Discussion

The studies described in this thesis concern various aspects of symptoms and symptom relief during the last phase of life of patients with advanced diseases. This chapter presents the key findings of the studies, followed by methodological considerations and a general discussion focusing on two important emerging themes in these studies, i.e. acknowledging different perspectives and communication. Finally some implications and recommendations for clinical practice and future research will be discussed.

KEY FINDINGS

In order to deliver good healthcare, it is important to know which symptoms occur during a specific disease or disease phase, as well as their impact on patients' daily functioning and quality of life. We studied the prevalence and impact of symptoms in two understudied patient groups (chapter 2 & 3). First, we focused on patients with incurable head and neck cancer (chapter 2) and found that these patients reported an average of 14 different symptoms (interval 0–26), of which 10 somatic symptoms and 4 psychosocial symptoms. The most frequently reported somatic symptoms were 'fatigue', 'pain' and 'weakness'. In the psychosocial area, these were 'worrying', 'sadness' and 'tenseness'. The symptom with the greatest impact on daily functioning, was 'dyspnoea'. We compared the reporting of patients and family members and found that in two thirds of cases, although not always significant, the occurrence rates and impact scores of physical symptom as estimated by family members were higher than those estimated by patients. For about 50% of the psychosocial symptoms we found a reverse trend. Second, we studied patients with advanced heart failure in South Africa (chapter 3). We found that patients, of whom 14% had completed high school and 26% had no income, reported a mean of 19 symptoms. Physical symptoms with the highest occurrence were 'shortness of breath', 'feeling drowsy/tired' and 'pain' . Psychological symptoms with the highest occurrence were 'worrying', 'feeling irritable' and 'feeling sad'. Symptoms with the highest burden were 'shortness of breath', 'numbness/ tingling in hands or feet' and 'I do not look like myself'. Higher symptom burden was associated with a higher age, having no income and fewer hospital admissions within the previous 12 months.

As death comes nearer, patients with advanced illness have been reported to experience many symptoms in their last week or days of life[1-11]. However, until now, research on the occurrence and impact of several symptoms in the dying phase has been scarce. This also holds for death rattle. We performed a systematic search of scientific literature concerning the prevalence of death rattle, its impact on patients, relatives and professional caregivers, and the effectiveness of interventions (chapter 4). We found that death rattle is a common symptom in dying patients. Approximately a third of patients will present with this symptom during the dying process. Death rattle leads to distress in both family members and professional caregivers, but it is doubtful if patients suffer from this symptom. Different medication regimes for the treatment of death rattle have been studied. Current evidence does not support the use of antimuscarinic drugs in the treatment of death rattle.

At the end of life, oral fluid intake is often reduced. Whether it is beneficial for patients to substitute decreasing oral intake with artificial hydration has been debated frequently[12-14]. This debate has mostly focused on two distinct symptoms: death rattle, which has been linked to over-hydration, and terminal restlessness, which has been linked to under-hydration. To investigate whether the amount of fluid intake, preceding and during the dying phase, is related to the occurrence of death rattle and terminal restlessness, we performed a multicentre prospective observational study in patients who were, according to their multidisciplinary care team, likely to die within a few days (chapter 5). We found that death rattle was reported at least once in 40% of patients during the dying phase, and in 35% of patients during the last 24 hours of life. The occurrence of death rattle increased with death coming nearer. Terminal restlessness was reported in 26% of patients during the dying phase and in 13% of patients during the last 24 hours of life. Terminal restlessness occurred almost evenly throughout the dying phase. We found no association between fluid intake and the occurrence of death rattle. Terminal restlessness during the last 24 hours of life was associated with a higher intake of fluid during the period 48-25 hours before death.

