

Relieving suffering or intentionally hastening death: Where do you draw the line?*

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Objective: End-of-life practices vary worldwide. The objective was to demonstrate that there is no clear-cut distinction between treatments administered to relieve pain and suffering and those intended to shorten the dying process.

Design: Secondary analysis of a prospective, observational study.

Setting: Thirty-seven intensive care units in 17 European countries.

Patients: Consecutive patients dying or with any limitation of therapy.

Interventions: Evaluation of the type of end-of-life category; dates and times of intensive care unit admission, death, or discharge; and decisions to limit therapy, medication, and doses used for active shortening of the dying process and the intent of the doctors prescribing the medication.

Measurements and Main Results: Limitation of life-sustaining therapy occurred in 3,086 (72.6%) of 4,248 patients, and 94 (2.2%) underwent active shortening of the dying process. Medication for

active shortening of the dying process included administration of opiates (morphine to 71 patients) or benzodiazepines (diazepam to 54 patients) alone or in combination. The median dosage for morphine was 25.0 mg/hr and for diazepam 20.8 mg/hr. Doses of opiates and benzodiazepines were no higher than mean doses used with withdrawal in previous studies in 20 of 66 patients and were within the ranges of doses used in all but one patient. Doctors considered that medications for active shortening of the dying process definitely led to the patient's death in 72 patients (77%), probably led to the patient's death in 11 (12%), and were unlikely to have led to death in 11 (12%) patients.

Conclusions: There is a gray area in end-of-life care between treatments administered to relieve pain and suffering and those intended to shorten the dying process. (Crit Care Med 2008; 36:8–13)

KEY WORDS: end-of-life decisions; euthanasia; shortening the dying process; withdrawing treatment; intensive care units; double effect

End-of-life actions are common in intensive care units (ICUs) around the world (1–4). Despite a widespread perception of excessive and inappropriate use of life-sustaining technology, withholding or withdrawing of treatment occurs in more than two thirds of patients dying in ICUs (1, 4) and has actually increased (5). The use of aggressive therapy has decreased

(5–7). While in the past most patients died in ICUs after cardiopulmonary resuscitation (CPR) (8), presently only approximately 20% of ICU patients who die undergo CPR (1, 4).

Discussions of end-of-life practices in ICUs generally imply that the lines between these practices are clear and well defined. Actions undertaken in the care of dying patients are grouped into distinct

categories, including CPR, withholding or withdrawing treatment, and active euthanasia or active shortening of the dying process (SDP) (1–5). Active euthanasia or SDP is assumed to be distinct from legal and ethically acceptable practices, such as withholding and withdrawing treatment.

Even though limitation of therapy is common, active euthanasia is controversial and only legal in The Netherlands and

*See also p. 331.

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Belgium (on the patient's direct request) (9, 10), and physician-assisted suicide is only allowed in Switzerland and Oregon in the United States (11). In these countries, where the law defines euthanasia as the act of deliberately terminating the life of another person at his or her request, active euthanasia practiced in the ICU for incompetent patients would be viewed as illegal. Palliative care, on the other hand, is widely practiced and encouraged (12). It is well known that the same medications given to ease pain and suffering can potentially cause or hasten death. It is exceedingly difficult to determine whether and when relief measures are undertaken with the implicit or explicit intention to shorten the dying process as opposed to just relieve pain and suffering.

Only three studies have examined the use of life-shortening practices in adult ICUs. In an attitudinal survey conducted in 16 European countries, 40% of physicians admitted to sometimes deliberately administering drugs to patients with no hope of survival until death ensues (13). The ETHICUS study documented SDP in seven of 17 European countries (4). Asch (14) noted that 17% of critical care nurses were asked by patients or relatives to perform euthanasia or assist in suicide, and 16% reported that they had engaged in such practices.

The purpose of this article is to make the argument and show evidence that there is no clear-cut distinction between treatments administered to relieve pain and suffering when withdrawing life-sustaining treatment and those intended to shorten the dying process. An in-depth examination of this gray area in end-of-life care has important moral and ethical implications for the practice of intensive care medicine. It also has implications for other acute care areas, long-term care, and community care, where there are similar concerns about pain management vs. actively assisting in the dying process. The article elaborates on the previous report (4), which only briefly touched on the findings on SDP. It analyzes the overlap between SDP and other end-of-life practices relying on three variables: doses of potentially life-shortening intravenous drugs, the time for patients to die after limitation of therapy, and the intent of the doctors who prescribed the medications.

