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Unexpected Death in Palliative Care: What to Expect When You are Not Expecting

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Abstract

Purpose of review—Death is a certainty in life. Yet, the timing of death is often uncertain. When death occurs suddenly and earlier than anticipated, it is considered an unexpected death. In this article, we shall discuss when is a death expected and unexpected, and review the frequency, impact, causes and approach to unexpected death in the palliative care setting.

Recent findings—Even in the palliative care setting in which death is relatively common, up to 5% of deaths in hospice and 10% of deaths in palliative care units were considered to be unexpected. Unexpected death has significant impact on care, including unrealized dreams and unfinished business among patients, a sense of uneasiness and complicated bereavement among caregivers, and uncertainty in decision making among healthcare providers. Clinicians may minimize the impact of unexpected events by improving their accuracy of prognostication, communicating the uncertainty with patients and families, and helping them to expect the unexpected by actively planning ahead. Furthermore, because of the emotional impact of unexpected death on bereaved caregivers, clinicians should provide close monitoring and offer prompt treatment for complicated grief.

Summary—Further research is needed to understand how we can better predict and address unexpected events.

Keywords

death; decision making; neoplasms; palliative care; prognosis; survival

Introduction

Unexpected death is death that occurs suddenly and earlier than anticipated.[1] A few implications related to this definition warrant discussion. First, it involves an acute event resulting in untimely death (other than violence), and is associated with an element of surprise. Second, “earlier than expected” is subject to interpretation by individual clinicians because the accuracy of prognostication determines what the clinician believes is “expected

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Conflicts of interest

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timing" and the clinician's own threshold for surprise determines what is considered "early". Third, the prevalence of unexpected is highly dependent on the disease setting. Fourth, this assessment can only be made post mortem instead of prospectively. Fifth, sudden unexpected deaths are often catastrophic events with significant emotional implications for family members and healthcare professionals. Finally, because of the rarity of these events and their unpredictable nature, the etiology is often unexplained and the course are more less well documented, making this topic more difficult to investigate.

Sudden unexpected deaths have mostly been studied in the settings of infancy,[2,3] adolescents, [4] epilepsy,[5–8] and cardiopulmonary disorders.[9–11] In contrast, they have not been well reported in the palliative care setting. This is partly because the life expectancy of patients seen by palliative care is often short, and death is often expected as a natural outcome. Surprisingly, recent studies revealed that a small but sizable proportion of patients in the palliative care setting have unexpected deaths. For instance, a death may be considered to be unexpected in a patient with metastatic pancreatic cancer and a life expectancy of a few weeks if she died within hours of an admission. In this article, we shall review the frequency, impact and management of unexpected death in the palliative care setting. To better examine the concept of unexpected death, we first need to understand when is death expected.

When is Death Expected?

In the advanced cancer setting, patients often develop characteristic symptoms and functional decline starting months before death, and continue to worsen in the last weeks of life.[12] The following symptoms can help clinicians prognosticate more accurately: (1) Deterioration in performance status. (2) Dyspnea, particularly at rest, (3) Delirium, and (4) Dysphagia, anorexia and cachexia.[13,14]

As patients approach the last phase of life, it is crucial for clinicians to be confident in making the diagnosis of impending death (i.e. expected survival of 3 days or less). Impending death is a diagnostic issue signaling the beginning of the end. The ability to make this diagnosis was associated with early establishment of supportive care plan, code status discussions, and discontinuation of cancer treatments.[15] Furthermore, clinicians can inform family members, who can in turn, make important personal decisions such as whether they should stay overnight or fly in to say goodbye.

The diagnosis of impending death is based on several physiologic changes associated with the dying process. In a prospective study, Morita et al. examined the process of dying in 100 cancer patients, and reported that death rattle, respiration with mandibular movement, cyanosis on extremities and pulselessness of the radial artery occurred with a median onset of 57, 7.6, 5.1 and 2.6 hours before death.[16] In another prospective study that included 178 cancer patients who died in a palliative care unit, Huang et al. found that death rattle had a positive predictive value of 74% and negative predictive value of 77% for death in 48 hours. [17] However, these studies only started documenting the signs when patients were recognized as dying, which may result in selection and ascertainment bias.

