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End-of-Life Practices in European Intensive Care Units

The Ethicus Study

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Context While the adoption of practice guidelines is standardizing many aspects of patient care, ethical dilemmas are occurring because of forgoing life-sustaining therapies in intensive care and are dealt with in diverse ways between different countries and cultures.

Objectives To determine the frequency and types of actual end-of-life practices in European intensive care units (ICUs) and to analyze the similarities and differences.

Design and Setting A prospective, observational study of European ICUs.

Participants Consecutive patients who died or had any limitation of therapy.

Intervention Prospectively defined end-of-life practices in 37 ICUs in 17 European countries were studied from January 1, 1999, to June 30, 2000.

Main Outcome Measures Comparison and analysis of the frequencies and patterns of end-of-life care by geographic regions and different patients and professionals.

Results Of 31 417 patients admitted to ICUs, 4248 patients (13.5%) died or had a limitation of life-sustaining therapy. Of these, 3086 patients (72.6%) had limitations of treatments (10% of admissions). Substantial intercountry variability was found in the limitations and the manner of dying: unsuccessful cardiopulmonary resuscitation in 20% (range, 5%-48%), brain death in 8% (range, 0%-15%), withholding therapy in 38% (range, 16%-70%), withdrawing therapy in 33% (range, 5%-69%), and active shortening of the dying process in 2% (range, 0%-19%). Shortening of the dying process was reported in 7 countries. Doses of opioids and benzodiazepines reported for shortening of the dying process were in the same range as those used for symptom relief in previous studies. Limitation of therapy vs continuation of life-sustaining therapy was associated with patient age, acute and chronic diagnoses, number of days in ICU, region, and religion ($P<.001$).

Conclusion The limiting of life-sustaining treatment in European ICUs is common and variable. Limitations were associated with patient age, diagnoses, ICU stay, and geographic and religious factors. Although shortening of the dying process is rare, clarity between withdrawing therapies and shortening of the dying process and between therapies intended to relieve pain and suffering and those intended to shorten the dying process may be lacking.

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While the principle that dying patients should be treated with respect and compassion is broadly accepted among health care professionals, medical practices for end-of-life care differ around the world. In the United States, medicine has moved from a paternalistic model to one that promotes autonomy and self-determination.[1,2] Patient expectations and preferences now help shape end-of-life practices, limiting the use of technologies that may prolong dying rather than facilitate recovery.[1,2] In Europe, patient-physician relationships are still somewhat paternalistic.[3-5]

Different cultures and countries deal in diverse ways with the ethical dilemmas arising as a consequence of the wider availability of life-sustaining therapies.[3,4,6] Some have not adopted the Western emphasis on patient autonomy or methods of terminating life support.[3,4,6] In the past, patients died in intensive care units (ICUs) despite ongoing aggressive therapy.[7] Theoretical discussions[7] and attitudes of critical care

For editorial comment see p 820.

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professionals concerning these issues have been reported.[4,8,9] In North America, observational studies documenting physician behavior have noted changes in the modes of patient deaths[10-17] and an earlier abandonment of life-sustaining treatments.[10] Although European observational studies have demonstrated withholding or withdrawing of life-sustaining treatments in 6% to 13.5% of patients admitted to the ICU and in 35% to 93% of dying patients, the results have come from individual countries.[5,17-21] The overall incidence of end-of-life practices in European ICUs is not known. Furthermore, no studies have been conducted to date comparing different European countries or regions to verify whether reported variations from questionnaire respondents[4] are accurate.

End-of-life actions in ICUs include withholding or withdrawing life-sustaining therapies,[5,7-21] and in Europe, community studies have described active euthanasia in the Netherlands[22] and Belgium.[23] At the time this study was conducted, euthanasia was legally practiced in only 1 European country, but withdrawing life-sustaining therapies was common.[5,19,21] It is not known whether regional variations in attitudes toward use of euthanasia has any influence on local ICU practice.

The objectives of this large multicenter study were to observe and describe actual end-of-life practices in ICUs of several European countries, to determine their overall incidence, to document variations in the pattern of practice, and to analyze similarities and differences in terms of variables that might explain the findings.

