End-of-life practices in traumatic brain injury patients: Report of a questionnaire from the CENTER-TBI study

Ernest van Veen, Mathieu van der Jagt, Giuseppe Citerio, Nino Stocchetti, Jelle L. Epker, Diederik Gommers, Lex Burdorf, David K. Menon, Andrew I.R. Maas, Hester F. Lingsma, Erwin J.O. Kompanje, the CENTER-TBI investigators and participants

Abstract

Purpose: We aimed to study variation regarding specific end-of-life (EoL) practices in the intensive care unit (ICU) in traumatic brain injury (TBI) patients.

Materials and methods: Respondents from 67 hospitals participating in The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study completed several questionnaires on management of TBI patients.

Results: In 60% of the centers, 50% of all patients with severe neurological damage dying in the ICU, die after withdrawal of life-sustaining measures (LSM). The decision to withhold/withdraw LSM was made following multidisciplinary consensus in every center. Legal representatives/relatives played a role in the decision-making process in 81% of the centers. In 82% of the centers, age played a role in the decision to withhold/withdraw LSM. Furthermore, palliative therapy was initiated in 79% of the centers after the decision to withdraw LSM was made. Last, withholding/withdrawing LSM was, generally, more often considered after more time had passed, in a patient with TBI, who remained in a very poor prognostic condition.

Conclusion: We found variation regarding EoL practices in TBI patients. These results provide insight into variability regarding important issues pertaining to EoL practices in TBI, which can be useful to stimulate discussions on EoL practices, comparative effectiveness research, and, ultimately, development of recommendations.

© 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

Life-sustaining measures (LSM), such as mechanical ventilation, have allowed physicians to prolong the life of patients. However, these LSM may sometimes be considered as disproportionate when they postpone unavoidable death and, as a consequence, may only result in prolonged suffering of patients and their relatives. Therefore, in many countries, it is seen as good medical practice to withhold or withdraw LSM in these situations and allow the patient to die when further treatment is judged as disproportionate [1,2].

A systematic review reported variation in the prevalence of withdrawing/withholding LSM [3] resulting from institutional factors [4–10], physician factors [10–14], and religion/geographic factors [14–16]. Recent studies have advised to also study variation pertaining to specific
end-of-life (EoL) practices [3,17]. A degree of variation in specific EoL practices is understandable, given the complexities of EoL care. However, if considerable variation negatively influences patient care, this variation may not be acceptable. One driving issue here is that withdrawal of life-sustaining measures (LSM) may be inappropriately instituted in individuals who have a chance of good quality survival. Furthermore, important issues may be that symptom control during withdrawal is suboptimal, interactions with families may be compromised, ethical issues may not be appropriately addressed, and organ donation may be affected. Studying variation may provide insight into these issues in patients with traumatic brain injury (TBI) on the intensive care unit (ICU), which can be useful to stimulate discussions regarding EoL best practices, and, ultimately, development of recommendations [3,17]. Furthermore, variation may inform comparative effectiveness research (CER), which entails studying the impact of differences in patient management on outcomes to inform best practices.

Therefore, we aimed to study variation regarding specific EoL practices in TBI patients. We investigated the occurrence of withdrawing life-sustaining measures (LSM), how the decision to withhold/withdraw LSM was made, the role of legal representatives/relatives, if age influenced the decision-making process, the initiation of palliative therapy, and the timing and execution of withholding/withdrawing LSM.

2. Methods

2.1. CENTER-TBI and study sample

The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI, www.center-tbi.eu) study is a prospective observational study on traumatic brain injury (TBI) [18,19]. For this, data on patient characteristics, management and outcomes were collected in centers from 20 countries across Europe and Israel (Fig. 1). Further, respondents from all participating centers in the CENTER-TBI study were asked to complete questionnaires which were used to create “provider profiles” of participating neurotrauma centers [20].

2.2. Questionnaire development and administration

The topics investigated for this provider profile study, are summarized in Table 1. In the questionnaires, we explicitly asked respondents to provide their understanding of the “general policy” for their institution. We defined this as the local standards used in more than 75% of patients, recognizing that there might be exceptions. Most questions used categorical answers. For some questions, the respondents had the option to fill in “other” and provide a free text response.

In an earlier publication from Cnossen et al. [20], detailed information about the development, administration, and content of the questionnaires is available.

