management is implemented by one or more clinicians. The time for implementation of SSRDs is ripe as clinicians are already formulating causal hypotheses about the treatments they deliver, and patient-reported outcomes are being tracked through self-report as part of distress screening programs. In the clinic, SSRDs foster more intentional approach to clinical hypothesis testing and treatment response.

SSRDs may be contraindicated when treatment response lacks significant individual variation, and when an acute course of symptoms precludes repeated assessment of symptoms or behaviors. SSRDs are also impractical when treatment effects occur after significant latencies because the causal lags become increasingly difficult to discern from history effects and other confounds. A similar concern arises when treatment effects are slow to washout (e.g., learning from behavior therapy, effects of SSRIs). In this case, reversal designs that remove the treatment, or alternating treatment designs that rotate them, are unlikely to yield clear functional relationships between treatment and outcome.

A final benefit to consider is the sense of compassion satisfaction clinicians experience when seeing positiveresponse to treatment. Similar to psychotherapy practice, palliative medicine may be difficult to learn from because many processes are in flux, and secondary loss may overshadow the fulfilling aspects of work. SSRDs have the potential to highlight the times where “unfixable” chronic conditions get systematically better, albeit sometimes in small or context-dependent ways.

Sincerely,

James Gerhart, PhD
Department of Psychology
Central Michigan University
Mt. Pleasant, Michigan
USA
E-mail: gerha1ji@cmich.edu

Dennis Hand, PhD
Thomas Jefferson University
Philadelphia, Pennsylvania, USA

Michael Hoerger, PhD
Tulane University
New Orleans, Louisiana, USA

Sean O’Mahony, MB, BCH, BAO
Rush University
Chicago, Illinois, USA

https://doi.org/10.1016/j.jpainsymman.2018.12.209

References

1. Kravitz RL, Duan N, Niedzinski EJ, Hay MC, Subramanian SK, Weisner TS. What ever happened to N-of-1 trials? Insiders’ perspectives and a look to the future. Milbank Q 2008;86:533–555.
2. Van Scheppingen C, Schroevers MJ, Pool G, et al. Is implementing screening for distress an efficient means to recruit patients to a psychological intervention trial? Psychooncology 2014;23:516–523.
3. Janosky JE, Libkuman TM, Leininger SL, Hoerger MP. Single Subject Designs in Biomedicine. Heidelberg: Springer Netherlands, 2009.
4. Duan N, Kravitz RL, Schmid CH. Single-patient (n-of-1) trials: a pragmatic clinical decision methodology for patient-centered comparative effectiveness research. J Clin Epidemiol 2013;66(8 Suppl):S21–S28.
5. Sidman M. Tactics of Scientific Research. New York, NY: Basic Books, 1960.
6. Dews PB. Studies on behavior. I. Differential sensitivity to pentobarbital of pecking performance in pigeons depending on the schedule of reward. J Pharmacol Exp Ther 1955;113:393–401.
7. Spira AP, Edelstein BA. Behavioral interventions for agitation in older adults with dementia: an evaluative review. Int Psychogeriatr 2006;18:195–225.
8. Kazdin A, ed. Research Design in Clinical Psychology, 3rd ed. Bost, MA: Allyn and Bacon, 1998.

Difference in Opinions About Continuous Deep Sedation Among Cancer Patients, Bereaved Families, and Physicians

To the Editor

Despite recent advances in palliative medicine, some symptoms are refractory to intensive palliative care, and then palliative sedation therapy is sometimes performed.[1,2] Continuous deep sedation (CDS) until death is regarded as one type of palliative sedation therapy, and it has recently become a focus of intense debate.[3–8] Although dying in one’s sleep is regarded as one type of good death in some cultures,[9] CDS may be labeled as a continuum of euthanasia, especially when performed for patients with relatively longer predicted survival.[3–8,10] Few empirical studies have been performed on what CDS means for patients and families themselves.[10] Comparing insights from patients and bereaved families with those from health care professionals is valuable. The primary aim of this study was to make rough comparisons of opinions about CDS among patients with cancer, bereaved families, home physicians, and palliative care specialists.

Subjects and Methods

A total of four questionnaire surveys were performed from August 2016 to February 2018 in Japan. The Institutional Review Board of the Seirei Mikatahara General Hospital approved the ethical and scientific validity of this study. If participants refused to participate in this survey, they were asked to return the questionnaire with no response.