METHODS

Study Population

All consecutive adult patients admitted to the ICU who died or had any limitation of life-saving interventions in the ICU from January 1, 1999, to June 30, 2000, were studied prospectively. Patients were followed until discharge from ICU, death, or 2 months from the decision to limit therapy.

Definitions of End-of-Life Categories

End-of-life categories were defined prospectively to enable the classification of each patient into 1 of 5 mutually exclusive categories: cardiopulmonary resuscitation (CPR); brain death; withholding life-sustaining treatment; withdrawing life-sustaining treatment; and active shortening of the dying process. *Withholding* treatment was defined as a decision that was made not to start or increase a life-sustaining intervention. Patients not undergoing CPR were classified as withholding therapy. *Withdrawing* treatment was defined as a decision that was made to actively stop a life-sustaining intervention presently being given. *Active shortening of the dying process* was defined 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 although withholding or withdrawing could occur prior to SDP. Examples included an intentional overdose of narcotics, anesthetics, or potassium chloride. *Cardiopulmonary resuscitation* was defined as a death despite use of ventilation and cardiac massage, that is, failed or unsuccesful CPR. *Brain death* was defined as a documented cessation of cerebral function and meeting the criteria for brain death.

The term "shortening of the dying process" was used instead of active euthanasia because Dutch investigators insisted that the term "active euthanasia" could not include most ICU patients who could not request the action. Several other terms were considered, but shortening of the dying process was accepted by all investigators as it describes the intent, the action that occurs, and is a more neutral term that physicians might more readily record. In addition, as some investigators might still be reluctant to admit to shortening of the dying process, another question was added to evaluate the highest possible incidence of actions that might be considered active euthanasia (although most of these actions were probably not active euthanasia). For each patient, physicians were asked whether any other action (not forgoing therapy) taken to relieve patient suffering may have contributed to the patient's death.

In each institution, the senior intensivist responsible for patient care and for end-of-life decisions determined the end-of-life practice and was responsible for filling out the study data form. A hierarchy for categorizing patients used the more active mode of limitation if more than 1 was recorded. Patients were classified as "withhold" only if that was the sole limitation made, as "withdraw" if treatment was both withheld and withdrawn, and as "shortening of the dying process" if withholding or withdrawing and shortening of the dying process decisions were involved. Patients who died without a treatment limitation either underwent CPR that was unsuccessful or were diagnosed with brain death. If a patient underwent successful CPR before withholding or withdrawing life-sustaining therapies, or was considered brain dead after withholding or withdrawing therapies, the patient was categorized as withholding or withdrawing according to the prioritization given above.

Ethical and Legal Considerations

No interventions or treatments were given, withheld, or withdrawn from patients as part of this observational study. Countries and centers were coded for the purpose of anonymity and study patients were numbered consecutively 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. Potential French centers could not participate as they could not obtain approval from their ethics committee.

Study Centers and Data Collection

National representatives of the Ethics Section of the European Society of Intensive Care Medicine were asked to coordinate the study for each country and

find several other ICUs in each respective country from a variety of institutions. Coordinators finalized definitions, data forms, and procedures (including a manual) for the study, and then met with principal investigators from each national center to explain the study, to describe inclusion and exclusion criteria, and to instruct on how to complete the forms. The forms were tested for reliability by giving them to investigators to complete for hypothetical test cases initially and again after 2 weeks. Agreement between the initial and repeat administrations was evaluated by κ coefficient of reliability, an interrater measure of agreement beyond chance. A value of 0.75 is considered excellent agreement, values between 0.40 and 0.75 are taken to represent fair or good agreement. Values of coefficients were above 0.6. Additional procedures to improve validity and consistency included actual test cases from centers before the study started, concurrent audit and feedback throughout the study, case audits, site visits, and an Internet site with frequently asked questions and meetings among investigators. Not all centers enrolled patients during the entire 18-month study.