2.3. Analyses

We calculated frequencies and percentages for all questions. The sample total of question two and six could exceed 100% because the respondents had the option to provide more than one response. For question six, we made a new response category. The result of this response category is the sum of centers that filled in all response categories for that question. Furthermore, for question seven, respondents could answer “never”, “sometimes”, “often”, or “always”. For the analyses we considered “never” and “sometimes” as “no general policy”, and “often” and “always” as “general policy”. Question five had six answers, of which four had a similar meaning. We combined these four answers to define one response category (Table 1).

We examined potential variation between and within seven regions based on the United Nations geo-scheme: Baltic States (Latvia, and Lithuania), Eastern Europe (Bosnia and Herzegovina, Hungary, Romania, and Serbia), Israel, Northern Europe (Denmark, Finland, Norway, and Sweden), Southern Europe (Italy, and Spain), the United Kingdom, and Western Europe (Austria, Belgium, France, Germany, the Netherlands, and Switzerland).

3. Results

3.1. Center characteristics

Of the 68 centers, 67 filled in the questionnaires and were included in the analysis. Between questions the response rate varied from 96 to 99%. Most participating centers were academic centers (N = 61, 91%), designated as a level I or II trauma center (N = 49, 73%). The average number of beds was 1187 of which on average 39 were ICU beds. In 2013, the median annual number of TBI patients was 92 (interquartile range (IQR) 53–159). The questionnaire about ethical aspects of the ICU was mostly completed by intensivists, neurosurgeons, and neurologists.

Of all patients with severe neurological damage who die in the ICU, approximately, how many die after withdrawal of life-sustaining measures?

In 60% of the centers, ≤50% of all patients with severe neurological damage who die in the ICU, died after withdrawal of LSM. In 40% of the centers, this was >50%. In 56% of the centers from Northern Europe, >75% of the patients with severe neurological damage who die in the ICU, died after withdrawing LSM. Contrary, in most centers from the Baltic States, Israel, and Southern Europe (80%, 100%, and 75% respectively), this was <25% (Fig. 2).

How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)?

In 67% of the centers, multidisciplinary discussion following consensus among all participating physicians was preferred. This was also preferred in most centers in Southern Europe, the United Kingdom (UK) and Western Europe (75%, 75%, and 84% respectively). In Northern European centers, however, this was preferred in 33% of the centers (Table 2).

Does the age of the patient influence your decision making about withholding and withdrawing life-sustaining treatment?

In 81% of the centers, age influenced the decision-making process, together with other criteria. This was also the case in all centers in Southern Europe. However, in the Baltic States and Eastern Europe, age did not play a role in 60%, and 50% of the centers respectively (Table 2).

To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?

In 19% of the centers, legal representatives/relatives played no role in the decision-making process before withdrawing/withdrawing LSM. This was the case in 67% of the centers in Northern Europe. Contrary, in all centers in Israel, and in 60% of the centers in Western Europe, legal representatives/relatives played a role in the decision-making process to some or to a great extent (Fig. 3).

If the decision is made to withdraw life-sustaining measures and before actual withdrawal, do you initiate palliative therapy in anticipation of distressing symptoms (such as pain, terminal restlessness, death rattle, stridor, dyspnoea)?

In 79% of the centers, palliative therapy in anticipation of distressing symptoms after the decision to withdraw/withdraw LSM was initiated. In Northern Europe, Southern Europe, and Western Europe this was the case in 78%, 92%, and 96% respectively. Contrary, in 60% of the centers from the Baltic States, palliative therapy was not initiated (Fig. 4).

If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patent, which life-sustaining measures do you stop?
In a comatose severely injured TBI patient, mechanical ventilation would be stopped in 63% of the centers, the administration of vasoactive medication would be stopped in 93% of the centers, renal replacement therapy would be stopped in 81% of the centers, the administration of intravenous fluids would be stopped in 34% of the centers, and nasogastric feeding would be stopped in 58% of the centers. In 25% of the centers, all of these LSM would be stopped after the decision to withdraw LSM (Table 3).

At what time after injury would you consider to withdraw life support in a patient with TBI, who is in a very poor prognostic condition (based on CT scan, GCS, clinic, ICP etc), but not brain dead?

In general, there was an increase in considering withholding/withdrawing LSM after more time had passed (ranging from 24 h to 2 weeks), in a patient with TBI, who was in a very poor prognostic condition but not brain dead. In 25% of the centers from Southern Europe, and in 16% of the centers from Western Europe, withholding/withdrawal LSM would be considered after 24 h. In 40% of the centers from the Baltic States, and in 25% of the centers from the UK this was considered after >2 weeks (Table 3).

