

Unsatisfactory example of a case study

Existential pain in advanced cancer

Word Count: 3414

Introduction

Many patients with advanced cancer experience existential pain and suffering near the end of life. The concepts of “existential pain” and “suffering” are difficult to define and the terms are sometimes used interchangeably. They are subjective and difficult to understand, measure, research and treat. As palliative care aims to improve quality of life, we must attempt to alleviate existential pain and suffering. The following case demonstrates some of the challenges in recognising and managing existential pain in a patient with advanced cancer at the end of life. The discussion explores the definitions of existential pain and existential suffering and considers interventions to treat them.

Case report

██████ was a fifty-seven year old mother of four, living in an outer metropolitan suburb ██████ with her husband. ██████ was an ex-smoker who was diagnosed with lung cancer in 2007. She had no other medical history. She underwent left upper lobectomy in 2007, with no adjuvant treatment, following which she considered her cancer to be cured. She had regular follow-up imaging with her Oncologist. Subsequent to her cancer treatment, ██████ had returned to managing a business that she owned with her husband. They sold their business in late 2010, at a loss, and were living off savings. They lived in public housing and were planning to start a new business. ██████ mobilised in a wheelchair due bilateral above knee amputations, complications of diabetes, and was independent with personal care. ██████, her husband and children identified themselves as not having any religion, while her mother had a strong Christian faith. ██████ favourite pastime was quilting and she was making an intricate design for her newest granddaughter, who was due in November 2011.

In January 2011 ██████ presented to her Oncologist with hip pain, leading to a diagnosis of widespread skeletal metastases. She commenced carboplatin and gemcitabine and received palliative radiotherapy to her pelvis, right

shoulder and thoracic spine. She began seeing a Palliative Care Physician at her local general hospital.

On 13/4/2011, two weeks after completing her third cycle of chemotherapy, ██████ visited her Palliative Care Physician. She had frequent vomiting that had escalated over the previous two weeks, to the point where she was not tolerating any oral intake, including medications. A recent computed tomography (CT) scan of the brain with intravenous contrast was reportedly normal. She had tried numerous anti-emetics, including oral metoclopramide, domperidone, and ondansetron, without benefit. Her nausea subsided only with subcutaneous metoclopramide administered by domiciliary nurses. She also reported a number of other symptoms during that review, including constipation; severe pain in the groin, abdomen and left lower chest wall; myoclonus; confusion; hot flushes and distressing nightmares. Her daily analgesia included 4g paracetamol, 1g naproxen, 600mg pregabalin, and 100mcg/hr fentanyl patch. Her pain was now uncontrolled despite 60mg immediate release oxycodone every two hours. Due to the above symptoms, ██████ was admitted to an inpatient palliative care unit (hospice) that day. She was eager for her symptoms to resolve within eight days, in time for a family reunion that she had organised.

At the hospice, ██████ fentanyl patch was rotated to a subcutaneous infusion of morphine and haloperidol, for pain, nausea and nightmares. Oral amitriptyline was commenced for neuropathic pain. Her nausea, pain and nightmares all resolved. Her bowels opened following methylnaltrexone. Her infusion was ceased on 16/4/11 and she recommenced fentanyl patches and daily oral haloperidol. Her nausea and pain remained controlled and she was discharged home on 18/4/2011.

██████ went on her holiday, three hours' drive from Perth, with her husband, mother ████████████████████ four adult children and nine grandchildren. She felt that her symptoms were well controlled until 27/4/11 when she began vomiting. She was taken by ambulance to a district hospital where she received parenteral metoclopramide. She was noted to have a temperature of

39 degrees Celsius. Her husband drove her home in their car, stopping every thirty minutes for [REDACTED] to vomit. Upon arriving home [REDACTED] developed visual hallucinations and phoned an ambulance. The ambulance was delayed and she waited three hours before arriving at the general hospital emergency department in the early hours of the morning. She was diagnosed with pneumonia and commenced intravenous antibiotics and metoclopramide. She remained nauseated but stopped vomiting. Her Palliative Care Physician was contacted via telephone and he arranged transfer to the hospice that day. Prior to transfer, [REDACTED] underwent a staging CT scan that had coincidentally been booked by her Oncologist for that day.

On arrival to the hospice, further symptoms were elicited including olfactory hallucinations, numbness in the left face in the distribution of the third branch of the trigeminal nerve, numbness in the right T9 dermatome, left thigh pain, fatigue and hot flushes. She commenced a subcutaneous infusion of metoclopramide and haloperidol, with resolution of her nausea and hallucinations. Dexamethasone was commenced for suspected cerebral metastases, following which the numbness and paraesthesia resolved.

Results of the staging CT scan became available, revealing consolidation in her left lung, multiple new metastases in the right lung, numerous small hepatic metastases, new skeletal metastases and pathological wedge fractures of multiple thoracic vertebrae. A CT scan of the brain, with contrast, was normal. [REDACTED] was disappointed but not surprised by the result. She cancelled follow-up appointments with her Medical Oncologist as she did not wish to travel to the appointment or to have further chemotherapy.

Magnetic resonance imaging (MRI) of the brain and spinal cord was planned to investigate for central nervous system metastases or spinal cord compression.

[REDACTED] underwent MRI of the spine on 1/5/2011 and experienced claustrophobia and panic. Due to this, she did not wish to progress to MRI of the brain even under sedation, nor would she wish to undergo whole brain

radiotherapy if found to have cerebral metastases. The MRI scan of the spine was normal other than the presence of vertebral metastases.

At this stage, [REDACTED] was seen by the hospice Counsellor and Pastoral Carer, who saw her and her family regularly for the remainder of the admission. The Counsellor employed humanistic and mindfulness strategies, acceptance and commitment therapy, and guided imagery techniques. [REDACTED] also commenced sublingual lorazepam, as required, for anxiety. [REDACTED] expressed repeatedly to staff that she was anxious and scared of being in pain; however, she felt secure being an inpatient at the hospice. She said that she wished to shield her family from her pain and suffering.

[REDACTED] fentanyl and amitriptyline doses were increased as her back pain worsened. She received radiotherapy to her thoracic spine. She developed new, non-specific visual symptoms, and her left facial neurological symptoms worsened. The subcutaneous infusion was converted to oral medications at [REDACTED] request, as she felt it was making her drowsy.

On 5/5/2011 [REDACTED] developed visual hallucinations and disorientation. She was mildly hypercalcaemic, having been normocalcaemic one week previously. This was treated with zoledronic acid and intravenous fluids. Other laboratory investigations revealed no cause of delirium. Her amitriptyline was ceased and haloperidol dose increased.

[REDACTED] hallucinations resolved but in the following days she was emotionally labile, at times tearful, irritated, or inappropriately familiar with staff. Her pain worsened and migrated to different sites. Her fentanyl patch was rotated to oral methadone, to try to improve neuropathic analgesia. She made frequent requests for breakthrough analgesia, even when she reported being free of pain. She also made requests for radiotherapy at various sites of her body. Her family visited from early morning until night. She began to phone them late at night after they returned home, distressed and agitated. Poor concentration stopped her from quilting.