The study data form included patient and institutional characteristics. Patient characteristics were sex, age, religious affiliation, ICU admission diagnosis, chronic disorders, type of end-of-life category, specific therapies limited, the method of shortening of the dying process (if relevant), whether interventions (other than forgoing life-sustaining treatments or shortening of the dying process) to relieve patient suffering may have contributed to patient mortality, and dates and times of (1) ICU admission, (2) death or discharge, and (3) decisions to limit therapy. Institutional data included country, hospital mortality rate, number of ICU admissions, practice (academic or nonacademic [private, public, or other]), and physician religious affiliation.

Statistical Analyses

Countries were divided into 3 geographic regions prior to data analysis: northern (Denmark, Finland, Ireland, the Netherlands, Sweden, and United Kingdom), central (Austria, Belgium, Czechia, Germany, and Switzerland), and southern (Greece, Israel, Italy, Portugal, Spain, and Turkey). The mean number of ICU admissions per month was used to categorize each institution by its turnover as small (≤30), intermediate (31-60), or large (≥61). The institutional variable practice was dichotomized into academic/nonacademic.

For each patient the main outcome variable was the end-of-life category. Univariate associations of end-of-life categories with the nonnumerical variables, sex, diagnosis, chronic disorder, region, practice, and religion were tested using the χ^2 test. When any cell had an expected frequency less than 5, an exact *P* value substituted the asymptotic one routinely calculated. Time lapse between 2 events (length of stay in the ICU, time from ICU admission until first limitation, time from the first decision to limit treatment until death, or time from the decision for the most active form of limitation of therapy until death) were shown to be in all cases very skewed and significantly deviated from normality by Lilliefors test. Descriptive statistics for those variables include medians and interquartile range (IQR), and differences among groups determined by region, practice, or religion were tested using the nonparametric Kruskal-Wallis rank test.

A multiple logistic regression was used to examine and test the associations of the odds for treatment limitations with the factors age, sex, diagnosis, chronic disorder, ICU length of stay, region, practice, and turnover. The outcome variable was the dichotomy "any limitation" (including withholding, withdrawing, or shortening of the dying process) vs "failed CPR." Collinearity of physician's religion and region prevented the inclusion of both variables in the model. The cumulative probability of death as a function of time from the most active limitation adjusted for age, sex, diagnosis, practice, turnover, and region was obtained using a Cox proportional hazards model.

Statistical analyses were performed using SPSS version 10 (SPSS Inc, Chicago, Ill) and StatXact version 4 (StatXact-Cytel Software Corp, Cambridge, Mass). A test was considered significant if $P<.05$. All *P* values reported are 2-sided. Funding sources had no involvement in the above methods.

RESULTS

During the study, 31 417 patients (range, 111-3118 patients per center) were admitted to ICUs in 37 centers located in 17 countries over 13.5 months (range, 1-18 months). Of the 31 417 patients, 4280 died or had life-sustaining treatments limited in some fashion. Of the 4280 patients, 32 were excluded, 27 were younger than 13 years old or were of unknown age, and 5 had no end-of-life information. Thus 4248 patients (13.5% of those admitted to ICUs) comprised the study population. Patient characteristics including age, sex, ICU admission diagnoses, religion, and mortality are shown in TABLE 1.

Limitation of life-sustaining therapy occurred in 3086 (72.6%) of 4248 patients, that is, 9.8% of ICU admissions and 76.0% of dying patients (3086/4058). The frequency of the different end-of-life categories together with the mortalities and range of percentages in the countries for the 4248 patients are shown in TABLE 2. Of the 3086 patients, 2734 (88.6%) received mechanical ventilation and at least 1815 (58.8%) were receiving vasopressor agents at the first limitation of therapy. Withholding preceded or accompanied withdrawal of therapy in 1335 of 1398 patients (95.4%) who underwent withdrawing treatment. All patients who underwent shortening of the dying process already had previous therapies withheld or withdrawn. Shortening of the dying process was used at 9 centers in 7 countries. A large proportion of the patients who underwent shortening of the dying process was reported in 1 center. Of the 94 patients who underwent shortening of the dying process, types of medications were available for all patients and doses used for shortening of the dying process were available for 50