### 4. Discussion

We aimed to study the variation regarding specific end-of-life (EoL) practices in critically ill traumatic brain injury (TBI) patients, using questionnaires filled in by experts in participating neurotrauma centers. We found variation in the occurrence of withdrawing LSM, how the decision to withhold/withdraw LSM was made, the role of legal representatives/relatives, the influence of age in the decision-making process, the initiation of palliative therapy, and the timing and execution of
withholding/withdrawing LSM. The results indicate important practice variation regarding EoL practices in TBI, which can be useful to stimulate discussions on EoL practices, comparative effectiveness research (CER), and recommendations.

First, we found variation in the occurrence of withdrawing LSM. This is in line with previous literature [3], showing not only variation within countries [4–6,10,21–27], but also within departments [12].

Second, we found variation regarding the decision-making process. All centers responded that they preferred multidisciplinary discussion before withdrawing/withholding LSM. This is in line with recommendations in previous literature [28–30]. However, the way this multidisciplinary discussion was implemented varied across centers. We also found variation regarding the extent of the role of legal representatives/relatives in this decision-making process. Previous literature stressed the importance of legal representatives/relatives in the decision-making process [29–31]. A Canadian questionnaire study showed that 39% of surrogate decision-makers wanted to share responsibility for the decision [32]. However, Wendler and Rid found that at least one third of the surrogate decision-makers could be emotionally burdened after making treatment decisions for incapacitated loved ones [33]. Healthcare providers should contemplate on whether or not they wish to communicate the uncertainty involved in EoL decision-making (when such prognostic uncertainty is indeed present), because it might have unpredictable impact on this emotional burden of legal representatives/relatives. Reasons to communicate about uncertainty have already been raised by Smith et al. and Lazaridis [34,35]. Smith et al. proposed a framework that should be adapted to the core values of the patient [34]. By following this framework, legal representatives/relatives should be involved in the decision-making process.

Fig. 2. Of all patients with severe neurological damage who die on the intensive care unit, approximately, how many die after withdrawal of life-sustaining measures?

Table 2
Practices around the decision-making process regarding withholding/withdrawing LSM.

| Regions                   | Sample total (N=67) | Baltic States (N=5) | Eastern Europe (N=6) | Israel (N=2) | Northern Europe (N=9) | Southern Europe (N=12) | United Kingdom (N=8) | Western Europe (N=25) |
|---------------------------|---------------------|---------------------|----------------------|--------------|-----------------------|------------------------|----------------------|------------------------|
| How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)? |                      |                     |                      |              |                      |                        |                      |                        |
| One physician (e.g. the most senior person) decides following multidisciplinary discussion | 10 (15%)             | 1 (20%)             | 0 (0%)               | 2 (100%)     | 3 (33%)               | 0 (0%)                 | 2 (25%)              | 2 (8%)                 |
| During multidisciplinary discussion in which the majority (more than 50%) has to agree | 14 (21%)             | 1 (20%)             | 2 (33%)              | 1 (50%)      | 3 (33%)               | 3 (25%)                | 0 (0%)               | 4 (16%)                |
| During multidisciplinary discussion in which there has to be unanimous consensus among all participating doctors | 45 (67%)             | 2 (40%)             | 4 (67%)              | 0 (0%)       | 3 (33%)               | 9 (75%)                | 6 (75%)              | 21 (84%)               |
| One physician decides (along with objective medical criteria) without multidisciplinary discussion (veto) | 0 (0%)               | 0 (0%)              | 0 (0%)               | 0 (0%)       | 0 (0%)                | 0 (0%)                 | 0 (0%)               | 0 (0%)                 |
| Other* | 2 (3%) | 1 (20%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (4%) |
| Does the age of the patient influence your decision making about withholding and withdrawing treatment? |                      |                     |                      |              |                      |                        |                      |                        |
| Yes, always, independent of other criteria | 11 (16%)             | 0 (0%)              | 0 (0%)               | 1 (50%)      | 0 (0%)                | 0 (0%)                 | 0 (0%)               | 0 (0%)                 |
| Yes, but only in combination with other criteria as CT scan, GCS, depth of coma | 54 (82%)             | 2 (40%)             | 3 (50%)              | 1 (50%)      | 7 (78%)               | 12 (100%)              | 6 (75%)              | 23 (92%)               |
| No, I only decide on the severity of the injury and anticipated prognosis | 12 (18%)             | 3 (60%)             | 3 (50%)              | 0 (0%)       | 2 (22%)               | 0 (0%)                 | 2 (25%)              | 2 (8%)                 |

Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, LSM: Life-sustaining measures.
relatives might experience more support when they are involved in EoL decisions. A multisociety statement recommended that the medical profession should lead public engagement efforts and advocate policies and legislation about the use of life-prolonging technologies [36]. These policies and legislation could be informative for the decision to involve legal representatives/relatives in the decision-making process.