METHODS

Study Population. This report is a secondary analysis of a previous prospective study (4). All consecutive adult patients who died or had

any limitation of lifesaving interventions in the ICU from January 1, 1999, to June 30, 2000, were studied prospectively (4). Patients were followed until discharge from ICU, death, or 2 months from the decision to limit therapy (4).

Definitions of End-of-Life Categories. End-of-life categories were defined prospectively as CPR, brain death, withholding life-sustaining treatment, withdrawing life-sustaining treatment, and SDP as previously reported (4). SDP was defined in the questionnaire as a circumstance in which someone performed an act with the specific intent of shortening the dying process. These acts did not include withholding or withdrawing treatment, and examples included intentional overdose of narcotics, anesthetics, or potassium chloride (4). A hierarchy for categorizing patients used the more active mode of limitation if more than one was recorded. Patients were classified as "withhold" only if that was the sole limitation made; "withdraw" included patients for whom treatment was both withheld and withdrawn; and "SDP" included cases involving withholding or withdrawing and SDP decisions.

Ethical and Legal Considerations. No interventions or treatments were given, withheld, or withdrawn from patients as part of the initial observational study (4). Countries, centers, and study patients were coded anonymously to ensure confidentiality and to allow clinicians to report practices of questionable legality. Individual institutional ethics committee approval with a waiver of informed consent was required and obtained from each participating institution.

Study Centers and Data Collection. National representatives of the Ethics Section of the European Society of Intensive Care Medicine coordinated the study for each country's participating ICUs. The prospectively collected data used specifically for this secondary analysis included type of end-of-life category (SDP and other categories were self-identified by the responsible physician) and dates and times of 1) ICU admission; 2) death or discharge; and 3) decisions to limit therapy, medication, and doses used for SDP and the intent of the doctors prescribing the medication or extubation. Physicians retrospectively classified the acts used for SDP as definitely, probably, or probably not the cause of the patient's death.

Statistical Analyses. Relative potency scales for analgesics were expressed in parenteral morphine equivalents (10 mg of morphine sulfate = 0.15 mg of fentanyl citrate = 0.0075 mg of sufentanil citrate) and sedatives in parenteral diazepam equivalents (10 mg of diazepam = 5 mg of midazolam) (3, 15). Drug doses were bolus or cumulative doses given over time. Differences in the numbers of withdrawals of endotracheal tubes were tested with the Fisher's exact test, and times from withdrawal of endotracheal tubes until death were tested by the Mann-Whitney test. Descriptive statistics for time variables are presented as median and interquartile range (IQR). Those

variables are markedly skewed, and therefore differences were tested using the nonparametric Kruskal-Wallis rank test. The Cox proportional-hazards model was used to evaluate the association between drug doses and time from SDP to death. The hazard ratios are expressed for a 10-mg/hr increase of either morphine or diazepam. Differences were considered significant if $p < .05$.

RESULTS

During the initial study, 31,417 patients were admitted to ICUs in 37 centers located in 17 countries (4). Of the 31,417 patients, 4,248 who died or had limitations of life-sustaining treatments comprised the study population. Limitation of life-sustaining therapy occurred in 3,086 (72.6%) of 4,248 patients, 9.8% of all ICU admissions, and 76.0% of dying patients. The frequencies of the different end-of-life categories were as follows: 832 (19.6%) of the patients received CPR, 330 (7.8%) were diagnosed with brain death, 1,594 (37.5%) had therapies withheld, 1,398 (32.9%) had therapies withdrawn, and 94 (2.2%) underwent SDP.

All SDP patients already had previous therapies withheld or withdrawn. SDP was performed in nine of the 37 centers in seven of the 17 countries, which was a minority of centers. Of the SDP patients, types of medications were available for all patients, and doses used for SDP were available for 66 (70%) patients. Table 1 demonstrates the medications and doses used (if available), the time from SDP until death, and whether the doctor administering the medication believed it caused the patient's death. Treatment modalities used for the patients who underwent SDP included administration of opiates or benzodiazepines alone or in combination; four patients also received muscle relaxants and seven received barbiturates. Potassium chloride was not used in any of the SDP cases. The most commonly used opiate was morphine (administered to 71 patients alone or in combination), ranging from 5 to 200 mg. The most commonly used benzodiazepine was diazepam (administered to 54 patients alone or in combination), ranging from 20 to 200 mg. The median dosage for morphine was 25.0 mg/hr and for diazepam 20.8 mg/hr. Although mean doses of opiates and benzodiazepines used for SDP were higher than mean doses used with withdrawing in previous studies (2, 3), they were no higher in 20 of 66 patients and were within the ranges of doses used in all but one patient (Table

