Variation in blood transfusion and coagulation management in Traumatic Brain Injury at the Intensive Care Unit: A survey in 66 neurotrauma centers participating in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study.

Running title

Transfusion and coagulation management

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Variation in transfusion and coagulation management in European neurotrauma centers

Authors

Jilske A. Huijben, MD. 1, Mathieu van der Jagt, MD, PhD. 2, Maryse C. Cnossen, MSc. 1, Marieke J.H.A. Kruip, MD, PhD. 3, Iain K. Haitsma, MD. 4, Nino Stocchetti, MD. 5, Andrew I.R. Maas, MD, PhD. 6, David K. Menon, MD, PhD. 7, Ari Ercole, MD, PhD. 7, Marc Maegle, MD, PhD. 8, Simon J. Stanworth, MD. 9, Giuseppe Citerio, MD. 10, Suzanne Polinder, PhD. 1, Ewout W. Steyerberg, PhD.1, 11 and Hester F. Lingsma, PhD. 1 on behalf of the CENTER-TBI investigators.

Affiliations

1. Center for Medical Decision Sciences, Department of Public Health, Erasmus MC – University Medical Center Rotterdam, Rotterdam, the Netherlands
2. Department of Intensive Care (Office H-611) and Erasmus MC Stroke Center, Erasmus Medical Center Rotterdam, P.O. Box 2040, 3000 CA - University Medical Center Rotterdam, Rotterdam, the Netherlands
3. Department of Hematology, Erasmus MC - University Medical Center Rotterdam, Rotterdam, the Netherlands
4. Department of Neurosurgery, Erasmus MC, 's Gravendijkwal 230, Kamer H-703, 3015, CE - University Medical Center Rotterdam, Rotterdam, the Netherlands
5. Department of Pathophysiology and Transplants, University of Milan, Italy and Fondazione IRCCS Ca’ Granda – Ospedale Maggiore Policlinico, Department of Anesthesia and Critical Care, Neuroscience Intensive Care Unit, Milan, Italy

6. Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium

7. Division of Anaesthesia, University of Cambridge, Addenbrooke’s Hospital, Cambridge, United Kingdom

8. Department of Traumatology, Orthopedic Surgery and Sportsmedicine, Cologne-Merheim Medical Center (CMMC) and the Institute for Research in Operative Medicine (IFOM), University of Witten/Herdecke, Cologne, Germany

9. NHS Blood and Transplant/Oxford University Hospitals NHS Trust, John Radcliffe Hospital, Oxford, United Kingdom

10. School of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy; Neurointensive care, San Gerardo Hospital, ASST-Monza, Monza, Italy

11. Department of Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, the Netherlands

Corresponding author

Jilske Huijben, MD

Full mailing address: P.O. Box 2040, 3000 CA Rotterdam, The Netherlands, internal postal address Na-2223

Contact information: Email: j.a.huijben@erasmusmc.nl, Telephone: 0031 10 703 84 53, Fax: 0031 107038475
Coauthors

Dr Mathieu van der Jagt

Full mailing address: Department Intensive Care, Erasmus MC, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands

Contact information (telephone, fax, and e-mail address): Email: m.vanderjagt@erasmusmc.nl, Telephone: +0031 010 703 0478

Maryse C. Cnossen, MSc

Full mailing address: P.O. Box 2040, 3000 CA Rotterdam, The Netherlands, internal postal address Na-2217

Contact information (telephone, fax, and e-mail address): Email m.c.cnossen@erasmusmc.nl, Telephone +31 10 703 89 94, Fax: 0031 107038475

Dr. Marieke J.H.A. Kruip

Full mailing address: Postbus 2040, 3000 CA Rotterdam, intern postal address Na-823, The Netherlands

Contact information (telephone, fax, and e-mail address): E-mail m.kruip@erasmusmc.nl | Telephone 010 703 31 23

Dr Iain K. Haitsma

Full mailing address: Department Neurochirurgie P.O. Box 2040, 3000 CA Rotterdam, The Netherlands

Contact information (telephone, fax, and e-mail address): Email: i.haitsma@erasmusmc.nl, Telephone: 00316-22 54 51 85

Prof Nino Stocchetti

Full mailing address: Department of physiopathology and transplant, Milan University, Neuro ICU
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.
Dr Simon Stanworth

Full mailing address: Headley Way, Headington, Oxford OX3 9DU John Radcliffe Hospital
United Kingdom

Contact information (telephone, fax, and e-mail address): Email: simon.stanworth@nhsbt.nhs.uk, Telephone: +44 (0)1865, Fax: +44 (0)1865

Dr Giuseppe Citerio

Full mailing address: Dipartimento di Medicina Perioperatoria e Terapie Intensive, Via Pergolesi 33

P.IVA e C.F.: 09314290967 H San Gerardo - Monza

Contact information (telephone, fax, and e-mail address): Email: giuseppe.citerio@unimib.it, Telephone: +390392334316, Fax +390392334340

Dr Suzanne Polinder

Full mailing address: P.O. Box 2040, 3000 CA Rotterdam, The Netherlands

Contact information (telephone, fax, and e-mail address): Email: s.polinder@erasmusmc.nl, Telephone +31 10 704 42 69 or +31 6 26 46 73 38

Prof Ewout W. Steyerberg

Full mailing address: Department of Medical Statistics LUMC PO Box 9600 2300 RC Leiden
The Netherlands

Contact information (telephone, fax, and e-mail address): Email: e.w.steyerberg@lumc.nl or E.Steyerberg@ErasmusMC.nl, Telephone: 31 71 5269700

Dr Hester F. Lingsma

Full mailing address: P.O. Box 2040, 3000 CA Rotterdam, The Netherlands

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Abstract

Our aim was to describe current approaches and to quantify variability between European intensive care units (ICUs) in patients with TBI. Therefore, we conducted a provider profiling survey as part of the ‘Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury’ (CENTER-TBI) study. The ICU Questionnaire was sent to 68 centers from 20 countries across Europe and Israel. For this study, we used ICU questions focused on 1) hemoglobin target level (Hb-TL), 2) coagulation management, and 3) deep venous thromboembolism (DVT) prophylaxis. Seventy-eight participants, mostly intensivists and neurosurgeons of 66 centers completed the ICU questionnaire. For ICU-patients, half of the centers (N=34; 52%) had a defined Hb-TL in their protocol. For patients with TBI, 26 centers (41%) indicated a Hb-TL between 70 and 90 g/l and 38 centers (59%) above 90 g/l. To treat trauma related hemostatic abnormalities the use of fresh frozen plasma (N=48; 73%) or platelets (N=34; 52%) was most often reported, followed by the supplementation of vitamin K (N=26; 39%). Most centers reported using DVT prophylaxis with anticoagulants frequently or always (N=62; 94%). In the absence of hemorrhagic brain lesions, 14 centers (21%) delayed DVT prophylaxis until 72 hours after trauma. If hemorrhagic brain lesions were present, the number of centers delaying DVT prophylaxis for 72 hours increased to 29 (46%). Overall, a lack of consensus exists between European ICUs on blood transfusion and coagulation management. The results provide a baseline for the CENTER-TBI study and the large between-center variation indicates multiple opportunities for comparative effectiveness research.

