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ETHICAL MATTERS

# Withdrawal of Life-Sustaining Treatment in a Mixed Intensive Care Unit: Most Common in Patients with Catastropic Brain Injury

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**Abstract**
*Objective* To determine the incidence of withdrawal of life-sustaining treatment in various groups of patients in a mixed intensive care unit (ICU).
*Design* Observational retrospective. Setting: University hospital mixed medical, neurological, neurosurgical and surgical ICU.
*Patients* All patients admitted to the ICU between 1 November 2006, and 31 October 2007.
*Results* 1,353 Patients were admitted to our ICU between 1 November 2006, and 31 October 2007. During this period, 218 (16.1%) patients died in the ICU, 10 of which were excluded for further analysis. In 174 (83.7%) of the remaining 208 patients, life-sustaining treatment was withdrawn. Severe CNS injury was in 86 patients (49.4%) being the reason for withdrawal of treatment, followed by MODS in 67 patients (38.5%). Notably, treatment was withdrawn in almost all patients (95%) who died of CNS failure. Patients who died in the ICU were significantly older, more often admitted for medical than surgical reasons, and had higher SOFA and APACHE II scores compared with those who survived their ICU stay. Also, SOFA scores before discharge/death were significantly different from admission scores. Of the 1,135 patients who survived their ICU stay, only 51 patients (4.5%) died within 28 days after ICU discharge.
*Conclusions* In 83, 7% of patients who die in the mixed ICU life-sustaining treatment is withdrawn. Severe cerebral damage was the leading reason to withdraw life-sustaining treatment.

**Keywords** Intensive care · End-of-life · Withdrawal of treatment · Subarachnoid haemorrhage · Traumatic brain injury

## Introduction

Over the last decades modern technology has allowed critically ill patients to survive longer. At the same time, it is increasingly accepted that continued aggressive intensive care unit (ICU) care is not always beneficial. Consequently, the dying process in the ICU frequently follows limitation of life-supporting therapies, with documented percentages up to 90% of all deaths preceded by some form of limitation [1–5].

Physician's behaviour of withholding or withdrawing life-supporting measures is changing in time [5, 6] and differs between regions and countries [7]. Withdrawing treatment is more common than withholding treatment in northern European countries and the USA than it is in comparison with southern European countries like Spain, Italy and Portugal [2]. Besides the severity of illness [8], cultural-religious motives influence the approach and practise of end-of-life care [2, 7].

The majority of studies to date have focused on either end-of-life issues [5, 9–11] or outcome for a single disease [12–16]. Less data are published concerning the ICU patient population as a whole, irrespective of the underlying disease [17]. This would provide better insight in the total group of patients, in which treatment is withdrawn.

The objective of this study was to evaluate the incidence of withdrawal of life-sustaining treatment in various groups

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of patients in a single centre university hospital mixed ICU in the Netherlands.

## Materials and Methods

### Study Design

We performed an observational retrospective study in the Erasmus MC University Hospital in Rotterdam, The Netherlands. The ICU is a mixed medical, neurological, neurosurgical and surgical ICU with a capacity of 28-beds. All patients admitted to the ICU between 1 November 2006 and 31 October 2007, were included. The Institutional Review Board approval was waived, as it is not required in the Netherlands, when research concerns the use of anonymous data of deceased patients.

### Data Collection

Data were collected using our patient data management system (PDMS), the electronic patient file and handwritten medical charts. We recorded demographics (age, gender), date of ICU admission, ICU admission diagnosis (Acute Physiology and Chronic Health Evaluation II diagnosis; APACHE II diagnosis), length of stay (LOS) in the ICU, severity of illness (APACHE II score), Sequential Organ Failure Assessment-score (SOFA-score) upon admission and before discharge/death, death in the ICU and the 28-day hospital mortality. Diagnoses were categorized as multiple organ dysfunction syndrome/multiple organ failure (MODS/MOF), severe central nervous system (CNS) injury, acute cardiac arrest, pulmonary failure, kidney failure, liver failure, or acute haemorrhage. Withdrawal of treatment was recorded in a binary fashion.

