Original Article

An Observational Study on a Protocol for Withdrawal of Life-Sustaining Measures on Two Non-Academic Intensive Care Units in The Netherlands: Few Signs of Distress, No Suffering?

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Abstract

Context. Because anticipation of death is common within the intensive care unit, attention must be paid to the prevention of distressing signs and symptoms, enabling the patient to die peacefully. In the relevant studies on this subject, there has been a lack of focus on measuring determinants of comfort in this population.

Objectives. To evaluate whether dying without distressing signs after the withdrawal of life-sustaining measures is possible using a newly introduced protocol and to analyze the potential influence of opioids and sedatives on time till death.

Methods. This was a prospective observational study, in two nonacademic Dutch intensive care units after the introduction of a national protocol for end-of-life care. The study lasted two years and included adult patients in whom mechanical ventilation and/or vasoactive medication was withdrawn. Exclusion criteria included all other causes of death.

Results. During the study period, 450 patients died; of these, 305 patients were eligible, and 241 were included. Ninety percent of patients were well sedated before and after withdrawal. Severe terminal restlessness, death rattle, or stridor was seen in less than 6%. Dosages of opioids and sedatives increased significantly after withdrawal, but did not contribute to a shorter time till death according the regression analysis.

Conclusion. The end-of-life protocol seems effective in realizing adequate patient comfort. Most patients in whom life-sustaining measures are withdrawn are well sedated and show few signs of distress. Dosages of opioids and sedatives increase significantly during treatment withdrawal but do not contribute to time until death. Dying with a minimum of distressing signs is thus practically possible and ethically feasible. J Pain Symptom Manage 2015;50:676–684.

Key Words
Signs of discomfort, intensive care, withdrawal of life-sustaining measures, time till death, opioids and sedatives, peak pressure

Introduction

The most used life-sustaining measures on the intensive care unit (ICU) are mechanical ventilation and vasoactive medications. As these measures are life-saving for many patients, over the last decade, a worrying trend has been noticed. Advanced life-sustaining measures are used in patients with poor long-term expectations secondary to more chronic organ dysfunction, comorbidity, and poor quality of life.[1] This can lead to the conclusion that the use of ICU measures in certain cases is disproportional. Withholding and/or withdrawing these life-sustaining measures (WOLSM) have become common decisions that precede death in ICUs worldwide. There are, however, striking differences regarding the frequency and practice of WOLSM among ICUs in Europe, North America and, for example, China.[2–5] Rates of WOLSM sometimes vary within the same country and may depend

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Accepted for publication: June 11, 2015.

0885-3924/$ - see front matter
http://dx.doi.org/10.1016/j.jpainsymman.2015.05.017

on the initial diagnosis;[6,7] rates range from 1.7% up to 85%.[5–8] The place where patients in terminal stages of illness die varies. For example, 20% of deaths in North America follow ICU admission, whereas, in The Netherlands, only 11% of deaths occur after admission to the ICU.[9–12]

Anticipated dying is common on the ICU, and much attention should be dedicated to the prevention and treatment of distressing symptoms and signs, as pain, anxiety, agitation, restlessness, and dyspnea to enable the patient to die peacefully.[13–16] Unfortunately, in some relevant studies on this subject, the level of (dis) comfort of the patients or the evaluation or prevention of distressing signs and symptoms are not clearly evaluated.[8,17–22] Several countries have published studies on their country-specific ICU populations and whether and how and when WOLSM is done.[8,18,19,21–25] The only available article from The Netherlands describes a single academic center retrospective study.[17]

In 2006, a concept guideline specifically designed for WOLSM, including advice on the prevention of distressing signs and symptoms on the ICU, was published.[26,27] This guideline was adopted as the national end-of-life protocol by the Dutch Intensive Care Society in 2008. Walling et al.[28] showed in that same year that a protocol for end-of-life care symptom management is indeed feasible and useful.

We studied end-of-life practices on two Dutch ICUs in the two years after the introduction of the national protocol, with a focus on distressing signs and symptoms and the use of opioids and sedatives after WOLSM. Opioids and sedatives are the medications of choice in treating pain and various forms of distress in end-of-life care. However, the assumption that the use of these medications might hasten death has made many doctors reluctant to use or increase dosages of these drugs. We wanted to analyze if the contribution of opioids and sedatives up to the time till death is relevant in the case of severely ill ICU patients. As far as we know, this is the first study that actually describes and quantifies the level of signs of discomfort in an ICU population after WOLSM.