Being aware that death is imminent is often seen as one of the features of a good death in modern Western culture[15-19]. We studied to what extent patients are aware of the imminence of their death by performing a secondary analysis of data from questionnaires filled in by nurses and bereaved family members, and data from patients' medical record (chapter 6). We found varying reports on whether patients were aware of the imminence of their death. According to the medical records, 51% of patients had been aware of the imminence of death, according to nurses this was true for 58% and according to family members for 62% of patients. Inter-rater agreement on patients' awareness of dying was fair. Whether a patient was aware of the imminence of dying was not clearly associated with the occurrence of symptoms that are common in the last days of life, such as fatigue, shortness of breath, pain, dysphagia or restlessness. Patients dying at home were more often aware of the imminence of death than patients who died in a hospital or in a nursing home. We also found that awareness of imminent death was associated with acceptance of dying: patients who were aware of the imminence of death were more often in peace with dying and more often felt that life had been worth living, than patients who had not been aware according to the family member.

Sometimes the symptoms which patients who are nearing death experience cannot be relieved with conventional therapeutic interventions. Palliative sedation is used to alleviate unbearable and refractory suffering in the last phase of life and has been linked to distress in nurses[20 21]. To explore the extent to which nurses experience distress when being involved in the practice of palliative sedation, we performed a secondary analysis of data from qualitative interviews with nurses (chapter 7). We found that whether or not a patient is experiencing unbearable suffering can be judged differently by the family, the physician or the nurse. Nurses described morally distressing situations in which they felt that providing palliative sedation was in the patient's best interest, but experienced (real or perceived) constraints from physicians that prevented them from taking action. In these situations nurses felt that starting palliative sedation was necessary to alleviate the patient's suffering, whereas the physician thought that it was too early. Nurses also described situations in which they experienced pressure from physicians or family members to be actively involved in the provision of palliative sedation, but felt that this was not in the patient's best interest. The latter situation was related to (1) starting palliative sedation when the nurse felt not all options to relieve suffering had been explored; (2) family requesting an increase of the sedation level where the nurse felt that this may involve hastening of death; (3) a decision by the physician to start palliative sedation where the patient had previously expressed an explicit wish for euthanasia.

METHODOLOGICAL AND OTHER CONSIDERATIONS

We used different methods in the studies described in this thesis: cross-sectional surveys among patients and family members; a systematic literature review; a prospective observational study; secondary analyses of (1) cross-sectional data collected through questionnaires and from the medical record, and (2) data from qualitative interviews. Methodological and other considerations will be discussed per study.

Cross-sectional surveys - Prevalence & impact of symptoms in 2 understudied patient groups

A cross-sectional study is an observational study that provides a snapshot of a certain population. For the data collection in the head and neck-study (chapter 2) we used instruments (i.e. Pal-C and Pal-SI) that were judged by the healthcare professionals as practical for gathering information on symptom prevalence in the least possible intrusive way. However, these instruments did not undergo a formal psychometric evaluation. In this study, data were provided by two separate groups: the first group consisted of 124 patients who provided information on symptom presence, the second group consisted of 24 patient and family member couples who both provided information on the impact of symptoms. The 44% non-response within the group that provided information on symptom prevalence is a limitation. Non-responding patients had a significantly shorter life expectancy and seemed to have a much worse condition than responding patients. The large nonresponse (more specifically, patients who did not respond because of their weak condition) within this group confirms how vulnerable this specific cancer population is. The number of patients and family members in the group that provided information on the impact of symptoms was small which limits the possibility to generalize results.

In the heart failure study (chapter 3), we used the Memorial Symptom Assessment Scale (MSAS), a widely used and well validated instrument. Patients were recruited over the course of a month at multiple wards of the hospital and the questionnaire was available in different languages. Although we had a high response rate, most patients who were included in the study were diagnosed with stage III heart failure. It is therefore possible that our results are not generalizable to patients with stage IV heart failure.

Systematic review - Death rattle prevalence, impact and interventions

We conducted a systematic review to synthesize current evidence concerning the symptom death rattle (chapter 4). We found that the reported death rattle prevalence varied widely between studies. This variation might be explained by several factors. First, there is a wide variety of labels used to describe death rattle, and whether various labels all refer to the exact same phenomenon is not clear. Second, different study designs were used. 34% were prospective studies and the weighted mean occurrence of death rattle in these studies was 45%. Sixty-four percent of the studies were retrospective studies and the weighted mean occurrence of death rattle in these studies was 30%. Third, methods to determine the prevalence of death rattle varied between the studies. Few studies used validated instruments, such as the death rattle scoring scale[22].