On 11/5/2011 the dexamethasone dose was weaned, methadone was increased and venlafaxine commenced to assist with anxiety, pain and worsening hot flushes. ██████ had been using lorazepam approximately once a day but this was thought to be causing drowsiness and she made the decision to stop it.

██████ neurological symptoms worsened, with the development of left-sided facial droop and dysphagia. ██████ began expressing guilt about many things. She experienced cyclical anger and guilt – anger that her family could not be at her bedside twenty-four hours a day, and guilt that she was being a burden on her family. She reported feeling scared, not of dying but of the uncertainty surrounding death.

On 18/5/2011, ██████ developed further neurological symptoms, including urinary retention and right foot drop. She developed dysphagia and could not swallow oral medications or fluid. A subcutaneous infusion of methadone and haloperidol was recommenced and oral medications ceased. Following a family meeting, ██████ commenced an end-of-life pathway. Due to ongoing nausea, agitation and anxiety, she commenced subcutaneous levomepromazine and sublingual clonazepam. Her agitation settled and drowsiness increased. She died five days later.

Discussion

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”¹ Although not perfectly understood, physical pain is well studied and there are plausible anatomical and physiological explanations for many of the pain syndromes encountered in advanced cancer, such as nociceptive, neuropathic and osseous pain. In addition, there are evidence-based guidelines or expert recommendations for treating these types of pain.²⁻⁴ A great challenge arises when, despite following these guidelines and treating pain aggressively with pharmacological, interventional and psychological measures, a patient’s pain

remains severe and distressing. In such cases, existential pain must be considered.

“Existential pain”, “existential distress” and “existential suffering” are all concepts that have been discussed in the palliative care literature. These terms are poorly defined and sometimes used interchangeably. There are literature reviews and quantitative studies that attempt to define these concepts.⁵⁻⁷ That they are relevant to the practice of palliative care is unquestionable. Strang et al⁸ interviewed 111 palliative physicians, of whom ninety-nine percent had managed patients with existential pain and most (85 of 111) felt existential pain to be “clearly relevant” to their practice.

Boston et al⁵ performed a systematic review of 156 articles referencing the above three terms. Only 32% of these were empirical research, 28% were peer-reviewed theoretical articles and the remainder case reports or opinion pieces. They found 64 articles to be relevant, after excluding those primarily related to spirituality, hope, transcendence, meaning, physical pain and depression. They identified fifty-six definitions of existential suffering, which tended to follow common themes such as “finding meaning”, “the loss of meaning or purpose in life”, and “What will happen to me after I die?” They found much overlap in the literature of the definitions of “existential”, “suffering” and “spiritual” and a large overlap of these with psychological diagnoses such as depression. They concluded that “existential suffering remains poorly understood and neglected in palliative care” and therefore difficult to treat.

A non-systematic review by Krikorian et al⁶ attempted to define “suffering” at the end of life. They found it to be a “unique, comprehensive holistic experience with physical, psychological, social and spiritual components...a complex negative affective and cognitive state with threat to self.” This reflects Cassell’s original work on suffering, where he defines suffering as “experienced by persons, not merely by bodies, [with] its source in challenges that threaten the intactness of the person as a complex social and psychological entity.”⁹ Krikorian et al⁶ also conclude that suffering is difficult to

assess and measure, due to its subjective nature. Another review found that “existential suffering” encompassed the concepts of “loss of personal meaning, loss of purpose of life, fear of death, despair, anguish, hopelessness, fear of being a burden to others, loss of dignity, helplessness and betrayal”. They concluded that existential pain is a metaphor for overall suffering.⁷

Strang et al⁸ also concluded that existential pain is a metaphor for suffering. They asked 150 hospital chaplains, 111 palliative care physicians and 90 pain physicians in Sweden, “How would you define the concept of existential pain?” They categorised the responses into four basic domains: “freedom”, “meaning and meaninglessness”, “existential isolation” and “death”. Using keyword frequency analysis, they found that palliative care physicians focused significantly more on “annihilation” and “impending separation” rather than physical pain, whereas pain physicians focused on the fact that “living is painful” and chaplains emphasised guilt issues and religious concerns. This further emphasises the inconsistencies in defining existential pain.

In a phenomenological study by Mount et al,¹⁰ 21 interviewees with life-threatening illness were questioned regarding the influence of spirituality and existential well-being upon their experience of illness. They found suffering to be associated with an “experience of isolation and meaninglessness.”

Williams¹¹ explored the concept of existential suffering in a qualitative study of 33 low socioeconomic status interviewees with advanced cancer, primarily female, black, middle-aged and unemployed. Subjects expressed guilt regarding dying young and therefore being unable to fulfill life’s responsibilities, such as raising children, and “persistent inability to control their destiny”.

Existential pain and distress often coincide with physical pain.¹² This raises questions such as: can unrelieved physical pain cause existential pain? Can existential pain result in the subjective sensation of physical pain? Is existential pain expressed as physical pain in patients who cannot articulate their suffering? In a case series by Strasser et al,¹³ the severe physical pain of

three patients with advanced cancer was alleviated by addressing their existential issues. Wilson et al¹² interviewed 381 patients with advanced cancer, of whom half felt that they were suffering, and one quarter that they were suffering at a moderate-to-extreme level. In a qualitative review, almost half of these attributed their suffering to physical complaints, 19% to social concerns, 18% to existential concerns and 14% to psychological. Pain was the most common physical complaint. However, on quantitative review, suffering was most strongly correlated with malaise, followed by weakness, pain and depression. In contrast, a prospective cohort study of hospice patients found there to be little association between physical symptoms and suffering. Rather, suffering was associated with worse psychological well-being and worse quality-of-life.¹⁴ In addition to physical symptoms, there is also a large overlap of existential pain or suffering with psychological disease, including depression and anxiety.¹² However, treating depression and anxiety does not necessarily alleviate existential pain.⁷

Cohen et al¹⁵ found terminally ill patients' quality of life to improve following admission to palliative care units, in those well enough to participate in the study. This included a significant improvement in their existential well-being, as measured on the McGill Quality of Life questionnaire. The possible interventions that led to improvement in existential wellbeing were not investigated. Finding a definition for existential pain may assist in identifying such interventions.

Several interventions have been offered for the management of existential pain. Strasser et al¹³ suggest addressing emotional distress, alexithymia (being unable to verbalise emotions) and delirium as a starting point to the treatment of existential pain.