Methods

Study Design

We conducted a two year prospective study from late 2008 until the middle of 2011. The study included all patients from two nonacademic Dutch ICUs in whom mechanical ventilation (MV) and/or vasoactive medication (VAM) was to be withdrawn.

Study ICUs

Two ICUs participated in this study. ICU-1 (14 beds) is one of the three largest level III nonacademic ICUs with both cardiopulmonary and traumatology facilities in The Netherlands. ICU-2 is a level I ICU that has six ICU beds and is part of a Protestant Christian teaching hospital. Both hospitals are situated in the populated western region of The Netherlands. These ICUs were selected because of their location, specific characteristics (as described previously), and the presence of a team of dedicated ICU research nurses. The study itself was designed to be fully nurse-driven to prevent physician bias in the timing of WOLSM and the administration or registration of drugs.

Inclusion and Exclusion Criteria

This study included only adult (18 years or older) patients in whom MV and/or VAM was scheduled to be withdrawn. Excluded from the study were brain-dead patients, patients who died spontaneously, and patients who died after euthanasia. Euthanasia, that is, death on clear request of the patient by medication that is intended to terminate the life instantaneously (Dutch law definition of euthanasia), although allowed by legal provision, is extremely rare in the ICU setting, even in The Netherlands, and, therefore, is not further discussed in this study.[29]

Data Collection

At the time when the definitive decision was made to change the focus of treatment from curative to palliative end-of-life care, which included the withdrawal of MV and/or VAM, the research nurses initiated the process of inclusion and data registration, without informing the physician involved. Information about the quality of decision-making and the motivation for the withdrawal decisions were extracted from the patient files, if documented, or else noted as observed by the nurses.

T0 was defined as the moment just before the actual withdrawal of life support. After T0, the patient's sedation level, signs of discomfort, and medication dosages were scored every 15 minutes. General patient data, as well as data on disease diagnosis, disease severity scores, and medication use, also were collected. For the analyses, the different opioids were all recalculated to morphine equivalents, as 10 μg fentanyl and 1 μg sufentanil are both equivalent to 1 mg morphine. Dosages of propofol and the VAMs are all expressed per kilogram of body weight. In total, 14 different disease categories were defined. Both the Richmond Agitation Sedation Scale and Ramsey Scale were used to measure sedation levels. Signs of discomfort, including death rattle, stridor, and terminal restlessness, were scored using a five-point scoring system (Table 1). Data for sequential organ failure assessment (SOFA) score calculations were collected retrospectively when necessary.

The potential predictors of the time until death after WOLSM were identified by a multidisciplinary intensive

Table 1
Discomfort Scoring Scales

Movement	1 No movements
	2 Occasional light movements of limbs
	3 Frequent movements of limbs (>10 times/minute)
	4 Frequent and strong movements of limbs (level of risk of dislocation of iv lines)
	5 Frequent and strong movements of head and limbs (the patients "crawls" in bed)
Stridor[a]	1 No stridor
	2 Soft stridor (audible next to the head-end of the bed)
	3 Clear stridor (audible from before the bed-end)
	4 Heavy stridor (already audible outside the room)
	5 Extreme stridor, that is, accompanied with intercostal indrawings
Death rattle[b]	1 No rattle audible
	2 Soft rattle (only audible just next to the head of the patient)
	3 Mild rattle (audible at the bedside of the patient)
	4 Clear rattle (audible from before the bed end)
	5 Loud rattle (already audible outside the box)

[a]The abnormal, high-pitched sound produced by turbulent airflow through a partially obstructed airway at the level of the supraglottis, glottis, subglottis, and/or trachea.
[b]The gurgling sound that originates from expirated air passing through a fluid collection (i.e., not swallowed saliva) in the oropharynx or retropharynx.

care research group before the study began and comprised the following: age, gender, body weight, SOFA score on Day 1, SOFA score on the day of withdrawal, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, dosages of (nor) epinephrine, positive end-expiratory pressure level, peak pressure, inspired oxygen fraction, length of stay, and change in dosages of opioids and sedatives.