**Table 1** Study population characteristics

| | All patients $n = 1{,}353$ | Survivors $n = 1{,}135$ | Non-survivors $n = 218$ |
|---|---|---|---|
| Age, years | 58 (44–69) | 57 (43–68) | 62 (50–75)* |
| Male sex (%) | 811 (59.9) | 677 (59.6) | 134 (61.5) |
| LOS, days | 4 (2–8) | 4 (2–7) | 4 (2–11) |
| APACHE II diagnosis (%)[a] | | | |
| Surgical | 539 (43.5) | 485 (47.5) | 54 (24.8)* |
| Cardiovascular | 92 (7.4) | 81 (7.9) | 11 (5.1) |
| Gastro-Intestinal | 199 (16.0) | 185 (18.1) | 14 (6.4) |
| Neurological | 154 (12.4) | 131 (12.8) | 23 (10.6) |
| Respiratory | 53 (4.3) | 48 (4.7) | 5 (2.3) |
| Renal | 21 (1.7) | 20 (2.0) | 1 (0.5) |
| Other | 20 (1.6) | 20 (2.0) | 0 (0) |
| Non-surgical | 701 (56.5) | 537 (52.5) | 164 (75.2) |
| Cardiovascular | 78 (6.3) | 64 (6.3) | 14 (6.4) |
| Gastro-Intestinal | 73 (5.9) | 60 (5.9) | 13 (6.0) |
| Neurological | 233 (18.8) | 175 (17.1) | 58 (26.6) |
| Respiratory | 203 (16.4) | 160 (15.7) | 43 (19.7) |
| Renal | 11 (0.9) | 9 (0.9) | 2 (0.9) |
| Sepsis | 49 (4.0) | 40 (3.9) | 9 (4.1) |
| After cardiac arrest | 26 (2.1) | 11 (1.1) | 15 (6.9) |
| Other | 28 (2.3) | 18 (1.8) | 10 (4.6) |
| APACHE II score, mean ± SD[b] | 20.5 ± 7.3 | 19.1 ± 6.7 | 27.7 ± 6.4* |
| SOFA score admission[c] | 7 (4–10) | 6 (4–9) | 9 (7–13)* |
| SOFA score discharge[d] | 5 (38) | 3 (2–5) | 10 (7–15)*° |

Values are represented as median (interquartile range), unless stated otherwise

*LOS* length of stay

* $P < 0.01$ compared to survivors;° $P < 0.05$ compared to SOFA score on admission for both survivors and non-survivors

[a] 113 missing values (113 survivors)

[b] 450 cases with ≥1 missing variable (377 survivors, 73 non-survivors)

[c] 359 cases with ≥1 missing variable (321 survivors, 38 non-survivors)

[d] 768 cases with ≥1 missing variable (729 survivors, 39 non-survivors)

### Study Definitions

Some APACHE II diagnoses appear in both the operative and non-operative group; our PDMS does not distinguish between sepsis, post cardiac arrest and post respiratory arrest. We assigned all patients in the aforementioned categories to the non-operative status. LOS was defined as the number of consecutive days a patient was admitted to the ICU. We recorded 1 day if the admission was less than 24-h, and the admission SOFA-score is identical to the SOFA-score at discharge/death. If the SOFA-score was incomplete, and no data were available for the concerning date, it was scored using previous values nearest in time. Only patients who died in the ICU were recorded as death in the ICU. CNS failure was defined as irreversible catastrophic cerebral damage. If (multiple) organ failure was secondary to CNS failure, reason to withdraw therapy was noted as CNS failure. Patients were declared brain death if they met all criteria set under Dutch law. The withdrawal of treatment included the withdrawal of mechanical ventilation and/or vaso-active drugs. If withholding treatment was the sole limitation, and no actual withdrawal took place, patients were classified as no withdrawal. Opioids and/or sedatives were administered in accordance with professional consensus and national guidelines. Occasionally, if delayed death was likely, patients were discharged to a ward and were categorized as ICU survivors.

### Statistical Analysis

Statistical analysis was performed using SPSS version 15 for Windows (SPSS Inc, Chicago, IL, USA). Descriptive statistics were computed for all variables. Results are expressed in numbers and percentages, mean ± standard deviation for continuous parametric variables and median and interquartile range (25–75% IQR) for continuous, non-parametric variables. Difference testing between groups was performed using the student *t*-test, Mann–Whitney U test, Wilcoxon signed rank test or Chi-square test as appropriate. A *P*-value of $<0.05$ was considered statistically significant. Missing values were excluded from analysis.

## Results

1,353 Patients were admitted to our ICU between 1 November 2006, and 31 October 2007. All patients were included in this study. During this period, 218 (16.1%) patients died in the ICU.

Population characteristics are shown in Table 1. Median age was 58 years, and 59.9% of patients were male. Patients who died in the ICU were significantly older, more often admitted for medical than surgical reasons, and had higher SOFA and APACHE II scores compared with those who survived their ICU stay. Also their SOFA scores before discharge/death were significantly different from admission scores. Of the 1,135 patients who survived their ICU stay, only 51 patients (4.5%) died within 28 days after ICU discharge.

