschillen. Wellicht wordt er anders omgegaan met oudere patiënten met terminale ziekte, worden zij minder vaak doorverwezen naar het ziekenhuis voor symptoombestrijding en indien zij zijn opgenomen worden zij minder vaak doorverwezen naar het palliatieteam.

Angst en depressie in de palliatieve fase worden door professionals ervaren als moeilijk observeerbare, bespreekbare en behandelbare symptomen. Vaak wordt aangenomen dat er een (wederkerige) relatie is met lichamelijke symptomen. Klinisch beleid is regelmatig op deze aanname gebaseerd. Daarom is onderzocht **wat de relatie is tussen angst, depressie en symptoomlijden**. Hiertoe is een analyse gedaan van 79 kanker patiënten in de palliatieve fase die werden opgenomen voor symptoombestrijding en doorverwezen voor een consult palliatieteam (UMC Utrecht). **Hoofdstuk 4** beschrijft deze studie. Angst en depressie werden gemeten met 3 verschillende instrumenten: 1) de Hospital Anxiety and Depression Scale (HADS), 2) de single-item vraag “voelt u zich angstig en/of somber?” en 3) de Edmonton Symptom Assessment System (ESAS). Lichamelijke symptomen werden in kaart gebracht met behulp van 1) een semi-gestructureerd interview met symptoom checklist en 2) de ESAS. Op basis van de HADS kwam bij 34% van de patiënten angst voor, bij 56% depressie en angst en depressie tegelijkertijd bij 29% van de mensen. De correlatie tussen de uitkomsten van de HADS, de single-item vraag en de ESAS was laag. Er werd geen associatie gevonden tussen angst en/of depressie en het voorkomen van lichamelijke symptomen. Patiënten die angstig of somber waren hadden hogere ESAS scores voor slaapproblemen en sufheid. De scores voor pijn, anorexie, vermoeidheid, misselijkheid en benauwdheid waren onafhankelijk van angst en/of depressie. Daaruit volgend is de relatie tussen angst en depressie en de aanwezigheid en intensiteit van lichamelijke symptomen bij opgenomen kanker patiënten in de palliatieve fase heel beperkt. Daardoor lijken symptoom voorkomen en intensiteit van de symptomen geen betrouwbare indicator van angst of depressie bij deze patiënten. Angst en depressie blijken ook erg weinig invloed te hebben op symptoomlijden. Het ontbreken van deze relaties in onze studie is tegengesteld aan wat in andere studies (met eveneens beperkte omvang) is gevonden en ook aan wat in de praktijk wordt aangenomen. Veel van die in de literatuur beschreven studies m.b.t. angst, depressie en symptomen werden vroeger in het ziekteproces uitgevoerd, terwijl onze studie focust op terminaal zieke mensen. De meest voor de hand liggende verklaring is dat een bestaande associatie tussen een symptoom, angst en/of somberheid wellicht verdwijnt gedurende het voortschrijdende ziekteproces, in die zin dat stemming een progressief dalende invloed heeft op symptomen en symptoomlijden naar mate de dood dichterbij komt.

Vermoeidheid is een ingewikkeld en moeilijk grijpbaar probleem voor professionals in de palliatieve zorg. Vaak blijven vragen van patiënten hieromtrent onbeantwoord. **Hoofdstuk 5** is de weergave van **een studie naar vermoeidheid** bij 100 kankerpatiënten opgenomen voor symptoombestrijding in de palliatieve fase