Most recently, the Investigating the Process of Dying study systematically documented the frequency, onset and diagnostic performance for impending death in 3 days in cancer patients admitted to an acute palliative care unit (APCU). This study was unique because it examined a comprehensive array of 62 physical signs among 357 consecutive patients with advanced cancer every 12 hours from the time of palliative care unit admission until hospital discharge or death, regardless of whether they were expected to die or not.[18,19] Fifteen of these physical signs were chosen for their ability to inform impending death, and were classified as either early signs or late signs based on their median onset in relation to death (<=3 days or >=3 days) (Table 1). The two early signs were decreased performance status and altered mentation. Both were found in a vast majority of patients before death, and had a moderate positive likelihood ratio for impending death. In contrast, the 13 late signs had lower frequencies in the last days of life, and had a high specificity (>90%) and high positive likelihood ratios (all had LR+>5, 8 had LR+>10) for impending death in 3 days. 7 late signs were related to neurocognitive decline (decreased response to verbal stimuli, decreased response to visual stimuli, Cheyne Stokes breathing, non-reactive pupils), 8 were related to neuromuscular alterations (drooping of nasolabial fold, respiration with mandibular movement, hyperextension of neck, inability to close eyelids, death rattle, grunting of vocal cords), and 7 were related to cardiovascular collapse (pulselessness of radial artery, peripheral cyanosis, decreased urine output). Gastrointestinal bleed was also found to have a very high likelihood for impending death, but occurred a very few patients. Future research should valid these signs further.

Are vital signs useful for the diagnosis of impending death? This question was also addressed in the Investigating the Process of Dying Study. In the last days of life, the average heart rate increases, the blood pressure decreases and the oxygen saturation decreases.[18,20] However, over half of the patients had vital signs in the normal range in the last 3 days. This may explain why both the absolute and relative changes in blood pressure and oxygen saturation only had low to moderate positive likelihood ratios for impending death.[18,20] At the same time, it should be emphasized that the cutoffs used to define abnormal vital signs in these studies were relatively conservative. More significant changes, such as decrease of systolic blood pressure from 140 mmHg to 50 mmHg, may indicate that the patient has hours or less to life.

Frequency of Unexpected Death

A national survey in Japan found that 18% of 1343 a random sample of adults had experienced an unexpected non-violent death.[21] However, only a handful of studies have examined the incidence of unexpected death in the palliative care/hospice setting. In one study from a hospice in the United Kingdom, Wilcock et al. categorized the nature of death in a weekly multidisciplinary team conference.[22] Among 100 consecutive deaths, 5 (5%) deaths were sudden and unexpected and 11 (11%) deaths were sudden but expected. In another study, Scott et al. examined the pattern of death in 208 patients who died in a hospice based on retrospective chart review. Only 1 (0.5%) death was sudden and expected and 2 (1%) patients died suddenly but not unexpectedly.[23]

The frequency of unexpected death has also been examined in APCUs. In the Investigating the Process of Dying Study, a death was considered to be unexpected if the attending physician answered “Yes” to the following question “Were you surprised by the timing of the death” following the event. 19/203 (10%) deaths were considered to be “unexpected”.[1] Using the same question, 22/203 (12%) deaths were considered to be unexpected by nurses. However, the inter-rater agreement was relatively low, albeit statistically significant (kappa 0.27). Interestingly, 22% of physicians and 27% of nurses answered “no” to the question “At 24 hours prior to his/her death, were you expecting this patient to die?” This suggested that even when clinicians did not expect a death to occur within 24 hours, some had a higher threshold for them to be “surprised”. Patients with unexpected deaths were significantly less likely than those with expected deaths to exhibit the physical signs of impending death in the last 3 days of life, such as inability to close eyelids, non-reactive populates, drooping of nasolabial folds, respiration with mandibular movement, peripheral cyanosis, and pulselessness of the radial artery.[1] Thus, this study highlights several important concepts regarding unexpected death:

1. Unexpected death is a subjective concept, with varying thresholds among individual clinicians for what they consider to be a “surprise”. This explains the relatively low inter-rater agreement.
2. Unexpected death occurred at relatively high frequency in the APCU setting (10%). Thus, clinicians should expect the unexpected when making plans.
3. The signs of impending death were associated with expected deaths. However, absence of these signs could not rule of impending death, and patients with unexpected deaths may sometimes exhibit these signs before death.[1]

Impact of unexpected death

Unexpected death has a negative impact on patients, families and healthcare professionals. Many decisions regarding diagnosis and treatments are dependent on a patient’s prognosis. With sudden unexpected death, decisions made based on expected survival may seem inappropriate in hindsight. For example, palliative chemotherapy should generally not be given to patients with less than 1 month of life expectancy because of the unfavorable risk-to-benefit ratio.[24] An oncologist who was expecting his patient with metastatic gastric cancer and a good performance status to live for several months initiated chemotherapy. However, the patient died unexpectedly 2 days after starting treatment. In retrospect, chemotherapy may seem unwarranted.