patients. Treatment modalities used for the patients who underwent shortening of the dying process included administration of opiates or benzodiazepines alone or in combination, with 4 patients also receiving muscle relaxants and 6 receiving barbiturates. Potassium chloride was not used in any of the shortening of the dying process cases. The most commonly used opiate was morphine (administered to 73 patients alone or combination), ranging from 5 to 200 mg. The most commonly used benzodiazepine was diazepam (administered to 54 patients alone or combination), ranging from 20 to 200 mg. The most common combination was morphine and diazepam (administered to 43 patients). The median dosage for morphine was 13.4 mg/h and for diazepam was 13.8 mg/h. Doses of opiates and benzodiazepines were no higher than mean doses used with withdrawing treatment in previous studies[12,14] in 22 of the 50 patients and were within the ranges of doses used in all but 5 patients. In 8 of 94 patients, the drug doses given would unlikely lead to death. Withdrawal of endotracheal tubes occurred in 17 of 94 patients (18.1%) who underwent shortening of the dying process and 125 (8.9%) of 1398 patients who underwent withdrawal of treatment ($P=.01$). None of these withdrawals occurred in patients who received muscle relaxants. One hundred thirty-nine of 2992 patients (4.6%) who did not undergo shortening of the dying process had actions taken other than forgoing therapies, which were classified by investigators as given to relieve patient suffering but which may have contributed to patient mortality.

The median (IQR, 25th to 75th percentiles) length of stay in the ICU for all study patients was 4.0 (1.0-11.1) days, and the median (IQR) time from ICU admission until the first limitation was 2.8 (0.6-9.8) days. The median (IQR) time from the first decision to limit treatment until death was 14.7 (2.9-54.7) hours. The median (IQR) time from the decision for the most active form of limitation of therapy until death was 6.6 (1.5-31.7) hours for all patients, 14.3 (2.2-67.1) hours for withholding, 4.0 (1.0-17.2) hours for withdrawing, and 3.5 (1.5-8.5) hours for shortening of the dying process ($P<.001$) patients. The predicted probability of death over time for the different limitations, adjusted for age, sex, diagnosis, practice, turnover, and region is shown in the FIGURE. The respective probabilities of death within 24, 48, and 72 hours were 50%, 61%, and 68% for withholding, 80%, 89%, and 93% for withdrawing, and 93%, 97%, and 99% for shortening of the dying process.

The distribution of patients by region was 1505 (35.4%) in the northern, 1209 (28.5%) in the central, and 1534 (36.1%) in the southern region. The frequency of the end-of-life categories by region is shown in Table 2. In the southern European countries, CPR was used more (30.1%) and withdrawing (17.9%) and shortening of the dying process (0%) were used less frequently than those in the central (17.9%, 33.8%, 6.5%) or northern (10.2%, 47.4%, 0.9%) countries ($P<.001$). The median (25th-75th percentiles) length of stay in the ICU was 2.3 (0.8-7.2) days in the northern countries, significantly shorter than those in the central and southern countries (5.0 [1.6-13.1] days and 5.9 [1.6-13.9] days, respectively; $P<.001$). The median time (IQR) from ICU admission until the first limitation was 1.6 (0.4-5.2) days in the northern, 3.3 (0.7-11.7) days in the central, and 5.7 (1.5-13.8) days in the southern countries ($P<.001$).

Withdrawal of life-sustaining treatment occurred more often if the physician was Catholic (41.2%), had no religious affiliation (35.6%), or Protestant (44.4%) (based on completed questionnaires) than if they were Jewish (15.7%), Greek Orthodox (13%), or Moslem (23.7%) ($P<.001$) (TABLE 3). Use of CPR and withholding treatment showed

Table 1. Study Population (N = 4248)

