Journal of Critical Care 58 (2020) 78–88

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

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

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ARTICLE INFO

Keywords:
Traumatic brain injury
Withdrawing life-sustaining measures
Withholding treatment
End-of-life
Critical care

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.

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

Abbreviations: ICU, intensive care unit; EoL, end-of-life; TBI, traumatic brain injury; LSM, life-sustaining measures; CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CT, computed tomography; IQR, interquartile range; UK, United Kingdom; GCS, Glasgow Coma Scale; ICP, intracranial pressure; CER, Comparative effectiveness research.

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https://doi.org/10.1016/j.jcrc.2020.04.001

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 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 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 withholding/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 withhold/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?

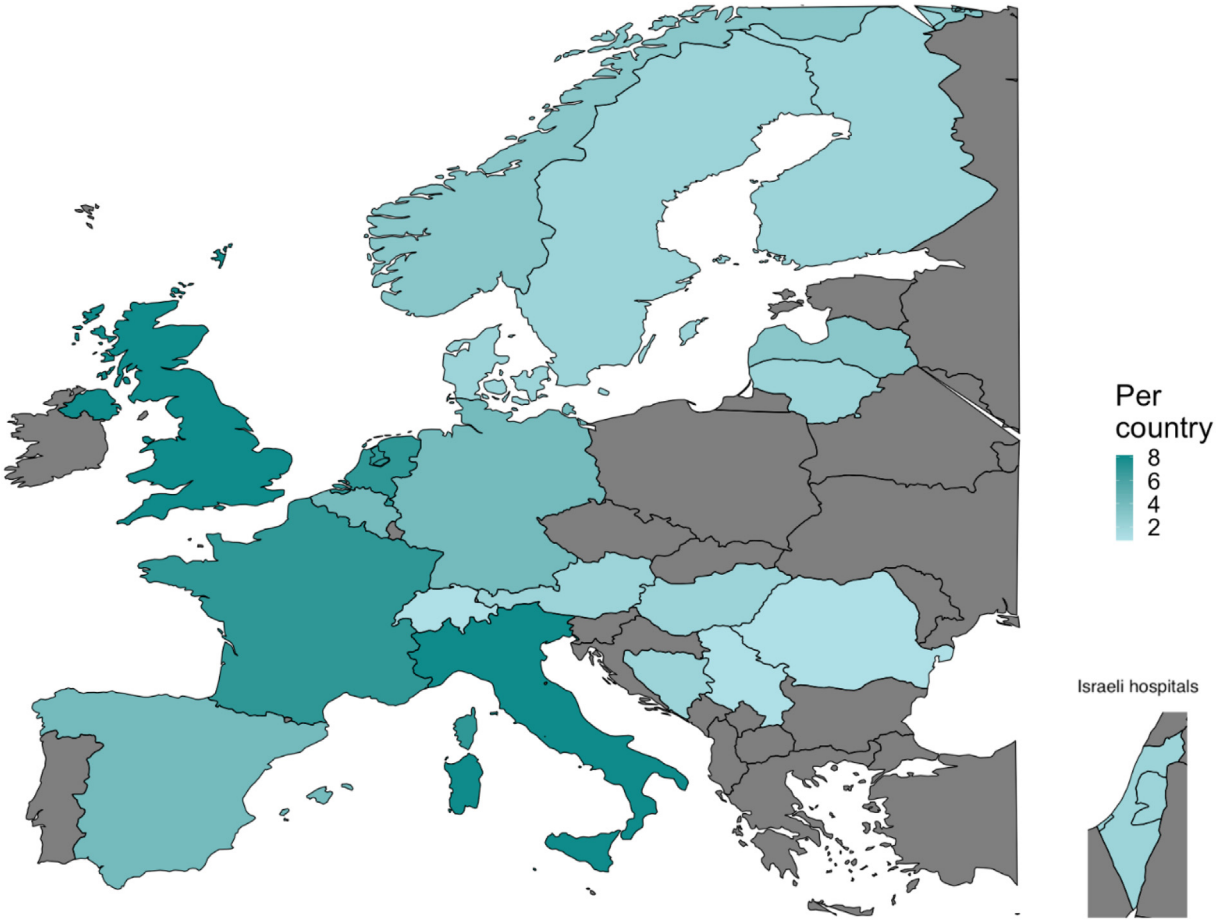

Fig. 1. Number of hospitals.

Table 1
Topics covered in this study, and the related questions to each topic.