Keywords: intensive care unit; traumatic brain injury; coagulopathy; transfusion; Europe
Introduction

The management of hemorrhage and disordered coagulation is a common and critically important challenge in trauma patients. This is particularly the case for patients with severe traumatic brain injury (TBI) where physicians have to balance the risks of progressive hemorrhage in the brain against secondary thrombotic complications including deep venous thrombosis (DVT). Many controversies continue to exist regarding the appropriate management for optimizing blood and coagulation status.

Transfusion thresholds for anaemia are a particularly controversial area in TBI. According to the guidelines 1, 2, transfusion in general critically ill patients is recommended at a restrictive hemoglobin target level (Hb-TL) of 70 g/l rather than a liberal Hb-TL of 90 g/l or 100 g/l. Whether such target levels also apply to patients with TBI is unclear. 3, 4 Inappropriate use of blood products exposes patients to a number of systemic risks and may even lead to progressive hemorrhagic injury following TBI. 3 However, cerebral oxygenation may be improved with higher hemoglobin concentrations 5, 6 whereas restrictive transfusion thresholds may predispose to brain tissue hypoxia and may increase the risk of early mortality. 7 On the other hand, a recent large retrospective cohort study indicated that a restrictive blood transfusion policy was not associated with increased mortality and can be cost-effective in patients with TBI. 8 An additional challenge for the management of both blood and coagulation status is the presence of coagulopathy. 9 Both pro- and anticoagulatory abnormalities can be observed after TBI in around one out of three patients. 10-12 Coagulopathy at admission is associated with increased mortality and poor neurological outcome. 12-14 Coagulopathy may result from defective clot initiation, poor clot formation or hyper fibrinolysis. Acidosis, hypothermia, coagulation factor consumption or dilution, and the more recently described acute coagulopathy of trauma-shock which results from widespread endothelial activation after hypoperfusion may contribute to coagulopathy. 15 Finally, patients with TBI are at increased risk of venous thromboembolism (VTE) (around 20%) 16 compared with general ICU patients (around 6-8%). 17 Here, the balance between the prevention of VTE and the risk of (progressive) hemorrhage of the brain depends largely on the timing of thromboprophylaxis with anticoagulants. However, current Brain Trauma Foundation guidelines do not make clear recommendations on coagulation management. 18
In summary, no definitive evidence exists to guide physicians in determining the transfusion and coagulation management in patients with (severe) TBI. This likely lead to variations in management. Our aim was to describe and quantify variability in European ICUs for blood transfusion and coagulation management in patients with TBI, using a survey among European neurotrauma centers participating in the Collaborative European Neurotrauma Effectiveness Research in TBI (CENTER-TBI) study. 

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Material and Methods

Participating centers

This study is part of the prospective, longitudinal ‘Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury’ (CENTER-TBI) study in 68 centers from 20 countries across Europe and Israel. The CENTER-TBI investigators and participants are listed in Supplemental Data 1. In 2014, before the start of inclusion of patients, the principle investigators of each center were asked to complete a set of questionnaires on structure and process of care: ‘the Provider Profiling Questionnaires’. The questionnaires were about TBI management irrespective of systemic injuries. One of these questionnaires concerned ICU management.

Provider Profiling Questionnaire

The provider profiling questionnaire was developed in a systematic manner. The literature (including guidelines and available surveys) was reviewed and experts of various disciplines (neurosurgeons, (neuro)intensivists, neurologists, emergency department physicians, rehabilitation physicians, medical ethicists, health care economists and epidemiologists) were consulted throughout the different phases in the development process. Preliminary questionnaires were pilot-tested in 16 of the participating centers for unexpected or missing values and ambiguity, and received feedback was incorporated. For more information about the development, administration and content of the total set of provider profiling questionnaires, see Cnossen et al., 2016. In this study, we focus on 10 questions (with additional sub questions) on hemoglobin target levels, trauma related coagulation management, and use and timing of thromboprophylaxis (Supplemental Data 2).

Hemoglobin target level and coagulation management

Participants were explicitly asked for their general policy rather than for individual treatment preferences. General policy was defined as ‘the way the large majority of patients (>75%) with a certain indication would be treated’. The ICU questionnaire

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Consisted mostly of multiple-choice questions and one open question; the Hb-TL in the protocol at the ICU for the general ICU population. For the hemoglobin unit conversion from mmol/L towards g/L we multiplied with the factor 1.6 and then rounded up to tens.

Statistical analysis

Descriptive statistics (frequencies and percentages) were used to describe the treatment policies reported by the participating centers. For some questions in which centers had to indicate how often a certain approach was taken by choosing ‘never’ (in 0-10% of cases), ‘rarely’ (in 10-30% of cases), ‘sometimes’ (in 30-70% of cases), ‘frequently’ (in 70-90% of cases) and ‘always’ (90-100% of cases), categories were combined (e.g. combining ‘always’ and ‘frequently’) because of low numbers in these categories.

To gain more insight into characteristics that determine treatment policies we divided centers in relatively high- and middle-income countries versus lower-income countries, and in countries from different geographic locations (North and West Europe versus South and East Europe and Israel). The designation into relatively lower-income countries was based on a 2007 report by the European Commission, and the designation into geographic location was based on the classification by the United Nations. Analyses were performed using the Statistical Package for Social Sciences (SPSS) version 21.

Results

Participating centers

Sixty-six centers of the 68 centers completed the ICU questionnaire (response rate=97%). The questionnaire was completed by intensivists (N=33; 50%), neurosurgeons (N=23; 35%), administrative staff (N=11; 17%), neurologists (N=5, 8%), anesthetists (N=5, 8%) and a trauma surgeon (N=1; 2%). Almost all the centers had an academic affiliation (N=60; 91%) and most centers were designated as a level I trauma center (N=44; 67%). Centers had a median of 33 (interquartile range 22-44) beds for general ICU patients and treated a

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Median of 92 (interquartile range: 52-160) patients with TBI, of all severities, annually. An extensive overview of all the center characteristics is described in a previous publication.