LeMay and Wilson¹⁶ performed a review of of eight group and individual interventions addressing existential issues in cancer patients. These employed psychological, spiritual, meaning-making dignity-improving measures. Only one of the interventions reviewed, long-term Supportive-

Expressive Group Therapy (SEGT), was “probably efficacious” using the American Psychological Association criteria for empirically-validated treatments, based on three randomised control trials. SEGT is an unstructured weekly group intervention for patients with advanced disease, with the aim of “improving self-worth, decreasing isolation and developing sources of support.” Participants are encouraged to interact outside sessions, and family meetings are held regularly.¹⁶

If existential pain is the result of a loss of meaning and a perceived threat to one’s person, then it is intuitive to treat it by attempting to reintroduce meaning to life and thereby minimise those threats. Psychotherapeutic meaning making,¹⁷ Meaning of Life Intervention,¹⁸ Temporal Existential Awareness and Meaning Making model¹⁹ and the Meaning-Making intervention²⁰ are some of the novel treatments hoping to address this. Some authors focus on hopefulness as a therapeutic intervention for existential pain and suffering.²¹⁻²³ Chochinov’s dignity therapy may also be useful for alleviating suffering at the end of life.²⁴

For more than a decade there has been much debate in the palliative care literature regarding the use of palliative sedation, also known as sedation to unconsciousness, as a treatment for unrelieved existential pain.²⁵⁻³² The unclear definition of existential pain may further confuse this debate. Blondeau et al²⁶ interviewed 100 doctors and 24 pharmacists working in palliative care and found that though most were favourable towards sedation as a treatment for physical pain, many felt sedation was not adequate treatment for existential suffering. A 2010 survey of 1880 physicians in the United States found that two in three opposed terminal sedation for the treatment of existential suffering.³¹ Rousseau³² recommends guidelines for the use of palliative sedation for existential suffering, including a trial of “respite sedation” to break the cycle of sleep deprivation and existential distress.³³

Conclusion

Existential pain and existential suffering at the end of life are concepts that overlap and are difficult to define. Existential pain may be thought of as a loss of sense of self, whereas existential suffering may be considered a loss of sense of meaning. Existential pain and suffering often coexist with physical symptoms like pain and malaise, although a causative relationship is uncertain. Despite difficulties in treatment, it is imperative that palliative care addresses existential pain and suffering in order to provide holistic care. Novel therapies such as meaning making and dignity therapy may assist but further studies are required. Consistent definitions of existential pain and suffering would assist with this. Terminal sedation remains a controversial treatment for existential pain and suffering.

Personal Reflection

I met ██████ during the first months of my palliative care training and her case raised a number of concerns for me, both at the time I was caring for her and retrospectively when reviewing her case. Had I a better understanding of existential pain, would I have cared for her better? ██████ distress and feelings of guilt were apparent. She felt that her cancer was a direct result of her former smoking. She felt guilty for dying young and therefore abandoning four generations of her family, including her elderly mother, disabled husband, children and grandchildren. She felt guilty that she was leaving her husband in a difficult financial position. Her quilting, which was very meaningful to her, was cut short by the physical side effects of her disease. Interlaced with her psychological and existential distress were significant physical symptoms, including neuropathic and osseous pain, nausea, hot flushes and neurological deficits.

I experienced a sense of helplessness that I could not alleviate her suffering, as well as frustration at the diagnostic uncertainty of the cause of her neurological symptoms. On discussion at our daily multidisciplinary team meetings, other staff members clearly felt the same. We faced this in different

ways – some sat silently with [REDACTED], others avoided her, while many of us tried to treat her suffering with medications. We bombarded her with analgesics, sedatives and antidepressants. Physical symptoms are much easier to understand, measure and treat than existential symptoms and there is less personal and emotional involvement required.

In retrospect, it is obvious to me that we made frequent changes to [REDACTED] medications. At the time, it felt as though our medication prescribing was slow and measured. Decisions were always made in consultation with other members of the multidisciplinary team. On reflection, I was surprised to realise how rapidly we changed her medications. I can rationalise all the prescribing decisions we made, all of which were with good intention, but upon reflection I wonder how much iatrogenic harm may have been caused. Whether through unpleasant side effects, by impairing her participation in psychological interventions or by contributing to delirium, the above may have exacerbated her existential pain. Published case studies of palliative care patients with existential pain show similar patterns of prescribing.^{13,34,35} I now wonder to what degree my prescribing was treating the patient, and how much it was treating my own helplessness and distress.

The inpatient setting impacted upon our decision-making. Had [REDACTED] been treated in the community setting, the frequent medication changes would have been impractical and uneconomical. In addition, staff members would not have been visiting [REDACTED], and observing her distress, many times throughout the day.

Reflecting on [REDACTED] case made me a more careful prescriber. It is very easy to prescribe a medication in order to treat difficult physical and psychological symptoms. It is gratifying and makes me feel useful as a doctor. However, it is often not the correct treatment decision to make, especially in cases of existential pain and suffering.

References

1. IASP Task Force on Autonomy. Part III: Pain terms, a current list with definitions and notes on usage. In: Merskey H, Bogduk N, editors. *Classification of Pain*, 2nd ed. Seattle: IASP Press; 1994. p. 209-14.
2. Moryl N, Coyle N, Foley K. Managing an acute pain crisis in a patient with advanced cancer: "This is as much of a crisis as a code". *JAMA* 2008; 229(12): 1457-67.
3. Dy SM. Evidence-based approaches to pain in advanced cancer. *Cancer Journal* 2010;16(5):500-6.
4. Smith HS. Painful osseous metastases. *Pain Physician* 2011; 14: E373-E405.
5. Boston P, Bruce A, Schreiber R. Existential suffering in the palliative care setting: an integrated literature review. *J Pain Symptom Manage* 2011; 41(3): 604-18.
6. Krikorian A, Limonero JT, Mate J. Suffering and distress at the end-of-life. *Psycho-Oncology* 2011:10 pages. Epub Oct 2011.
7. Bruce A, Boston P. Relieving existential suffering through palliative sedation: discussion of an uneasy practice. *J Advanced Nurs* 2011; 67(12): 2732-40.
8. Strang P, Strang S, Hultborn R, Arner S. Existential pain - an entity, a provocation, or a challenge? *J Pain Symptom Manage* 2004; 27(3): 241-50.
9. Cassel EJ. The nature of suffering and the goals of medicine. *New Engl J Med* 1982; 306(11): 639-45.

10. Mount BM, Boston PH, Cohen SR. Healing connections: on moving from suffering to a sense of well-being. *J Pain Symptom Manage* 2007; 33(4): 372-88.
11. Williams BR. Dying young, dying poor: a sociological examination of existential suffering among low-socioeconomic status patients. *J Palliat Med* 2004; 7(1): 27-37.
12. Wilson KG, Chochinov H, McPherson CJ, LeMay K, Allard P, Chary S, et al. Suffering with advanced cancer. *J Clin Onc* 2007; 25(13): 1691-7.
13. Strasser F, Walker P, Bruera E. Palliative pain management: when both pain and suffering hurt. *J Palliat Care* 2005; 21(2): 69-79.
14. Abraham A, Kutner J, Beaty B. Suffering at the end of life in the setting of low physical symptom distress. *J Palliat Med* 2006; 9(3): 658-65.
15. Cohen SR, Boston P, Mount BM, Porterfield P. Changes in quality of life following admission to palliative care units. *Palliat Med* 2001; 15: 363-71.
16. LeMay K, Wilson G. Treatment of existential distress in life threatening illness: a review of manualized interventions. *Clin Psychol Rev* 2008;28:472-93.
17. Breitbart W, Gibson C, Poppito SR, Berg A. Psychotherapeutic intervention at the end of life: a focus on meaning and spirituality. *Can J Psychiatry* 2004; 49(6): 366-72.
18. Mok E, Lau K, Lai T, Ching S. The Meaning of Life Intervention for patients with advanced-stage cancer: development and pilot study. *Oncol Nurs Forum* 2012;39:E480-8.