Occurrence of withdrawing LSM
1. **Of all patients with severe neurological damage who die in the ICU, approximately, how many die after withdrawal of life-sustaining measures?**
Practices around the decision-making process
2. **How is the decision reached to withhold/withdraw life-sustaining measures (e.g. mechanical ventilation, vasoactive medication, renal replacement therapy, intravenous fluid administration)?**
3. **To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?**
4. **Does the age of the patient influence your decision making about withholding and withdrawing life sustaining treatment?**
Practices before withholding/withdrawing LSM
5. **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)?**
Timing and execution of withholding/withdrawing LSM
6. **If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patent, which life-sustaining measures do you stop?**
7. **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?**

Abbreviations: CT: Computed Tomography, GCS: Glasgow Coma Scale, ICP: Intracranial Pressure, ICU: Intensive Care Unit, LSM: Life-sustaining measures, TBI: Traumatic brain injury.

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/withdrawing 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

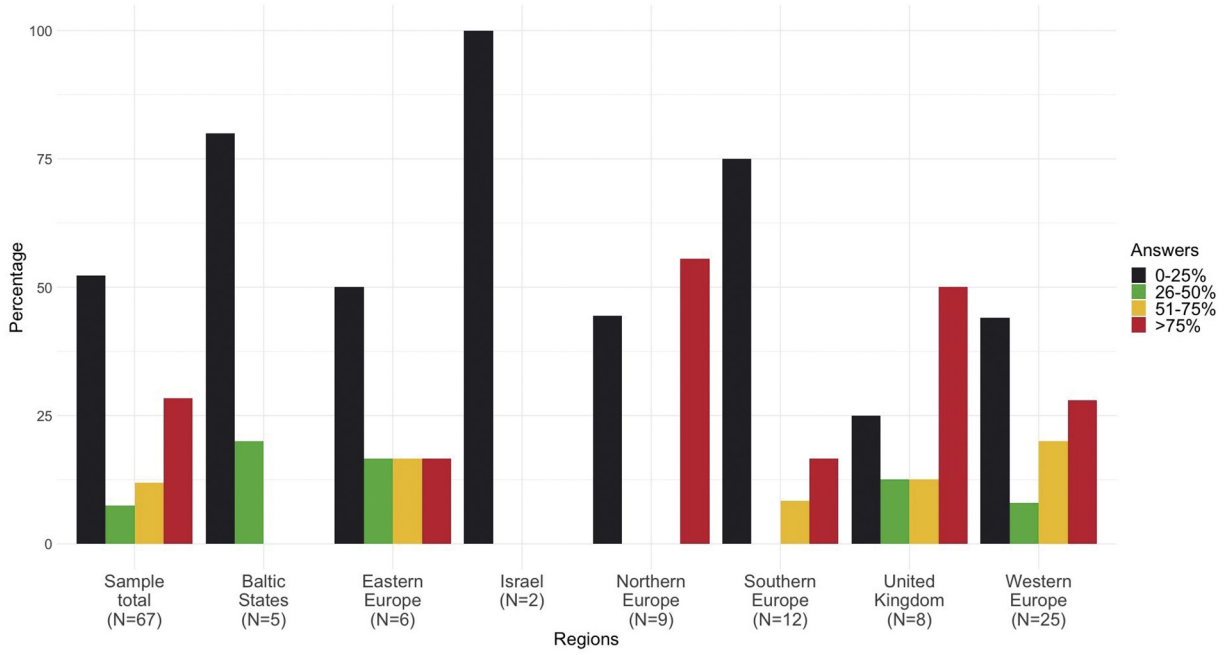

Fig. 2. Of all patients with severe neurological damage who die on the intensive care unit, approximately, how many die after withdrawal of life-sustaining measures?

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/

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

	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 multidisciplinarydiscussion (veto)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Other[a]	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	1(1%)	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.

