We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Chapter

Communication with Families in the Last Days of a Patient's Life and Optimal Delivery of a Death Pronouncement

Soichiro Okamoto, Yu Uneno, Masanori Mori, Takashi Yamaguchi and Nobuhisa Nakajima

Abstract

Communicating with family members is critically important when a severely ill patient is experiencing their last few days of life. However, healthcare professionals (HCPs) have limited opportunities to learn effective and respectful ways to perform this communication. In recent decades, significant effort has been put forth to identify the phenomena that indicate the last hours and days of life and the optimal methods to deliver a death pronouncement, which will potentially help HCPs communicate compassionately with family members throughout the dying process. In this chapter, we will review the literature regarding the phenomena that indicate the last hours and days of life and the death pronouncement. Furthermore, we will discuss clinical implications derived from those articles and future research perspectives.

Keywords: communication, impending death, bereaving family, death pronouncement

1. Introduction

The death and dying of a loved one can place a serious emotional burden on his/her family members [1]. The methods of communication during the dying process and the death pronouncement are critically important because they can affect the families' acute emotional responses and their long-term psychological well-being [2]. However, there are limited opportunities to learn effective and respectful methods of how to communicate at the end of life and the pronouncement of a patient's death even though healthcare professionals (HCPs) often experience such challenges in daily practice.

Over the last decade, cumulative evidence has revealed various phenomena that indicate the patient is experiencing their last hours and days of life (e.g., death rattle, cyanoses, or Cheyne-Stokes respiration) [3, 4]. Sharing these bedside clinical signs with families can allow them to understand the patients' condition, estimate prognosis, and prepare for the impending event. Moreover, a recent unique research study regarding the death pronouncement (e.g., a video-vignette study design) revealed effective and respectful ways to deliver this pronouncement [5].

The communication processes between HCPs and family members can potentially reduce the unpleasant emotional responses of the families.

In this chapter, we will review the reported literature regarding communication during the dying process and death pronouncement. Furthermore, we will discuss clinical implications derived from those articles and future research perspectives.

2. Phenomena indicating the last hours and days of life

As the time of death approaches, patients with advanced cancer follow various clinical courses and commonly experience serious burdens such as pain, dyspnea, or delirium [4, 6]. Previous literature has reported that patients and their family members hope to be free from physical and emotional distress at the end of life, and it is challenging for HCPs to assess the patients' distress and deliver optimal care during end-of-life situations [7]. Understanding the bedside trajectory of the patients' symptoms and distress will potentially allow HCPs to develop a reasonable end-of-life care pathway, which enables them to share the patient's condition and promotes family members to prepare for the impending event [3, 8]. Actually, leaflet-based interventions that describe physical impending death signs have been revealed to improve family members' knowledge and distress throughout the dying process [9, 10].

We herein review the literature regarding representative and common phenomena that indicate the last hours and days of life.

2.1 Common symptoms in the last weeks of life

During the last 2 weeks of life, dyspnea, pain, increased bronchial secretions, and confusion occur with prevalence of 56.7, 52.4, 51.4, and 50.1%, respectively [4]. As death approaches, the prevalence of dyspnea and confusion increases [8]. Meanwhile, pain was reported to reach a stable level of intensity [8]. Thus, HCPs must not underestimate those common symptoms and other hidden signs of distress and symptoms in patients.

Accordingly, performance status also deteriorates throughout the dying process [8, 11]. Because of muscle weakness and refractory cachexia, time spent in bed increases. Moreover, patients experience difficulties with performing daily activities such as changing clothes, bathing, swallowing, etc. At this point, because of the loss of autonomy, patients often feel emotionally and spiritually burdened, and supportive communication to cope with these distresses must be encouraged.

2.2 Common symptoms in the last days of life

In 2013, a Delphi method study including a panel of palliative care experts reached a consensus that the following seven clinical signs serve as impending death signs: changing breathing rhythm and patterns (e.g., Cheyne-Stokes respiration, apnea), irreversible deterioration of consciousness, no fluid or food intake, marble-like skin, changing emotional status (e.g., restlessness, agitation), rapid degradation of general condition, and intuition of professionals (gut feeling) [12]. A unique longitudinal observational study revealed a detailed symptom trajectory in the last days of life [13]. In this study, apnea, Cheyne-Stokes respiration, increased bronchial secretions, dysphasia of liquids, a decreased level of consciousness, a palliative performance scale score $\leq$ 20%, peripheral cyanosis, pulselessness of the radial artery, respiration with mandibulae movement, and decreased urine output were recognized as impending death signs. Particularly, a palliative performance scale score $\leq$ 20%, decreased levels of consciousness, and dysphasia of liquids