Ethical Approval

In The Netherlands, by law, purely observational studies with no intervention(s) are, without exception, exempt from institutional review board approval. The study described in this report was strictly observational, and patients were treated with the standard of care. Therefore, a request for approval for this study by the ethics committee was waived.

Moreover under Dutch law, data of deceased patients may be used for publications and scientific research without specific consent if the data are fully redacted.[30] Because all the patients in our study died, all data were freely available from the hospital records without the specific permission of the patients or proxies.

Statistical Analysis

Patient data that were generated from consecutive observations, such as SOFA scores, were compared using paired *t*-tests. Potential predictors of time until death after WOLSM were evaluated using standard linear regression models instead of Cox regression as all patients died. So, the only between-patient variation in outcome is the time to the event (death) and not the event itself. Statistical analyses were performed, and graphs were created using IBM SPSS Statistics, version 22.0, for Mac (IBM Corp., Armonk, NY) and Prism 5 for Mac OS X (GraphPad Software Inc., San Diego, CA).

Results

General Characteristics of the Study Population

During the study period, 430 patients died. All ICU deaths in the study period were extracted from the general hospital administration and compared with the ICU study population deaths. Because 24 hours a day/seven days a week coverage for eligibility screening by the research nurses could not be offered during the study period, 125 patients were not screened. No patients were missed during the presence of the research nurses. In the eligible group, 79% of the patients died in the ICU after the withdrawal of MV and/or VAM. Eventually, 241 patients were included, as shown in Fig. 1. The general characteristics of these 241 patients are described in Table 2.

There were no statistical differences between the general patient characteristics of the first and the second study year. The mean age of the noneligible patients was 68.1 years and was not significantly different from that of the patients who were included in the study ($P = 0.16$). The mean APACHE II score in the unscreened patient group was 27.3 ($P = 0.02$).

Diagnostic Categories

The distribution of the different admission categories is shown in Table 2.

Decision-Making, Responsibility, and Motivation

The most common reasons that were mentioned as motivation for WOLSM were futility and/or the disproportionate use of ICU resources. In 56% of the cases, the decision was made after a multidisciplinary consultation. In 20% of the cases, the decision was made by the medical ICU team but without a multidisciplinary consultation. In 13% of the cases, a single physician was responsible for the decision; however, 90% of these individual decisions were made during weekends, evenings, or night shifts. Fully shared decision-making was mentioned in 9% of cases. WOLSM occurred twice by request of the patient, and in two cases, family demand was the primary motivation.

Vasoactive Medication, Opioids, Sedatives, and Muscle Relaxants

The dosage characteristics of the intravenous medications that were used during the study period are described in Table 3. The overall dosages of propofol,