Characteristics	
Age, mean (SD [range]), y	63 (17 [13-98])
Sex, No. (%)*	
Male	2587 (60.9)
Female	1658 (39.1)
Patients by country region, No. (%)	
Northern	1505 (35.4)
Central	1209 (28.5)
Southern	1534 (36.1)
ICU admission disorders, No. (%)	
Respiratory	937 (22.1)
Cardiovascular	730 (17.2)
Neurologic	656 (15.4)
Gastrointestinal	591 (13.9)
Surgery	426 (10.0)
Sepsis	403 (9.5)
Trauma	283 (6.7)
Metabolic	117 (2.8)
Hematologic	38 (0.9)
Multiple organ system failure	28 (0.7)
Other	14 (0.3)
Missing	25 (0.6)
Patient religion, No. (%)	
Catholic	1346 (31.7)
Protestant	861 (20.3)
Greek Orthodox	334 (7.9)
Jewish	243 (5.7)
Islam	117 (2.8)
None	118 (2.8)
Unknown	1159 (27.3)
Other	70 (1.6)
Outcome	
Lived	190 (4.5)
Died	4058 (95.5)

*Information for 3 patients is missing (N = 4245).

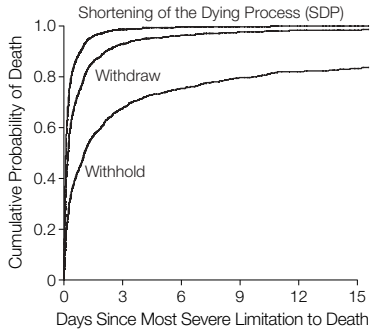
Table 2. Frequencies of Patient End-of-Life Categories by Region (N = 4248)*

	Patients, No (%)				
	Unsuccessful CPR	Brain Death	Withholding Life-Sustaining Treatment	Withdrawing Life-Sustaining Treatment	Active Shortening of the Dying Process
Region					
Northern (n = 1505)	154 (10.2)	48 (3.2)	575 (38.2)	714 (47.4)	14 (0.9)
Central (n = 1209)	217 (17.9)	92 (7.6)	412 (34.1)	409 (33.8)	79 (6.5)
Southern (n = 1534)	461 (30.1)	190 (12.4)	607 (39.6)	275 (17.9)	1 (0.1)
Total (N = 4248)	832 (19.6)	330 (7.8)	1594 (37.5)	1398 (32.9)	94 (2.2)
Range between countries, %	5-48	0-15	16-70	5-69	0-19
Hospital mortality, %	100	100	89	99	100

Abbreviation: CPR, cardiopulmonary resuscitation.
*$P<.001$, χ^2 test for the association between region and end-of-life practice. Brain death was excluded from the analysis.

differences based on physician's religion. Patient religious affiliations were Catholic (30%), Protestant (24%), Jewish (6%), Greek Orthodox (6%), none (3%), Moslem (2%), other (2%), and unknown (27%). Differences in CPR use, withholding, and withdrawing therapy based on patient religious affiliations were similar to those found for physicians (data not shown). Multivariate analyses revealed more withholding and withdrawing therapies than use of CPR as patient age and days in ICU increased, in northern countries, in ICUs with intermediate patient turnover, and in patient acute and chronic diagnoses (TABLE 4). Withholding treatment alone also was more common than CPR use in northern and central countries ($P<.001$).

Figure. Probability of Death Over Time for Withholding, Withdrawing, or Active Shortening of the Dying Process (SDP)



No. at Risk

SDP	94	2	0	0	0	0
Withdraw	1192	80	42	33	25	24
Withhold	1542	491	385	320	285	263

Adjusted RR (relative risk): 2.3 for withdraw (95% confidence interval [CI], 2.2-2.6), and 3.8 for shortening of the dying process (95% CI, 3.1-4.8). Risks are relative to withhold and adjusted for age, sex, diagnosis, practice, turnover, and region. The RR for shortening of the dying process relative to withdraw is 1.6 (95% CI, 1.3-2.0). Probabilities and adjusted RR obtained from a Cox proportional hazard regression model.

COMMENT

This is the first observational study to date to evaluate multiple countries for the various ICU end-of-life practices, to examine religion as a factor in end-of-life practices, to study time to death after different types of therapeutic limitations, and to speculate about a lack of clarity between therapies intended to relieve pain and suffering in patients and those intended to shorten the dying process or cause death.