In another example, the APCU palliative care team was planning to discharge a patient who was expected to live for a few weeks to home hospice. The team diligently communicated with the patient and her family about the prognosis and care plan. However, the patient died suddenly and unexpectedly overnight. Her family regretted the decision to stay home instead of by the bedside, and did not have the last opportunity to “say goodbye”. Because unexpected death, by definition, occurs earlier than expected, it takes precious time away from patients and family, when many may not have had the opportunity to plan ahead or engage in advance care planning. Indeed, patients who died unexpectedly were more likely to receive inappropriate cardiopulmonary resuscitation.[25,26]

Complicated grief is another potential concern for bereaved family caregivers.[27] Untimely death is often linked to the element of surprise, and could exacerbate the emotional distress and the lack of sense of control among caregivers. Furthermore, unexpected death may sometimes be preceded by catastrophic complications such as massive gastrointestinal bleeding, stroke, and acute respiratory failure that can be particularly distressing to caregivers. In other cases, the causes may not be identified even after an autopsy. Understandably, unexpected death is associated with higher rates of complicated grief, major depressive disorder, panic disorder, substance use, and mortality in bereaved caregivers.[28–31]

Causes of Unexpected Death

To our knowledge, the causes of unexpected death have not been studied in the palliative care setting. This is partly because (1) diagnostic investigations are not always done to maximize comfort at the end-of-life; (2) autopsies which are the gold standard for determining the cause(s) of death are rarely conducted;[32,33] and (2) patients often have multiple potentially life threatening complications making attribution difficult. This is illustrated by a study that examined 23 acute symptomatic complications in patients admitted to APCUs.[34] Delirium, pneumonia and bowel obstruction were the most common complications, occurring in 43%, 20% and 16% of patients on admission, and 70%, 46% and 35% during the entire APCU stay, respectively. Delirium ($P<0.001$), pneumonia ($P=0.003$), peritonitis ($P=0.03$), metabolic acidosis ($P<0.001$) and upper gastrointestinal bleed ($P=0.03$) were associated with worse survival. A greater number of symptomatic complications on admission was also associated with poorer survival ($P<0.001$). Patients who died in the APCU had a slightly higher number of symptomatic complications during the entire APCU stay (median 5 vs. 4; $P=0.03$) compared to patients who were discharged alive.[34] Another study examined the causes of death at autopsy in 48 patients who died in an inpatient hospice unit. Pneumonia was present in 38/48 (79%) patients, and appeared to be the major cause of death in 44% of patients.[35] However, neither study specifically examined causes of unexpected death.

In the oncology setting, the causes of unexpected death have only been reported in a few studies. Autopsy of 28 cancer patients who died unexpectedly revealed that 15 (54%) died of non-cancer related cardiovascular events (myocardial infarction, n=13; aortic dissection, n=1; pulmonary embolism, n=1), and 10 (36%) died of cancer-related complications (cardiac involvement, n=4; esophagoaortic fistula, n=2; duodenal-inferior vena cava fistula, n=1; hepatic rupture, n=2; tumor embolism, n=1), and the other 3 died of iatrogenic causes (adverse event related to anticholinergic drugs, diuretic and antineoplastic medication, 1 each).[36] Other case reports have reported bowel perforation and tumor embolisms as causes of unexpected death.[37,38]

Management Strategies

Death is a certainty in life. Yet, the timing of death is often uncertain. Unexpected death occurs even in palliative care setting, when patients often have a short expected survival.

Given that consequences on care planning and the emotional toll related to unexpected death, how can clinicians approach these situations?

1. **Maximizing accuracy in prognostication.** Studies have repeatedly shown that clinicians overestimate survival systematically.[39–41] Inaccurate prognostication may contribute to higher incidence of unexpected death. Objective prognostic factors, prognostic models, serial prognostication, and recognition of the signs of impending death may help clinicians to formulate prognosis more accurately.[18–20,42–44]

2. **Optimizing communication with patients and family. In addition to over-estimating survival,** Clinicians often inflate the prognosis when communicating with patients, which may contribute to heightened optimism and unrealistic expectations. It is important to have candid discussions regarding life expectancy with patients and family. When discussing prognosis, the use of the best and worst case scenarios (e.g. weeks to months) may help to paint a realistic picture.[45] Given the relatively high frequency of unexpected death in the palliative care setting, it is important to emphasize the uncertainty in prognostication, and to ask patients and families to expect the unexpected ("hope for the best, and prepared for when things do not go as planned"). End-of-life discussions have been shown to be associated with less aggressive of care in the last days of life.[46,47] Advance care planning should be discussed early in the disease trajectory because these documents are for unexpected events.[48] For patients at risk for bleeding, bleeding packs may be useful.[49]

3. **Minimize iatrogenic causes of unexpected death.** Invasive procedures and certain medications such as chemotherapy can be associated with significant adverse events, particularly when given to patients with a short life expectancy and poor performance status.