19. Lee V, Loiselle CG. The salience of existential concerns across the cancer control continuum. *Palliat Support Care* 2012;10:123-33.
20. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer* 2008; 16: 779-85.
21. McCullough E. Is there hope for a peaceful death? *J Palliat Med* 2011; 14(3): 380.
22. Alidina K, Tettero I. Exploring the therapeutic value of hope in palliative nursing. *Palliat Support Care* 2010; 8(3): 353-8.
23. Mok E, Lau KP, Lam WM, Chan LN, Ng J, Chan KS. Health-care professionals' perspective on hope in the palliative care setting. *J Palliat Med* 2010; 13(7): 877-83.
24. Chochinov HM, Hack T, Hassard T, Kristjanson LJ, McClement S, Harlos M. Dignity therapy: a novel psychotherapeutic intervention for patients near the end of life. *J Clin Oncol* 2005; 23(24): 5520-5.
25. Morita T, Tsunoda J, Inoue S, Chihara S. Terminal sedation for existential distress. *Am J Hosp Palliat Care* 2000; 17(3): 189-95.
26. Blondeau D, Roy L, Dumont S, Godin G, Martineau I. Physicians' and pharmacists' attitudes toward the use of sedation at the end of life: influence of prognosis and type of suffering. *J Palliat Care* 2005; 21(4): 238-45.
27. Taylor BR, McCann RM. Controlled sedation for physical and existential suffering? *J Palliat Med* 2005; 8(1): 144-7.
28. Berlinger N. Taking existential suffering seriously. *J Pain Symptom Manage* 2007; 34(1): 108-10.

29. Cassell EJ, Rich JD. Intractable end-of-life suffering and the ethics of palliative sedation. *Pain Med.* 2010; 11(3): 435-8.
30. Juth N, Lindblad A, Lynoe N, Sjostrand M, Helgesson G. European Association for Palliative Care (EAPC) framework for palliative sedation: an ethical discussion. *BMC Palliat Care* 2010; 9: 20.
31. Putman MS, Yoon JD, Rasinski KA, Curlin FA. Intentional sedation to unconsciousness at the end of life: findings from a national physician survey. *J Pain Symptom Manage* 2012; Epub 2012/12/06.
32. Rousseau P. Existential suffering and palliative sedation: a brief commentary with a proposal for clinical guidelines. *Am J Hosp Palliat Care* 2001;18:151-3.
33. Rousseau P. Existential distress and palliative sedation [letter]. *Anesth Analg* 2005; 101(2): 611-12.
34. Mori M, Elsayem A, Reddy SK, Bruera E, Fadul NA. Unrelieved pain and suffering in patients with advanced cancer. *Am J Hosp Palliat Care* 2011; Epub 2011/07/22.
35. Sudore RL, Villars P, Carey EC. Sitting with you in your suffering: lessons about intractable pain at the end of life. *J Palliat Med* 2010; 13(6): 779-82.

Palliative Medicine Advanced Training Program Scoresheet for the Case Study

Name of Trainee: [REDACTED]

Name of Assessor: [REDACTED]

Date: 1 [REDACTED]

The aim of this Case Study is to help ground the trainee in the cultures of Palliative Medicine and interdisciplinary palliative care.

The advanced trainee is required to write a Case Study of a patient whom they have managed. This study will not focus solely on the clinical aspects of the individual patient's disease, but will also consider the global issues of palliative care and the role of the doctor as a provider of Palliative Medicine to this patient. The trainee will explore the impact that caring for the particular patient and their family had on them personally.

Even though the Case Study would not normally be submitted to a peer reviewed journal for consideration for publication, the Case Study must still be of sufficient standard.

The Case Study must receive a *Satisfactory* result against each major criterion sections listed below in order to receive an overall result of *Satisfactory*.

1. Introduction

Does the introduction explain the theme/issues of the case study? **X Yes**

2. Case Presentation

Comments: Thorough and comprehensive details with logical flow and easy understanding. More detail of clinical thinking may have been helpful –i.e. what was considered the possible differential diagnosis of progressive neurological symptoms despite non-diagnostic investigations.

Criterion	Yes	No
Is the case presentation well thought out?	x	<input type="checkbox"/>
Is an adequate medical history provided?	x	<input type="checkbox"/>
Is an adequate psychosocial history provided?	x	<input type="checkbox"/>
Are the important issues adequately described?	x	<input type="checkbox"/>

Overall mark for this section: x Satisfactory

3. Discussion

This should form 50-60% of the case study

Comments: The literature review is thorough and relevant and demonstrates wide reading. The many references mean that each is briefly presented with little discussion. There is no correlation with the case study. Many of the references from the literature are relevant to the case study and the trainee needs to make these connections clearly. There is clinical discussion of palliative sedation, but no ethical discussion. No other ethical issues related to the case are mentioned.

Criterion	Yes	No
Has the trainee discussed the case issues?	x	<input type="checkbox"/>
Has the trainee connected the discussion to the case study?	<input type="checkbox"/>	x
If appropriate, have ethical issues been considered?	<input type="checkbox"/>	x
Has the trainee presented a succinct report supported, where appropriate, by reference to the relevant literature?	x	<input type="checkbox"/>
Is there evidence of purposeful reading and thoughtful appraisal in discussion of the case/issues?	x	<input type="checkbox"/>
Is there inclusion of relevant, up-to-date material?	x	<input type="checkbox"/>

Overall mark for this section:

x Unsatisfactory

4. Personal Reflection

This should be approximately 400-500 words and can be written in first person

Comments: The trainee demonstrates personal and professional development as a result of the experiences involved in the case.

Criterion	Yes	No
Has the trainee included an adequate reflection on their personal experience as related to the case study?	x	<input type="checkbox"/>

Overall mark for this section:

x Satisfactory

5. Style and Lucidity

The structure, quality and style of writing are expected to be of a standard suitable for submission to a peer reviewed journal or research ethics committee

Comments: Easy to read and comprehend. Well structured.

General Comments: This case study describes a challenging and important aspect of Palliative Care very well. More information about clinical thinking could be provided. The discussion extensively reviews relevant literature and draws conclusions, but there is no connection to the case study as it occurred, or consideration how the management could have been approached differently. The reflection shows personal and professional development as a result of the case.

Signature of Assessor: _____  _____

Date: _____  _____

Please return to:
Education Officer
Palliative Medicine Education Committee
The Royal Australasian College of Physicians
145 Macquarie Street, Sydney NSW 2000
PalliativeMedTraining@racp.edu.au
Fax: +61 2 9256 9698

**Resubmitted case study which was
marked as satisfactory**

Existential pain in advanced cancer

Word Count: 3496



The Royal Australasian
College of Physicians

The Royal Australasian Chapter of Palliative Medicine
Palliative Medicine Education Committee

Case Study Resubmission Cover Sheet

This page must be completed and attached to the front of the Resubmitted Case Study when submitted to the College for review.