The study demonstrates that end-of-life actions are routine in European ICUs. Life support was limited in 73% of study patients and 10% of ICU admissions. Both withholding and withdrawing of life support seem to be accepted by most European intensivists while shortening of the dying process, despite occurring in a few cases, remains rare. The study provides useful data for physicians and families for approximate times to death after various limitations. This information should help those involved with the dying patient prepare for the inevitable outcome.

The choice of limiting therapy rather than continuing life-sustaining therapy was related to patient age, acute and chronic diagnoses, number of days in ICU, frequency of patient turnover, region, and physician religion. Previous studies have shown greater limitations for elderly patients,[14,17,18,21] severity of illness scores,[5,17,21] length of ICU stay,[14,18,21] and certain diagnostic categories such as cirrhosis, severe cardiac and respiratory failure, organ system failure, cancer, and cardiac arrests.[5,18] The greatest frequency of limitations in the present study occurred for acute neurologic diseases and human immunodeficiency virus for chronic disorders. The northern region had more limitations, decreased CPR use, less time until a limitation of treatment was determined, and perhaps consequent shorter ICU stays. Regional differences may be related to religious differences that were closely intertwined.

Physician and patient religion showed significant differences in use of end-of-life therapies. These differences may be because of the varying religions and cultures of European countries. A large US study failed to show regional differences.[13] Religious affiliation was not evaluated,[13] but the greater differences in Europe may be related to more religious homogeneity within European countries than the United States. Responses to bioethical issues have been shown to vary throughout Europe.[24] In the only other large international multicenter study on ICU practices, differences in CPR directives were observed depending on country; religion was not evaluated.[17] Religious affiliations have been shown to influence physician attitudes toward withdrawal of life support in hypothetical situations.[4,22,25] Catholic physicians were less willing to withhold or withdraw therapy[4,22,25]; and in 1 study, Jewish physicians were more willing to limit therapy[8] and in another study less willing.[25] The present study demonstrated that physicians who were Protestant, Catholic, or with no religion more frequently used withdrawal of life-sustaining treatments than physicians who were Greek Orthodox, Jewish, or Moslem. A previous Israeli study with

Table 3. Distribution of End-of-Life Practices by Physician's Religion*

Physician's Religion	Total No. of Patients	No. (%)			
		Unsuccessful CPR	Withholding Life-Sustaining Treatment	Withdrawing Life-Sustaining Treatment	Active Shortening of the Dying Process
Catholic	1415	317 (22.4)	450 (31.8)	583 (41.2)	65 (4.6)
Protestant	854	84 (9.8)	380 (44.5)	379 (44.4)	11 (1.3)
Greek Orthodox	277	109 (39.4)	131 (47.3)	37 (13.4)	0
Jewish	369	60 (16.3)	251 (68.0)	58 (15.7)	0
Islam	38	14 (36.8)	15 (39.5)	9 (23.7)	0
None	878	209 (23.8)	338 (38.5)	313 (35.6)	18 (2.1)
Unknown/other	87	39 (44.8)	29 (33.3)	19 (21.8)	0
Total	**3918**	**832 (21.2)**	**1594 (40.6)**	**1398 (35.7)**	**94 (2.4)**

Abbreviation: CPR, cardiopulmonary resuscitation.
*$P<.001$, χ^2 test for the association between physician's religion and end-of-life practice. Brain death and religion unknown/other categories were excluded from the analysis.

only Jewish physicians demonstrated only withholding and no withdrawing of life-sustaining treatments.[20]

Several factors account for the great variability in the end-of-life categories between countries. First are the different religions and cultures noted herein. Second, physician values and practices seem to differ from country to country.[3,4,6] Major variations were noted for both continuation and limitation of life-sustaining treatment. The rate for CPR use was 48% and for withdrawing treatment 5%, which may indicate inordinate continuation of treatment, whereas rates for CPR use of 5% and for withdrawing of 69% may signify insufficient energetic care. Cook et al[17] have noted variability in medical centers within cities. Another possible explanation for the differences between countries and regions may relate to the difference in case mix. Finally, the variability may be related to the ongoing evolution of end-of-life practices[7,10] occurring at different rates and to different degrees among various countries.[13]