Third, we found variation in practices before withholding/withdrawing LSM. Decisions regarding palliative therapy were not formalized in a protocol in the majority of centers. Despite this, palliative therapy was initiated in most centers after the decision to withhold/withdraw LSM. Where such care was not reported, the response might have been influenced by the wording of our questionnaire, which may have been construed as starting such therapy in advance of, rather than at the time of, withdrawing LSM. Palliative therapy might be common practice in general, but not in anticipation of distressing symptoms. Past recommendations stressed the importance of good palliative care [29,30,37]. Previous literature described that there should be no maximum dosage of narcotics or sedatives [30,37]. The right amount of drugs should be adapted to the need of the individual patient. Furthermore, Hawryluck et al. described, that pre-emptive dosing in anticipation of pain and suffering should be considered as good palliative care if the intent of the physician is clear and well documented [37].

Fourth, we found variation regarding which LSM to stop after the decision to withhold/withdraw LSM was made. In a quarter of centers, all LSM were stopped after the decision to withhold/withdraw LSM.
Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, ICP: Intracranial Pressure, LSM: Life-sustaining measures, TBI: Traumatic brain injury.

Previous literature suggested to critically evaluate all LSM that provide no comfort to dying patients, for whom the chances for meaningful recovery are absent. [28,30]. Asch et al. reported that blood products and hemodialysis, were among the LSM most preferably withdrawn by physicians, while tube feeding and intravenous fluids were least preferred to be withdrawn [38]. This is in line with our results. One reason for the reluctance to withdraw tube feeding and intravenous fluids could be that physicians believe that this could be perceived as starving the patient. On the other hand, continuing feeding and fluids might also prolong suffering at the end-of-life because the patient may live longer due to this “active” treatment.

Last, we found variation in when withdrawal of LSM was considered, and how often age influenced the decision-making process of withdrawing LSM. A previous study found that brain injury was an important trigger for withdrawing LSM [39]. Our results show that withdrawing LSM in a patient with very poor prognostic conditions but who is not brain dead was considered after 4–7 days in more than a quarter of the centers, and that age was a criterion for the decision to withdraw life-sustaining measures in many centers. Obviously, there is a general tendency to practice the “benefit of the doubt” in poor grade patients early in the course. The use of “considered” in our question meant that we could not be sure of the frequency with which such consideration actually led to the withdrawal of LSM. Consequently, caution is needed in interpreting the responses to this question. In general, physicians should exercise extreme caution regarding early prognostication and withdrawal of LSM following severe traumatic brain injury in spite of the existence of validated prognostic models [40,41]. Based on our results, in Northern European centers, patients in the intensive care unit (ICU) with severe neurological damage may have died more frequently because of withdrawal of LSM compared to other regions. This finding could lead to one of two diametrically opposing inferences. On one hand, the practice in Northern Europe may be appropriate, and ensure that patients who have no prospect of an acceptable functional outcome have withdrawal of LSM, thus minimizing the burden of suffering to the patient and family, and optimizing the use of limited health care resources. On the other hand, given that there was less unanimous consensus needed for the decision to withdraw LSM in Northern European countries, this practice could indicate a potential for self-fulfilling prophecies [42]. Self-fulfilling prophecies may exist in TBI too [43]. Early withholding/withdrawing of LSM, and withholding of treatment of patients that are “too old”, could lead to those self-fulfilling prophecies. On the Durban World Congress, ethics experts concluded that age should not be the sole criterion upon which to decide to withhold/withdraw LSM [44]. Although age is an important factor in prognostic models in TBI [40,41], and even though increasing age has been found to be independently associated with the decision to withdraw LSM [6,45], clinicians should be cautious taking age as a dominant criterion to withdraw LSM. Regarding the timing of withdrawing LSM, in a position statement from the Neurocritical Care Society, the recommendation was to wait at least 72 h before withdrawing LSM in patients with devastating brain injury [29]. “Early” withdrawal of LSM might be unwise due to too much uncertainty of the prognosis. On the other hand, “late” withdrawal of LSM would not always be in the best interest of the patient because of the potential for prolonged suffering. Finding the balance between resolving prognostic uncertainty and preventing harm and suffering in individual patients remains a difficult and incompletely resolved clinical problem. Our study has limitations that should be considered when interpreting the results. First, our results are based on the perceptions of practices reported by respondents rather than actual clinical practice data. However, even if this is the case, the fact that responders’ answers vary between centers, already provides insight in variation across European and Israeli neurotrauma centers. Second, some of our questions were open to ambiguity and may not have been interpreted correctly by the respondents. For example, in the questionnaire, we made no distinction between withholding and withdrawing life-sustaining measures. Because clinical choices could be different between the two, this may have influenced the results. In any case, a questionnaire cannot capture all the nuances that underpin clinical practice, which involves many complex potential alternative options that cannot be captured by questionnaires. Third, our results should invoke discussions rather than be considered as definitive, given the nature and room for
interpretations of our survey questions. Fourth, the data obtained may not be representative for all neurotrauma centers within the geographical areas studied, because the participating neurotrauma centers represent a select group. Fifth, the results come from data obtained in 2013. Last, it is possible that a more favorable picture or individual preferences may have been presented (even unwittingly), instead of the general policy in a center.