Patients with cancer were recruited from a commercially database. Although we were aware of a potential sampling bias, the primary aim of this study was a rough comparison, and thus we decided to use this sample. This database consists of more than 1,000,000 Japanese who voluntarily registered, and participants were invited via Internet. Inclusion criteria were adult patients with cancer receiving regular outpatient treatment and aware of the diagnosis of malignancy. Invitation was made via the e-mail at a time; and if the requested number of the participants completed, survey was closed (i.e., the actual number of potential participants who invited were unknown). Each patient received a small reward, and a total of 400 responses were requested.

Bereaved families were consecutively recruited from the families of patients who died at 71 certified inpatient hospices/palliative care units. Primary physicians identified potential participants following the inclusion criteria: adult bereaved family members of an adult patient with cancer (one family member was selected for each patient), capable of replying to a self-reported questionnaire, and aware of the diagnosis of malignancy. Families were surveyed 6 to 12 months after the patients' deaths by mail. One reminder was sent.

Home physicians and palliative care specialists were recruited from the national registry of certified physicians of the Japanese Academy of Home Care Physicians and Japanese Society of Palliative Medicine, respectively. Questionnaires were sent to all registered physicians by mail, with two reminders.

Measurements

The questionnaire was developed by the authors on the basis of a literature review.[1–8] We defined CDS as the continuous use of sedatives to relieve intolerable and refractory symptoms with loss of consciousness until death according to national guideline.[1,2] To avoid confusion due to different interpretations of CDS, we paraphrased CDS throughout the questionnaire.

We examined the level of agreement with the statements on a six-point Likert-type scale from 1 (strongly disagree) to 6 (strongly agree) using "death in sleep after total unconsciousness by sedatives is one type of good death for imminently dying patients" (good death). We also examined whether the respondents viewed CDS as appropriate in four situations (Fig. 1), such as 1) physical symptoms/predicted survival of days, 2) psychological suffering/days, 3) physical symptoms/months, and 4) psychological suffering/months. CDS were paraphrased, such as "total unconsciousness by sedatives until death is appropriate if a patient has refractory and intense suffering and his/her survival is estimated as days (months)." Levels of agreement were measured on a six-point Likert-type scale from one (strongly disagree) to six (strongly agree). Respondent backgrounds were obtained from the respondents themselves.

Statistical Analyses

Mean scores were compared using the analysis of variance (ANOVA) and Tulsky method as a post hoc test. Sex and age were adjusted. Owing to multiple comparisons, a P-value of 0.010 was regarded as significant. All analyses were performed using the Statistical Package for the Social Sciences (ver. 11.0).

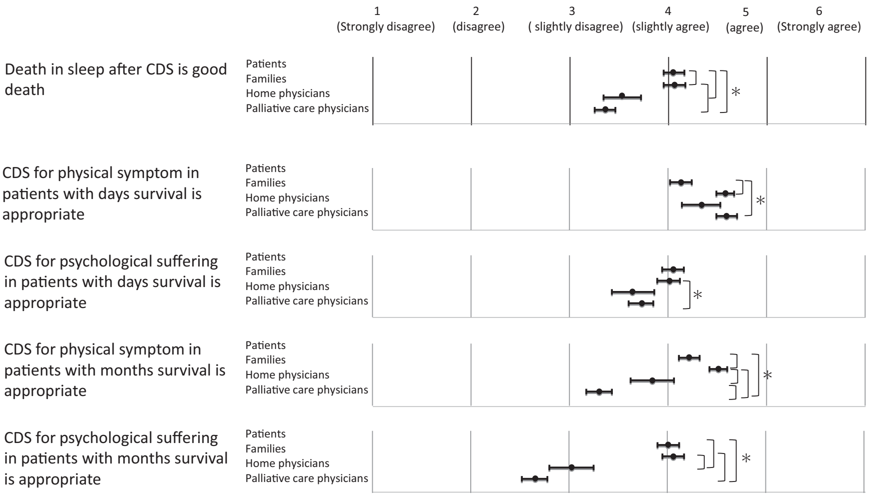

Fig. 1. Mean and 95% confidence intervals were shown. *: $P < 0.01$ adjusted for age and sex; Patients, $n = 412$; bereaved families, $n = 512$; home physicians, $n = 131$; and palliative care physicians, $n = 440$. CDS = continuous deep sedation.