Table 1. Active shortening of the dying process (SDP): medications, doses in morphine and diazepam equivalents (mg/hr), time from SDP until death, and whether SDP caused death

| | Medication | Morphine, mg/hr | Valium, mg/hr | Time from SDP to Death, hrs | SDP Caused Death ^a |
|----|-----------------------------------|-----------------|---------------|-----------------------------|-------------------------------|
| 1 | Morphine, diazepam | | | 1.5 | 1 |
| 2 | Sufentanil | 33.4 | | 7.5 | 1 |
| 3 | Morphine, diazepam | | | 1.75 | 1 |
| 4 | Morphine | | | 3.9 | 1 |
| 5 | Morphine, diazepam | | | 6.0 | 1 |
| 6 | Morphine, diazepam, pancuronium | 11.7 | 5.9 | 8.5 | 1 |
| 7 | Morphine, diazepam | 38.5 | 15.4 | 1.3 | 1 |
| 8 | Morphine, diazepam | 10.5 | 21.1 | 4.75 | 1 |
| 9 | Sufentanil | 66.7 | | 1.5 | 1 |
| 10 | Morphine, diazepam | 33.3 | 33.3 | 3.0 | 1 |
| 11 | Morphine, diazepam | 7.1 | 35.7 | 7.0 | 1 |
| 12 | Morphine | | | 2.5 | 1 |
| 13 | Morphine, diazepam | | | 1.3 | 1 |
| 14 | Morphine, diazepam | | | 4.25 | 1 |
| 15 | Morphine, diazepam | 59.9 | | 1.67 | 1 |
| 16 | Morphine, diazepam | 44.4 | 44.4 | 2.25 | 1 |
| 17 | Sufentanil, midazolam | 66.9 | 20.4 | 2.75 | 1 |
| 18 | Morphine, diazepam | | | 1.5 | 1 |
| 19 | Morphine, diazepam | 66 | 40 | 0.5 | 1 |
| 20 | Morphine, diazepam | 14.3 | 14.3 | 3.5 | 1 |
| 21 | Sufentanil | 167.2 | | 1.5 | 1 |
| 22 | Morphine, diazepam | 10.5 | 42.1 | 4.75 | 1 |
| 23 | Sufentanil, midazolam | | | 2.9 | 1 |
| 24 | Sufentanil, midazolam | 33.4 | 13.3 | 3.0 | 1 |
| 25 | Morphine, diazepam | | | 0.4 | 1 |
| 26 | Sufentanil, diazepam | 66.7 | 16.7 | 3.0 | 1 |
| 27 | Sufentanil, diazepam | 42 | 15 | 2.0 | 1 |
| 28 | Morphine, diazepam, thiopental | 19 | 38.1 | 5.25 | 1 |
| 29 | Morphine, diazepam | | | 12.4 | 1 |
| 30 | Morphine, diazepam | 30 | 30 | 2.0 | 1 |
| 31 | Morphine, diazepam | 120 | 120 | 2.0 | 1 |
| 32 | Morphine, diazepam | | | 6.0 | 1 |
| 33 | Morphine, diazepam | 20.4 | 20.4 | 4.9 | 1 |
| 34 | Sufentanil, pentothal | 3.8 | | 1.75 | 1 |
| 35 | Morphine, diazepam | 200 | 200 | 0.5 | 1 |
| 36 | Sufentanil | 100.1 | | 3.0 | 1 |
| 37 | Morphine, diazepam, thiopental | 160 | 160 | 0.5 | 1 |
| 38 | Morphine, diazepam, cisatracurium | 25 | 25 | 4.0 | 1 |
| 39 | Morphine, diazepam, cisatracurium | 16.3 | 4.1 | 12.3 | 1 |
| 40 | Morphine, diazepam | | | 5.0 | 1 |
| 41 | Morphine, diazepam | 125 | 125 | 0.4 | 1 |
| 42 | Morphine, diazepam | | | 2.0 | 1 |
| 43 | Morphine, diazepam | | | 2.75 | 1 |
| 44 | Morphine | | | 0.5 | 1 |
| 45 | Morphine, propofol | | | 1.75 | 1 |
| 46 | Morphine, diazepam | 11.8 | 7.8 | 12.75 | 1 |
| 47 | Morphine | | | 1.0 | 1 |
| 48 | Morphine, diazepam | 25 | 30 | 2.0 | 1 |
| 49 | Morphine, thiopental | 800 | | 0.25 | 1 |
| 50 | Diazepam | | | 3.5 | 1 |
| 51 | Morphine, diazepam, thiopental | 100 | 200 | 0.1 | 1 |
| 52 | Morphine, diazepam | 90.9 | | 1.1 | 1 |
| 53 | Morphine, diazepam | 10 | 10 | 5.0 | 1 |
| 54 | Morphine | 74.6 | | 0.67 | 1 |
| 55 | Morphine, diazepam | 12.5 | 7.5 | 4.0 | 1 |
| 56 | Morphine | 100 | | 1.0 | 1 |
| 57 | Cisatracurium, morphine | | | 0.1 | 1 |
| 58 | Morphine, diazepam | 12.5 | | 4.0 | 1 |
| 59 | Morphine, diazepam | 25 | | 2.0 | 1 |