commonly occur in the last 3 days of life. The authors suggested dividing impending death signs into two categories: early and late signs [13]. Early signs (e.g., decreased performance status, decreased oral intake, and decreased level of consciousness) are observed relatively frequently. Because of their low specificity, these signs are not reliable predictive markers of a death event within 3 days. By contrast, late signs emerge only in the last few days of life in a smaller proportion of patients and had a high positive likelihood ratio for impending death within 3 days. The author concluded that late physical signs may assist clinicians in making a diagnosis of impending death [13]. The same research groups reported an inability to close the eyelids, drooping of the nasolabial fold, hyperextension of the neck, and grunting of vocal cords as promising impending death signs [14].

2.3 Detailed discussion of common symptoms and clinical signs

2.3.1 Pain

Pain control is a common clinical challenge at any stage of disease [15]. Pain in the last 2 weeks of life and 48 hours before death occurs with a prevalence of 44 and 54%, respectively [4, 7]. With inappropriate pain control, both patients and caregivers are likely to complain of fatigue, anorexia, and insomnia [16].

Various agents have been investigated to relieve cancer pain and pathophysiological assessments of pain (e.g., nociceptive, somatic, and visceral pain); therefore, selecting a reasonable treatment strategy is essential [17–21]. During the end-of-life stage, many patients suffer from swallowing difficulties, and in such cases, HCPs must consider alternative routes for administering analgesics to achieve appropriate pain control without interruption. Intravenous and subcutaneous administrations are stable, less invasive methods [22].

2.3.2 Dyspnea

Dyspnea results from several causes, including atelectasis due to tumor growth, pleural effusion, superior vena cava syndrome, pulmonary embolism, anemia, etc. [15, 23, 24]. The prevalence of dyspnea in the last 2 weeks of life is 56.7% [4]. Patient dyspnea is well known to be associated with family members' distress [25].

The effect of morphine on alleviating dyspnea has been well investigated [26]. Because of the deteriorated capacity of drug metabolism and excretory abilities during the end-of-life period, the administration of morphine requires careful monitoring of adverse events (e.g., impaired conscious state and decreased respiration rate) [26]. Given the concerns of those adverse events, physicians are less confident with prescribing opioids for dyspnea than for pain, which can result in the undertreatment of dyspnea [27]. Optimal clinical training is warranted in this setting. In addition, benzodiazepines can be a treatment option against refractory dyspnea [25].

In addition to pharmacological treatment, some non-pharmacological approaches are also promising for dyspnea. Recently, a unique study revealed that fan therapy toward the face is effective for patients with advanced lung cancer [28, 29]. Moreover, it is empirically known that changing body posture and discharging sputum are also effective methods of dyspnea care.

2.3.3 Increased bronchial secretions

With impending death, a rattle sound can be heard during both the inspiratory and expiratory phases around the upper respiratory tract area. Bennett divided this symptom into two subtypes: type I and II [30]. Type I is mainly

caused by the accumulation of salivary secretions due to a decrease in consciousness and swallowing reflex [30]. Generally, anticholinergic drugs that suppress secretions from the salivary glands and endobronchial mucous are promising strategies to treat type I. Since type II is believed to be caused by purulent sputum such as tumor-derived secretions and pneumonia, anticholinergics are considered ineffective [30].

Classical anticholinergic drugs such as atropine, scopolamine hydrobromide, and glycopyrronium, which reduce secretions from the salivary glands and bronchial mucosa, are commonly used [31]. These medications can be administered sublingually, subcutaneously, and intravenously. Despite the cumulative experience of administering classical anticholinergic drugs among HCPs, there is a lack of sufficient investigations on their effects. A double-blinded clinical trial from Germany showed the superior efficacy of glycopyrronium compared to scopolamine hydrobromide [32]. In a randomized controlled trial conducted in Belgium, the subcutaneous administration of atropine, scopolamine butylbromide, and scopolamine hydrobromide showed an improvement of approximately 40% on a pre-post basis; no significant difference between the drugs was reported [33]. Recently, the prophylactic administration of hyoscine butylbromide was shown to effectively prevent the death rattle [34]. However, because a randomized controlled study found that atropine was not superior to a placebo control, anticholinergic drugs are not widely recognized as the gold standard treatment [35].