Of the 218 patients who died in the ICU, nine patients were brain death and data of one patient were untraceable, leaving 208 patients available for analysis (Fig. 1). In 174 (83.7%) of these patients, life-sustaining treatment was withdrawn. Severe CNS injury was in 86 patients (49.4%) being the reason for withdrawal of treatment, followed by MODS in 67 patients (38.5%). In patients who died of primary CNS failure, treatment was withdrawn in 95%. The majority of patients with severe CNS injury were admitted with primary intracranial disorders (73%). Patients with intracerebral-, subdural- or subarachnoid-haemorrhage (ICH/SDH/SAH) and traumatic brain injury (TBI) accounted for 42.9% and 27.0% in the non-surgical and surgical group, respectively (Fig. 2). Craniotomy for ICH/SDH/SAH made up 69.6% of the surgical group.

## Discussion

This study determines the incidence of withdrawal of life-sustaining measures in various groups of patients in a mixed intensive care unit. In our population, 16.1% of

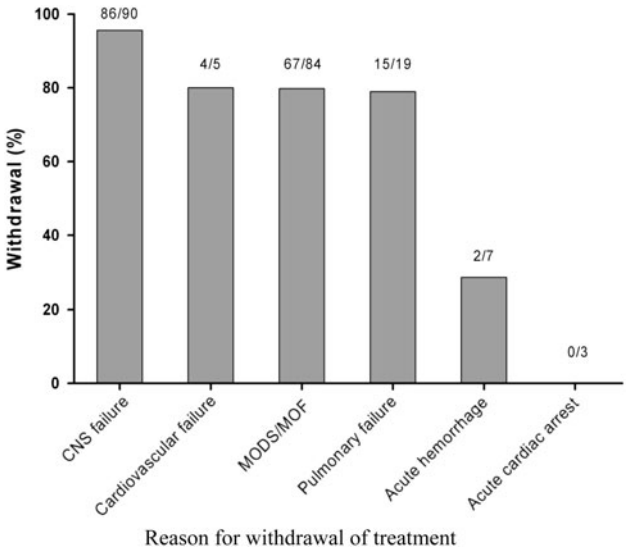


**Fig. 1** Withdrawal of treatment ($n = 174$). Values are presented as percentages; numbers above columns represent cases of withdrawal and total number of cases per cause of death. *CNS failure* central nervous system failure, *MODS/MOF* multiple organ dysfunction syndrome/multiple organ failure

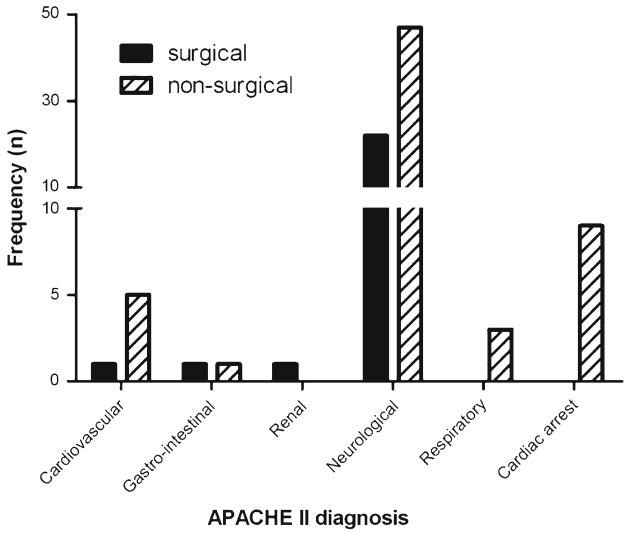


**Fig. 2** CNS failure/APACHE II diagnosis ($n = 90$)

| | surgical | non-surgical |
|---|---|---|
| cardiovasc | 1 | 5 |
| GI | 1 | 1 |
| renal | 1 | 0 |
| neuro | 22<br>▪ (2x no WD craniot ICH/SDH/SAH)<br>▪ 3x cran neopl, 1x SHL, 18x ICH/SAB | 47<br>▪ (1x no WD ICH)<br>▪ 17x SHL, 28x SAB/ICH, 2x epil |
| resp | 0 | 3 |
| cardiac arrest | - | 9 (1x no WD) |
| | 25 | 65 |

patients admitted to the ICU in the studied period died, this is in accordance with other European ICUs [2, 3].

The primary cause of death was severe central nervous system (CNS) injury, whereas MODS was the second most common cause. This finding is in agreement with Mayr et al. [17], who identified both CNS and cardiovascular failure as the most important risk factors for death in the ICU. However, in their study, MODS was the leading cause of death. The difference in cause of death is likely due to the differences in case mix. In contrast to our study, nearly half of their patients were admitted after cardiac surgery, whereas catastrophic CNS failure occurred only in a minority of patients.