For the management of TBI at the ICU, most centers indicated to follow the 2007 Brain Trauma Foundation (BTF) guidelines (N=28; 42%), which were broadly based on BTF and/or national guidelines. Some centers indicated they did not have specific guidelines for management of TBI (N=11; 17%) or that they developed a guideline independently from available guidelines (N=2; 3%).

Hemoglobin target level

Half of the centers (N=34; 52%) reported to have hemoglobin target levels (Hb-TL) described in their protocol for general/non-TBI ICU patients. The reported Hb-TL varied (open question): 110 g/l (N=1; 3%), 100 g/L (N=8; 28%), 90 g/L (N=4; 14%), 80 g/L (N=9; 31%), 70 g/L (N=5; 18%), 80-100 g/L (N=1; 3%), and above 100 g/l (N=18; 28%). In non-neurological critically ill patients, 35 of the centers (56%) reported a Hb-TL between 70 and 80 g/l. However, twice as many centers (N=16; 25%) between 90 g/l and 100 g/l (N=20; 31%) and above 100 g/l (N=18; 28%).

Coagulation management

Transfusion with fresh frozen plasma was most often reported for correction of trauma related coagulopathy (N=48; 73%), followed by the use of platelets (N=34; 52%) or recombinant factor VIIa (N=3; 5%). One center reported to use Desmopressin in addition to Tranexamic Acid. (Figure 1)

Coagulopathy was most often managed with vitamin K (N=26; 39%), Fibrinogen (N=27; 41%), Prothrombin Complex Concentrate (N=17; 26%), Tranexamic acid (N=7; 11%), or Desmopressin (N=3; 5%).

Most centers indicated that they use deep venous thrombosis (DVT) prophylaxis with anticoagulants frequently (N=18; 27%), or always (N=14; 67%) in patients with TBI.

Most centers indicated that they use deep venous thrombosis (DVT) prophylaxis in the absence of hemorrhagic brain lesions. However, twice as many centers (N=16; 25%) between 90 g/l and 100 g/l (N=20; 31%) and above 100 g/l (N=18; 28%).

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that number of centers (N=29; 46%) indicated to wait 72 hours after trauma in the presence of hemorrhagic brain lesions. Low molecular weight heparin was most commonly indicated as the prophylactic drug of choice (N=54; 82%), followed by subcutaneous unfractioned heparin (N=7; 11%) and intravenous heparin (N=1; 2%). (Table 2)

Most centers indicated that they would always test a coagulation panel prior to the insertion of a parenchymal sensor (N=45; 69%) or a ventricular catheter (N=46; 71%). The reported minimum platelet count for the insertion of a ventricular catheter was variable: >100 x10^9/L (N=30; 46%), >80 x10^9/L (N=9; 14%) or >50 x10^9/L (N=9; 14%). In most of the remaining centers the minimum platelet count depended on the surgeon (N=13; 20%). Also, the reported minimum International Normalized Ratio (INR) considered safe for placement of a ventricular catheter was variable: <1.4 (N=21; 33%), <1.3 (N=17; 26%) or <1.2 (N=8; 12%). Again, in most of the remaining centers the minimum INR was indicated to depend on surgeon’s individual preferences (N=15; 23%). There were no centers that answered ‘never’ on all questions. (Table 3)

Twenty-nine centers indicated identical policies for coagulation management (always using DVT prophylaxis, and always obtaining a coagulation panel prior to insertion of a parenchymal or ventricular catheter). The majority of these centers are located in South and East Europe and Israel (N=13, 56%) versus (N=16, 37%) in North and West Europe and the majority are located in high income countries (N=26, 47%), versus (N=3, 27%) in lower income countries.

Discussion

This study shows large between-center variation in blood transfusion and coagulation-directed policies in critically ill patients with TBI. More centers indicated a restrictive Hb-TL (between 70 g/l and 80 g/L) in general ICU patients compared to patients with TBI. Reported coagulation management was variable regarding timing of deep venous

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Thrombosis (DVT) prophylaxis with anticoagulants, minimum platelet count and INR values prior to ICP probe insertion, and correction of trauma-related coagulopathy.

The large between-center differences are likely in part explained by a lack of evidence on optimal management of patients with TBI. A majority of centers in our study reported to adhere to the 2007 Brain Trauma Foundation (BTF) guidelines for the treatment of patients with TBI, but this guideline does not provide specific recommendations on red blood cell transfusion or coagulopathy management. Equally, some trauma guidelines have stated policies on blood transfusion and coagulation in trauma patients of which some pertain to patients with TBI, but recommendations are still scarce.1, 2, 23 A recent update of the Cochrane Review of all Red Cell Transfusion trials reported on 12587 patients identified in 31 randomized trials and suggested that a restrictive rather than liberal transfusion practice improves outcomes but noted the data was very limited for neurocritical care.24 Regarding patients with TBI, several trials have been conducted on blood transfusion guidance.25, 26, and the reversal of coagulopathy has been associated with significantly less time with fever, higher cost-effectiveness and a lower risk of mortality compared with a liberal Hb-TL. Another explanation for the variation in management would be the between-center variation in the content of available protocols. E.g., we found that even between centers that do have a protocol on red blood cell transfusion policy, the reported Hb-TL still varied substantially. Overall in TBI patients admitted to the intensive care,27, 28 there was a trend toward a more restrictive policy. However, in the recent large retrospective single-center study in TBI patients conducted by Croa et al.,29 the reported Hb-TL was still associated with significantly less time with fever, higher cost-effectiveness and a lower risk of mortality compared with a liberal Hb-TL.

In addition, coagulation management in TBI is further complicated by the recent introduction of newer anticoagulants, such as direct thrombin inhibitors (dabigatran, argatroban), which might even become more complex. Concurrent use of anticoagulant and antplatelet medications is a growing concern. Prior warfarin treatment for example is associated with increased risk of poor outcome.29 In addition, coagulation treatment for example is associated with an increased risk of poor outcome.30
For DVT prophylaxis the BTF guidelines do provide a recommendation, which was formulated quite broadly: DVT prophylaxis with anticoagulants can be started if the brain injury is stable and the benefit is considered to outweigh the risk of increased intracranial hemorrhage. Recommendations on the preferred agent, dose, or timing are lacking. In our study only 65% of centers indicated that they always would implement DVT prophylaxis. A review including 15 studies and 4,491 patients on DVT occurrence in TBI published in 2015 showed that DVT incidence is significantly increased (18% versus approximately 2%) when pharmaceutical prophylaxis is not given in the first 8 days. For the timing issue in DVT prophylaxis a novel theoretical prophylaxis protocol, ‘the Parkland Protocol’ has been recently described. The protocol takes into account the likelihood of natural progression of brain hemorrhage and in that way determines the timing of anticoagulation. The risk classification is based on the stability of the brain hemorrhage at a computed tomography (CT) scan, the modified Berne Norwood criteria (subdural hematoma >8 mm, epidural hematoma >8 mm, contusion or intraventricular hemorrhage >2 cm, multiple contusions per lobe, subarachnoid hemorrhage with abnormal CT angiography), and the presence of an ICP monitor or craniectomy. A randomized controlled trial (RCT) including 62 low risk patients showed the safety of this protocol for this group: no progression of brain hemorrhage with the use of low molecular weight heparin at 24 hours post injury and one DVT with the use of placebo at 24 hours post injury. However, more evidence is needed before this protocol can be widely accepted for the guidelines.