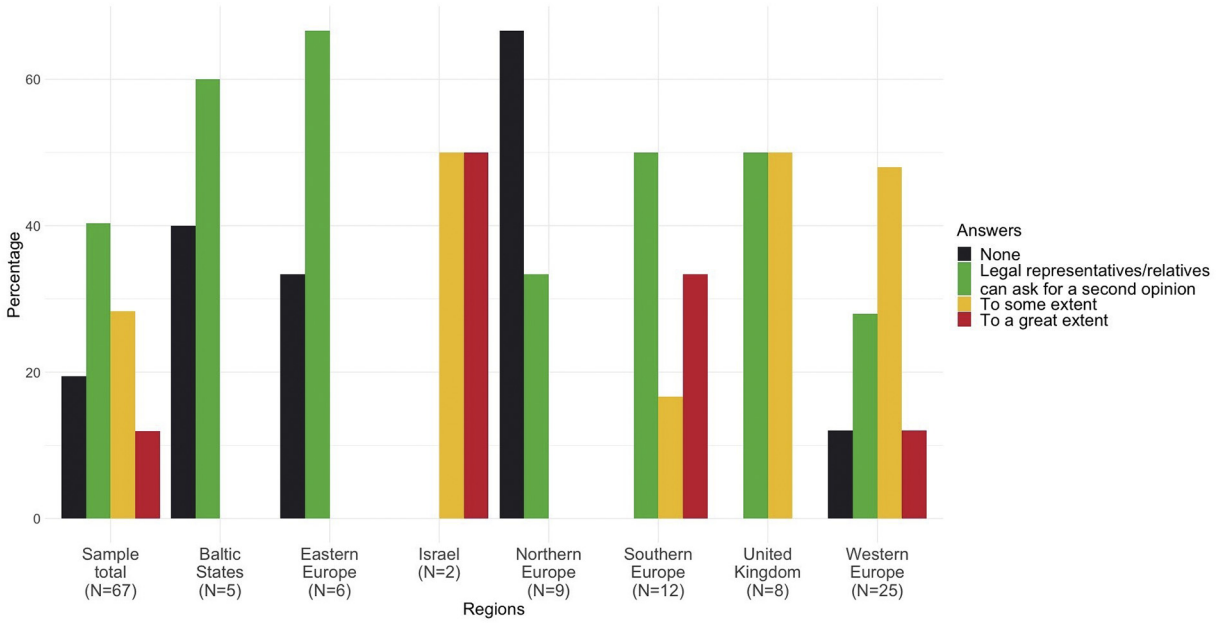

Fig. 3. To what extent do opinions of legal representatives/relatives play a role in decision-making about withdrawal/withholding of life-sustaining measures?

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.

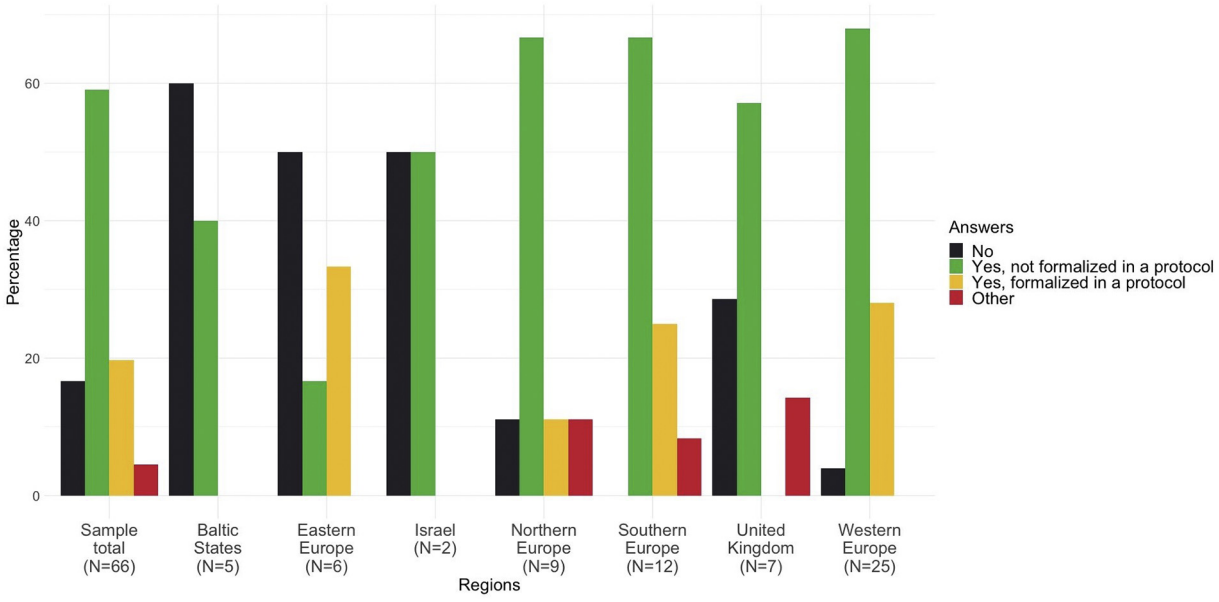

Fig. 4. If the decision is made to withdraw life-sustaining measures and before actual withdrawal, do you initiate palliative therapy in anticipation of distressing symptoms (such as pain, terminal restlessness, death rattle, stridor, dyspnoea)?