Since the rattle sound due to increased bronchial secretions may cause family members to anticipate patient distress, appropriate information sharing among family members and HCPs is crucial [36]. A survey for bereaved family members revealed that 66% felt distress due to the rattle sound and 53% reported the need to improve this symptom [36]. Conversely, another study found that the death rattle may not be associated with respiratory distress in coma patients [37]. In cases of refractory rattle sounds, HCPs must explain to family members that the patients are experiencing limited distress, and HCPs should continue care for their grief and suffering [37].

2.3.4 Delirium

Delirium at the terminal stage is occasionally described as agitation or terminal restlessness, which occurs as an irreversible symptom due to organ dysfunction [38]. Delirium occurred in 44% of patients during the last 7 days of life, and 88% of cancer patients with delirium had incurable end-stage delirium [38]. Delirium not only causes patients unbearable distress, but more than half (54%) of the family members reported distress as well [39].

To treat a patient's delirium, the reversible causes must be examined and treated (e.g., infection, electrolyte abnormalities, nutritional deficiency, dehydration, and medications). The administration of olanzapine, quetiapine, and aripiprazole may provide some benefits for the patient [40]. Although a clinical study showed that neither oral haloperidol nor risperidone had a demonstrable benefit on the symptomatic management of mild-to-moderate delirium, antipsychiatry drugs including haloperidol and chlorpromazine are generally used for delirium in end-stage patients [41, 42]. Administering haloperidol with lorazepam may benefit terminal cancer patients (median overall survival of 73 hours) with agitated delirium [43]. Since these drugs can be administered intravenously, subcutaneously, or intramuscularly, suitable administration is possible even in end-of-life patients. However, since it may fail to show improvements despite appropriate treatment and care, delirium is one of the most common reasons for the decision to initiate sedative therapy (57.1%) [44].

2.3.5 Vital signs

Vital signs include the level of consciousness, blood pressure, pulse rate, respiratory rate, O_2 saturation, etc. [45]. Vital signs are indicators that can reflect several abnormal and altered states of human biological status [46]. These indicators can often be surrogate markers of distress such as pain or dyspnea, even in patients with loss of consciousness. However, vital signs may have a limited role as prognosis predictors. Previous literature has revealed that blood pressure and O_2 saturation tend to decrease and body temperature tends to increase in the last 3 days of life, but their sensitivity and specificity to predict death within 3 days were 30 and 80%, respectively [45]. Thus, routine monitoring of vital signs may not be essential in end-of-life clinical practice.

2.3.6 Other clinical signs

Patients with Cheyne-Stokes respiration display abnormal respiration patterns that repeat cycles of apnea and a gradually increasing and decreasing respiratory rate [13]. During the last 3 days of life, 41% of patients experience this symptom [47].

Respiration with mandibulae movement is known as a late impending death sign. Patients unintentionally move their lower jaw up and down, commonly with loss of consciousness [13]. During the last 3 days of life, 56% of patients experience this symptom, which may predict death occurrence within 7.6 (±2.5) hours [48].

Cyanosis is caused by increased deoxyhemoglobin within the peripheral tissue. Central cyanosis is commonly derived from shock status and congestive heart failure, whereas peripheral cyanosis commonly affects local lesions caused by peripheral vascular disease [13]. At the end of life, cyanosis is believed to be caused by contraction of the peripheral vessels. During the last 3 days of life, 56% of patients experience this symptom, which can predict death occurrence within 5.1 (±1.0) hours [48].

2.3.7 Prognosis prediction

Prognosis prediction is also a critical issue in end-of-life care and is partially composed of the abovementioned symptoms and clinical signs. Several user-friendly clinical tools have been developed in previous studies, such as the palliative prognostic score, the palliative prognostic index, and prognostic in palliative care study predictor models [49–51]. Detailed discussion regarding this topic is described elsewhere [52].

3. Death pronouncement

When a patient dies, physicians must relay this information to his/her family members. Generally, to diagnose the patient's death, physicians examine the vanished pulse, respiratory cycles, and heart sounds [53]. This procedure is not only a clinical practice but is also a valuable opportunity for compassionate communication with his/her family members and can help alleviate their grief and emotional burden [53, 54]. Recent evidence has disclosed the optimal way to deliver a death pronouncement. However, the death pronouncement can be a considerably stressful event even for physicians, which potentially leads to unfavorable outcomes such as insomnia, anxiety, or depression. Brown et al. revealed that the death pronouncement can cause serious distress even in simulation settings [55]. Education for HCPs and healthcare students may play an essential role in coping with this distress. To

date, several educational activities regarding death pronouncement and procedure guides have been developed.