Please submit one electronic copy in **word format (not PDF)** to the email address
PallMedDiploma@racp.edu.au

Name of Trainee

Name of Supervisor

Title of Case Study

Resubmission 1: Existential Pain in Advanced Cancer

Please ensure that the trainee has proof-read the case study and has marked off each of the following items on the checklist prior to submission.

- | | |
|-----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> Introduction | <input checked="" type="checkbox"/> Spelling / grammar check |
| <input checked="" type="checkbox"/> Discussion | <input checked="" type="checkbox"/> Vancouver Referencing followed |
| <input checked="" type="checkbox"/> Personal Reflection | <input checked="" type="checkbox"/> Generic drug names written in lower case (<i>first letter only</i>) |
| <input checked="" type="checkbox"/> Conclusion | <input checked="" type="checkbox"/> Proprietary drug names written in upper case (<i>first letter only</i>) |
| <input checked="" type="checkbox"/> Reference List | <input checked="" type="checkbox"/> Medicine doses written in standard units |
| <input checked="" type="checkbox"/> Word count <3500 (<i>references not included</i>) | <input checked="" type="checkbox"/> Word count (<i>please state</i>): 3496 |

The trainee and supervisor confirm that this resubmission has been amended in response to comments received from the reviewers. Where recommended changes have not been made, a separate explanatory note is provided.

Please comment on the quality of the project material. (Mandatory)

Supervisor comments: (please attach further pages as required)

The trainee has provided a comprehensive report on a case that was challenging for her early in her palliative care training. She has discussed the case in relation to current evidence and literature on the definition of existential pain and suffering and the use of palliative sedation therapy for existential pain and suffering. She has also discussed the ethical issues and ongoing debate regarding the appropriateness of palliative sedation therapy for existential suffering and pain. She has now linked the case study to the literature discussed. I believe her case study is now satisfactory in what is a challenging area of palliative care practice.

Signature of Supervisor:

15// 04 / 2014

(Please print name): _____

Trainee Declaration

Please tick to indicate that you understand the following statements.

I declare that:

- This assessment is my own original work, except where I have appropriately cited the original source.
 - This assessment complies with the marking criteria score sheet
 - This assessment has been amended in response to comments received from the reviewers
 - This assessment has not been previously submitted for assessment in this or any other context.
- If the assessment has been previously submitted, please note the details below:

Please attach to the Case Study and forward to:

Education Officer, Palliative Medicine Education Committee PallMedDiploma@racp.edu.au

Submitted previously for the same assessment.
Amendments have been made for resubmission.

- This assessment complies with the College's [Academic Honesty and Plagiarism](#) policy.

For the purposes of assessment, I give the assessor of this assignment permission to:

- Reproduce this assessment for marking purposes, and;
 Take steps to authenticate the assessment, including communicating a copy of this assessment to a checking service (which may retain a copy on its database for future plagiarism checking).

Date of submission: 15/04/2014/

Signature of Trainee:

Introduction

Many patients with advanced cancer experience existential pain and suffering near the end of life. The concepts of “existential pain” and “suffering” are difficult to define and the terms are sometimes used interchangeably. They are subjective and difficult to understand, measure, research and treat. As palliative care aims to improve quality of life, we must attempt to alleviate existential pain and suffering. The following case demonstrates some of the challenges in recognising and managing existential pain in a patient with advanced cancer at the end of life. The discussion explores the definitions of existential pain and existential suffering and considers interventions to treat them.

Case report

██████████ was a fifty-seven year old mother of four, living in ██████████ with her husband. ██████████ was an ex-smoker who was diagnosed with lung cancer in 2007. She had no other medical history. She underwent left upper lobectomy in 2007, with no adjuvant treatment, following which she considered her cancer to be cured. She had regular follow-up imaging with her Oncologist. Subsequent to her cancer treatment, ██████████ had returned to managing a business that she owned with her husband. They sold their business in late 2010, at a loss, and were living off savings. They lived in public housing and were planning a new business. ██████████ mobilised in a wheelchair due to diabetes-related above knee amputations. ██████████ her husband and children identified themselves as having no religion, while her mother had a strong Christian faith. ██████████ favourite pastime was quilting and she was making an intricate design for her granddaughter, due in November 2011.

In January 2011 ██████████ presented to her Oncologist with hip pain, leading to a diagnosis of widespread skeletal metastases. She commenced chemotherapy and palliative radiotherapy to her pelvis, right shoulder and thoracic spine. She began seeing a Palliative Care Physician at her local general hospital.

On 13/4/2011, during her third cycle of chemotherapy, ██████████ had frequent vomiting that escalated over two weeks, to the point where she was not tolerating any oral intake. A recent computed tomography (CT) scan of the brain with intravenous contrast was normal. She had tried numerous oral anti-emetics without benefit. Nausea subsided only with subcutaneous metoclopramide administered by domiciliary nurses. She also reported a number of other symptoms at that time, including severe pain in the groin, abdomen and chest wall; myoclonus; confusion; hot flushes and nightmares. Her daily analgesia included 4g paracetamol, 1g naproxen, 600mg pregabalin, and 100mcg/hour fentanyl patch. Pain was now uncontrolled despite two-hourly 60mg immediate release. Due to the above symptoms, ██████████ was admitted to an inpatient palliative care unit (hospice) that day. She

was eager for her symptoms to resolve within eight days, in time for a family reunion she had organised.

At the hospice, ██████ commenced a subcutaneous infusion of morphine and haloperidol, for pain, nausea and nightmares. Amitriptyline was commenced for neuropathic pain. Nausea, pain and nightmares all resolved. The infusion was ceased on 16/4/11 and she recommenced fentanyl patches and daily oral haloperidol. Nausea and pain remained controlled and she was discharged on 18/4/2011.

██████ attended her family reunion, three hours' drive from Perth, with her husband, mother, four adult children and nine grandchildren. She felt that her symptoms were well controlled until 27/4/11 when she began vomiting. She was taken by ambulance to a district hospital where she received parenteral metoclopramide. She was noted to be febrile. Her husband drove her home, stopping every thirty minutes for ██████ to vomit. She attended her local general hospital emergency department, where she was diagnosed with pneumonia and commenced intravenous antibiotics and metoclopramide. She remained nauseated but stopped vomiting. Her Palliative Care Physician was contacted via telephone and he arranged transfer to the hospice that day. Prior to transfer, ██████ underwent a re-staging CT scan that had coincidentally been booked for that day.

On arrival to the hospice, further symptoms were elicited including olfactory hallucinations, numbness in the left and right T9 dermatome, left thigh pain, fatigue and hot flushes. She commenced a subcutaneous infusion of metoclopramide and haloperidol, with resolution of nausea and hallucinations. Dexamethasone was commenced for suspected cerebral metastases, following which the numbness and paraesthesia resolved.