Medical practices are affected by the cultural climate of the society in which they exist [46]. Therefore, culture may explain some of the observed variation, such as the lack of influence of legal representatives/relatives in the decision-making process. Other variation, such as the possibility to withdrawing LSM may have a more legal basis. For example, in Israel withdrawing mechanical ventilation is against the law [47]. However, much variation found in our study also appears to be within regions, and even within the countries in those regions. Thus, on the basis of our results, we cannot easily attribute the variation to specific region or country characteristics such as most prevalent religion.

Our data comes from diverse sources, representing many cultural, religious and legal backgrounds. Our intent is not to change the daily practices of clinicians but to provide insight into systems used in other countries with a view to establishing common ground. Furthermore, withdrawing LSM should not preempt the availability and affordability of palliative care. Future research should study reasons for the found variation (e.g. cultural differences, and differences pertaining to legislation). Moreover, future research should evaluate the effect of the variation (e.g. cultural differences, and differences pertaining to legislation). Thus, on the basis of our results, we cannot clearly attribute the variation to specific region or country characteristics such as most prevalent religion.

The possibility to withdraw LSM may have a more legal basis. For example, relatives in the decision-making process. Other variation, such as the lack of influence of legal representatives/relatives in the decision-making process. Other variation, such as the possibility to withdrawing LSM may have a more legal basis. For example, in Israel withdrawing mechanical ventilation is against the law [47]. However, much variation found in our study also appears to be within regions, and even within the countries in those regions. Thus, on the basis of our results, we cannot easily attribute the variation to specific region or country characteristics such as most prevalent religion.
1 Department of Physiology and Pharmacology, Section of Perioperative Medicine and Intensive Care, Karolinska Institutet, Stockholm, Sweden
2 János Szentágóthai Research Centre, University of Pécs, Pécs, Hungary
3 Division of Surgery and Clinical Neuroscience, Department of Physiological Medicine and Rehabilitation, Oslo University Hospital and University of Oslo, Oslo, Norway
4 Department of Neurosurgery, University Hospital Northern Norway, Tromso, Norway
5 Department of Physical Medicine and Rehabilitation, University Hospital Northern Norway, Tromso, Norway
6 Trauma Surgery, Medical University Vienna, Vienna, Austria
7 Department of Anesthesiology & Intensive Care, University Hospital Nancy, Nancy, France
8 Raymond Poincare hospital, Assistance Publique – Hopitaux de Paris, Paris, France
9 Department of Anesthesiology & Intensive Care, S Raffaele University Hospital, Milan, Italy
10 Department of Neurosurgery, Radboud University Medical Center, Nijmegen, The Netherlands
11 Department of Neurosurgery, University of Szeged, Szeged, Hungary
12 International Projects Management, ARTTIC, Munchen, Germany
13 Department of Neurology, Neurological Intensive Care Unit, Medical University of Innsbruck, Innsbruck, Austria
14 Department of Neurosurgery & Anesthesia & intensive care medicine, Karolinska University Hospital, Stockholm, Sweden
15 NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham, UK
16 Anesthesia-Réanimation, Assistance Publique – Hopitaux de Paris, Paris, France
17 Department of Anesthesiology & ICU, AOU Città della Salute e della Scienza di Torino - Orthopedic and Trauma Center, Turin, Italy
18 Department of Neurology, Odense University Hospital, Odense, Denmark
19 BehaviourWorks Australia, Monash Sustainability Institute, Monash University, Victoria, Australia
20 Department of Public Health, Faculty of Health Sciences and Social Work, Tmava University, Tmava, Slovakia
21 Quesgen Systems Inc., Burlingame, California, USA
22 Australian & New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