We herein review the previous literature regarding the optimal method of delivering the death pronouncement and education on this topic.

3.1 History of death pronouncement education

Initially, narrative guidelines for death pronouncements were proposed in the early 1990s. In 1992, Terri A. Schmidt et al. proposed a program that included 17 recommendations on how to conduct interactions with survivors following a patient's sudden death in the emergency department [56]. This program required 2 1/2 hours to complete and allowed residents to practice their communication skills in a protected setting [56]. In the same year, the Office of Attorney General of Iowa proposed a recommended procedure for the death pronouncement called "in person, in time." This recommendation conveyed the following five concepts: "in person" (respect for privacy and for free emotional reactions), "in time" (information should be delivered as soon as possible), "in pairs" (news should be delivered by a team of two notifiers), "in plain language" (the message should be relayed directly; the notifier ought to speak slowly and in single sentences, giving details and answering questions), and "with compassion" (empathy, the attempt to understand emotions accompanying individuals who are notified about the death of a close relative, is essential) [57]. In 1998, Lucille Marchand et al. introduced brief clinical tips for residents, which included six steps (the phone call, the patient floor, in the room, the pronouncement, documentation, and when to call the corner), to clarify how the death pronouncement process should proceed [58].

3.2 Educational intervention regarding the death pronouncement

In conjunction with those narrative approach efforts mentioned above, the efficacy of the educational intervention was investigated. Marc et al. reported that one and a half lectures regarding the death pronouncement improved the skills of resident physicians who attended an ACLS course [59]. Lucille Marchand et al. reported on outcomes derived from a workshop based on six essential competencies (patient care, medical knowledge, practice-based learning and improvement, systems-based practice, professionalism, and interpersonal skills communication) proposed by the Accreditation Council for Graduate Medical Education's Outcome Project [60]. This workshop provided the opportunities to learn poetry, prose, and narratives on delivering death pronouncements by senior residents; reviews and discussion of protocols for death pronouncement, autopsy, and organ donation; and a roleplay of a death pronouncement with the opportunity for reflection [60]. In 2005, Bailey et al. examined the effectiveness of a 10-minute death pronouncement module and pocket-card guideline approach [54]. This intervention improved five self-assessed competencies, including three procedure skills (clinical examination for pronouncing death, writing the death note, and completing the death certificate) and two communication skills (informing the family about the death and assessing/managing family bereavement) [54]. In 2008, Hobgood et al. investigated the efficacy of a 2-hour teaching module based on the mnemonic "The GRIE_VING," which included small group discussion, roleplay, and didactic experiences [61]. This module improved resident confidence and competency scores on a pre-post basis [61]. The authors also reported on the efficacy of this intervention in fourth-year medical students [62]. In 2011, Nordstrom et al. reported a unique approach employing a marathon death exercise. This exercise was designed to enable fourth-year medical students to gain insight into the emotional and formal procedure of delivering a death pronouncement [63].

As mentioned above, a considerable number of studies that used lectures and/or roleplay for pre/post medical education showed promising efficacy.

3.3 Optimal method of delivering the death pronouncement

In addition to considering and discussing the optimal way to deliver a death pronouncement among HCPs, it may be helpful to acquire opinions from viewpoints of family members, which potentially include definite answers. Kusakabe et al. performed a survey of bereaved family members [64]. The families experienced a death pronouncement in home care settings, and 89% reported that there were no deficiencies throughout the process [64]. Family members reported that positive physician behaviors included acting calmly (not rushed), having a suitable appearance for the situation, introducing themselves to the family members, explaining the cause of death explicitly, and conducting a check using a light and stethoscope for the death pronouncement. Negative behaviors included a lack of clearly verifying the time of death and leaving the patient's clothes disheveled. Interestingly, Japanese family members did not appreciate touching the family members' backs or shoulders as an expression of empathy [64]. Hatano et al. also conducted a survey of bereaved family members from hospice or palliative care unit settings [65]. Overall, 86% of bereaved caregivers reported satisfaction with physician behavior toward the death pronouncement; however, 22% felt there were several areas requiring improvement. The bereaved caregivers did not appreciate automatic or routine pronouncement behaviors. Likewise, a logistic regression analysis revealed that "polite behavior" and the "physician introduced himself/herself to the family" were preferred behaviors. Confirmation by the primary responsible physician was significantly preferred than that by an unfamiliar physician [65]. Based on these findings of optimal behaviors, Mori et al. performed a unique study applying a randomized, scripted, video-vignette study design [5]. In this randomized, video-vignette study, volunteer participants viewed two videos of death pronouncements by an on-call physician with or without compassion-enhanced behaviors [5]. This behavior included five components: "waiting until the families calm themselves down, explaining that the physician has received a sign-out containing information of the patient's condition, performing the examination respectfully, ascertaining the time of death with a wristwatch (vs. a smartphone), and reassuring the families that the patient did not experience pain." Participants who viewed the compassion-enhanced behaviors video assigned significantly higher scores for physician compassion and trust in the physician and lower scores for anger, sadness, fear, and disgust. This study proposed recommendations that physicians should initiate a prompt examination, explain that they have received a sign-out, perform the examination respectfully, ascertain the time of death with a wristwatch, and reassure the families that the patient did not experience pain [5].