4. **Psychosocial care for the caregiver.** Given the significant emotional impact of death on bereaved caregivers, especially when unexpected, it is important to support them longitudinally and monitor for complicated grief.[50] Agnew et al. provided a comprehensive review of bereavement assessment tools.[51] There are few published guidelines available on the bereavement process in the palliative care setting, and the few existing guidelines barely discussed unexpected death.[52,53] Using a quasi-experimental design, Wagner et al. examined a preventive, internet-based, cognitive-behavioral intervention in the context of unexpected non-violent death, and reported that it was successful in reducing emotional distress. Further research is needed to confirm its benefits.[54]

5. **More research on unexpected death is needed.** Currently, different studies defined unexpected death differently, making it difficult to synthesize the data. A standardized operational definition is needed. Future studies are needed to better characterize the frequency, impact, and causes of unexpected death in the palliative care setting, and to develop specific interventions targeting this group of bereaved caregivers who are at high risk of developing complicated grief.

Conclusion

Unexpected death is death that occurs suddenly and earlier than anticipated. Even in the palliative care setting, up to 10% of deaths were considered to be unexpected, with negative consequences for patients, bereaved caregivers and health professionals. Clinicians may minimize the impact of unexpected death by improving their accuracy of prognostication, communicating the uncertainty with patients and families, and helping them to expect the unexpected by actively planning ahead. Furthermore, because of the emotional impact of unexpected death on bereaved caregivers, clinicians should provide close monitoring and offer prompt treatment for complicated grief. Moving forward, we need to standardize the definition of unexpected death in the palliative care setting, and to further characterize this phenomenon and minimize its impact on patients, caregivers and healthcare providers.

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Key points

- Unexpected death is death that occurs suddenly and earlier than anticipated.
- Unexpected death is associated with truncated care plans and more aggressive end-of-life care for patients and significant emotional distress among bereaved caregivers.
- Clinicians may minimize the impact of unexpected death by improving their accuracy of prognostication, communicating the uncertainty with patients and families, and helping them to expect the unexpected by actively planning ahead.

Table 1

Bedside Physical Signs associated with Impending Death in 3 Days[18,19]

Physical Signs	Frequency of sign in last 3 days of life, %	Median Onset in days (Q1-Q3)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)
Cheyne Stokes breathing	41	2.0 (1.0–2.0)	98.5 (98.4–98.7)	12.4 (10.8–13.9)
Death rattle	66	1.5 (1.0–2.0)	97.1 (96.9–97.3)	9 (8.1–9.8)
Decreased response to verbal stimuli	69	2.0 (1.5–4.0)	96 (95.8–96.3)	8.3 (7.7–9)
Decreased response to visual stimuli	70	3.0 (2.0–4.0)	94.9 (94.6–95.1)	6.7 (6.3–7.1)
Drooping of nasolabial fold	78	2.5 (1.5–3.0)	95.5 (95.3–95.8)	8.3 (7.7–8.9)
Grunting of vocal cords	54	1.5 (1.0–2.0)	97.9 (97.7–98.1)	11.8 (10.3–13.4)
Hyperextension of neck	46	2.5 (2.0–3.0)	96.7 (96.5–96.9)	7.3 (6.7–8)
Inability to close eyelids	57	1.5 (1.0–1.5)	97.9 (97.7–98.1)	13.6 (11.7–15.5)
Non-reactive pupils	38	2.0 (1.5–3.0)	99 (98.8–99.1)	16.7 (14.9–18.6)
Palliative performance scale ≤20%	93	4.0 (3.5–6.0)	81.3 (80.9–81.7)	3.5 (3.4–3.6)
Peripheral cyanosis	59	3.0 (2.0–4.5)	94.9 (94.7–95.2)	5.7 (5.4–6.1)
Pulselessness of radial artery	38	1.0 (0.5–1.0)	99.3 (99.2–99.5)	15.6 (13.7–17.4)
Respiration with mandibular movement	56	1.5 (1.0–2.0)	97.5 (97.3–97.6)	10 (9.1–10.9)
Richmond Agitation Sedation Scale ≤-2	90	4.5 (3–6)	89.3 (88.9–89.7)	4.9 (4.7–5)
Upper gastrointestinal bleed	5	5.5 (0.5–17.0)	99.7 (99.6–99.7)	10.3 (9.5–11.1)
Urine output over last 12 h <100 ml	72	1.5 (1.0–2.5)	98.2 (98–98.5)	15.2 (13.4–17.1)

Abbreviations: CI, confidence interval; Q1-Q3, interquartile range