23 Department of Surgery and Perioperative Science, Umeå University, Umeå, Sweden
24 Department of Neurosurgery, Medical School, University of Pécs, Hungary and Neurotrauma Research Group, János Szentágóthai Research Centre, University of Pécs, Hungary
25 Department of Medical Psychology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
26 Brain Physics Lab, Division of Neurosciences, Dept of Clinical Neurosciences, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK
27 Neuro ICU, Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico, Milan, Italy
28 ANZIC Research Centre, Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Victoria, Australia
29 Department of Neurosurgery, Hospital of Cruces, Bilbao, Spain
30 NeuroIntensive Care, Niguarda Hospital, Milan, Italy
31 School of Medicine and Surgery, Università Milano Bicocca, Milan, Italy
32 NeuroIntensive Care, ASST di Monza, Monza, Italy
33 Department of Public Health, Erasmus Medical Center-University Medical Center, Rotterdam, The Netherlands
34 Department of Anaesthesiology, University Hospital of Aachen, Aachen, Germany
35 Department of Anesthesia & Neurointensive Care, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK
36 School of Public Health & PM, Monash University and The Alfred Hospital, Melbourne, Victoria, Australia
37 Radiology/MRI department, MRC Cognition and Brain Sciences Unit, Cambridge, UK
38 Institute of Medical Psychology and Medical Sociology, Universitätmedizin Göttingen, Göttingen, Germany
39 Oxford University Hospitals NHS Trust, Oxford, UK
40 Intensive Care Unit, CHU Poitiers, Poitiers, France
41 Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK
42 Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium
43 Department of Anaesthesia & Intensive Care, Maggiore Della Carità Hospital, Novara, Italy
44 Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium
45 Department of Neurosurgery, clinical centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
46 Division of Anaesthesia, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK
47 Center for Stroke Research Berlin, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany
48 Intensive Care Unit, CHR Citadelle, Liège, Belgium
49 Department of Anaesthesiology and Intensive Therapy, University of Pécs, Pécs, Hungary
50 Departments of Neurology, Clinical Neurophysiology and Neuroanesthesiology, Region Hovedstaden Rigshospitalet, Copenhagen, Denmark
51 National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand
52 Department of Neurology, Erasmus MC, Rotterdam, the Netherlands
53 Department of Anaesthesiology and Intensive care, University Hospital Northern Norway, Tromso, Norway
54 Department of Neurosurgery, Hadassah-hebrew University Medical center, Jerusalem, Israel
55 Fundación Instituto Valenciano de Neurorehabilitación (FIVAN), Valencia, Spain
56 Department of Neurosurgery, Shanghai Renji hospital, Shanghai
57 Karolinska Institutet, INCF International Neuroinformatics Coordinating Facility, Stockholm, Sweden
58 Emergency Department, CHU, Liège, Belgium
59 Neurosurgery clinic, Pauls Stradins Clinical University Hospital, Riga, Latvia
60 Department of Computing, Imperial College London, London, UK
61 Department of Neurosurgery, Hospital Universitario 12 de Octubre, Madrid, Spain
62 Department of Anesthesia, Critical Care and Pain Medicine, Medical University of Vienna, Austria
63 College of Health and Medicine, Australian National University, Canberra, Australia
64 Department of Neurosurgery, Neurosciences Centre & JPN Apex trauma centre, All India Institute of Medical Sciences, New Delhi-110029, India
65 Department of Neurosurgery, Erasmus MC, Rotterdam, the Netherlands
66 Department of Neurosurgery, Oslo University Hospital, Oslo, Norway
67 Division of Psychology, University of Stirling, Stirling, UK
The authors declare that they have no conflicts of interest.

Funding

Data used in preparation of this manuscript were obtained in the context of CENTER-TBI, a large collaborative project, supported by the Framework 7 program of the European Union (602150). The funder had no role in the design of the study, the collection, analysis, and interpretation of data, or in writing the manuscript.