3.4 Future perspectives

As described above, several educational intervention models have been developed, and reasonable methods of delivering the death pronouncement have been proposed. However, one study suggested that only 35% of the procedures were judged as acceptable [66]. We must continue to grasp and improve the overall quality of the death pronouncement delivery by HCPs. Moreover, to determine the HCPs' burden in this setting, a scale that measures the difficulties of delivering a death pronouncement must be developed.

The next steps must investigate whether those interventions or behaviors truly improve the outcomes of bereaved family members (e.g., depression, anxiety, or

substance abuse.) Accordingly, investigating the efficacy of alleviating the emotional burden of HCPs is also necessary. Continuous efforts to develop effective educational interventions and implement practical models that can meet the needs of several medical contexts are also warranted.

4. Conclusions

In this chapter, we narratively reviewed various phenomena that indicate the impending last hours and days of life and the death pronouncement within a scientific context. These findings can help enable HCPs to engage in compassionate communication with the family members who share the same ultimate goals. Further efforts to integrate and enhance this knowledge and these activities are warranted to alleviate the burden and distress of patients, family members, and HCPs.

Acknowledgements

This work was supported by JSPS KAKENHI Grant Number JP18K15396.

Conflict of interest

No conflicts of interest are declared.

Author details

Soichiro Okamoto[1], Yu Uneno[2*], Masanori Mori[3], Takashi Yamaguchi[4] and Nobuhisa Nakajima[5]

1 Asoka Vihara Hospital, Kyoto, Japan

2 Seirei Hospice, Seirei Mikatahara General Hospital, Shizuoka, Japan

3 Palliative Care Team, Seirei Mikataraha General Hospital, Shizuoka, Japan

4 Division of Palliative Care, Department of Medicine, Konan Hospital, Japan

5 Division of Community-based Medicine and Primary Care, University of the Ryukyus Hospital, Okinawa, Japan

*Address all correspondence to: yuuneno@kuhp.kyoto-u.ac.jp

IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. CC BY

References

[1] Krawczyk M, Gallagher R. Communicating prognostic uncertainty in potential end-of-life contexts: Experiences of family members. BMC Palliative Care. 2016;**15**:59

[2] Steinhauser KE, Christakis NA, Clipp EC, McNeilly M, McIntyre L, Tulsky JA. Factors considered important at the end of life by patients, family, physicians, and other care providers. Journal of the American Medical Association. 2000;**284**(19):2476-2482

[3] Seow H, Barbera L, Sutradhar R, Howell D, Dudgeon D, Atzema C, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 2011;**29**(9):1151-1158

[4] Kehl KA, Kowalkowski JA. A systematic review of the prevalence of signs of impending death and symptoms in the last 2 weeks of life. American Journal of Hospice and Palliative Medicine. 2013;**30**(6):601-616

[5] Mori M, Fujimori M, Hamano J, Naito AS, Morita T. Which physicians' behaviors on death pronouncement affect family-perceived physician compassion? A randomized, scripted, video-vignette study. Journal of Pain and Symptom Management. 2018;**55**(2):189-97.e4

[6] de la Cruz M, Noguera A, San Miguel-Arregui MT, Williams J, Chisholm G, Bruera E. Delirium, agitation, and symptom distress within the final seven days of life among cancer patients receiving hospice care. Palliative & Supportive Care. 2015;**13**(2):211-216

[7] Ellershaw J, Smith C, Overill S, Walker SE, Aldridge J. Care of the dying: Setting standards for symptom control in the last 48 hours of life. Journal of Pain and Symptom Management. 2001;**21**(1):12-17

[8] Mercadante S, Casuccio A, Fulfaro F. The course of symptom frequency and intensity in advanced cancer patients followed at home. Journal of Pain and Symptom Management. 2000;**20**(2):104-112