2). In retrospect, doctors considered that the doses of medications they gave for SDP definitely led to the patient's death in 72 patients (77%), probably led to the patient's death in 11 (12%), and were unlikely to have led to the patients death in 11 (12%) (Table 1).

Withdrawal of endotracheal tubes occurred in 17 of the 94 SDP patients (18.1%) and 125 (8.9%) of 1,398 patients who underwent withdrawal of treatment ($p = .01$). In the SDP patients, the median (IQR) time from the withdrawal of endotracheal tubes until death was 7.0 hrs (12.4 hrs) vs. 3.5 hrs (6.6 hrs) from the time of all other withdrawals of treatments until death ($p < .05$). There was no difference in the median time to death in the seven patients with prior limitations before withdrawal of endotracheal tube—42.0 hrs (63.6 hrs)—vs. the ten patients without prior limitations—50.0 hrs (129.3 hrs).

The median (IQR) time from the first decision to limit treatment until death was 14.7 hrs (51.0 hrs). The median (IQR) time from the decision for the most active form of limitation of therapy until death was 6.6 hrs (30.2 hrs) for all patients, 14.3 hrs (64.6 hrs) for withholding, 4.0 hrs (16.2 hrs) for withdrawing, and 3.5 hrs (7.0 hrs) for SDP ($p < .001$). Increasing doses of opiates and benzodiazepines were associated with a shorter time to death (hazard ratio for morphine, 1.10; 95% confidence interval, 1.04–1.16; hazard ratio for diazepam, 1.12; 95% confidence interval, 1.03–1.22) (Fig. 1).

DISCUSSION

Although end-of-life medical actions are commonly grouped into distinct categories, in actual practice they form a continuum—from aggressive resuscitation to active euthanasia—and the dividing lines between different actions are not always easy to define. A thorough and frank discussion of the differences, similarities, and overlaps between different end-of-life practices is vital to ensure optimal and responsible critical care.

An example of the complexity in defining different categories of ICU care is the relationship between withholding and withdrawing life-sustaining therapies. The conventional ethical view is that there is no moral distinction between the two (13), but this belief is not universal (16), and studies show that some health-care professionals are more reluctant to withdraw than withhold therapies (13,