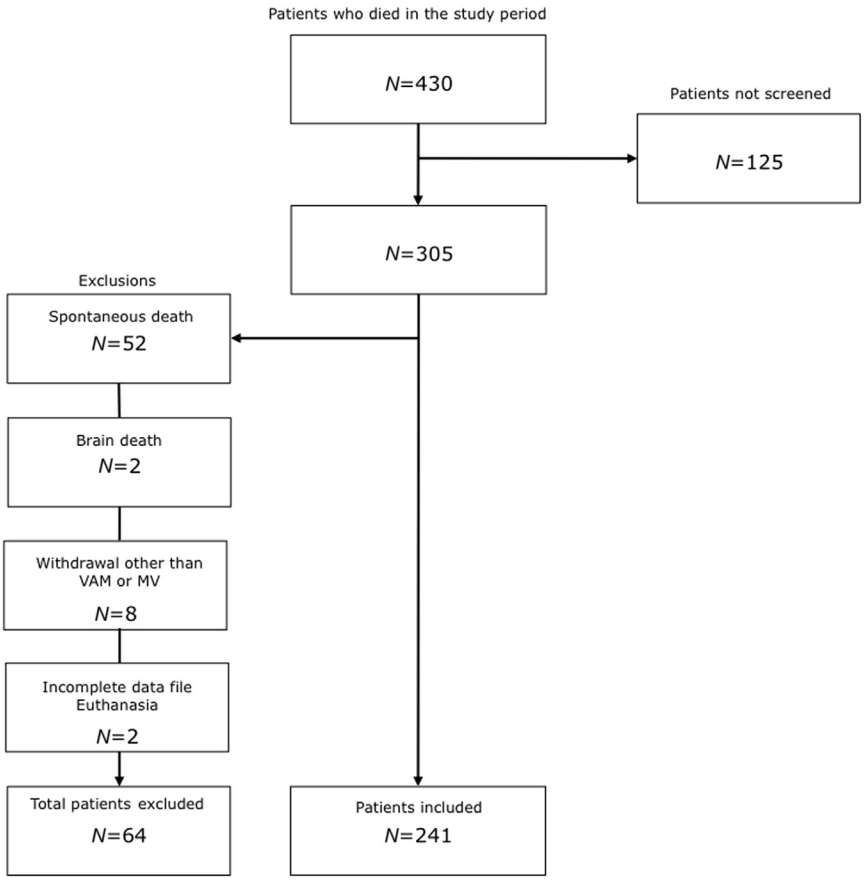

Fig. 1. Flow diagram of the patients in the study.

midazolam, and morphine equivalents increased significantly from T0 to T-final. In ICU-2, the rise in opioid dosages after withdrawal was not statistically significant. Muscle relaxants were used in only one patient with therapy-resistant myoclonus; ventilation, however, was continued until circulatory arrest.

Withdrawal Rates and Discomfort and Sedation Scales

The incidences of WOLSM-related signs of discomfort and the sedation scales are described in Table 4. During the second year of the study, there were significantly more extubations. Overall, the incidence in the first year was 47% compared with 74% in the second year ($P < 0.001$); however, incidence and severity of stridor and death rattle remained the same.

Eight patients received butylscopolamine and/or diuretics for the prevention of death rattle. One patient received steroids in anticipation of stridor. None of these patients eventually scored Grade 4 or 5 (severe) on the discomfort scale.

At T0, 15 patients had a Richmond Agitation Sedation Scale score between −1 and 2 and a Ramsey score between 1 and 4. A change in sedation scores after withdrawal was observed in 47 patients, but these changes were observed mainly in lightly sedated patients because of the initiation of or increase in sedatives and/or opioids in this group.

Time Until Death

The median time from withdrawal until death was 20 minutes (Table 4). None of the 241 patients survived after WOLSM. Within 90 minutes of WOLSM, 80% of the patients had expired.

Regression analysis of the potential predictors of the time until death in our model ($R^2 = 0.236$ and $F = 3769$, $P < 0.0001$) showed that ventilation peak pressure was the only significant predictor of a shorter time until death (beta $= -0.205$, $P = 0.032$). The only significant predictor of a longer time till death was the change in opioid equivalents (beta 0.326, $P = 0.003$).

The complete overview of the regression analysis coefficients is shown in Table 5.

Discussion

Characterization of factors that predict time to death after WOLSM may help physicians inform

Table 2
The General Characteristics of the Study Population and the Reasons for Admission

Characteristics	Result/Number	Percentage
Age (mean in yrs ± SD)	70.51 ± 0.855, $n = 241$	
Male	142	58.9
Female	99	41.1
Length of stay (mean in days ± SD)	6.95 ± 0.548	
APACHE II score (mean)	30.5 ± 9.6, $n = 215$	89
SOFA score Day 1 (mean ± SD)	10.24 ± 3.5, $n = 241$	100
SOFA score Day 2 (mean ± SD)	10.47 ± 3.49, $n = 169$	70
SOFA score at day of withdrawal (mean ± SD)	12.26 ± 3.5[a], $n = 241$	100
Weight (mean in kg ± SD)	77.33 ± 1.045, $n = 237$	98
Peak pressure of ventilation (mean in mm Hg ± SD)	27.15 ± 0.633, $n = 212$	88
Reason for admission	$n = 241$	100
Sepsis	71	29
Out-of-hospital cardiac arrest	50	21
Primary cardiac disease	27	11
Respiratory	21	9
Postcardiac surgery	20	8
Neurological or neurosurgical	15	6
Bleed (non-GI)	7	3
Hematologic disease	7	3
Other	23	10

APACHE II = Acute Physiology and Chronic Health Evaluation II; SOFA = sequential organ failure assessment; GI = gastrointestinal.
[a]$P < 0.0001$ compared with the SOFA score on Day 1.