The large between center-variation we found is in line with previous studies. For critically ill trauma patients, several surveys have been conducted to study the management of trauma related hemorrhage and coagulopathy. These studies also found large differences in clinical practices, even among level 1 trauma centers, for example in the use of viscoelastic testing. In the survey of Hamada et al. the reported Hb-TLs in critically ill trauma patients were compared with patients with TBI, and were significantly higher in patients with TBI, like in our study. In addition, two previous surveys were conducted that report the percentage respondents that chose specific Hb-TLs and the rationale for blood transfusion in patients with TBI (coagulation management was not assessed). In the study of Sena et al. a newly developed multiple-choice survey...
was completed by 312 physicians of the trauma surgery-, neurosurgery-, and ICU department of level I trauma centers in the United States. In the study of Badenes et al., a newly developed multiple-choice survey was used as well, but was completed by 868 respondents, mostly specialists in anesthesiology and intensive care, worldwide. In the study of Sena et al., 55% of respondents chose a restrictive policy of 70 g/l or less. Likewise, in the study of Badenes et al., 50% of respondents chose a low Hb-TL of 70 or 80 g/l, while in our study 16% chose a Hb-TL between 70 and 80 g/l. The difference could either be explained by a difference in patient population (severely injured patients with TBI in the study of Sena et al.), by a difference in answer options (we did not have an answer option below 70 g/l), or by a difference in policy between Europe and other continents.

Strengths of our study include the comprehensive development process of the questionnaires and the high response rate of 97%. Limitations include the survey-design, resulting in perceived practices rather than actual practices. Although we explicitly asked for general policy and data were anonymously collected, we cannot exclude differences between current findings and actual treatment in the participating centers. In addition, questions were aimed to assess general policy and contained no specific details on patient characteristics. This is not representative for clinical practice (possibly making the questions more difficult to answer). In addition, we could not make a distinction between pharmaceutical versus mechanical DVT prophylaxis. A further limitation comprises the representativeness of our sample. The majority of centers were Academic level I trauma centers with a special interest in neurotrauma. Findings are therefore not generalizable to non-specialized centers. In addition, differences between centers could represent differences in case-mix instead of true practice.

The practice variability we report supports that evidence on optimal treatment approaches is needed. Such evidence can potentially be obtained in a non-randomized design by comparing outcomes between centers with different treatment policies. Such a Comparative Effectiveness Research approach exploits the existing between-center variation. Data on real time patient management and clinically relevant outcomes in the CENTER-TBI study are now being collected. Future research on blood transfusion and coagulation management in patients with TBI could lead to prevention of progressive brain hemorrhage and secondary problems like coagulopathy and VTE. For now, the optimal
transfusion strategies to correct coagulopathy. It is important to note that there is no consensus on the optimal strategy for managing coagulopathy, and the choice of strategy may depend on various factors such as the type and severity of injury, patient characteristics, and availability of resources.

In conclusion, we showed substantial variation in blood and coagulation management in patients with TBI at the ICUs in Europe and Israel participating in the CENTER-TBI study. This variation may be largely attributable to the lack of guidelines and high-quality evidence on these topics. The large practice variation provides an opportunity to study the effectiveness of different policies in comparative effectiveness research.

Conclusions

In conclusion, we showed substantial variation in blood and coagulation management in patients with TBI at the ICUs in Europe and Israel participating in the CENTER-TBI study. This variation may be largely attributable to the lack of guidelines and high-quality evidence on these topics. The large practice variation provides an opportunity to study the effectiveness of different policies in comparative effectiveness research.
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Author disclosure statement

No competing financial interests exist.

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Table 1. Red blood cell transfusion policy

<table>
<thead>
<tr>
<th>Items</th>
<th>Number completed</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol at the ICU</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Protocol questionnaire</td>
<td>34</td>
<td>52% (28%)</td>
</tr>
<tr>
<td>Presence of a protocol with a Hb-TL</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Absence of a protocol with a Hb-TL</td>
<td>14</td>
<td>48% (28%)</td>
</tr>
</tbody>
</table>

| Transfusion at Hb-TL in protocol (open question) | 29 |      |
| >100 g/L | 18 | 63 (31%) |
| Between 90 g/L and 100 g/L | 20 | 63 (33%) |
| Between 70 g/L and 80 g/L | 16 | 63 (56%) |

| Transfusion at Hb-TL in protocol (closed question) | 29 |      |
| >100 g/L | 18 | 63 (31%) |
| Between 90 g/L and 100 g/L | 20 | 63 (33%) |
| Between 70 g/L and 80 g/L | 16 | 63 (56%) |

| Transfusion at Hb-TL | 63 |      |
| >100 g/L | 18 | 63 (28%) |
| Between 90 g/L and 100 g/L | 20 | 63 (31%) |
| Between 70 g/L and 80 g/L | 16 | 63 (33%) |

Note: Items are described in the table with different transfusion thresholds for red blood cell (RBC) transfusion in patients with traumatic brain injury (TBI) and non-neurological critically ill patients. The table provides a summary of the transfusion protocols and the number of patients who fall into each category. The percentages indicate the proportion of patients within each category.
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Frequencies and percentage of centers with corresponding answers, ICU: Intensive Care Unit, Hb-TL: hemoglobin target levels, TBI: traumatic brain injury, g/L: grams per liter

a) General policy: the way the large majority of patients (>75%) with a certain indication would be treated at the intensive care
b) Policy in the acute phase
Table 2. Coagulation policies, deep venous thrombosis *