Table 1. —Continued

| | Medication | Morphine, mg/hr | Valium, mg/hr | Time from SDP to Death, hrs | SDP Caused Death ^a |
|----|--------------------------------|-----------------|---------------|-----------------------------|-------------------------------|
| 60 | Morphine, diazepam, thiopental | 250 | 250 | 0.2 | 1 |
| 61 | Thiopental | | | 0.2 | 1 |
| 62 | Morphine, diazepam | | | 6.6 | 1 |
| 63 | Sufentanil | 66.7 | | 2.0 | 1 |
| 64 | Morphine, diazepam | 7.7 | 7.7 | 13.0 | 1 |
| 65 | Sufentanil, midazolam | 133.4 | 40 | 3.25 | 1 |
| 66 | Sufentanil, diazepam | 100.1 | 100 | 2.0 | 1 |
| 67 | Morphine, diazepam | 11.4 | 11.4 | 3.5 | 1 |
| 68 | Morphine, diazepam | 20 | 20 | 5.0 | 1 |
| 69 | Morphine, diazepam | 37.5 | 37.5 | 4.0 | 1 |
| 70 | Diazepam | | 44.4 | 2.25 | 1 |
| 71 | Morphine | 1.2 | | 25.0 | 1 |
| 72 | Morphine | 30 | | 1.5 | 1 |
| 73 | Sufentanil, diazepam | | | 8.0 | 2 |
| 74 | Morphine, diazepam | | | 3.1 | 2 |
| 75 | Morphine, diazepam | 3.4 | 3.4 | 11.75 | 2 |
| 76 | Morphine | 7.5 | | 10.0 | 2 |
| 77 | Benzodiazepine, opioids | | | 0.6 | 2 |
| 78 | Morphine, midazolam | 8 | 16 | 8.75 | 2 |
| 79 | Morphine, midazolam | 10 | 1.1 | 8.5 | 2 |
| 80 | Midazolam | 2.1 | 2.1 | 9.5 | 2 |
| 81 | Morphine | 3.1 | | 6.5 | 2 |
| 82 | Morphine | 8.5 | | 4.25 | 2 |
| 83 | Morphine | 1.2 | | 16.5 | 2 |
| 84 | Morphine | | | 2.6 | 3 |
| 85 | Sufentanil, midazolam | 41.7 | 10 | 1.25 | 3 |
| 86 | Sufentanil | 190.1 | | 4.75 | 3 |
| 87 | Sufentanil | 33.4 | | 1.0 | 3 |
| 88 | Morphine | 10 | | 6.2 | 3 |
| 89 | Fentanyl | 6.7 | | 8.75 | 3 |
| 90 | Morphine | 2.3 | | 22.0 | 3 |
| 91 | Morphine, diazepam | | | 92 | 3 |
| 92 | Fentanyl, propofol | | | 10.65 | 3 |
| 93 | Morphine | 12 | | 0.5 | 3 |
| 94 | Morphine | 0.1 | | 29.1 | 3 |

^aMedication definitely (1), probably (2), or probably not (3) caused the patient's death. The median times from SDP to death were 3.0 hrs (for definitely), 8.5 hrs (for probably), and 6.2 hrs (for probably not) ($p < .05$).

Table 2. Medications given during active shortening of the dying process in ETHICUS and during withholding and withdrawing in other studies

| | ETHICUS (n = 66) | Wilson et al. (3) (n = 33) | Keenan et al. (2) (n = 359) |
|---|---------------------|-------------------------------|--------------------------------|
| Opiate—morphine equivalent mg/hr | | | |
| Mean ± SD | 59.3 ± 108.3 | 11.2 ± 11.5 | 21.0 ± 33.0 |
| Median | 25 | — | 14.4 |
| Range | 0.1–800 | — | 0.7–350 |
| Benzodiazepine—diazepam equivalent, mg/hr | | | |
| Mean ± SD | 46.0 ± 60.8 | 9.8 ± 18.4 | 8.6 ± 11.0 |
| Median | 20.8 | — | 14.4 |
| Range | 1.1–250 | — | 0.7–350 |

17). In fact, different studies have defined not restarting an intravenous vasopressor infusion as either withholding (18) or withdrawing (4).

The blurred line between different categories is also exemplified by the confusion among physicians, which causes them to misclassify or misrepresent their

own actions: A U.S. survey suggested that the actual practice of euthanasia or physician-assisted suicide in the United States and other countries may be overstated by >20% (19). In the survey, many oncologists who initially reported that they had intentionally ended a patient's life revealed through in-depth interviews

that in fact they had performed withholding of life-sustaining treatment or provided potentially life-shortening narcotics for pain relief, which are neither euthanasia nor assisted suicide (19).

Only one previous study in neonatal ICUs specifically evaluated the controversial overlap between the use of potentially life-shortening drugs and mercy killing (20). Van der Heide et al. (20) found “a rather large overlap between decisions to administer drugs with and without the intention of hastening death, with respect to the type and dose of the drugs given, aspects of decision making, [and] prognostic factors.” They reported that potentially life-shortening drugs were given in 37% of 299 deaths; of these, the possibility that death would be hastened was taken into account in 52% of patients, hastening of death was partly intended in 22%, and hastening of death was explicitly intended in 26% (20). All respondents who explicitly intended to hasten death stated that they also acted to alleviate pain or other symptoms (19). Median doses of drugs and length of time by which life was shortened were higher when hastening death was explicitly intended (20). The authors stated that whether drugs were administered with or without the intention of hastening death was not always clear (20). Wilson et al. (3) showed that physicians ordered drugs to hasten death in 39% of cases but always with other reasons, such as relieving pain. A Dutch governmental multidisciplinary task force on end-of-life decisions also underlined that hastening death in patients may be difficult to distinguish from the palliative effects of drugs (21). The issue is further complicated by the fact that medications given concomitantly with withdrawal of therapy may instead of shortening the time to death actually sometimes delay an inevitable death (22, 23).