(Daniel den Hoed kliniek). In een multidimensioneel model werden niveaus van vermoeidheid en correlaten met relevante medische en psychologische variabelen bepaald binnen verschillende dimensies van vermoeidheid. De hypothese daarbij was dat verschillende dimensies van vermoeidheid verschillende niveaus en correlaten hebben. Met de Multidimensional Fatigue Inventory (MFI) werden 5 dimensies van vermoeidheid gemeten: algemene vermoeidheid (GF), lichamelijke vermoeidheid (PF), beperkingen in activiteit (RA), beperkingen in motivatie (RM) en mentale vermoeidheid (MF). De onderzochte correlaten waren lichamelijke symptomen (gemeten met de EORTC QLQ C-30), stemming (gemeten met de HADS), tumor load, hemoglobine spiegels, biochemische serum variabelen, voorgaande anti tumor behandeling en medicatie gebruik. De mediane scores voor GF, PF en RA kwamen dichtbij de maximum score van de schalen. De mediane RM en MF scores waren matig en significant verschillend van de GF, PF en RA scores. Multiple regressie analyse liet een correlatie zien tussen verlies van eetlust en somberheid met alle dimensies van vermoeidheid. Misselijkheid, benauwdheid, angst, ALAT en Hb, voorgaande immunotherapie, gebruik van opioïden en anticonvulsiva waren andere correlaten van diverse dimensies van vermoeidheid. Slaap problemen lieten geen correlatie met een van de dimensies zien. Het percentage verklaarde variantie was niet groter dan matig tot gemiddeld. De resultaten geven inzicht in de verschillende niveaus van vermoeidheid, afhankelijk van de dimensie van vermoeidheid, waarbij iedere dimensie eigen correlaten heeft. Symptomen die niet eerder geïdentificeerd werden als correlaten van vermoeidheid zoals gebrek aan eetlust, misselijkheid en braken, bleken in onze studie wel belangrijk gecorreleerd. De resultaten van deze studie bevestigen de noodzaak van de benadering van vermoeidheid met een multidimensioneel concept.

Vanwege de altijd terugkerende vraag in de palliatieve fase “hoe lang heb ik nog?”, werd de **prognostische waarde van symptomen voor overleving** onderzocht. Het onderzoek is beschreven in **hoofdstuk 6**. Er werd een prospectieve analyse gedaan van 181 opgenomen kankerpatiënten in de palliatieve fase, alle patiënten werden voor symptoombestrijding verwezen naar het palliatieteam (UMC Utrecht). Gemeten werden de symptoom prevalentie (symptoom checklist in semi-gestructureerd interview) en overlevingsduur (vanaf het moment van het eerste consult bij het palliatieteam tot aan het overlijden). De gemiddelde overlevingsduur was 53 dagen. Met behulp van een Cox regressie model werd een voorspellend overlevingsmodel gebouwd. Er waren 20 symptomen die bij >10% van de patiënten voor kwamen, het mediaan aantal symptomen was 4. Multivariate analyse liet misselijkheid, slikstoornissen, benauwdheid, verwardheid en het ontbreken van

somberheid zien als onafhankelijke prognostische factoren voor overleving

($p < 0.05$), met een relatief risico van respectievelijk 1.96, 1.81, 1.79, 2.35 en 1.79. Patiënten met 2, 3 of 4 van deze symptomen tegelijkertijd hadden een relatief risico om te sterven van respectievelijk 2.7, 2.1 en 9.0. Een cluster van symptomen met misselijkheid, slikstoornissen, benauwdheid, verwardheid en het ontbreken van somberheid zou kunnen worden gebruikt om de overlevingsduur van opgenomen kankerpatiënten in de palliatieve fase met meer zekerheid te voorspellen. Dit zou artsen en verpleegkundigen kunnen ondersteunen bij het ontwikkelen van een op maat gesneden beleid voor symptoom bestrijding, om daardoor onnodige behandelingen en of transfers tussen thuis en ziekenhuis te voorkomen. Dat alles zou kunnen resulteren in een realistische planning van professionele en logistieke ondersteuning voor de patiënt waardoor de resterende tijd voor de patiënt en naasten kan worden verbeterd.