Results of the staging CT scan became available, revealing consolidation in her left lung, multiple new metastases in the right lung, numerous small hepatic metastases, new skeletal metastases and pathological wedge fractures of multiple thoracic vertebrae. A CT scan of the brain, with contrast, was normal. ██████ was disappointed but not surprised by the result. She cancelled follow-up appointments with her Medical Oncologist as she did not wish to have further chemotherapy.

Magnetic resonance imaging (MRI) of the brain and spinal cord was planned to investigate for central nervous system metastases or spinal cord compression.

██████ underwent MRI of the spine on 1/5/2011 and experienced claustrophobia and panic. Due to this, she did not wish to progress to MRI of the brain even under sedation, nor would she wish to undergo whole brain radiotherapy if found to have cerebral metastases. The MRI scan of the spine was normal other than the presence of vertebral metastases.

At this stage, ██████ was seen by the hospice Counsellor and Pastoral Carer, who saw her and her family regularly for the remainder of the admission. The

Counsellor employed humanistic and mindfulness strategies, acceptance and commitment therapy, and guided imagery techniques. [REDACTED] also commenced sublingual lorazepam, as required, for anxiety. [REDACTED] expressed repeatedly to staff that she was anxious and scared of being in pain, although she felt secure in the hospice. She said she wished to shield her family from her suffering.

[REDACTED] fentanyl and amitriptyline doses were increased as her back pain worsened. She received radiotherapy to her thoracic spine. She developed new, non-specific visual symptoms, and her neurological symptoms worsened. The subcutaneous infusion was converted to oral medications at [REDACTED] request, as she felt it was making her drowsy.

On 5/5/2011 [REDACTED] developed visual hallucinations and disorientation. She was mildly hypercalcaemic, having been normocalcaemic one week previously. This was treated with zoledronic acid and intravenous fluids. Other laboratory investigations revealed no cause of delirium. Her amitriptyline was ceased and haloperidol dose increased.

[REDACTED] hallucinations resolved but in the following days she was emotionally labile, at times tearful, irritated, or inappropriately familiar with staff. Her pain worsened and migrated to different sites. Her fentanyl patch was changed to oral methadone, to try to improve neuropathic pain. She made frequent requests for breakthrough analgesia, even when she reported being free of pain. She also made requests for radiotherapy at various sites of her body. Her family visited from early morning until night. She began to phone them late at night after they returned home, distressed and agitated. Poor concentration stopped her from quilting.

On 11/5/2011 the dexamethasone dose was weaned, methadone was increased and venlafaxine commenced to assist with anxiety, pain and worsening hot flushes. [REDACTED] had been using lorazepam approximately once a day but she decided to stop it as she felt it was causing drowsiness.

[REDACTED] neurological symptoms worsened, with the development of facial droop and dysphagia. [REDACTED] began expressing guilt about many things. She experienced cyclical anger and guilt – anger that her family could not be at her bedside twenty-four hours a day, and guilt that she was being a burden on them. She reported feeling scared, not of dying but of the uncertainty surrounding death.

On 18/5/2011, [REDACTED] developed further neurological symptoms, including urinary retention and foot drop. She developed dysphagia so a subcutaneous infusion of methadone and haloperidol was recommenced and oral medications ceased. Following a family meeting, [REDACTED] commenced an end-of-life pathway. Due to ongoing nausea, agitation and anxiety, she commenced subcutaneous levomepromazine and sublingual clonazepam. Her agitation settled and drowsiness increased. She died five days later.

Discussion

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”¹ Although not perfectly understood, physical pain is well studied and there are plausible anatomical and physiological explanations for many of the pain syndromes encountered in advanced cancer, such as nociceptive, neuropathic and osseous pain. In addition, there are evidence-based guidelines or expert recommendations for treating these types of pain.²⁻⁴ As in the case of ██████████, a great challenge arises when, despite following these guidelines and treating pain aggressively with pharmacological, interventional and psychological measures, a patient’s pain remains severe and distressing. In such cases, existential pain must be considered.

“Existential pain”, “existential distress” and “existential suffering” are all concepts that have been discussed in the palliative care literature. These terms are poorly defined and sometimes used interchangeably. There are literature reviews and quantitative studies that attempt to define these concepts.⁵⁻⁷ That they are relevant to the practice of palliative care is unquestionable. Strang et al⁸ interviewed 111 palliative physicians, of whom ninety-nine percent had managed patients with existential pain and most (85 of 111) felt existential pain to be “clearly relevant” to their practice.

Boston et al⁵ performed a systematic review of 156 articles referencing the above three terms. Only 32% of these were empirical research, 28% were peer-reviewed theoretical articles and the remainder case reports or opinion pieces. They found 64 articles to be relevant, after excluding those primarily related to spirituality, hope, transcendence, meaning, physical pain and depression. They identified fifty-six definitions of existential suffering, which tended to follow common themes such as “finding meaning”, “the loss of meaning or purpose in life”, and “What will happen to me after I die?”. They found much overlap in the literature of the definitions of “existential”, “suffering” and “spiritual” and a large overlap of these with psychological diagnoses such as depression. They concluded that “existential suffering remains poorly understood and neglected in palliative care” and therefore difficult to treat.

A non-systematic review by Krikorian et al⁶ attempted to define “suffering” at the end of life. They found it to be a “unique, comprehensive holistic experience with physical, psychological, social and spiritual components...a complex negative affective and cognitive state with threat to self.” This reflects Cassell’s original work on suffering, where he defines suffering as “experienced by persons, not merely by bodies, [with] its source in challenges that threaten the intactness of the person as a complex social and psychological entity.”⁹ These themes were all expressed by ██████████ in her second hospice admission. Krikorian et al⁶ also conclude that suffering is difficult to assess and measure, due to its subjective nature. Another review found that “existential suffering” encompassed the concepts of “loss of personal meaning, loss of purpose of life, fear of death, despair, anguish,

hopelessness, fear of being a burden to others, loss of dignity, helplessness and betrayal". They concluded that existential pain is a metaphor for overall suffering.⁷

Strang et al⁸ also concluded that existential pain is a metaphor for suffering. They asked 150 hospital chaplains, 111 palliative care physicians and 90 pain physicians in Sweden, "How would you define the concept of existential pain?" They categorised the responses into four basic domains: "freedom", "meaning and meaninglessness", "existential isolation" and "death". Using keyword frequency analysis, they found that palliative care physicians focused significantly more on "annihilation" and "impending separation" rather than physical pain, whereas pain physicians focused on the fact that "living is painful" and chaplains emphasised guilt issues and religious concerns. This further emphasises the inconsistencies in defining existential pain.