The purpose of this article is to shed light on one of the most controversial areas in end-of-life practices: the lack of clear or easily determined distinctions between SDP or euthanasia and therapies intended to relieve pain and suffering administered when withdrawing life-sustaining therapies. Differentiation between the two is complicated and may be impossible because the physicians' true intentions are often difficult to ascertain. In an emotionally charged, life-and-death setting, such as the ICU, these intentions are likely to be multilayered, complex, and ambiguous (12, 24, 25).

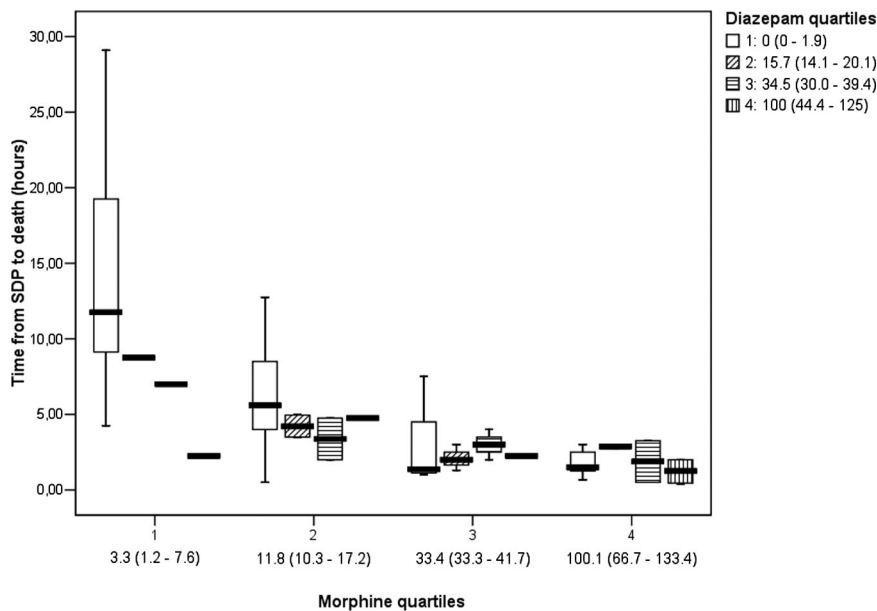


Figure 1. Time from shortening of dying process (SDP) to death according to the doses of the medication (morphine and diazepam equivalents, mg/hr) administered (quartiles). This analysis includes only observations where no drugs other than morphine or diazepam were used.

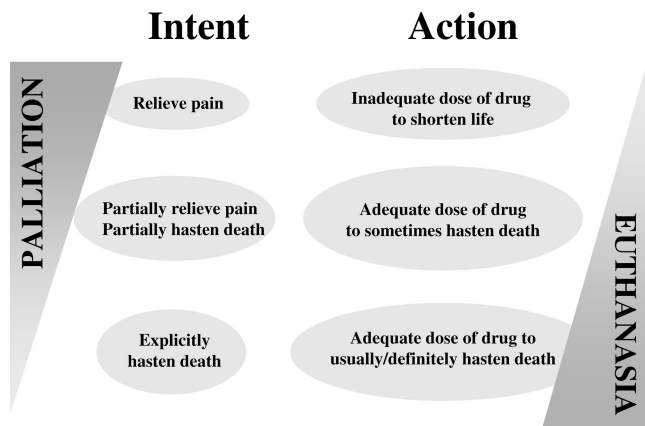


Figure 2. The spectrum of actions between palliative care and euthanasia.