The conventional ethical view is that there is no moral distinction between withholding and withdrawing life-sustaining therapies.[26,27] This belief is not universal,[11] and some health care professionals are more reluctant to withdraw than withhold therapies.[4,8] This study indicates that both withdrawing and withholding of life support have widespread acceptance in Europe. The present study, however, demonstrates clinical differences between withholding and withdrawing treatments: withdrawal of therapy was associated with earlier and more frequent mortality. Previous studies in which questionnaires were used or which had smaller numbers of patients led to similar conclusions.[5,28] Another possible explanation for this finding is that withdrawal of therapy occurred in more unstable patients.

At the time of this study, euthanasia was illegal in all European countries, although legally pardoned in the Netherlands. A previous study also noted euthanasia in Belgium,[23] but evidence of euthanasia in ICU practice was not available. This study confirms that active shortening of the dying process, although reported in the ICUs of 7 countries, remains rare. One possible reason for the infrequent use of active shortening of the dying process in ICUs may be the dependency of ICU patients on life support. Withdrawing or withholding life-support often leads to death thus minimizing any perceived need for shortening of the dy-

Table 4. Logistic Regression of Any Limitation of Therapy (Witholding Life-Sustaining Treatment, Withdrawing Life-Sustaining Treatment, or Actively Shortening the Dying Process) vs Unsuccessful Cardiopulmonary Resuscitation on Patient Variables (Age, Sex, and Acute Diagnosis, Chronic Disorder, and Days in ICU) and ICU Characteristics (Turnover, Practice, and Region)*

	Patients, No. (%)†	OR (95% CI)‡	*P* Value
Age	3857 (100)	1.02 (1.01-1.02)	<.001
Days in ICU	3857 (100)	1.03 (1.02-1.04)	<.001
Sex			
Male	2338 (60.6)	1	
Female	1519 (39.4)	1.11 (0.93-1.33)	.24
Region			
Southern	1314 (34.1)	1	
Central	1112 (28.8)	3.84 (2.91-5.07)	<.001
Northern	1431 (37.1)	7.39 (5.77-9.47)	<.001
Turnover			
Large	1798 (46.6)	1	
Intermediate	1517 (39.3)	2.03 (1.57-2.63)	<.001
Small	542 (14.1)	1.07 (0.81-1.41)	.63
Practice			
Nonacademic	605 (15.7)	1	
Academic	3252 (84.3)	1.25 (0.97-1.62)	.09
Acute diagnosis			
Surgery	413 (10.7)	1	
Neurologic	467 (12.1)	7.18 (4.81-10.73)	<.001
Respiratory	912 (23.6)	2.22 (1.62-3.03)	<.001
Cardiovascular	706 (18.3)	1.47 (1.09-1.97)	.01
Gastrointestinal	583 (15.1)	2.33 (1.68-3.24)	<.001
Metabolic	111 (2.9)	1.98 (1.09-3.59)	.02
Trauma	193 (5.0)	1.92 (1.26-2.93)	.002
Sepsis	396 (10.3)	2.85 (1.97-4.14)	<.001
Other	76 (2.0)	1.74 (0.96-3.17)	.07
Chronic disorder			
None	686 (17.8)	1	
Cancer	504 (13.1)	2.66 (1.90-3.73)	<.001
AIDS/HIV	36 (0.9)	10.66 (3.55-32.01)	<.001
CVA	139 (3.6)	1.64 (0.99-2.72)	.55
Hepatic failure	53 (1.4)	3.94 (1.49-10.43)	.006
Congestive heart failure	266 (6.9)	1.49 (1.02-2.18)	.04
COPD	424 (11.0)	1.91 (1.37-2.68)	<.001
Cardiovascular	849 (22.0)	1.52 (1.15-1.99)	.003
Neurologic, cognitive, muscular	155 (4.0)	1.82 (1.11-3.00)	.02
Pulmonary	121 (3.1)	3.20 (1.77-5.81)	<.001
Kidney, urinary system	78 (2.0)	1.29 (0.72-2.31)	.39
Digestive system	148 (3.8)	3.42 (2.02-5.77)	<.001
Immunologic system	38 (1.0)	1.04 (0.49-2.21)	.91
Miscellaneous	360 (9.3)	1.57 (1.12-2.19)	.01