The most optimal study design to evaluate the effectiveness of medical therapy and other interventions for death rattle is a controlled study. We found no studies that included a placebo group. Further, randomized controlled trials among patients who are in the dying phase are rare, mainly because of ethical and practical considerations related to randomization, informed consent, use of placebo and follow-up[1-5.]

Prospective observational study - Hydration and symptoms in the last days of life

A randomized controlled trial would also be the most optimal design to study the effects of fluid intake on the occurrence of symptoms, but would pose ethical challenges. In the Netherlands, healthcare professionals tend to be reserved about prescribing artificial hydration at the end of life.[23] In daily practice, fluid intake and administration of hydration vary. Therefore, we conducted a prospective observational study, to explore whether there is a relation between fluid intake in daily practice and the occurrence of death rattle and terminal restlessness (chapter 5). We prospectively collected information on fluid intake at three moments in time: the week before the start of the Care Program for the Dying (CPD), the day before the start of the CPD and 4 hourly during the dying phase, i.e. after the CPD was started. The occurrence of symptoms was also measured 4 hourly during the dying phase. To avoid mixing cause and effect, we calculated the total amount of fluid intake during the time period 48-25 hours before death and related this to occurrence of death rattle and terminal restlessness during the last 24 hours of life. Whereas terminal restlessness occurred almost evenly throughout the dying phase and often only once, it is possible that patients who were classified as having no terminal restlessness during the last 24 hours of life actually presented with terminal restlessness before the last 24 hours of life but were successfully treated, e.g. by providing them with palliative sedation. However, we found no evidence that patients with terminal restlessness were more often sedated than patients without terminal restlessness. At the start of this study no instrument to measure terminal restlessness was available. We therefore decided to use the calmness scale of the Vancouver Interaction and Calmness Scale. Whereas the value of this instrument to measure terminal restlessness has not been assessed, it is possible that patients were misclassified. The prevalence found in our study is however in line with other studies on restlessness in the terminal phase of life. Occurrence of death rattle was measured using the validated Death rattle scoring scale by Back et al[22].

Secondary analyses – Awareness of dying & Palliative sedation and moral distress

An advantage of secondary analyses of research data is that it is a form of efficient use of research data. Especially for research in palliative care with its potentially fragile patients it is an advantage when data can be used as efficient as possible. However, when using data from qualitative studies, (chapter 7) it is unclear if the number of interviews was sufficient to achieve saturation of information on the researched topic. It is possible that relevant information is missed. In both secondary analyses, (chapter 6 & 7) data were used that were collected after the death of a patient. A certain degree of recall bias can therefore not be precluded. For the qualitative interviews, we tried to limit this bias by focusing on specific and recent cases.

INTERPRETATION OF THE FINDINGS

Acknowledging different perspectives

The studies in this thesis cover various aspects of the burden and management of symptoms during the last phase of life of patients with an advanced illness. A recurrent theme in the studies in this thesis is the presence of different perspectives. A specific situation can be viewed upon differently by different observers. Also, 'what you see is not always all there is to see'. In palliative care, this was already suggested when Dame Cicely Saunders in 1964 introduced the concept of 'total pain', which includes the physical, emotional, social, and spiritual dimensions of distress and thus encompasses more than might be expected when discussing pain[24].

In several specific situations studied in this thesis different perspectives appeared to be present: symptom prevalence and burden in patients with head and neck cancer may vary according to patients and family members (chapter 2), awareness of dying of a patient may vary according to healthcare professionals and family members (chapter 6) and what is in the best interest of a patient may vary according to nurses, physicians and family members in our study on palliative sedation (chapter 7).