Table 3
Timing and execution of withholding/withdrawing life-sustaining measures (LSM).

	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)
If the decision is made to withdraw life-sustaining measures in a comatose severely injured TBI patient, which life-sustaining measures do you stop?								
We stop mechanical ventilation	42 (63%)	4 (80%)	1 (17%)	0 (0%)	8 (89%)	3 (25%)	8 (100%)	18 (72%)
We stop administration of vasoactive medication	62 (93%)	5 (100%)	4 (67%)	2 (100%)	8 (89%)	10 (83%)	8 (100%)	25 (100%)
We stop renal replacement therapy	54 (81%)	4 (80%)	1 (17%)	2 (100%)	8 (89%)	9 (75%)	7 (88%)	23 (92%)
We stop administration of intravenous fluids	23 (34%)	3 (60%)	1 (17%)	1 (50%)	4 (44%)	1 (8%)	2 (25%)	11 (44%)
We stop nasogastric feeding	39 (58%)	3 (60%)	2 (33%)	1 (50%)	8 (89%)	5 (42%)	3 (38%)	17 (68%)
Number of centers that indicated to stop all of the above life-sustaining measures	17 (25%)	3 (60%)	0 (0%)	0 (0%)	4 (44%)	0 (0%)	1 (13%)	9 (36%)
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? [a]								
24 h	7 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (25%)	0 (0%)	4 (16%)
2–4 days	13 (19%)	0 (0%)	0 (0%)	0 (0%)	2 (22%)	4 (33%)	1 (13%)	6 (24%)
4–7 days	18 (27%)	0 (0%)	1 (17%)	0 (0%)	4 (44%)	5 (42%)	2 (25%)	6 (24%)
>1 week	25 (37%)	0 (0%)	0 (0%)	1 (50%)	5 (56%)	7 (58%)	1 (13%)	11 (44%)
>2 weeks	30 (45%)	2 (40%)	0 (0%)	1 (50%)	5 (56%)	5 (42%)	2 (25%)	15 (60%)

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 my 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 respondents' 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 withdraw LSM may have a more legal basis. For example, in Israel withdrawing mechanical ventilation is against the law [47]. However, most 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 clearly 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 of specific EoL practices on clinically relevant outcomes using comparative effectiveness research. Such research should incorporate both mortality and long-term functional outcome to be able to interpret the outcome data. The complexity of some of the drivers of reported practice makes the case for mixed methods approaches to this problem, with a potentially substantive role for qualitative research methods. These strategies are important in order to inform preferred approaches to improve the quality of care for patients and relatives, and to prevent self-fulfilling prophecies.

Some variation between regions might always remain because of differences in patients, physician preferences and experience, and institutional factors. A recent study showed that this variation is primarily caused by differences between providers [48]. However, the WELPICUS study, published in 2014 [49] showed that theoretical consensus regarding EoL practices can be established. In order to put this theoretical consensus into practice, recommendations for specific EoL practices should be developed. The development of such recommendations can be facilitated through insight regarding important variations in practice, further discussion, and CER. Where possible, multidisciplinary and (inter)national groups should be involved in this development, as should patient representatives, as this may promote acceptance of recommendations on a broader scale.

5. Conclusion

We found variation regarding EoL practices in critically ill TBI patients, using questionnaires filled in by experts in European and Israeli neurotrauma centers. Specific issues that vary and need to be considered in discussions on EoL practices, CER, and recommendations, are the influence of legal representatives/relatives, the role of age in the decision-making process, what LSM to withdraw/withhold, and the timing of withdrawing/withholding LSM. Our results may give impetus to the design of (prospective) studies on EoL practices, exploring the role of self-fulfilling prophecies, further updating prediction models on prognosis and optimizing palliative care.

CENTER-TBI investigators and participants

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Financial/nonfinancial disclosure

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 National Institute for Health Research (UK). The funder had no role in the design of the study, the collection, analysis, and interpretation of data, or in writing the manuscript.

Authors' contributions

EvV analyzed the data and drafted the manuscript, and the supplementary tables and figures. All coauthors gave feedback on the manuscript. EJOK supervised the project. All coauthors gave feedback on (and approved) the final version of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2020.04.001.

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