<table>
<thead>
<tr>
<th>Items</th>
<th>Number completed</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of DVT prophylaxis</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Never (0-10%)</td>
<td>1</td>
<td>1</td>
<td>(2%)</td>
</tr>
<tr>
<td>- Rarely (10-30%)</td>
<td>0</td>
<td>0</td>
<td>(0%)</td>
</tr>
<tr>
<td>- Sometimes (30-70%)</td>
<td>3</td>
<td>3</td>
<td>(4%)</td>
</tr>
<tr>
<td>- Frequently (70-90%)</td>
<td>18</td>
<td>18</td>
<td>(27%)</td>
</tr>
<tr>
<td>- Always (90-100%)</td>
<td>44</td>
<td>44</td>
<td>(67%)</td>
</tr>
<tr>
<td>Start in the absence of hemorrhagic lesions</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- &lt; 24 hours</td>
<td>24</td>
<td>24</td>
<td>(37%)</td>
</tr>
<tr>
<td>- 24-72 hours</td>
<td>14</td>
<td>14</td>
<td>(21%)</td>
</tr>
<tr>
<td>- &gt; 72 hours</td>
<td>1</td>
<td>1</td>
<td>(2%)</td>
</tr>
<tr>
<td>- Never</td>
<td>26</td>
<td>26</td>
<td>(40%)</td>
</tr>
<tr>
<td>Start in the presence of hemorrhagic lesions</td>
<td>5</td>
<td></td>
<td>(8%)</td>
</tr>
<tr>
<td>- &lt; 24 hours</td>
<td>29</td>
<td>29</td>
<td>(46%)</td>
</tr>
<tr>
<td>- 24-72 hours</td>
<td>4</td>
<td>4</td>
<td>(6%)</td>
</tr>
<tr>
<td>- &gt; 72 hours</td>
<td>64</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>- Never</td>
<td>10</td>
<td>10</td>
<td>(16%)</td>
</tr>
<tr>
<td>Start after intracranial surgery</td>
<td>31</td>
<td></td>
<td>(48%)</td>
</tr>
<tr>
<td>- &lt; 24 hours</td>
<td>21</td>
<td>21</td>
<td>(33%)</td>
</tr>
<tr>
<td>- 24-72 hours</td>
<td>2</td>
<td>2</td>
<td>(3%)</td>
</tr>
<tr>
<td>- &gt; 72 hours</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Never</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacological DVT prophylaxis</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Subcutaneous unfractioned heparin</td>
<td>7</td>
<td>7</td>
<td>(11%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td>(2%)</td>
</tr>
</tbody>
</table>
### Intravenous Heparin vs. Low-Molecular Weight Heparin

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Heparin</td>
<td>54</td>
<td>82%</td>
</tr>
<tr>
<td>Low-Molecular Weight Heparin</td>
<td>10</td>
<td>18%</td>
</tr>
</tbody>
</table>

**General Policy:** The way the large majority of patients (>75%) with a certain indication would be treated at the intensive care unit.

**DVT:** deep venous thrombosis

**General policy:** the way the large majority of patients (>75%) with a certain indication would be treated at the intensive care unit.
Table 3. Coagulation policies, ICP monitoring a

<table>
<thead>
<tr>
<th>Items</th>
<th>Number</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checks prior to insertion of parenchymal sensor for ICP monitoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation panel</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Never (0-10%)</td>
<td>4</td>
<td>(6%)</td>
<td></td>
</tr>
<tr>
<td>- Rarely (10-30%)</td>
<td>2</td>
<td>(3%)</td>
<td></td>
</tr>
<tr>
<td>- Sometimes (30-70%)</td>
<td>5</td>
<td>(8%)</td>
<td></td>
</tr>
<tr>
<td>- Frequently (70-90%)</td>
<td>5</td>
<td>(8%)</td>
<td></td>
</tr>
<tr>
<td>- Always (90-100%)</td>
<td>45</td>
<td>(69%)</td>
<td></td>
</tr>
<tr>
<td>- Not available b</td>
<td>4</td>
<td>(6%)</td>
<td></td>
</tr>
<tr>
<td>Checks prior to insertion ventricular catheter for ICP monitoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation panel</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Never (0-10%)</td>
<td>3</td>
<td>(4%)</td>
<td></td>
</tr>
<tr>
<td>- Rarely (10-30%)</td>
<td>2</td>
<td>(3%)</td>
<td></td>
</tr>
<tr>
<td>- Sometimes (30-70%)</td>
<td>5</td>
<td>(8%)</td>
<td></td>
</tr>
<tr>
<td>- Frequently (70-90%)</td>
<td>4</td>
<td>(6%)</td>
<td></td>
</tr>
<tr>
<td>- Always (90-100%)</td>
<td>46</td>
<td>(71%)</td>
<td></td>
</tr>
<tr>
<td>- Not available b</td>
<td>5</td>
<td>(8%)</td>
<td></td>
</tr>
<tr>
<td>Minimum platelet count</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- &gt;150 x10⁹/L</td>
<td>1</td>
<td>(2%)</td>
<td></td>
</tr>
<tr>
<td>- &gt;100 x10⁹/L</td>
<td>30</td>
<td>(46%)</td>
<td></td>
</tr>
<tr>
<td>- &gt; 80 x10⁹/L</td>
<td>9</td>
<td>(14%)</td>
<td></td>
</tr>
<tr>
<td>- &gt; 50 x10⁹/L</td>
<td>9</td>
<td>(14%)</td>
<td></td>
</tr>
<tr>
<td>- Depending on the surgeon</td>
<td>13</td>
<td>(20%)</td>
<td></td>
</tr>
<tr>
<td>- No minimum</td>
<td>0</td>
<td>(0%)</td>
<td></td>
</tr>
<tr>
<td>- Other</td>
<td>3</td>
<td>(4%)</td>
<td></td>
</tr>
<tr>
<td>Minimum INR</td>
<td>65</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Frequencies and percentage of centers with corresponding answers

DVT: deep venous thrombosis, ICP: intracranial pressure, INR: International Normalized Ratio, L: liter

<table>
<thead>
<tr>
<th>Depending on the surgeon</th>
<th>Other</th>
<th>&lt;1.2</th>
<th>&lt;1.3</th>
<th>&lt;1.4</th>
<th>No minimum</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (0%)</td>
<td>15 (23%)</td>
<td>8 (12%)</td>
<td>17 (26%)</td>
<td>4 (6%)</td>
<td>21 (33%)</td>
<td>29</td>
</tr>
</tbody>
</table>

General policy: the way the large majority of patients >75% with a certain indication would be treated at the intensive care by Centers that did not have this technique.