relatives of the dying patient and alleviate some of the anxiety resulting from uncertainty regarding the time course to death.[31] Until now, six studies have addressed the subject of time till death after WOLSM for severely ill ICU patients.[12,32–36] However, although each study in itself is interesting and illustrative for the local habits and practice of WOLSM, they all have unfortunately one or more major shortcomings; for example, small sample size,[33] not including sedatives or opioids in the analysis,[34–36] the use of retrospective data,[12] or being a single center study.[32,34,36] Several other studies have described the practice of WOLSM and the dosages of opioids and sedatives used but failed to report whether the patients were comfortable or well sedated or not. The absence of such essential information makes it impossible to compare results regarding how well end-of-life care was provided.

Sedation Levels and Signs of Discomfort

Pain, anxiety, and dyspnea are probably the most important signs and symptoms to prevent when life-sustaining measures are withdrawn; it is, however, very difficult to asses these "symptoms" in a population that is already deeply sedated and treated with opioids even before WOLSM. This is logical because most patients are severely ill and mechanically ventilated and, therefore, would be in pain and distress if no medication was given.[37] Therefore, we focused on terminal restlessness as a representative sign for pain and dyspnea as well as anxiety. Death rattle and stridor might be distressing for the patient, but most of the time it is a stress factor for the family and, therefore, should be anticipated.[16]

Most patients were already well sedated even before WOLSM; only a few patients showed more signs of awareness after WOLSM than before. Most patients who had a change in sedation level changed from a shallow level of sedation to a deeper level. This is in concordance with the marked increase of opioid and sedative dosages in the same period.

The most frequently scored combination of moderate and severe signs of discomfort was death rattle, with an incidence of 17%. This is not surprising

Table 3
Intravenous Perfusorpump Medications Used in the Study

	Number	Percentage	Mean ± SD	Median	IQR
Dobutamin, maximum dosage[b]	94	39	4.6 ± 3.188	4.0	2.0–6.0
Norepinephrine, maximum dosage[b]	170	71	0.62 ± 0.6	0.4	0.15–0.96
Adrenaline, maximum dosage[b]	20	8	1.11 ± 1.2	0.7	0.2–1.8
Opioids					
Start dosage T0	185	77	11.7 ± 8.38	10	5–15
Maximum dosage[c]	213	88	14.04 ± 8.34[a]	12	6–18
Midazolam					
Start dosage T0	111	46	12.2 ± 7.5	10	5–17
Maximum dosage[d]	129	54	13.8 ± 9.8[a]	10	8–20
Propofol					
Start dosage	78	32	186.8 ± 96.91	200	100–250
Maximum dosage[d]	83	34	213.7 ± 113.2[a]	200	150–300
Propofol, maximum dosage[e]	83	34	2.98 ± 1.57	2.6	1.76–3.6

IQR = interquartile range.
[a]Significant change $P < 0.002$.
[b]Microgram per kilogram per minute.
[c]Morphine equivalents in milligram per hour.
[d]Milligram per hour.
[e]Milligram per kilogram per hour.

Table 4
Withdrawal Rates, Sedation Levels, Discomfort Scales, and Time till Death

Withdrawal Rates	Number	Percentage
Mechanical ventilation present (MV)	231	95
Withdrawal of MV	216	93
Detubation after withdrawal of MV	141	65
Tracheostomy	9	4
Vasoactive medication present (VAM)	196	81
No VAM	45	19
VAM withdrawn	180	92
MV and VAM withdrawn together	157	65
VAM not withdrawn	16	8
Sedation levels		
Rass T0 −5/−4	188/19	78/8
Ramsey T0 6/5	185/34	77/14
Discomfort symptom scales		
Terminal restlessness		
Severe (Grade 4/5)	11	5
Moderate (Grade 3)	7	3
Death rattle		
Severe (Grade 4/5)	10	4
Moderate (Grade 3)	31	13
Stridor		
Severe (Grade 4/5)	8	3
Moderate (Grade 3)	17	7
Time until death	$n = 241$	100
Mean in minutes ± SD	111.64 ± 17.16	
Median in minutes	20	

because terminal extubation is an essential part of the new WOLSM protocol. Moreover, death rattle is also a very frequently observed sign in dying patients outside the ICU. The incidence of severe death rattle was only 4%. The incidences of terminal restlessness and stridor appear to be low, but this is hard to interpret because there are, as far as we know, no publications on this issue available.