Figure 2 demonstrates the spectrum of actions between palliative care and euthanasia. Palliative care is given to relieve pain and suffering with doses of drugs that are usually inadequate to shorten a patient's life but may at times hasten death without the intent to do so. Euthanasia or SDP occurs when a doctor administers drugs in doses adequate to shorten a patient's life with the explicit intent to hasten death. Differentiation may be difficult as intentions are subjective and private and only self-reporting or an analysis of extreme actions will be determinant (12). This study is one of the few that prospectively recorded the intensivists' intentions along with their practices. The most striking finding of the study was that although doses of opioids and benzodiazepines reportedly used to

shorten the dying process with the intention to cause death were higher than those used for symptom relief in earlier studies (2, 3), mean doses in close to one third of patients were similar and ranges for all patients were analogous to those in earlier studies. Surprisingly, the time to death for SDP patients was not different than that for patients in whom withdrawal was performed. This is probably related to the fact that doses of drugs used for SDP were not sufficient to cause an immediate death. Some physicians who performed SDP may have thought of their actions as "the double effect" and not as euthanasia despite the definition. An important finding of this study was that larger doses used for SDP did, however, correlate with a quicker death. Previous smaller studies have not shown a

correlation between higher doses of narcotics and/or benzodiazepines and shorter patient survival (22, 26). Although the practices of palliative care and SDP are very different, distinguishing the two may be extremely difficult.

The confusion in end-of-life decisions is also seen within the SDP patients. All doctors explicitly intended to hasten death in SDP patients. In a retrospective evaluation of these actions based on doses of medications given and the length of time until death, the actions were not so clear. Physicians believed that the doses they gave were definitely the cause of death in 77% of patients, probably the cause in 12%, and probably not the cause in 11%. It is recognized that absolute doses may not be indicative of euthanasia or SDP, because prior exposure, tolerance, and duration of medications are important. Inadequate doses of drugs might be related to a doctor's feelings of guilt or fear of prosecution and may explain the surprising finding that even when SDP was intended, patients took several hours to die, almost as long as cases of in therapy withdrawal. Another unexpected discovery was that extubated patients lived longer than nonextubated patients. These findings suggest that the gray area between relief measures and SDP extends in both directions: While in some cases physicians may be hastening the patient's death by providing what is classified as relief measures, in other cases physicians supposedly intending to cause death may in fact be providing drugs that are only capable of relieving pain and suffering. Therefore, the distinction between therapies intended to relieve pain and suffering and those intended to cause death may not be as clear as previously thought.

A major strength of the present study is that it provides empirical data for an ethical debate that often remains theoretical due to scarcity of facts. Other strong features include the prospective design, enrollment of a large number of consecutive patients from 37 ICUs in 17 countries, evaluation of all limitations and deaths in all admitted patients, and analysis of the intent and self-reporting of actions rather than theoretical responses to a questionnaire. Anonymity and contemporaneous documentation probably resulted in honest and more accurate reporting.

There are, however, limitations to the present study. Drug doses were not available for some of the SDP patients and for

patients who had therapies withheld or withdrawn. There may have been a selection bias in the doses that were reported. In addition, participants by their special interest in ethical issues may not necessarily share the attitudes of unselected ICU physicians. Severity scores of the patients were not analyzed, and underreporting of practices for fear of legal ramifications cannot be excluded.

The present report provides evidence that some physicians may be giving much larger doses of medications than needed for relief of pain or suffering so that the patient can die with dignity, but these physicians do not call this practice euthanasia. Yet in fact, physicians administering these perfectly legal relief treatments may in fact consciously or unconsciously be practicing a disguised form of mercy killing. It is unclear how many physicians or nurses around the world, in providing relief measures to terminal patients, also intend to shorten the dying process.

This complex empirical picture of actual ICU practice, rather than an idealized list of distinct, neatly separated actions, should form the basis for an open discussion of end-of-life practices. We need to arrive at a level of transparency at which proper safeguards for end-of-life medical care (18, 22) can be developed and maintained. Palliation with potentially life-shortening drugs may be given with no intent, partial intent, or explicit intent to hasten death. Markedly increasing doses of these drugs may be considered homicide by some and an appropriate form of terminal care by others. Physicians should administer drugs in sufficient amounts to relieve pain and suffering because the importance of palliative care cannot be overemphasized, but the drugs should not be intended to directly cause death (12). Physicians must recognize that appropriate palliative care may lead to a patient's death although unintended. One important safeguard should be proper documentation of the use of potentially life-shortening measures, including keeping records on the timing and doses of the drug and the physician's intention at each step.

Such documentation can help protect the physician wrongly accused of deliberately ending a patient's life. No less important, it may reduce the use of inappropriately large doses of medications to shorten the dying process given in the guise of relieving pain and suffering.