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Figure 1. Trauma related coagulopathy treatment

Bars represent the percentage of centers that indicated to use this treatment as general policy (the way the large majority of patients >75% with a certain indication would be treated). In order of always and frequently summed. Always: in 90-100% of cases; Frequently: in 70-90% of cases; Sometimes: in 30-70% of cases; Rarely: in 10-30% of cases; Never: in 0-10% of cases.
Supplemental data 1. Center-TBI investigators and participants

Adams Hadie 1, Alessandro Masala 2, Allanson Judith 3, Amrein Krisztina 4,
Andaluz Norberto 5, Andelic Nada 6, Andrea Nanni 2, Andreassen Lasse 7, Anke Audny 8,
Antoni Anna 9, Ardon Hilko 10, Audibert Gérard 11, Auslands Kaspars 12, Azouvi Philippe 13,
Baciu Camelia 14, Bacon Andrew 15, Badenes Rafael 16, Baglin Trevor 17, Bartels Ronald 18,
Barzó Pál 19, Bauerfeind Ursula 20, Beer Ronny 21, Belda Francisco Javier 16,
Bellander Bo-Michael 22, Belli Antonio 23, Bellier Rémy 24, Benali Habib 25, Benard Thierry 24,
Berardino Maurizio 26, Beretta Luigi 27, Beynon Christopher 28, Bilotta Federico 16,
Binder Harald 9, Biqiri Erta 14, Blaabjerg Morten 29, Borgen Lund Stine 30, Bouzat Pierre 31,
Bragge Peter 32, Brazinova Alexandra 33, Brehar Felix 34, Brorsson Camilla 35, Buki Andras 36,
Bullinger Monika 37, Buková Veronika 33, Calappi Emiliana 38, Cameron Peter 39,
Carbayo Lozano Guillermo 40, Carise Elsa 24, Carpenter K. 41, Castaño-León Ana M. 42,
Causin Francesco 43, Chevallard Giorgio 14, Chiergato Arturo 14, Citerio Giuseppe 44,45,
Chosen Maryse 46, Coburn Mark Coburn 47, Coles Jonathan 48, Cooper Jamie D. 49,
Correa Marta 50, Covic Amra 51, Curry Nicola 52, Czeiter Endre 53, Czosnyka Marek 54,
Dahyot-Fizelier Claire 24, Damas François 55, Damas Pierre 56, Dawes Helen 57,
De Keyser Véronique 58, Della Corte Francesco 59, Depreitere Bart 60, Ding Shenghao 61,
Dippel Diederik 62, Dizdarevic Kemal 63, Dulière Guy-Loup 55, Dzeko Adelaida 64,
Eapen George 15, Engemann Heiko 51, Ercole Ari 65, Esser Patrick 57, Ezer Erzsébet 66,
Fabricius Martin 67, Feigin Valery L. 68, Feng Junfeng 61, Foks Kelly 62, Fossi Francesca 14,
Francony Gilles 31, Frantzén Janek 69, Freo Ulderico 70, Frisvold Shirin 71, Furmanov Alex 72,
Gagliardo Pablo 73, Galanado Damien 25, Gao Guoyi 74, Geleijns Karin 41,
Ghysens Alexandre 75, Giraud Benoit 24, Glocker Ben 76, Gomez Pedro A. 42,
Grossi Francesca 59, Gruen Russell L. 77, Gupta Deepak 78, Haagsma Juanita A. 46,
Hadzic Ermin 64, Haitsma Iain L. 79, Hartings Jed A. 80, Helbok Raimund 21, Helseth Eirik 81,
Hertle Daniel 28, Hill Sean 82, Hoedemaekers Astrid 83, Hoefer Stefan 51,
Hutchinson Peter J. 1, Håberg Asta Kristine 84, Jacobs Bram 85, Janciak Ivan 86,
Janssens Koen 58, Ji Motor 74, Jones Kelly 87, Kalala Jean-Pierre 88,
Kamitsas Konstantinos 76, Karan Mladen 89, Karau Jana 20, Katila Ari 69, Kaukonen Maija 90,
Keeling David 52, Kerforne Thomas 24, Ketharanathan Naomi 41, Kettunen Johannes 91,


1 Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke’s Hospital & University of Cambridge, Cambridge, UK

2 Department of Anesthesia & Intensive Care, M. Bufalini Hospital, Cesena, Italy

3 Department of Clinical Neurosciences, Addenbrooke’s Hospital & University of Cambridge, Cambridge, UK

4 János Szentágothai Research Centre, University of Pécs, Pécs, Hungary

5 University of Cincinnati, Cincinnati, Ohio, United States

6 Division of Surgery and Clinical Neuroscience, Department of Physical Medicine and Rehabilitation, Oslo University Hospital and University of Oslo, Oslo, Norway

7 Department of Neurosurgery, University Hospital Northern Norway, Tromso, Norway

8 Department of Physical Medicine and Rehabilitation, University Hospital Northern Norway

9 Trauma Surgery, Medical University Vienna, Vienna, Austria

10 Department of Neurosurgery, Elisabeth-Tweesteden Ziekenhuis, Tilburg, the Netherlands

11 Department of Anesthesiology & Intensive Care, University Hospital Nancy, Nancy, France

12 Riga Eastern Clinical University Hospital, Riga, Latvia

13 Raymond Poincare hospital, Assistance Publique – Hopitaux de Paris, Paris, France

14 NeuroIntensive Care, Niguarda Hospital

15 NeuroIntensive Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

16 Department Anesthesiology and Surgical-Trauma Intensive Care, Hospital Clinic Universitari de Valencia, Spain

17 Cambridge University Hospitals, Cambridge, UK

18 Department of Neurosurgery, Radboud University Medical Center

19 Department of Neurosurgery, University of Szeged, Szeged, Hungary

20 Institute for Transfusion Medicine (ITM), Witten/Herdecke University, Cologne, Germany

21 Department of Neurocritical care, Innsbruck Medical University, Innsbruck, Austria
22 Department of Neurosurgery & Anesthesia & intensive care medicine, Karolinska University Hospital, Stockholm, Sweden

23 NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham, UK

24 Intensive care Unit, CHU Poitiers, Poitiers, France

25 Anesthesie-Réanimation, Assistance Publique – Hopitaux de Paris, Paris, France

26 Department of Anesthesia & ICU, AOU Città della Salute e della Scienza di Torino - Orthopedic and Trauma Center, Torino, Italy