Results

Of the 787 bereaved family members, 219 home physicians, and 695 palliative care specialists who were mailed, 592 (75%), 141 (64%), and 469 (67%) returned the questionnaire, respectively. Of them, 80, 4, and 29 refused to participate, respectively, and an additional 0, 6, and 0 returned invalid answers, respectively; thus, finally, 512 (65%) bereaved family members, 131 (60%) home physicians, and 440 (63%) palliative care specialists were analyzed. A total of 412 patients completed the questionnaire. Backgrounds of the respondents are summarized in Table 1.

Patients and the bereaved families were significantly more likely to agree that death followed by CDS is one type of good death than both home and palliative care physicians (Fig. 1). Compared with differences in opinions about the appropriateness of CDS in patients with a predicted survival of days, there were apparent discrepancies in opinions between patients/families and physicians for patients with a predicted survival of months (Fig. 1). Patients and families were more likely to agree that CDS is appropriate for patients with refractory and intense physical or psychological suffering than physicians. Predicted survivals made less influence on the perceived appropriateness of CDS in patients and families.

Table 1
Characteristics of the Respondents

Variables	Patients, $N = 412$	Bereaved Families, $N = 512$	Home Physicians, $N = 131$	Palliative Care Specialists, $N = 440$
Sex				
Male	256 (62%)	170 (33%)	95 (73%)	350 (80%)
Female	156 (38%)	334 (65%)	36 (27%)	81 (18%)
Missing	0 (0%)	0 (0%)	0 (0%)	9 (2.0%)
Age, years				
<40	21 (5.1%)	27 (5.4%)	33 (25%)	26 (6.0%)
40–49	67 (16%)	50 (10%)	38 (29%)	122 (28%)
50–59	100 (24%)	127 (25%)	44 (34%)	192 (45%)
60–69	110 (27%)	159 (32%)	15 (11%)	81 (19%)
70–79	88 (21%)	109 (22%)	1 (0.8%)	10 (2.3%)
≥80	26 (6.3%)	31 (6.2%)	0 (0%)	0 (0%)
Religion				
None	214 (52%)	181 (35%)	99 (76%)	290 (66%)
Buddhism	176 (43%)	273 (53%)	18 (14%)	78 (18%)
Christianity	9 (2.2%)	14 (2.7%)	6 (4.6%)	48 (11%)
Others	13 (3.1%)	26 (5.0%)	7 (5.3%)	12 (2.7%)
Missing	0 (0%)	13 (2.5%)	1 (0.8%)	12 (2.7%)
Education				
High school	160 (39%)	261 (51%)	0	0
Junior college	71 (17%)	114 (22%)	0	0
University/college	181 (44%)	117 (23%)	131 (100%)	440 (100%)
Missing	0 (0%)	20 (3.9%)	0	0
Income (10^3 yen/year)			N.A.	N.A.
<20,000	19 (4.6%)	139 (27%)		
20,000-40,000	123 (30%)	195 (38%)		
40,000-60,000	81 (20%)	69 (14%)		
60,000-80,000	51 (12%)	40 (7.8%)		
≥80,000	78 (19%)	39 (7.6%)		
Missing	60 (15%)	30 (5.8%)		
Primary sites			N.A.	N.A.
Lung	38 (9.2%)	99 (19%)		
Stomach	20 (4.9%)	58 (11%)		
Colon, rectum	0 (0%)	68 (13%)		
Esophagus	36 (8.7%)	17 (3.3%)		
Breast	89 (22%)	25 (4.9%)		
Prostate, testis	24 (5.8%)	12 (2.3%)		
Ovary, uterus	79 (19%)	29 (5.6%)		
Kidney, bladder	36 (8.8%)	19 (3.7%)		
Pancreas, bile ducts	12 (2.9%)	74 (15%)		
Liver	1 (0.2%)	30 (5.9%)		
Head and neck	28 (6.8%)	21 (4.3%)		
Bloods, lymph nodes	35 (8.5%)	14 (2.8%)		
Unknown	0 (0%)	5 (1.0%)		
Others	13 (3.2%)	40 (7.9%)		
Missing	0 (0%)	0 (0%)		

N.A. = not available.