David K. Menon was supported by a Senior Investigator Award from the Canadian Institutes of Health Research and the Canada Research Chair in Critical Care and Emergency Medicine at the University of Ottawa, Canada. Piers Keenan was supported by a Senior Investigator Award from the Canadian Institutes of Health Research and the Canada Research Chair in Critical Care and Emergency Medicine at the University of Ottawa, Canada. The Centre for End of Life Research and Education (CENTRE-TBI) is a collaborative project among the University of Ottawa, Ottawa, Ontario, Canada; University of Maastricht, Maastricht, the Netherlands; and the University of Florida Health, Jacksonville, Florida, USA. Funding for data collection and analysis is supported by the Canadian Institutes of Health Research, Ottawa, Ontario, Canada; the University of Maastricht, Maastricht, the Netherlands; and the University of Florida Health, Jacksonville, Florida, USA. The database used in preparation of this manuscript were obtained in the CENTER-TBI Study. PLoS One 2016;11(8):e0161367.

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(4):1163–7.

Ferrand E, Robert R, Ingrand P, Lemaire F, French LG. Withholding and withdrawal of life support in intensive care units in France: a prospective survey. French LATEMBEA Group. Lancet 2001;357(9249):9–14.

Esteban A, Gordo F, Solsona JF, E et al. Withdrawing and withholding life support in the intensive care unit: a Spanish prospective multi-centre observational study. Intensive Care Med 2001;27(1):174–9.

Keenan SP, Buske KD, Chen LM, E et al. Withdrawing and withholding of life support in the intensive care unit: a comparison of teaching and community hospitals. The Southwestern Ontario Critical Care Research Network. Crit Care Med 1998;26(2):245–51.

Keenan SP, Buske KD, Chen LM, E et al. A retrospective review of a large cohort of patients undergoing the process of withdrawing or withholding of life support. Crit Care Med 1997;25(8):1324–31.

Ouanes I, Stambouli N, Dachraoui F, E et al. Pattern of end-of-life decisions in two Tunisian intensive care units: the role of culture and intensivists’ training. Intensive Care Med 2012;38(4):710–7.

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(1):15–20.

Traug RD, Campbell ML, Curtis JR, E et al. Recommendations for end-of-life care in the intensive care unit: a consensus statement by the American College [corrected] of Critical Care Medicine. Crit Care Med 2008;36(3):953–63.

Sprung CL, Cohen SI, Sjovestad P, E et al. End-of-life practices in European intensive care units: the Ethics Study. JAMA 2003;290(6):790–7.

Buloh HH, Sprung CL, Baras M, E et al. Are religion and religiosity important to end-of-life decisions and patient autonomy in the ICU? The Ethicot study. Intensive Care Med 2007;33(10):1732–9.

Sprung CL, Cohen SI, Sjovestad P, E et al. End-of-life practices in European intensive care units: the Ethics Study. JAMA 2003;290(6):790–7.

Buloh HH, Sprung CL, Baras M, E et al. Are religion and religiosity important to end-of-life decisions and patient autonomy in the ICU? The Ethicot study. Intensive Care Med 2007;33(10):1732–9.

Maas AJ, Menon DK, Steyerberg EW, E et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): a prospective longitudinal observational study. Neurosurgery 2015;76(1):67–80.

Maas AJ, Menon DK, Adelson PD, E et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol 2017;16(12):1087–1048.

Crossen MC, Polinder S, Lingma HF, E et al. Variation in structure and process of care in traumatic brain injury: provider profiles of European neurotrauma centers participating in the CENTER-TBI Study. PLoS One 2016;11(8):e0161367.

Sprung CL, Maa J, Baras M, E et al. The importance of religious affiliation and culture on end-of-life decisions in European intensive care units. Intensive Care Med 2007;33(10):1732–9.

Sprung CL, Cohen SI, Sjovestad P, E et al. End-of-life practices in European intensive care units: the Ethics Study. JAMA 2003;290(6):790–7.

Buloh HH, Sprung CL, Baras M, E et al. Are religion and religiosity important to end-of-life decisions and patient autonomy in the ICU? The Ethicot study. Intensive Care Med 2007;33(10):1732–9.

Sprung CL, Cohen SI, Sjovestad P, E et al. End-of-life practices in European intensive care units: the Ethics Study. JAMA 2003;290(6):790–7.

Buloh HH, Sprung CL, Baras M, E et al. Are religion and religiosity important to end-of-life decisions and patient autonomy in the ICU? The Ethicot study. Intensive Care Med 2007;33(10):1732–9.

Maas AJ, Menon DK, Adelson PD, E et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol 2017;16(12):1087–1048.

Crossen MC, Polinder S, Lingma HF, E et al. Variation in structure and process of care in traumatic brain injury: provider profiles of European neurotrauma centers participating in the CENTER-TBI Study. PLoS One 2016;11(8):e0161367.

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(4):1163–7.