[9] Otani H, Morita T, Uno S, Yamamoto R, Hirose H, Matsubara T, et al. Effect of leaflet-based intervention on family members of terminally ill patients with cancer having delirium: Historical control study. American Journal of Hospice and Palliative Medicine. 2014;**31**(3):322-326

[10] Otani H, Morita T, Uno S, Yamamoto R, Hirose H, Matsubara T, et al. Usefulness of the leaflet-based intervention for family members of terminally ill cancer patients with delirium. Journal of Palliative Medicine. 2013;**16**(4):419-422

[11] Hui D, dos Santos R, Chisholm GB, Bruera E. Symptom expression in the last seven days of life among cancer patients admitted to acute palliative care units. Journal of Pain and Symptom Management. 2015;**50**(4):488-494

[12] Domeisen Benedetti F, Ostgathe C, Clark J, Costantini M, Daud ML, Grossenbacher-Gschwend B, et al. International palliative care experts' view on phenomena indicating the last hours and days of life. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer. 2013;**21**(6):1509-1517

[13] Hui D, dos Santos R, Chisholm G, Bansal S, Silva TB, Kilgore K, et al. Clinical signs of impending death in cancer patients. The Oncologist. 2014;**19**(6):681-687

[14] Hui D, Dos Santos R, Chisholm G, Bansal S, Souza Crovador C, Bruera E. Bedside clinical signs associated with impending death in patients with advanced cancer: Preliminary findings of a prospective, longitudinal cohort study. Cancer. 2015;**121**(6):960-967

[15] Teunissen SC, Wesker W, Kruitwagen C, de Haes HC, Voest EE, de Graeff A. Symptom prevalence in patients with incurable cancer: A systematic review. Journal of Pain and Symptom Management. 2007;**34**(1):94-104

[16] Ovayolu O, Ovayolu N, Aytac S, Serce S, Sevinc A. Pain in cancer patients: Pain assessment by patients and family caregivers and problems experienced by caregivers. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer. 2015;**23**(7):1857-1864

[17] Armstrong P, Wilkinson P, McCorry NK. Use of parecoxib by continuous subcutaneous infusion for cancer pain in a hospice population. BMJ Supportive & Palliative Care. 2018;**8**(1):25-29

[18] Myers KG, Trotman IF. Use of ketorolac by continuous subcutaneous infusion for the control of cancer-related pain. Postgraduate Medical Journal. 1994;**70**(823):359-362

[19] Negro S, Martin A, Azuara ML, Sanchez Y, Barcia E. Stability of tramadol and haloperidol for continuous subcutaneous infusion at home. Journal of Pain and Symptom Management. 2005;**30**(2):192-199

[20] Mercadante S, Lodi F, Sapio M, Calligara M, Serretta R. Long-term ketamine subcutaneous continuous infusion in neuropathic cancer pain. Journal of Pain and Symptom Management. 1995;**10**(7):564-568

[21] Centeno C, Vara F. Intermittent subcutaneous methadone administration in the management of cancer pain. Journal of Pain & Palliative Care Pharmacotherapy. 2005;**19**(2):7-12

[22] Dickman A, Bickerstaff M, Jackson R, Schneider J, Mason S, Ellershaw J. Identification of drug combinations administered by continuous subcutaneous infusion that require analysis for compatibility and stability. BMC Palliative Care. 2017;**16**(1):22

[23] Campbell ML, Kiernan JM, Strandmark J, Yarandi HN. Trajectory of dyspnea and respiratory distress among patients in the last month of life. Journal of Palliative Medicine. 2018;**21**(2):194-199

[24] Guirimand F, Sahut d'izarn M, Laporte L, Francillard M, Richard JF, Aegerter P. Sequential occurrence of dyspnea at the end of life in palliative care, according to the underlying cancer. Cancer Medicine. 2015;**4**(4):532-539

[25] Okamoto Y, Morita T, Tsuneto S, Aoyama M, Kizawa Y, Shima Y, et al. Bereaved family members' perceptions of the distressing symptoms of terminal patients with cancer. American Journal of Hospice and Palliative Medicine. 2018;**35**(7):972-977

[26] Jansen K, Haugen DF, Pont L, Ruths S. Safety and effectiveness of palliative drug treatment in the last days of life-a systematic literature review. Journal of Pain and Symptom Management. 2018;**55**(2):508-21.e3

[27] Hadjiphilippou S, Odogwu SE, Dand P. Doctors' attitudes towards prescribing opioids for refractory dyspnoea: A single-centred study. BMJ Supportive & Palliative Care. 2014;**4**(2):190-192