27 Department of Anesthesiology & Intensive Care, S Raffaele University Hospital, Milan, Italy

28 Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany

29 Department of Neurology, Odense University Hospital, Odense, Denmark

30 Departments of Neuroscience and Nursing Science, Norwegian University of Science and Technology, Trondheim, Norway

31 Department of Anesthesiology & Intensive Care, University Hospital of Grenoble, Grenoble, France

32 BehaviourWorks Australia, Monash Sustainability Institute, Monash University, Victoria, Australia

33 Department of Public Health, Faculty of Health Sciences and Social Work, Trnava University, Trnava, Slovakia

34 Department of Neurosurgery, Bagdasar-Arseni Emergency Clinical Hospital, Bucharest, Romania

35 Department of Neurosurgery, Umea University Hospital, Umea, Sweden

36 Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program, Pecs, Hungary

37 Department of Medical Psychology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany

38 Neuro ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy

39 Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia

40 Department of Neurosurgery, Hospital of Cruces, Bilbao, Spain

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Intensive Care and Department of Pediatric Surgery, Erasmus Medical Center, Sophia Children’s Hospital, Rotterdam, The Netherlands

Department of Neurosurgery, Hospital Universitario 12 de Octubre, Madrid, Spain

Department of Neuroscience, Azienda Ospedaliera Università di Padova, Padova, Italy

NeuroIntensive Care, Azienda Ospedaliera San Gerardo di Monza, Monza, Italy

School of Medicine and Surgery, Università Milano Bicocca, Milano, Italy

Department of Public Health, Erasmus Medical Center-University Medical Center, Rotterdam, The Netherlands

Department of Anaesthesiology, University Hospital of Aachen, Aachen, Germany

Department of Anesthesia & Neurointensive Care, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK

School of Public Health & PM, Monash University and The Alfred Hospital, Melbourne, Victoria, Australia

Radiology/MRI department, MRC Cognition and Brain Sciences Unit, Cambridge, UK

Institute of Medical Psychology and Medical Sociology, Universitätsmedizin Göttingen, Göttingen, Germany

Oxford University Hospitals NHS Trust, Oxford, UK

Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program (Grant No. KTIA 13 NAP-II/8), Pecs, Hungary

Brain Physics Lab, Division of Neurosurgery, Dept of Clinical Neurosciences, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK

Intensive Care Unit, CHR Citadelle, Liège, Belgium

Intensive Care Unit, CHU, Liège, Belgium

Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK

Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium

Department of Anesthesia & Intensive Care, Maggiore Della Carità Hospital, Novara, Italy

Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium

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61 Department of Neurosurgery, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
62 Department of Neurology, Erasmus MC, Rotterdam, the Netherlands
63 Department of Neurosurgery, Medical Faculty and clinical center University of Sarajevo, Sarajevo, Bosnia Herzegovina
64 Department of Neurosurgery, Regional Medical Center Dr Safet Mujić, Mostar, Bosnia Herzegovina
65 Division of Anaesthesia, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK
66 Department of Anaesthesiology and Intensive Therapy, University of Pécs, Pécs, Hungary
67 Departments of Neurology, Clinical Neurophysiology and Neuroanesthesiology, Region Hovedstaden Rigshospitalet, Copenhagen, Denmark
68 National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand
69 Rehabilitation and Brain Trauma, Turku University Central Hospital and University of Turku, Turku, Finland
70 Department of Medicine, Azienda Ospedaliera Università di Padova, Padova, Italy
71 Department of Anesthesiology and Intensive care, University Hospital Northern Norway, Tromso, Norway
72 Department of Neurosurgery, Hadassah-hebrew University Medical center, Jerusalem, Israel
73 Fundación Instituto Valenciano de Neurorrehabilitación (FIVAN), Valencia, Spain
74 Department of Neurosurgery, Shanghai Renji hospital, Shanghai Jiaotong University/school of medicine, Shanghai, China
75 Emergency Department, CHU, Liège, Belgium
76 Department of Computing, Imperial College London, London, UK
77 Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; and Monash University, Australia
78 Department of Neurosurgery, Neurosciences Centre & JPN Apex trauma centre, All India Institute of Medical Sciences, New Delhi-110029, India
79 Department of Neurosurgery, Erasmus MC, Rotterdam, the Netherlands
80 Department of Neurosurgery, University of Cincinnati, Cincinnati, Ohio, USA
81 Department of Neurosurgery, Oslo University Hospital, Oslo, Norway
82 Department of Physiology and Pharmacology, Section of Perioperative Medicine and Intensive Care, Karolinska Institutet, Stockholm, Sweden
83 Department of Intensive Care Medicine, Radboud University Medical Center
84 Department of Medical Imaging, St. Olav's Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway
85 Department of Neurology, University Medical Center Groningen, Groningen, Netherlands
86 International Neurotrauma Research Organisation, Vienna, Austria
87 National Institute for Stroke & Applied Neurosciences of the AUT University, Auckland, New Zealand
88 Department of Neurosurgery, UZ Gent, Gent, Belgium
89 Department of Neurosurgery, Clinical centre of Vojvodina, Novi Sad, Serbia
90 Helsinki University Central Hospital
91 Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland
92 Hungarian Brain Research Program - Grant No. KTIA 13 NAP-A-II/8, University of Pécs, Pécs, Hungary
93 Department of Intensive Care and Department of Ethics and Philosophy of Medicine, Erasmus Medical Center, Rotterdam, The Netherlands
94 Department of Neurological & Spinal Surgery, Markusovszky University Teaching Hospital, Szombathely, Hungary
95 Cyclotron Research Center, University of Liège, Liège, Belgium
96 Emergency Medicine Research in Sheffield, Health Services Research Section, School of Health and Related Research (ScHARR), University of Sheffield, Sheffield, UK
97 Institute of Research in Operative Medicine (IFOM), Witten/Herdecke University, Cologne, Germany
98 VP Global Project Management CNS, ICON, Paris, France
99 Department of Neurosurgery, Rambam Medical Center, Haifa, Israel
100 Department of Anesthesiology & Intensive Care, University Hospitals Southampton NHS Trust, Southampton, UK