Ferrand E, Robert R, Ingrand P, Lemaire F, French LG. Withholding and withdrawal of life support in intensive care units in France: a prospective survey. French LATEMBEA Group. Lancet 2001;357(9249):9–14.

Esteban A, Gordo F, Solsona JF, E et al. Withdrawing and withholding life support in the intensive care unit: a Spanish prospective multi-centre observational study. Intensive Care Med 2001;27(1):174–9.

Keenan SP, Buske KD, Chen LM, E et al. Withdrawing and withholding of life support in the intensive care unit: a comparison of teaching and community hospitals. The Southwestern Ontario Critical Care Research Network. Crit Care Med 1998;26(2):245–51.

Keenan SP, Buske KD, Chen LM, E et al. A retrospective review of a large cohort of patients undergoing the process of withdrawing or withholding of life support. Crit Care Med 1997;25(8):1324–31.

Ouanes I, Stambouli N, Dachraoui F, E et al. Pattern of end-of-life decisions in two Tunisian intensive care units: the role of culture and intensivists’ training. Intensive Care Med 2012;38(4):710–7.

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(1):15–20.

Traug RD, Campbell ML, Curtis JR, E et al. Recommendations for end-of-life care in the intensive care unit: a consensus statement by the American College [corrected] of Critical Care Medicine. Crit Care Med 2008;36(3):953–63.

Souter MJ, Blissett PA, Blosser S, E et al. Recommendations for the Critical Care Management of Devastating Brain Injury: prognostication, psychosocial, and ethical management: a position statement for healthcare professionals from the Neurocritical care society. Neurocrit Care 2015;23(1):4–13.

Dowrow J, Delaney JW, Hawryluck L, Kenny L. Guidelines for the withdrawal of withdrawal sustaining measures. Intensive Care Medicine 2016;42(6):1003–17.

Kon AA, Davidson JE, Morrison W, Danis M, White DB. Shared Decision Making in ICUs: an American College of Critical Care Medicine and American Thoracic Society Policy Statement. Crit Care Med 2016;44(1):188–201.

Heyland DK, Cook DJ, Rockefeller GM, E et al. Decision-making in the ICU: perspectives of the substitute decision-maker. Intensive Care Med 2003;29(1):75–82.

Wendler D, Rz A. Systematic review: the effect on surrogates of making treatment decisions for others. Ann Intern Med 2011;154(5):336–46.

Smith AK, White DB, Arnold RM. Uncertainty over others? Intrinsic attributes of life-sustaining treatments are associated with physicians’ preferences. Med Care 1996;34(2):103–11.

Joynt GM, Lipman J, Hartog C, E et al. The Durban World Congress Ethics Round Table IV: health care professional end-of-life decision-making. J Crit Care 2015;30(2):224–30.

Steyerberg EW, Mushkudiani N, Peetel P, E et al. Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. PLoS Med 2006;3(8):e165 discussion e.

Collaborators MCT, Peetel P, Arango M, E et al. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008;336(7641):425–9.

Merton RK. The self-fulfilling prophecy. Antioch Rev 1948;8(2):193–210.
Izzy S, Compton R, Carandang R, Hall W, Muehlschlegel S. Self-fulfilling prophecies through withdrawal of care: do they exist in traumatic brain injury, too? Neurocrit Care 2013;19(3):347–63.

Guidet B, Hodgson E, Feldman C, et al. The Durban World Congress Ethics Round Table Conference Report: II. Withholding or withdrawing of treatment in elderly patients admitted to the intensive care unit. J Crit Care 2014;29(6):896–901.

Nessler N, Roquilly A, Lasocki S, et al. Patient factors and outcomes associated with the withdrawal or withholding of life-sustaining therapies in mechanically ventilated brain-injured patients: an observational multicentre study. Eur J Anaesthesiol 2018;35(7):511–8.

Payer L. Medicine & culture: varieties of treatment in the United States, England, West Germany, and France. 1st ed. New York: H Holt; 1988; 204.

Steinberg A, Sprung CL. The dying patient: new Israeli legislation. Intensive Care Med 2006;32(8):1234–7.

Long AC, Brumback LC, Curtis JR, et al. Agreement with consensus statements on end-of-life care: a description of variability at the level of the provider, hospital, and country. Crit Care Med 2019;47(10):1396–401.

Sprung CL, Truog RD, Curtis JR, et al. Seeking worldwide professional consensus on the principles of end-of-life care for the critically ill. The Consensus for Worldwide End-of-Life Practice for Patients in Intensive Care Units (WELPICUS) study. Am J Respir Crit Care Med 2014;190(8):855–66.