[28] Puspawati N, Sitorus R, Herawati T. Hand-held fan airflow stimulation relieves dyspnea in lung cancer patients. Asia-Pacific Journal of Oncology Nursing. 2017;**4**(2):162-167

[29] Kako J, Morita T, Yamaguchi T, Kobayashi M, Sekimoto A, Kinoshita H, et al. Fan therapy is effective in relieving dyspnea in patients with terminally ill cancer: A parallel-arm, randomized controlled trial. Journal of Pain and Symptom Management. 2018;**56**(4):493-500

[30] Bennett MI. Death rattle: An audit of hyoscine (scopolamine) use and review of management. Journal of Pain and Symptom Management. 1996;**12**(4):229-233

[31] Lokker ME, van Zuylen L, van der Rijt CC, van der Heide A. Prevalence, impact, and treatment of death rattle: A systematic review. Journal of Pain and Symptom Management. 2014;**47**(1):105-122

[32] Likar R, Rupacher E, Kager H, Molnar M, Pipam W, Sittl R. Efficacy of glycopyrronium bromide and scopolamine hydrobromide in patients with death rattle: A randomized controlled study. Wiener Klinische Wochenschrift. 2008;**120**(21-22):679-683

[33] Wildiers H, Dhaenekint C, Demeulenaere P, Clement PM, Desmet M, Van Nuffelen R, et al. Atropine, hyoscine butylbromide, or scopolamine are equally effective for the treatment of death rattle in terminal care. Journal of Pain and Symptom Management. 2009;**38**(1):124-133

[34] Mercadante S, Marinangeli F, Masedu F, Valenti M, Russo D, Ursini L, et al. Hyoscine butylbromide for the management of death rattle: Sooner rather than later. Journal of Pain and Symptom Management. 2018;**56**(6):902-907

[35] Heisler M, Hamilton G, Abbott A, Chengalaram A, Koceja T, Gerkin R. Randomized double-blind trial of sublingual atropine vs. placebo for the management of death rattle. Journal of Pain and Symptom Management. 2013;**45**(1):14-22

[36] Shimizu Y, Miyashita M, Morita T, Sato K, Tsuneto S, Shima Y. Care strategy for death rattle in terminally ill cancer patients and their family members: Recommendations from a cross-sectional nationwide survey of bereaved family members' perceptions. Journal of Pain and Symptom Management. 2014;**48**(1):2-12

[37] Campbell ML, Yarandi HN. Death rattle is not associated with patient respiratory distress: Is pharmacologic treatment indicated? Journal of Palliative Medicine. 2013;**16**(10):1255-1259

[38] Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: A prospective study. Archives of Internal Medicine. 2000;**160**(6):786-794

[39] Morita T, Akechi T, Ikenaga M, Inoue S, Kohara H, Matsubara T, et al. Terminal delirium: Recommendations from bereaved families' experiences. Journal of Pain and Symptom Management. 2007;**34**(6):579-589

[40] Bush SH, Lawlor PG, Ryan K, Centeno C, Lucchesi M, Kanji S, et al. Delirium in adult cancer patients: ESMO clinical practice guidelines. Annals of Oncology: Official Journal of the European Society for Medical Oncology (ESMO). 2018;**29**(Supplement_4):iv143-iiv65

[41] Agar MR, Lawlor PG, Quinn S, Draper B, Caplan GA, Rowett D, et al. Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: A randomized clinical trial. JAMA Internal Medicine. 2017;**177**(1):34-42

[42] Candy B, Jackson KC, Jones L, Leurent B, Tookman A, King M. Drug therapy for delirium in terminally ill adult patients. The Cochrane Database of Systematic Reviews. 2012;**11**:Cd004770

[43] Hui D, Frisbee-Hume S, Wilson A, Dibaj SS, Nguyen T, De La Cruz M, et al. Effect of lorazepam with haloperidol vs haloperidol alone on agitated delirium in patients with advanced cancer receiving palliative care: A randomized clinical trial. Journal of the American Medical Association. 2017;**318**(11):1047-1056

[44] Maltoni M, Scarpi E, Rosati M, Derni S, Fabbri L, Martini F, et al. Palliative sedation in end-of-life care and survival: A systematic review. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 2012;**30**(12):1378-1383

[45] Bruera S, Chisholm G, Dos Santos R, Crovador C, Bruera E, Hui D. Variations in vital signs in the last days of life in patients with advanced cancer. Journal of Pain and Symptom Management. 2014;**48**(4):510-517