Discussion

The most important finding of this study was the clarification of significant discrepancies in opinions about CDS among patients with cancer, bereaved families, and physicians. Compared with physicians, patients with cancer and families were more likely to agree that death in one's sleep as a result of CDS is one type of good death and were more likely to regard CDS as appropriate even if the predicted survival of the patient is months.

Death in one's sleep after CDS is regarded as a good death by patients/bereaved families more than by physicians, and there were no significant differences between patients and families. A possible interpretation is that, for physicians, performing CDS may mean the failure of symptom management, but for patients and families, there is no distinction between a natural decline in consciousness and sleep after CDS.[10] The concept of a good death differs among cultures,[9] and so further cross-cultural study is of value to understand cultural meaning of consciousness in the dying process.

Of note was the fact that patients and bereaved families were more likely to regard CDS as appropriate even if the predicted survival of the patient is months. For physicians, the influence of the patient's predicted survival was great when determining whether CDS is appropriate. This finding suggests that physicians might consider the possibility of life-shortening as one of the important factors in determining whether CDS is proportionally appropriate,[2] but patients and families put more value on reducing suffering and less on survival in this situation. The indication of CDS for not imminently dying patients is a focus of recent debate, such as legalization of sedation in France or Italy.[7,8] Patient/family view should be included into further discussion.

This study has some limitations. The patient sample was from Internet sample and biased. Response rates are acceptable but moderate. Questionnaires were developed for this study, and their reliability and validity were not formally confirmed. Finally, definitions about CDS and good death may lead to different results, although we carefully used these terminologies.

In conclusion, patients and families may have a different view from physicians about the meaning of CDS. Further study is highly needed.

Tatsuya Morita, MD
Department of Palliative and Supportive Care
Palliative Care Team
Seirei Mikatahara General Hospital
Hamamatsu, Shizuoka
Japan
E-mail: tmorita@sis.seirei.or.jp

Daisuke Kiuchi, MD
Department of Palliative Medicine
National Cancer Center Hospital
Tokyo
Japan

Masayuki Ikenaga, MD
Hospice Palliative Medicine
Yodogawa Christian Hospital
Osaka
Japan

Hirofumi Abo, MD
Department of Palliative Medicine
Rokko Hospital
Kobe, Hyogo
Japan

Sayaka Maeda, MD
Palliative Care Center
Department of Palliative Medicine
Kyoto University Hospital
Kyoto
Japan

Maho Aoyama, RN, MNS
Department of Palliative Nursing
Health Sciences
Tohoku University Graduate School of Medicine
Sendai, Miyagi
Japan

Takuya Shinjo, MD
Shinjo Clinic
Kobe, Hyogo
Japan

Yoshiyuki Kizawa, MD, PhD, FJSIM
Department of Palliative Medicine
Kobe University Graduate School of Medicine
Kobe, Hyogo
Japan

Satoru Tsuneto, MD, PhD
Department of Human Health Sciences
Graduate School of Medicine
Kyoto University
Kyoto
Japan

Mitsunori Miyashita, RN, PhD
Department of Palliative Nursing
Health Sciences
Tohoku University Graduate School of Medicine
Sendai, Miyagi
Japan

https://doi.org/10.1016/j.jpainsymman.2018.11.025

Disclosures and Acknowledgments

This study was funded by the Japanese Society of Palliative Medicine, the Japan Hospice Palliative Care Foundation, JSPS KAKENHI Grant Number JP16KT0007, and the Yuumi Memorial Foundation for Home Health Care. The authors have no conflicts of interest.