In our study, withdrawal of treatment preceded death in 84% of cases, which is high compared with the percentages reported by Sprung et al. (47.4%) [2], and Spronk et al. (53%) [1]. Differences in cultural and religious background may explain this difference. Indeed, the ETHICUS study group has shown that limitations in life-sustaining therapy vary in practice between regions and different religions. Physicians in the northern countries were more likely to withdraw treatment than their southern colleagues [2]. In addition, Catholic, Protestant and physicians with no religious affiliation tended to withdraw rather than withhold treatment as the form of limitation in life-supporting therapy compared with their Jewish, Greek orthodox and Moslem colleagues [9]. Finally, moral judgements on withholding vs. withdrawing treatment may vary among physicians and medical staff. Although from an ethical point of view consensus exists that there is no moral difference between withdrawing and withholding treatment [18, 19], this is not generally accepted [20] and physicians may be more reluctant towards withdrawing than withholding treatment [21]. In our hospital, the decision to withdraw therapy is made by the multidisciplinary team. A noticeable difference compared with the USA, where such decisions are made by the responsible physician in collaboration with family members or a surrogate decision

maker of the patient [19, 22]. When treatment is believed to be futile by the multidisciplinary team, in most cases treatment is withdrawn rather than withheld [23].

Among patients in whom treatment was withdrawn, a large percentage of patients with severe CNS failure were presented. Moreover, we found that treatment was withdrawn in almost all of the patients (95%) who died of CNS failure. Although the percentage found is high, this is in line with results reported by Sprung et al. where therapy limitations were most often made for acute cerebral diseases [2]. In addition, neurological failure was the second most quoted reason to limit treatment, and the reason in one of five cases in northern regions [11]. Again, differences in religion, culture and moral judgements may cause the difference in percentage in withdrawal of treatment in patients with severe neurological damage in our study and other authors. Hypothetically, another explanation exists and causes some concern. The decision to withdraw treatment depends on the expectation that patients with severe neurological damage have a 'poor' prognosis and that ongoing treatment is futile. To differentiate 'poor' from 'good' prognosis and to determine what is and what is not futile remains difficult. Also, withdrawing treatment inevitable leads to death in these cases and hence, the hazard exists of a self-fulfilling prophecy in regards to withdrawing life-sustaining therapy in patients with severe neurological damage [24]. To avoid this particular trap, caring physicians ought to determine the prognosis grounded on evidence-based studies lacking a large group of patients in which treatment is withheld or withdrawn.

We found a readmission rate of 11.4% which is comparable with rates reported in a large review [25], but higher than reported in recent studies (5.1–7.4%) [26, 27]. This difference can be partially accounted for by differences in case mix. It is also possible that there are differences in ICU admission and discharge policies, because our hospital does not have high or medium care units.

Cook et al. [28] studied withdrawal of mechanical ventilation in anticipation of death in the ICU. All patients were mechanically ventilated, 66.3% were successfully weaned from the ventilator, 17.2% died while receiving ventilation, and 19.5% had mechanical ventilation withdrawn, of whom 87.3% died in the ICU. More than 66% died after withdrawal of mechanical ventilation, vasoactive agents and/or dialysis. Physician's perception that the patient preferred not to use life support, and the physician's prediction of a low likelihood of ICU survival were major determinants of withdrawal of mechanical ventilation. However, severity of illness and organ dysfunction were not associated with withdrawal of mechanical ventilation. In our study population, ICU non-survivors had a SOFA score of 12.5 (IQR 9–17) before death. Patients, in whom treatment was withdrawn, had a median SOFA-score of 12 (9–17), compared with 14 (9–18) in patients with no withdrawal. When subdividing patients who died after withdrawal into CNS failure and no CNS failure, SOFA-scores are 10 (7–14) and 15 (11.25–17), respectively. This seems to be in accordance with Cook et al. [28], but no conclusions can be drawn from these observations in the present study, because the missing values outnumbered the valid values.

## Limitations

This was a single centre, single country study, which may limit the generalizability of our results to other centres and countries. In addition, our population comprised a high proportion of patients with catastrophic cerebral injury; which in part can be explained by the fact that our hospital is one of the ten trauma centres in the Netherlands (all patients with severe TBI in a region of 2.1 million inhabitants are admitted to our hospital) and because we serve as a regional centre for the (surgical/endovascular) treatment of patients with subarachnoid haemorrhage. Also, the withdrawal rate in this study may be underestimated. Although not standard practice, some patients were transferred to the ward after withdrawal of therapy when delayed death was likely. These patients were excluded from non-survivor analysis, and thus, clouded both survivor and non-survivor data.

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