REFERENCES

- Prendergast TJ, Claessens MT, Luce JM: A national survey of end-of-life care for critically ill patients. *Am J Respir Crit Care Med* 1998; 158:1163-1167
- Keenan SP, Busche KD, Chen LM, et al: A retrospective review of a large cohort of patients undergoing the process of withholding or withdrawal of life support. *Crit Care Med* 1997; 25:1324-1331
- Wilson WC, Smedira NG, Fink C, et al: Ordering and administration of sedatives and analgesics during the withholding and withdrawal of life support from critically ill patients. *JAMA* 1992; 267:949-953
- Sprung CL, Cohen SL, Sjøkvist P, et al: End-of-life practices in European intensive care units. The Ethicus Study. *JAMA* 2003; 290: 790-797
- Prendergast TJ, Luce JM: Increasing incidence of withholding and withdrawal of life support from the critically ill. *Am J Respir Crit Care Med* 1997; 155:15-20
- Wilson D: A report of an investigation of end-of-life care practices in health care facilities and the influences on those practices. *J Palliat Care* 1997; 13:34-40
- Wilson D: Addressing myths about end-of-life care: Research into the use of acute care hospitals over the last five years of life. *J Palliat Care* 2002; 18:29-38
- Sprung CL, Eidelman LA, Pizov R: Changes in forgoing life-sustaining treatments in the United States: Concern for the future. *Mayo Clin Proc* 1996; 71:512-516
- Van der Maas BJ, Van der Wal, Haver Kate I, et al: Euthanasia, physician-assisted suicide and other medical practices involving end of life in the Netherlands, 1990-1995. *N Engl J Med* 1996; 335:1699-1705
- Delliens L, Mortier F, Bilsen J, et al: End-of-life decisions in medical practice in Flanders, Belgium: A nationwide survey. *Lancet* 2000; 356:1806-1811
- Burkhardt S, La Harpe R, Harding TW, et al: Euthanasia and assisted suicide: Comparison of legal aspects in Switzerland and other countries. *Med Sci Law* 2006; 46:287-294
- Truog RD, Cist AFM, Brackett SE, et al: Recommendations for end of life care in the intensive care unit: The Ethics Committee of the Society of Critical Care Medicine. *Crit Care Med* 2001; 29:2332-2348
- Vincent JL: Forgoing life support in western European intensive care units: The results of an ethical questionnaire. *Crit Care Med* 1999; 27:1626-1633
- Asch DA: The role of critical care nurses in euthanasia and assisted suicide. *N Engl J Med* 1996; 334:1374-1379
- Coda BA: Opioids. In: Clinical Anesthesia. Fifth Edition. Barash PG, Cullen BF, Stoelting RK (Eds). Philadelphia, Lippincott Williams & Wilkins, 2006, pp 353-383
- Steinberg A, Sprung CL: The dying patient: New Israeli legislation. *Intensive Care Med* 2006; 32:1234-1237
- The Society of Critical Care Medicine Ethics Committee. Attitudes of critical care medicine professionals concerning forgoing life-sustaining treatments. *Crit Care Med* 1992; 20:320-326
- Eidelman LA, Jakobson DJ, Pizov R, et al: Forgoing life-sustaining treatment in an Israeli ICU. *Intensive Care Med* 1998; 24: 162-166
- Emanuel EJ, Daniels ER, Fairclough D, et al: The practice of euthanasia and physician-assisted suicide in the United States. Adherence to proposed safeguards and effects on physicians. *JAMA* 1998; 280:507-513
- Van der Heide A, van der Maas P, van der Wal G, et al: Using potentially life-shortening drugs in neonates and infants. *Crit Care Med* 2000; 28:2595-2599
- Overleggoep Toetsing Zorgvuldig Medische Handelen Rond het Levenseinde bij Pasgeborenen: Toetsing als Spiegel van de Medische Praktijk. Ministerie van Volksgezondheid, Welzijn en Sport, 1997
- Chan JD, Treece PD, Engleberg RA, et al: Narcotic and benzodiazepine use after withdrawal of life support. *Chest* 2004; 126: 286-293
- Edwards MJ: Opioids and benzodiazepines appear paradoxically to delay inevitable death after ventilator withdrawal. *J Palliat Care* 2005; 21:299-302
- Quill TE: The ambiguity of clinical intentions. *N Engl J Med* 1993; 329:1039-1040
- Quill TE, Lo B, Brock DW: Palliative options of last resort. *JAMA* 1997; 278:2090-2104
- Campbell ML, Bizek KS, Thill M: Patient responses during rapid terminal weaning from mechanical ventilation: A prospective study. *Crit Care Med* 1999; 27:73-77