As already mentioned in the Results section, the incidence of terminal extubation increased over the two year study period. Nevertheless, the incidence of death rattle and stridor did not increase. Apparently, the reluctance to remove the tube after withdrawal of life-sustaining measures declined gradually, most likely because of the low incidences of distress factors encountered and the effectiveness of the preventive measures advised in the protocol.

Opioid and Sedative Use

Most of our population was receiving sedatives and opioids as a standard of care, resulting in adequate sedation at T0. Similar to what is described in other studies, we saw a significant rise in the dosages of opioids and sedatives in the last hours of life.[17,32,34] We think that when death is imminent, these medications should be increased in a goal-directed way, not focusing on the dosage level but on the individual patient so that suffering is alleviated and optimal patient comfort is achieved. The median dosage of morphine (12 mg/hour) is lower than described in previous reports.[25,32] The fact that the opioid doses did not increase significantly in the Protestant hospital is in concordance with the fact that religious Dutch people are reluctant to use opioids if an earlier death may be the result.[38] The statistically significant attribution of the increase in opioids to the lengthening of time till death, however, supports the hypothesis that goal-directed use of opioids is "ethically" safe.[34,39] Chan

Table 5
Overview of the Regression Coefficients in the Model

Coefficients[a]

	Unstandardized Coefficients		Standardized Coefficients		
Model	B	SE	Beta	*t*	Sig.
1					
(Constant)	344.377	246.627		1.396	0.164
Age	0.635	1.509	0.030	0.421	0.674
Sex	49.742	42.350	0.086	1.175	0.242
Body weight	−1.069	1.348	−0.058	−0.793	0.429
LOS ICU	4.624	2.596	0.128	1.781	0.077
SOFA score admission day	−2.764	7.434	−0.032	−0.372	0.710
SOFA score withdrawal day	−3.998	7.289	−0.049	−0.549	0.584
APACHE II score	−0.364	2.324	−0.012	−0.157	0.876
PEEP level	−2.509	6.656	−0.036	−0.377	0.707
Peak pressure	−6.671	3.097	−0.205	−2.154	0.033
FiO2	0.185	0.732	0.019	0.252	0.801
Withdrawal of MV	7.865	69.482	0.008	0.113	0.910
Norepinephrine	−30.635	41.780	−0.061	−0.733	0.464
Maximum morphine equivalents	−2.027	2.399	−0.092	−0.845	0.399
Change in opioids	8.310	2.728	0.327	3.046	0.003
Propofol (mg/kg/h)	3.866	13.216	0.023	0.293	0.770

LOS = length of stay; SOFA = sequential organ failure assessment; APACHE II = Acute Physiology and Chronic Health Evaluation II; PEEP = positive end-expiratory pressure; FiO2 = inspired oxygen fraction; MV = mechanical ventilation.
[a]Dependent variable: minutes till death after withdrawal of life-sustaining measures.

et al.[32] report the use of sedatives in only 40% of the total population and Rocker et al.[25] in 45%, with only 3.4% using propofol.

The comparison of sedatives is more complicated because, in contrast to the previously mentioned studies, in our study propofol was used as an alternative for benzodiazepines in 40% of patients receiving a sedative (86%). Notably, in our study, the mean maximum dosage after withdrawal adjusted for body weight does not exceed 3 mg/kg/hour.

The dosages of midazolam seem to be slightly higher than reported by Rocker et al. and Chan et al. However, in their studies, lorazepam in higher dosages is described, which is rarely seen in Dutch ICUs because lorazepam is recognized as an independent risk factor for delirium and, therefore, not used.[40,41]

Age and Disease Severity

The patients in our study were six years older than the average Dutch ICU patient.[10] The mean APACHE II and SOFA scores in our cohort were 31 and 12, respectively. The combination of advanced age and (multi)organ failure is a strong predictor of death.[42,43] The frequently observed combination of the two explains why inappropriateness of therapy is often mentioned as the key point in the decision-making process of WOLSM in this study.