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; HIV, human immunodeficiency virus; ICU, intensive care unit; OR, odds ratio.
*Patients were excluded if they did not have information for all variables or were considered brain dead.
†Percentages may not add up to 100% due to rounding.
‡For the continuous variables, the OR equals the relative change in the OR when the variable is increased by 1 unit.

ing process. The fact that all shortening of the dying process therapies were preceded by withholding or withdrawing and that the time course until death was similar for shortening of the dying process and withdrawing might mean that a process of withdrawal is observed for a while and then actions are taken to shorten the life of the patient. If physicians were shortening the dying process from the outset, a quicker death may have been observed.

Whether or not shortening of the dying process is considered euthanasia is controversial. Active euthanasia includes the intent to cause death plus the action that causes death. The purpose of shortening of the dying process was to specify an action that directly caused the intentional death of the patient. Discussions with investigators reporting shortening of the dying process decisions confirmed that hastening death was the intention in all shortening of the dying process cases. A small number of physicians have used shortening of the dying process for intent, but without actions causing death most likely because the definition for shortening of the dying process emphasized the intent to shorten the dying process without specifying (except for examples) specific actions required to cause death. The majority of cases of shortening of the dying process can be equated with euthanasia as physicians showed intent and actions that caused death.

The distinction between therapies intended to relieve pain and suffering and those intended to shorten the dying process or hasten death may not be so clear or easily determined. Differentiation may be difficult as intentions are subjective and private and only self-reporting or an analysis of extreme actions will be determinant.[29] In fact, most end-of-life decisions have multilayered intentions that are complex, ambiguous, and often contradictory.[30] It is unclear how many physicians around the world who withdraw treatments and give therapies to relieve pain or suffering also intend to shorten the dying process. Some physicians give much larger doses of medications than are required for relief of pain or suffering so that the patient can die with dignity, but do not call this euthanasia. The present findings that doses of opioids and benzodiazepines reported for shortening of the dying process treatment with the intent to cause death were in the same range as those used for symptom relief in earlier studies[12,14] and leading to death within similar times as in patients undergoing withdrawing treatment, leads to the speculation that the distinction between treatments to cause death and to relieve suffering in dying patients may be unclear. It is recognized that absolute doses may not be indicative of euthanasia as prior exposure, tolerance, and duration of medications are important. That the distinction is not sharp is further supported by the fact that 5% of the patients (not receiving shortening of the dying process treatment) received therapies that may have contributed to mortality, raising the possibility that the adjunct drugs contributed to death in some non–shortening of the dying process cases too.

Strengths of the present study include the prospective design and enrollment of a large number of consecutive patients from 37 ICUs in 17 countries, evaluation of all limitations and deaths in all admitted patients, analysis of the apparent reasons for the findings, and direct reporting of actions rather than theoretical responses to a questionnaire. Anonymity and contemporaneous documentation probably resulted in honest and more accurate reporting. However, the present study has limitations. The patients studied may not be representative of the ICU population of each European country. Since only 1 to 4 centers participated from each country, it was recognized a priori that the participating ICUs did not necessarily represent the practices of all ICUs in that country. Therefore, regions were evaluated. 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. Underreporting of practices for fear of legal ramifications cannot be excluded. The findings of the present study do reflect what physicians from different countries say they do.[4]

Despite the importance of end-of-life physician practices, many related questions remain unanswered. For instance, what are the perspectives of physicians, nurses, patients, and families regarding the ICU and potential dying experiences in different countries with different cultures? The present group has started such a study. Only with knowledge of actual physician behavior, such as that observed in this study, can future studies hope to ask the appropriate questions and then can proper public debate occur.

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