Communicatie wordt door artsen, verpleegkundigen en paramedici in de palliatieve fase als een verbindend en cruciaal instrument beschouwd. Daarmee is een adequate invulling niet gegarandeerd. **Hoofdstuk 7 is een overzicht van de literatuur die in 2004** werd gepubliceerd rondom het thema communicatie tussen patiënten, naasten en professionals in de palliatieve fase van kanker. Er zijn een aantal conclusies getrokken:

- vertrouwen blijkt een van de belangrijkste factoren in het opbouwen van een relatie
- zelfrapportage van klachten en problemen door de patiënt blijkt de methode met de grootste voorkeur voor informatie verzameling om het inzicht in de prevalentie, duur, frequentie en interferentie van symptomen te verbeteren
- besluitvorming in de palliatieve fase vraagt om een complexe integratie van conceptuele kennis, ethische en juridische implicaties en communicatieve vaardigheden
- ondanks het feit dat professionals verondersteld worden in gesprek te gaan over emoties, blijkt existentieel lijden van patiënten en hun mantelzorgers vaak te worden gemist in de laatste levensfase.

Aanvullend werd de noodzaak voor educatie van professionals en 'zorg voor de zorgenden' in de literatuur benadrukt. Interdisciplinaire communicatie kreeg ook aandacht.

Er werd weinig literatuur gevonden over de groeiende populatie oudere patiënten. Ook observationele studies werden nauwelijks gevonden waardoor de actuele praktijk van communicatie in de palliatieve fase onzichtbaar blijft. Conclusie is dat er meer empirisch werk nodig is om de kwaliteit van de benodigde communicatie in

In Nederland zijn sinds de Centra voor Ontwikkeling van Palliatieve Zorg in iedere regio expert teams beschikbaar voor consultatie in de palliatieve fase t.b.v. de verspreiding en toepassing van kennis en kunde op het gebied van o.a. symptoom management. In de regio van het Integraal Kankercentrum Midden Nederland bestaat het Palliatieteam Midden Nederland sinds 1999. Vanwege de ontwikkelingen sinds de start werd besloten tot een **evaluatie van de telefonische helpdesk functie** over een periode van **5 jaar (2001-2005)**. **Hoofdstuk 8** beschrijft die studie. Gedurende de studie werd een toenemend aantal consulten geregistreerd: 1794 consulten werden geregistreerd. Van de patiënten die het betrof, was 51% man, was de gemiddelde leeftijd 65 (0-104) en werd 84% thuis behandeld door de huisarts. Tweederde van deze patiënten had een gemiddelde levensverwachting (zoals in geschat door de consulterend arts) van minder dan 4 weken. De meest gestelde vragen hadden betrekking op pijn (49%), delier (20%), misselijkheid en braken (16%) en benauwdheid (12%). Het mediaan aantal symptomen dat werd besproken per consult was 1 (0-6). Van de gestelde vragen was 54% farmacologisch van aard, 19% had betrekking op psychologische problemen en 21% op de organisatie van zorg. Daarnaast vroeg 17% van de consulterende professionals ondersteuning voor zichzelf. Dilemma's betreffende besluitvorming rondom het levenseinde kwamen voor in 14% van de consulten: 11% m.b.t. palliatieve sedatie en 3% m.b.t. euthanasie. De 24-uurs telefonische consultatie service PTMN blijkt na meer dan 5 jaar te voorzien in een behoefte van huisartsen in relatie tot hun dilemma's in de dagelijkse praktijk van palliatieve zorg thuis. Het ontbreken van consulten van artsen en verpleegkundigen uit zieken- en verpleeghuizen zou verklaard kunnen worden door de beschikbaarheid van eigen protocollen, interne mogelijkheden voor collegiale consultatie en de multidisciplinaire samenwerking in deze organisaties.