In a phenomenological study by Mount et al,¹⁰ 21 interviewees with life-threatening illness were questioned regarding the influence of spirituality and existential well-being upon their experience of illness. They found suffering to be associated with an "experience of isolation and meaninglessness." Williams¹¹ explored the concept of existential suffering in a qualitative study of 33 low socioeconomic status interviewees with advanced cancer, primarily female, black, middle-aged and unemployed. Subjects expressed guilt regarding dying young and therefore being unable to fulfill life's responsibilities, such as raising children, and "persistent inability to control their destiny". ██████ experienced similar guilt about her perceived abandonment of her family and failure to fulfil her roles of wife, mother, daughter and carer.

As in ██████ case, existential pain and distress often coincide with physical pain.¹ This raises questions such as: can unrelieved physical pain cause existential pain? Can existential pain result in the subjective sensation of physical pain? Is existential pain expressed as physical pain in patients who cannot articulate their suffering? In a case series by Strasser et al,¹³ the severe physical pain of three patients with advanced cancer was alleviated by addressing their existential issues. Wilson et al¹² interviewed 381 patients with advanced cancer, of whom half felt that they were suffering, and one quarter that they were suffering at a moderate-to-extreme level. In a qualitative review, almost half of these attributed their suffering to physical complaints, 19% to social concerns, 18% to existential concerns and 14% to psychological. Pain was the most common physical complaint. However, on quantitative review, suffering was most strongly correlated with malaise, followed by weakness, pain and depression. In contrast, a prospective cohort study of hospice patients found there to be little association between physical symptoms and suffering. Rather, suffering was associated with worse psychological well-being and worse quality-of-life.¹⁴ In addition to physical symptoms, there is also a large overlap of existential pain or suffering with psychological disease, including depression and anxiety.¹² However, treating depression and anxiety does not necessarily alleviate existential pain.⁷

Cohen et al¹⁵ found terminally ill patients' quality of life to improve following admission to palliative care units, in those well enough to participate in the study. This included a significant improvement in their existential well-being, as measured on the McGill Quality of Life questionnaire. The possible interventions that led to improvement in existential wellbeing were not investigated. ██████ reported a sense of security in the hospice environment, with ready access to a multidisciplinary team and perceived ability to "shield" her family from some of her suffering, which she would not be able to do at home. Finding a definition for existential pain may assist in identifying specific interventions that improve existential wellbeing.

Several interventions have been offered for the management of existential pain. Strasser et al¹³ suggest addressing emotional distress, alexithymia (being unable to verbalise emotions) and delirium as a starting point to the treatment of existential pain.

LeMay and Wilson¹⁶ performed a review of eight group and individual interventions addressing existential issues in cancer patients. These employed psychological, spiritual, meaning-making dignity-improving measures. Only one of the interventions reviewed, long-term Supportive-Expressive Group Therapy (SEGT), was "probably efficacious" using the American Psychological Association criteria for empirically-validated treatments, based on three randomised control trials. SEGT is an unstructured weekly group intervention for patients with advanced disease, with the aim of "improving self-worth, decreasing isolation and developing sources of support." Participants are encouraged to interact outside sessions, and family meetings are held regularly.¹⁶

If existential pain is the result of a loss of meaning and a perceived threat to one's person, then it is intuitive to treat it by attempting to reintroduce meaning to life and thereby minimise those threats. Psychotherapeutic meaning making,¹⁷ Meaning of Life Intervention,¹⁸ Temporal Existential Awareness and Meaning Making model¹⁹ and the Meaning-Making intervention²⁰ are some of the novel treatments hoping to address this. Some authors focus on hopefulness as a therapeutic intervention for existential pain and suffering.²¹⁻²³ Chochinov's dignity therapy may also be useful for alleviating suffering at the end of life.²⁴ In ██████ case, it was employed in an informal manner by the clinical psychologist.

For more than a decade there has been much debate in the palliative care literature regarding the use of palliative sedation, also known as sedation to unconsciousness, as a treatment for unrelieved existential pain.²⁵⁻³² The unclear definition of existential pain may further confuse this debate. The European Association for Palliative Care has published a framework for the use of palliative sedation³³, with considerations given for "refractory existential or psychological distress". They acknowledge that special consideration are necessary because "it is much more difficult to establish [that existential or psychological distress] are truly refractory." Blondeau et al²⁶ interviewed 100 doctors and 24 pharmacists working in palliative care and found that though most were favourable towards sedation

as a treatment for physical pain, many felt sedation was not adequate treatment for existential suffering. A 2010 survey of 1880 physicians in the United States found that two in three opposed terminal sedation for the treatment of existential suffering.³¹ Rousseau³² recommends guidelines for the use of palliative sedation for existential suffering, including a trial of “respite sedation” to break the cycle of sleep deprivation and existential distress.³⁴

Conclusion

The case of ██████ exposed the difficult concepts of existential pain and existential suffering at the end of life, which are concepts that overlap and are difficult to define. Existential pain may be thought of as a loss of sense of self, whereas existential suffering may be considered a loss of sense of meaning. Existential pain and suffering often coexist with physical symptoms like pain and malaise, although a causative relationship is uncertain. Despite difficulties in treatment, it is imperative that palliative care addresses existential pain and suffering in order to provide holistic care. Novel therapies such as meaning making and dignity therapy may assist but further studies are required. Consistent definitions of existential pain and suffering would assist with this. Palliative sedation, as used in the case of ██████, remains a controversial treatment for existential pain and suffering.

Personal Reflection

I met ██████ during the first months of my palliative care training and her case raised a number of concerns for me, both at the time I was caring for her and retrospectively when reviewing her case. Had I a better understanding of existential pain, would I have cared for her better? ██████ distress and feelings of guilt were apparent. She felt that her cancer was a direct result of her former smoking. She felt guilty for dying young and leaving four generations of her family, including her elderly mother, disabled husband, children and grandchildren. She felt guilty for leaving her husband in a difficult financial position. Her quilting, which was meaningful to her, was made difficult by her illness. Interlaced with her psychological and existential distress were significant physical symptoms, including pain, nausea, hot flushes and neurological deficits.

I experienced a sense of helplessness that I could not alleviate her suffering, as well as frustration at the diagnostic uncertainty of the cause of her neurological symptoms. On discussion at our daily multidisciplinary team meetings, other staff members clearly felt the same. We faced this in different ways – some sat silently with ██████, others avoided her, while many of us tried to treat her suffering with medications. We bombarded her with analgesics, sedatives and antidepressants. Physical symptoms are much easier to understand, measure and treat than existential symptoms and there is less personal and emotional involvement required.

In retrospect, it is obvious that we made frequent changes to [REDACTED] medications. At the time, it felt as though our prescribing was slow and measured. Decisions were always made in consultation with the multidisciplinary team. On reflection, I was surprised to realise how rapidly we changed her medications. I can rationalise all the prescribing decisions we made, all of which were with good intention, but upon reflection I wonder how much iatrogenic harm may have been caused. Whether through unpleasant side effects, by impairing her participation in psychological interventions or by contributing to delirium, the above may have exacerbated her existential pain. Published case studies of palliative care patients with existential pain show similar patterns of prescribing.^{13,35,36} I now wonder to what degree my prescribing was treating the patient, and how much it was treating my own helplessness and distress.