WOLSM Process, Time till Death, and Severity of Suffering

Predicting time till death is not easy in a general ICU population as demonstrated by Munshi et al.[44] However, some representative studies showed concurrence with our data that high ventilator settings like positive end-expiratory pressure, inspired oxygen fraction, or peak pressure are reliable predictors of a shorter time till death.[36,45]

In our previous study on opioids and sedatives and time till death, we demonstrated that time between the withdrawal of the different treatment entities and death was short.[17] In this study, in 157 patients (65%) both VAM and MV were withdrawn at the very same time. This was only ethically possible because most patients was already adequately sedated and treated with opioids before the WOLSM decision was made.

This approach has several important advantages. First, when life-sustaining measures are stopped at once, it is almost certain that the patient will die within four hours (±90% of patients). For families, this is very reliable and, hence, important information.[15] Second, when the patient dies very quickly after cessation of life support, families realize how dependent the patient had become on all the supportive measures, and thereby, the acceptance of the withdrawal decision might be facilitated. For understanding Dutch values, it is very important to note that the Dutch general public is strongly against continuing treatment when no cure or improvement is to be expected and that they are, with regard to end-of-life decisions, often even more progressive than Dutch medical specialists.[38]

Severity of suffering in dying ICU patients can be formulated as a function of pain, discomfort, anxiety, fear, other forms of psychological distress, and time. Treatment of pain, discomfort, and psychological distress should be optimal in end-of-life care; however, the factor time is often not taken into account. Slowly withdrawing often means also slowly dying. In our population, the imaginary area under the curve of a "time till death graph" is very small. When in that same population pain discomfort and distress are also adequately treated, the total load of suffering is per definition low. We think that we certainly never should deliberately aim to hasten death, but unnecessarily postponing death might be equally ethically objectionable from this perspective.

Study Limitations

There are several limitations to this study. Because patient inclusion was the responsibility of the research nurses, the study was fully dependent on their presence. The fact that 125 patients were missed for eligibility screening because of periods of research nurse absence can be interpreted as a major drawback. However, there is no reason to think that this might have led to patient selection or inclusion/exclusion bias; on the contrary, because the study was fully nurse driven, physicians involved were unaware of the study being done and, therefore, could not have been influenced by their presence or absence.

Although the two selected hospitals are complementary in background, size, and patient categories and, therefore, are on average an adequate representation of the different nonacademic ICUs in The Netherlands, a multicenter study would yield more homogeneous data and more reliable results. However, because the protocol has been implemented nationwide and medical educational programs are mostly centrally organized in a small country like The Netherlands, medical practices are very homogeneous and differences are expected only to be subtle, as already demonstrated by Spronk et al.[46]

Another limitation is that we began the observations just before the treatment was withdrawn (T0). Because most patients were already well sedated at T0, and we know that there is almost always a significant increase in opioids and sedatives in the last hours and that the highest dosages are always reported after treatment withdrawal, we think that describing the prewithdrawal

period would not yield additional information necessary for answering our study questions.[17,32,34]

Because patient comfort is the most important goal after WOLSM, this study focused on patient signs and patient comfort alone. Evaluation of family satisfaction, of course, must be part of a follow-up study evaluating this protocol.

Conclusions

Dutch ICU patients in whom life-sustaining measures are withdrawn are relatively old and are severely ill. These patients do not seem to benefit medically from ICU treatment; therefore, continuation of invasive ICU therapy does not seem to be in proportion. Most decisions for WOLSM are made in a multidisciplinary setting and are based on the disproportionateness of the treatment. Opioids and sedatives are widely used and dosages increase by a significant amount during the process of WOLSM; dosages are, however, comparable with the dose ranges previous observed by others and do not contribute to a shorter time till death. Patients in Dutch ICUs die rapidly, resulting in a dignified death with a low burden of suffering and little signs of discomfort. Further research is required to evaluate family satisfaction with this protocol.

Disclosures and Acknowledgments

No funding was received for this study, and the authors declare no conflicts of interest.

The authors are extremely grateful to Dr. Jeanette Schoonderbeek and Dr. Michael Franken, who gave us permission to run this study on their intensive care units. Without the efforts of Lettie van de Berg and Hanneke van Embden and their fellow research nurse colleagues, this study would not have been possible. We thank them for their enthusiastic and stimulating participation and above all for their meticulous data collection.

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