Algemene conclusie

Het onderzoek dat is weer gegeven in dit boekje voegt kennis toe over symptomen en het management ervan. Het laat ook zien hoeveel vragen professionals hebben over de hantering ervan in de praktijk van alledag. In de palliatieve fase zijn symptomen alles bepalend. De basis voor een adequaat palliatief beleid en de basis voor de ruimte die de patiënt heeft voor alles wat hij meer is dan zijn ziekte. Hoe goed het systeem van ondersteunende zorg ook is, hoe zeer betrokkenen ook streven naar optimalisering van de resterende kwaliteit van leven, als symptomen niet adequaat worden bestreden is er geen ruimte bij de patiënt om optimaal te profiteren van het overige zorg aanbod. Aldus, is goed symptoom management in onze overtuiging een noodzakelijke voorwaarde om patiënten de gelegenheid te geven aandacht te besteden aan de andere dimensies in hun leven. Passende aandacht voor

In palliative cancer care symptoms mean everything

symptoom lijden op iedere mogelijke locatie waar de patiënt verblijft, moet de basis zijn voor op maat aangepaste behandeling gericht op handhaving en verbetering van de kwaliteit van leven. Verder onderzoek met creatieve benaderingen is daarvoor heel hard nodig.

In palliative cancer care symptoms mean everything

Dankwoord

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De Raad van Bestuur Integraal Kankercentrum Midden Nederland: Drs. Ria Koppejan.

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In palliative cancer care symptoms mean everything

Over de auteur

Saskia Teunissen werd op 21 februari 1963 geboren in Molenhoek (L) en ging naar het Nijmeegs Jezuïeten Canisius College. Daarna volgde zij de in-service opleiding tot A-verpleegkundige in het Canisius Wilhelmina Ziekenhuis (CWZ) vanwege de combinatie met zorg thuis voor haar vader met ALS. Na de afronding (1984) werden de vervolgoopleiding oncologieverpleegkunde en diverse andere specialistische en management opleidingen voltooid. Vanaf eind jaren tachtig was zij mede-initiator van innovatieve zorgprojecten in de transmurale oncologische en palliatieve zorg. Veel stages in het buitenland werden daartoe afgelegd. Zij werkte in gecombineerde leidinggevende en expert functies binnen de hemato-oncologie van het CWZ en het Integraal Kankercentrum Oost te Nijmegen. Tussentijds volgde zij de deeltijd studie Gezondheidswetenschappen in Maastricht. Na de voltooiing daarvan in 1995 vertrok zij naar de Dr. Daniel den Hoed Kliniek te Rotterdam als leidinggevende van de Palliatieve Zorg Unit. Daar werden de eerste stappen in onderzoek gezet. In 1998 maakte zij de overstap naar het UMC Utrecht vanwege de opzet van een consultatie project palliatieve zorg. Zij vervulde 5 jaar de gecombineerde rol van programma coördinator Centrum voor Ontwikkeling van Palliatieve Zorg Utrecht en consulent palliatieve zorg. In die periode kreeg het lang geambieerde promotietraject concrete invulling en werd ook het leiderschapstraject Orion gevolgd. Naast werk, studie en onderzoek heeft zij altijd een actieve rol vervuld in regionale en landelijke commissies en besturen en werden bijdragen geleverd aan boeken, multi media projecten, onderwijs, symposia en congressen. Deze neven activiteiten en de ontmoeting met professionals van allerlei soort waren in veel opzichten leerzaam en inspirerend. Momenteel maakt zij deel uit van het clusterbestuur van het cluster Medische Oncologie en Hematologie UMC Utrecht, vervult zij de rol van consulent organisatie en ontwikkeling palliatieve zorg bij het Integraal Kankercentrum Midden Nederland en is zij bestuurslid van het Academisch Hospice Demeter. Gedurende 25 jaar is er sprake van een 'luxe probleem': de non-keuze tussen inhoud en organisatie van de kankerzorg. De combinatie blijft inspireren, uitdagen en steeds weer nieuwe ideeën genereren om zorg voor patiënten, professionals, onderwijs en onderzoek te verbeteren.

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*wat voor en achter ons ligt
zijn kleinigheden
vergeleken met
wat in ons ligt*

Oliver Wendell Holmes

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