References

1. Beller EM, van Driel ML, McGregor L, Truong S, Mitchell G. Palliative pharmacological sedation for terminally ill adults. Cochrane Database Syst Rev 2015;1:CD010206.
2. Cherny NI, ESMO Guidelines Working Group. ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation. Ann Oncol 2014;25(Suppl 3):iii143–iii152.
3. Papavasiliou EE, Payne S, Brearley S. Current debates on end-of-life sedation: an international expert elicitation study. Support Care Cancer 2014;22:2141–2149.
4. Rys S, Deschepper R, Mortier F, et al. The moral difference or equivalence between continuous sedation until death and physician-assisted death: word games or war games?: a qualitative content analysis of opinion pieces in the indexed medical and nursing literature. J Bioeth Inq 2012;9:171–183.
5. Rys S, Mortier F, Deliens L, et al. Continuous sedation until death: moral justifications of physicians and nurses–a content analysis of opinion pieces. Med Health Care Philos 2013;16:533–542.
6. Materstvedt LJ, Bosshard G. Deep and continuous palliative sedation (terminal sedation): clinical-ethical and philosophical aspects. Lancet Oncol 2009;10:622–627.
7. Raus K, Chambaere K, Sterckx S. Controversies surrounding continuous deep sedation at the end of life: the parliamentary and societal debates in France. BMC Med Ethics 2016;17:36.
8. Miccinesi G, Caraceni A, Maltoni M. Palliative sedation: ethical aspects. Minerva Anestesiol 2017;83:1317–1323.
9. Sanjo M, Miyashita M, Morita T, et al. Preferences regarding end-of-life cancer care and associations with good-death concepts: a population-based survey in Japan. Ann Oncol 2007;18:1539–1547.
10. Morita T, Hirai K, Akechi T, Uchitomi Y. Similarity and difference among standard medical care, palliative sedation therapy, and euthanasia: a multidimensional scaling analysis on physicians' and the general population's opinions. J Pain Symptom Manage 2003;25:357–362.

Palliative Care Consultation Before Left Ventricular Assist Device Implantation

Dear Editor

In a recent article published in the *Journal of Pain and Symptom Management*, Chuzi et al.[1] report on palliative care (PC) consultations before left ventricular assist device (LVAD) implantation. The authors conclude that a one-time PC consultation immediately before implantation is insufficient to complete preparedness planning and to delineate patients' preferences and goals. The authors pointed out several reasons for this finding. The first is that PC consultations were offered acutely before surgery. The second is that PC clinicians may be unfamiliar with LVAD-related complications.

Acknowledging the suggestions by Dr. Chuzi, we would like to offer an additional perspective based on our experience. We started a mandatory PC consultation before LVAD implantation (preVAD) for both destination therapy and bridge to transplant in 2014.[2] A semistructured script to minimize the differences among PC clinicians was developed (Table 1), and to date, we have met with close to 300 patients for those who have already decided to undergo LVAD therapy. The content of the conversations is documented in the medical record descriptively. After LVAD implantation, PC is consulted whenever needed, when there are catastrophic events or concerns about the overall condition (i.e., repeated hospitalizations or declining functional status). We agree that it would be ideal for preVAD to be operationalized much earlier before LVAD implantation. However, given the disease trajectory of heart failure, which can deteriorate very quickly, and thus requires relatively acute decision-making, it is challenging for that to happen in all cases. Indeed, we have found that preVAD occurred only 3 days (median) before implantation surgery.[2] We have also encountered many patients who are in the intensive care unit and are expecting surgery the next day. Providing a consultation in this setting could be overwhelming and counterproductive. Nonetheless, in our study, where we examined if patients could respond to questions of 3 and 5 in a semistructured script (Table 1), all the patients were still able to express what makes their life meaningful. In addition, 92% could discuss possible complications of LVAD therapy, and 70% could articulate what would be an unacceptable health state.[2]

We believe that our intervention using a semistructured script worked well because it does not necessarily focus on the specific medical intervention or life-sustaining treatments but rather focuses more on the conditions of what would be a meaningful life, and what are the underlying values and goals of the patient. As we have noticed with advance directives, it is difficult for patients to understand the specific interventions (e.g., mechanical ventilation, renal replacement therapy, or blood transfusions) in the inherently more complex medical state when they need to make such decisions.[3] Furthermore, as shown by the authors,[1] it would be even more overwhelming for patients in that emotionally charged situation to consider the possibility of device malfunction or other progressive comorbid condition, such as old age or malignancy. Regardless of the reason of deterioration, such as LVAD-associated complications, device malfunctions, or progressive complications, decisions about the goals of care would ultimately come down to the patients' attitudes toward his/her quality of life, beliefs about suffering, tradeoffs, and what is an unacceptable state; and this is inherently subjective and unique to the specific patient. In addition, this approach would not necessarily require clinicians to be familiar with all