A patient's assessment is often seen as the gold standard source to collect information about their health status. But even a patient's rating may not always be in accordance with reality, because patients may e.g. underreport symptoms because they do not want to be a burden, or prefer not to worry their family members[25-29]. At the end of life and especially in after-death research, so called proxy-ratings are often used, i.e. a healthcare professional or a family member is asked to provide information on the patient's situation. Studies have shown that patients' ratings of e.g. symptoms may differ from proxy ratings[25 30]. It does not seem to matter in this respect who the proxy is (i.e. healthcare professional or family member)[25]. Proxies have been shown to reliably report on the more objectively observable symptoms. Agreement is poorer when the reporting is about more subjective symptoms, such as pain, feelings and thoughts, anxiety and depression[30]. This is in line with the results in our study in patients with head and neck cancer, in which we saw overreporting by family members of dyspnoea and underreporting of powerlessness and anxiety (chapter 2). The level of patient-proxy agreement appears to be dependent, to a certain degree, on the health status of the patient. Several studies have suggested a U-shaped relationship, meaning that agreement is better when the patient's health status is either very good or very poor[25]. However, views on whether or not patients are aware of the imminence of death diverged between different caregivers (chapter 6). In our study on palliative sedation, the nurse, the physician and the family members appeared to potentially have different views on whether or not a patient was experiencing unbearable suffering (chapter 7). Nurses, physicians and family members usually differ on their level of knowledge and they have different roles and responsibilities when it comes to end of life care and decision making. We found in our study that nurses feel that they are very capable of estimating dying patients' needs, because of their experience and nearness to the patient. They however do not have the authority to make decisions on medical care and treatment, only physicians are legally responsible for making such decisions[31 32].

In our study on symptoms in patients with advanced heart failure, we found that patients reported more symptoms than expected (chapter 3). Many of the reported symptoms are not generally thought of as being caused by heart failure[33 34]. These symptoms might be related to treatment, but the causes of symptoms such as pain remain unclear. Two reviews have focused on symptoms in the last year of life and compared patients with cancer to those with other diagnoses[35 36]. They found that irrespective of the primary diagnosis, commonalities in the prevalence of symptoms were evident. The recommendation following that conclusion is that healthcare professionals should be aware that patients with life-limiting illnesses may exhibit problems and needs that are not strictly associated with their specific diagnosis. This suggests that there is a need for broad symptom screening, also because multimorbidity is currently becoming the norm at the end of life[37].

It is evident that different perspectives exist in the last phase of life. These different perspectives may result from a different appreciation of a phenomenon, a lack of evidence on what the most beneficial intervention would be, or from a lack of communication among those involved. Evidence and communication are to a certain extent within our reach to tackle, but some causes of different perspectives will remain. It is important to be aware of the potential presence of these different perspectives, to acknowledge them and to make them part of the continuous communication about the patients' health status, with patients, family members and within the healthcare team.

'Acknowledging different perspectives: it needs words.'

Communication

Honest and sensitive communication has been identified by patients and family members as one of the most important elements of care during the last phase of life[38-40]. Care during the last phase of life is often delivered by a multidisciplinary team, which requires continuous communication and shared insights within the team and regular conversations between team members, patients, and family members[41].

A systematic review on the preferences for end-of-life communication of patients with advanced diseases and their family members showed their need for clear information at all stages of the illness trajectory, about the illness itself, prognosis and symptom management[40]. It is important to inform the patient and family members about what can be expected during the last phase of life. This information should be repeated regularly and tailored to existing or expected symptoms. Also, discussions about what is experienced by the patient and family members are important. Being a family member of someone who is in the last phase of life is often an intense and difficult experience. It can be the family member's first actual encounter with dying and death[42]. Even if family members are aware of the imminence of death, this does not mean that they are prepared for it[43]. A death from a chronic illness that is expected by healthcare professionals may be experienced as unexpected and traumatic by family members who are focusing on caregiving rather than on preparing themselves for bereavement[44-47]. In our study on palliative sedation (chapter 7) nurses described requests from family members to start palliative sedation or to expedite the patient's dying trajectory after palliative sedation had been started, which were from the perspective of the nurse not indicated or appropriate yet. Watching how a close relative is dying can be a heavy burden for family members, sometimes an even greater burden than for the patient him- or herself, which may result in such requests. It is important for healthcare professionals to listen to the family members, acknowledge their experiences and to communicate with the distressed family members to explain why their request may not be appropriate yet.