The inpatient setting impacted upon our decision-making. Had [REDACTED] been treated in the community setting, the frequent medication changes would have been impractical and uneconomical. In addition, staff members would not have been visiting [REDACTED], and observing her distress, many times throughout the day.

As with any decision to sedate a patient to the point of unconsciousness, ethical considerations arose. Was [REDACTED] existential pain refractory or could it have been alleviated with further non-pharmacological interventions or “respite sedation”? Was delirium affecting her capacity to consent to palliative sedation? In this case, our decision-making was ultimately made easier by her unambiguous physical deterioration and her explicit wishes for palliative sedation expressed to her family and us.

Reflecting on [REDACTED] case has made me a more careful prescriber. It is easy to prescribe a medication to treat difficult physical and psychological symptoms. It is gratifying and makes me feel useful as a doctor. However, it is often not the correct treatment decision to make, especially in cases of existential pain and suffering.

References

1. IASP Task Force on Autonomy. Part III: Pain terms, a current list with definitions and notes on usage. In: Merskey H, Bogduk N, editors. *Classification of Pain*, 2nd ed. Seattle: IASP Press; 1994. p. 209-14.
2. Moryl N, Coyle N, Foley K. Managing an acute pain crisis in a patient with advanced cancer: "This is as much of a crisis as a code". *JAMA* 2008; 229(12): 1457-67.
3. Dy SM. Evidence-based approaches to pain in advanced cancer. *Cancer Journal* 2010;16(5):500-6.
4. Smith HS. Painful osseous metastases. *Pain Physician* 2011; 14: E373-E405.
5. Boston P, Bruce A, Schreiber R. Existential suffering in the palliative care setting: an integrated literature review. *J Pain Symptom Manage* 2011; 41(3): 604-18.
6. Krikorian A, Limonero JT, Mate J. Suffering and distress at the end-of-life. *Psycho-Oncology* 2011:10 pages. Epub Oct 2011.
7. Bruce A, Boston P. Relieving existential suffering through palliative sedation: discussion of an uneasy practice. *J Advanced Nurs* 2011; 67(12): 2732-40.
8. Strang P, Strang S, Hultborn R, Arner S. Existential pain - an entity, a provocation, or a challenge? *J Pain Symptom Manage* 2004; 27(3): 241-50.
9. Cassel EJ. The nature of suffering and the goals of medicine. *New Engl J Med* 1982; 306(11): 639-45.
10. Mount BM, Boston PH, Cohen SR. Healing connections: on moving from suffering to a sense of well-being. *J Pain Symptom Manage* 2007; 33(4): 372-88.
11. Williams BR. Dying young, dying poor: a sociological examination of existential suffering among low-socioeconomic status patients. *J Palliat Med* 2004; 7(1): 27-37.
12. Wilson KG, Chochinov H, McPherson CJ, LeMay K, Allard P, Chary S, et al. Suffering with advanced cancer. *J Clin Onc* 2007; 25(13): 1691-7.
13. Strasser F, Walker P, Bruera E. Palliative pain management: when both pain and suffering hurt. *J Palliat Care* 2005; 21(2): 69-79.

14. Abraham A, Kutner J, Beaty B. Suffering at the end of life in the setting of low physical symptom distress. *J Palliat Med* 2006; 9(3): 658-65.
15. Cohen SR, Boston P, Mount BM, Porterfield P. Changes in quality of life following admission to palliative care units. *Palliat Med* 2001; 15: 363-71.
16. LeMay K, Wilson G. Treatment of existential distress in life threatening illness: a review of manualized interventions. *Clin Psychol Rev* 2008;28:472-93.
17. Breitbart W, Gibson C, Poppito SR, Berg A. Psychotherapeutic intervention at the end of life: a focus on meaning and spirituality. *Can J Psychiatry* 2004; 49(6): 366-72.
18. Mok E, Lau K, Lai T, Ching S. The Meaning of Life Intervention for patients with advanced-stage cancer: development and pilot study. *Oncol Nurs Forum* 2012;39:E480-8.
19. Lee V, Loiselle CG. The salience of existential concerns across the cancer control continuum. *Palliat Support Care* 2012;10:123-33.
20. Lee V. The existential plight of cancer: meaning making as a concrete approach to the intangible search for meaning. *Support Care Cancer* 2008; 16: 779-85.
21. McCullough E. Is there hope for a peaceful death? *J Palliat Med* 2011; 14(3): 380.
22. Alidina K, Tettero I. Exploring the therapeutic value of hope in palliative nursing. *Palliat Support Care* 2010; 8(3): 353-8.
23. Mok E, Lau KP, Lam WM, Chan LN, Ng J, Chan KS. Health-care professionals' perspective on hope in the palliative care setting. *J Palliat Med* 2010; 13(7): 877-83.
24. Chochinov HM, Hack T, Hassard T, Kristjanson LJ, McClement S, Harlos M. Dignity therapy: a novel psychotherapeutic intervention for patients near the end of life. *J Clin Oncol* 2005; 23(24): 5520-5.
25. Morita T, Tsunoda J, Inoue S, Chihara S. Terminal sedation for existential distress. *Am J Hosp Palliat Care* 2000; 17(3): 189-95.
26. Blondeau D, Roy L, Dumont S, Godin G, Martineau I. Physicians' and pharmacists' attitudes toward the use of sedation at the end of life: influence of prognosis and type of suffering. *J Palliat Care* 2005; 21(4): 238-45.
27. Taylor BR, McCann RM. Controlled sedation for physical and existential suffering? *J Palliat Med* 2005; 8(1): 144-7.

28. Berlinger N. Taking existential suffering seriously. *J Pain Symptom Manage* 2007; 34(1): 108-10.
29. Cassell EJ, Rich JD. Intractable end-of-life suffering and the ethics of palliative sedation. *Pain Med*. 2010; 11(3): 435-8.
30. Juth N, Lindblad A, Lynoe N, Sjostrand M, Helgesson G. European Association for Palliative Care (EAPC) framework for palliative sedation: an ethical discussion. *BMC Palliat Care* 2010; 9: 20.
31. Putman MS, Yoon JD, Rasinski KA, Curlin FA. Intentional sedation to unconsciousness at the end of life: findings from a national physician survey. *J Pain Symptom Manage* 2012; Epub 2012/12/06.
32. Rousseau P. Existential suffering and palliative sedation: a brief commentary with a proposal for clinical guidelines. *Am J Hosp Palliat Care* 2001;18:151-3.
33. Cherny NI, Radbruch L; Board of the European Association for Palliative Care. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med* 2009; 23(7):581-93.
34. Rousseau P. Existential distress and palliative sedation [letter]. *Anesth Analg* 2005; 101(2): 611-12.
35. Mori M, Elsayem A, Reddy SK, Bruera E, Fadul NA. Unrelieved pain and suffering in patients with advanced cancer. *Am J Hosp Palliat Care* 2011; Epub 2011/07/22.
36. Sudore RL, Villars P, Carey EC. Sitting with you in your suffering: lessons about intractable pain at the end of life. *J Palliat Med* 2010; 13(6): 779-82.