[46] Hwang IC, Ahn HY, Park SM, Shim JY, Kim KK. Clinical changes in terminally ill cancer patients and death within 48 h: When should we refer patients to a separate room? Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer. 2013;**21**(3):835-840

[47] Hui D, Hess K, dos Santos R, Chisholm G, Bruera E. A diagnostic model for impending death in cancer patients: Preliminary report. Cancer. 2015;**121**(21):3914-3921

[48] Morita T, Ichiki T, Tsunoda J, Inoue S, Chihara S. A prospective study on the dying process in terminally ill cancer patients. American Journal of Hospice and Palliative Medicine. 1998;**15**(4):217-222

[49] Morita T, Tsunoda J, Inoue S, Chihara S. The palliative prognostic index: A scoring system for survival prediction of terminally ill cancer patients. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer. 1999;**7**(3):128-133

[50] Glare PA, Eychmueller S, McMahon P. Diagnostic accuracy of the palliative prognostic score in hospitalized patients with advanced cancer. Journal of Clinical Oncology. 2004;**22**(23):4823-4828

[51] Gwilliam B, Keeley V, Todd C, Gittins M, Roberts C, Kelly L, et al. Development of prognosis in palliative care study (PiPS) predictor models to improve prognostication in advanced cancer: Prospective cohort study. British Medical Journal (Clinical Research Edition). 2011;**343**:d4920

[52] Uneno Y, Kanai M. Prognosis Prediction Models and their Clinical Utility in Palliative Care. In book: Highlights on Several Underestimated Topics in Palliative Care. Intech. 2017. DOI: 10.5772/intechopen.69663

[53] Hallenbeck J. Palliative care in the final days of life: "They were expecting it at any time". Journal of the American Medical Association. 2005;**293**(18):2265-2271

[54] Bailey FA, Williams BR. Preparation of residents for death pronouncement: A sensitive and supportive method. Palliative & Supportive Care. 2005;**3**(2):107-114

[55] Brown R, Dunn S, Byrnes K, Morris R, Heinrich P, Shaw J. Doctors' stress responses and poor communication performance in simulated bad-news consultations. Academic

Medicine: Journal of the Association of American Medical Colleges. 2009;**84**(11):1595-1602

[56] Schmidt TA, Norton RL, Tolle SW. Sudden death in the ED: Educating residents to compassionately inform families. The Journal of Emergency Medicine. 1992;**10**(5):643-647

[57] Sobczak K. The procedure for death notification-"In person, in time...". Anaesthesiology Intensive Therapy. 2013;**45**(4):241-243

[58] Marchand LR, Kushner KP, Siewert L. Death pronouncement: Survival tips for residents. American Family Physician. 1998;**58**(1):284-285

[59] Pollack M. Educating new resident physicians in death notification. Academic Medicine : Journal of the Association of American Medical Colleges. 1999;**74**(6):721

[60] Marchand L, Kushner K. Death pronouncements: Using the teachable moment in end-of-life care residency training. Journal of Palliative Medicine. 2004;**7**(1):80-84

[61] Hobgood C, Harward D, Newton K, Davis W. The educational intervention "GRIEV_ING" improves the death notification skills of residents. Academic Emergency Medicine. 2005;**12**(4):296-301

[62] Hobgood CD, Tamayo-Sarver JH, Hollar DW Jr, Sawning S. Griev_Ing: Death notification skills and applications for fourth-year medical students. Teaching and Learning in Medicine. 2009;**21**(3):207-219

[63] Nordstrom A, Fjellman-Wiklund A, Grysell T. Drama as a pedagogical tool for practicing death notification-experiences from Swedish medical students. BMC Medical Education. 2011;**11**:74

[64] Kusakabe A, Naito AS, Hirano K, Ikenaga K, Saitou N, Mikan H, et al. Death pronouncements: Recommendations based on a survey of bereaved family members. Journal of Palliative Medicine. 2016;**19**(6):646-651

[65] Hatano Y, Morita T, Otani H, Igarashi N, Shima Y, Miyashita M. Physician behavior toward death pronouncement in palliative care units. Journal of Palliative Medicine. 2018;**21**(3):368-372

[66] Ferrand E, Jabre P, Vincent-Genod C, Aubry R, Badet M, Badia P, et al. Circumstances of death in hospitalized patients and nurses' perceptions: French multicenter Mort-a-l'Hopital survey. Archives of Internal Medicine. 2008;**168**(8):867-875