When focusing on two distinct symptoms of the dying phase, death rattle and terminal restlessness (chapter 4 and 5), there are different perspectives on how these symptoms should be addressed. For death rattle, this seems to be related to whether this symptom is seen as a normal phenomenon at the end of life. When death rattle is seen as a distressing symptom which should be managed, communication and actions are most likely different from situations where the symptom is seen as a normal and non-burdening phenomenon of the dying phase[48 49].

When healthcare professionals communicate within the healthcare team, and with patients and their family members during the last phase of life, it is important to be sensitive about what is said and about how and when and by whom it is said. In addition, they need to listen to what patients and family members say, but also 'hear' what they do not (explicitly) say. Being sensitive to non-verbal cues and 'reading between the lines' is sometimes necessary to 'hear' what worries patients, family, or other healthcare professionals have, and what questions or fears for the near future.

IMPLICATIONS AND RECOMMENDATIONS

For clinical practice

Systematic screening of common symptoms is needed for patients with advanced illness, to be able to address the symptoms that are most distressing or burdensome for a patient. Screening of symptoms should not be limited to their presence, but should include a measure of the extent to which they cause distress or impact on daily functioning. For this screening, many (generic) symptom assessment instruments are available[50 51]. Bearing in mind the deteriorating condition of the patient, the length of such screening instruments should be kept to a minimum. Digital tools like computerized adaptive testing should be considered where possible. For care during the dying phase, the Care Program for the Dying can be used as a clinical instrument, because it includes systematic screening of the most common symptoms during the dying phase.

Care during the last phase of life should include continuous communication about the patients' health status, with patients and family members to identify potential differences in perspectives and appreciations of the patient's situation. The expected course of the illness, which symptoms could occur and the available treatment options should be discussed regularly. Palliative care is interdisciplinary care in which the complementary competences from different healthcare professionals are combined[52]. Ongoing communication within the healthcare team should be an integral part of palliative care. By doing so, physicians and nurses should be better able to understand each other's viewpoints and argumentation.

Proactive care planning and anticipatory prescription of medication are of the essence. Decisions to start palliative sedation for patients with refractory and unbearable suffering should not come as a 'surprise' to the involved health care professionals; instead, it should be the anticipated potential follow-up of efforts to control symptoms near the end of life.

For research

The number of studies focusing on symptoms in patients with advanced diseases has increased during the last decades. Future research should focus on understudied non-cancer groups and effectiveness of interventions for certain understudied symptoms during the last phase of life, such as death rattle. Our systematic review showed that death rattle leads to distress in both family members and professional caregivers, and that there is a lack of evidence for the effectiveness of any antimuscarinic medication in the treatment of death rattle (chapter 4). From a pharmacological perspective, antimuscarinic medications are unable to reduce existing secretions[53]. There are however indications that antimuscarinic medication might have a prophylactic effect[53-55]. Studies on the effectiveness of prophylactic prescription of antimuscarinic medication on the development of death rattle are therefore needed. Studies are also needed on the effectiveness of nursing interventions to address death rattle, such as repositioning of the patient and suctioning of secretions. The effectiveness of nursing interventions also needs to be investigated for many other symptoms, as the medical interventions often have limited results in the last phase of life[56-58].

Our findings on awareness of dying suggest that communication during patients' dying phase is not yet optimal (chapter 6). The optimal time and strategy to enhance open communication about the dying phase cannot be concluded from our data and should be a topic in future research.

In this thesis, various aspects of symptoms and symptom relief during the last phase of life of patients with advanced diseases have been discussed. To be able to provide good quality of care during the last phase of life, we need to systematically screen for common symptoms, acknowledge different perspectives, communicate continually and tailor our care to the needs of the individual patient and their family members.

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