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101 icometrix NV, Leuven, Belgium
102 Cologne-Merheim Medical Center (CMMC), Department of Traumatology, Orthopedic Surgery and Sportmedicine, Witten/Herdecke University, Cologne, Germany
103 Centrum für Schlaganfallforschung, Charité – Universitätsmedizin Berlin, Berlin, Germany
104 Intensive Care Unit, Southmead Hospital, Bristol, Bristol, UK
105 Department of Neurological Surgery, University of California, San Francisco, California, USA
106 Department of Neurosurgery, CHU, Liège, Belgium
107 Department of Neurosurgery, The Walton centre NHS Foundation Trust, Liverpool, UK
108 Department of Medical Genetics, University of Pécs, Pécs, Hungary
109 National Trauma Research Institute, The Alfred Hospital, Monash University, Melbourne, Victoria, Australia
110 Department Health and Prevention, University Greifswald, Greifswald, Germany
111 Department of Neurosurgery, Emergency County Hospital Timisoara, Timisoara, Romania
112 Centre Hospitalier Universitaire Vaudois
113 Department of Intensive Care, Elisabeth-Tweesteden Ziekenhuis, Tilburg, the Netherlands
114 Department of Systems Medicine, Steno Diabetes Center, Gentofte, Denmark
115 Analytic and Translational Genetics Unit, Department of Medicine; Psychiatric & Neurodevelopmental Genetics Unit, Department of Psychiatry; Department of Neurology, Massachusetts General Hospital, Boston, MA, USA
116 Program in Medical and Population Genetics; The Stanley Center for Psychiatric Research, The Broad Institute of MIT and Harvard, Cambridge, MA, USA
117 Department of Radiology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium
118 NeuroIntensive Care Unit, Department of Anesthesia & Intensive Care Azienda Ospedaliera San Gerardo di Monza, Monza, Italy
119 International Projects Management, ARTTIC, Munchen, Germany
120 Department of Anesthesia & Intensive Care, Azienda Ospedaliera Università di Padova, Padova, Italy

121 Dept. of Neurosurgery, Leiden University Medical Center, Leiden, The Netherlands and Dept. of Neurosurgery, Medical Center Haaglanden, The Hague, The Netherlands

122 Intensive Care Unit, CHU Dupuytren, Limoges, France

123 Intensive Care Unit, CHRU de Besançon, Besançon, France

124 Department of Anesthesiology and Critical Care, Pitié-Salpêtrière Teaching Hospital, Assistance Publique, Hôpitaux de Paris and University Pierre et Marie Curie, Paris, France

125 Department of Neurosurgery, Kaunas University of technology and Vilnius University, Vilnius, Lithuania

126 Rezekne Hospital, Latvia

127 Department of Anaesthesia, Critical Care & Pain Medicine, NHS Lothian & University of Edinburgh, Edinburgh, UK

128 Director, MRC Biostatistics Unit, Cambridge Institute of Public Health, Cambridge, UK

129 Department of Physical Medicine and Rehabilitation, Oslo University Hospital/University of Oslo, Oslo, Norway

130 Division of Surgery and Clinical Neuroscience, Oslo University Hospital, Oslo, Norway

131 Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands

132 Broad Institute, Cambridge MA Harvard Medical School, Boston MA, Massachusetts General Hospital, Boston MA, USA

133 Department of Neurosurgery, Odense University Hospital, Odense, Denmark

134 Department of Neurosurgery, Vall d'Hebron University Hospital, Barcelona, Spain

135 Klinik für Neurochirurgie, Klinikum Ludwigsburg, Ludwigsburg, Germany

136 University Hospital Heidelberg, Heidelberg, Germany

137 Division of Biostatistics and Epidemiology, Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary

138 Department of Traumasurgery, Leiden University Medical Center, Leiden, The Netherlands

139 Department of Anaesthesiology and Intensive Care, AUVA Trauma Hospital, Salzburg, Austria

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1. Director of Neurocritical Care, University of California Los Angeles, USA
2. Department of Neurosurgery, St. Ola's Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway
3. Department of Neurosurgery, Kaunas University of Health Sciences, Kaunas, Lithuania
4. Department of Psychiatry, University of Florida, Gainesville, Florida, USA
5. Division of Psychology, University of Stirling, Stirling, UK
6. VTT Technical Research Centre, Tampere, Finland
7. University of Florida, Gainesville, Florida, USA
8. Department of Neurosurgery, The HAGA Hospital, The Hague, The Netherlands
9. Department of Intensive Care, Erasmus MC, Rotterdam, the Netherlands

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Supplemental data 2. Provider Profiling Questionnaire (ICU part)

The following questions about ICU policies are included in the manuscript.

Information about the completion of the questionnaire

Other than the CENTER-TBI investigator, which of the following individuals was involved in completion of this questionnaire?

- Neurologist
- Neurosurgeon
- Trauma Surgeon
- ED physician
- Administrative staff member / data manager / financial department
- Neuroscientist
- Other, please specify

Select all that apply.

The Local investigator is the senior clinician(s) at your hospital involved in supervision of CENTER TBI.

NA. The questionnaire is solely completed by the CENTER TBI local investigator.

The Local investigator is the senior clinician(s) at your hospital involved in supervision of CENTER TBI.

General patient statistics

With reference to guidelines for Intensive Care Unit (ICU) management of Traumatic Brain Injury (TBI), does your ICU:

1. 2012: ………………………………………..
2. 2013: ………………………………………..
3. 2012: ………………………………………..
4. 2013: ………………………………………..

What is the number of patients treated in your Intensive Care Unit (ICU) annually?

1. What is the number of Traumatic Brain Injury (TBI) patients treated in your Intensive Care Unit (ICU) annually?

2012: ………………………………………..
2013: ………………………………………..

What is the number of patients treated in your Intensive Care Unit (ICU) annually?

- Not have specific guidelines for management
- Follow the Brain Trauma Foundation Guidelines
- Follow National Guidelines (Please specify: .........................................................)
- Have institutional guidelines which are broadly based on BTF and/or National Guidelines
- Have separate guidelines which you have developed independently
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<table>
<thead>
<tr>
<th>Question</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>23. Is a coagulation panel assessed prior to insertion of an ICP monitor?</td>
<td>Never (0-10%), Rarely (10-30%), Sometimes (30-70%), Frequently (70-90%), Always (90-100%), N/A, we do not have this technique</td>
</tr>
<tr>
<td>24. What is considered a minimum platelet count for insertion of a ventricular catheter in your Intensive Care Unit (ICU)?</td>
<td>&gt;150K, &gt;100K, &gt;80K, &gt;50K, Variable, depends on surgeon, Other, please specify</td>
</tr>
<tr>
<td>25. What is considered the minimum INR for safe placement of a ventricular catheter in your Intensive Care Unit (ICU)?</td>
<td>&lt;1.4, &lt;1.3, &lt;1.2</td>
</tr>
</tbody>
</table>
Variable, depending on surgeon

No minimum

Other, please specify
Deep venous thrombosis (DVT) prophylaxis

The responses to the following questions should represent, as best as practicable, a general consensus on treatment at your centre, rather than individual management preferences.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never (0-10%)</th>
<th>Rarely (10-30%)</th>
<th>Sometimes (30-70%)</th>
<th>Frequently (70-90%)</th>
<th>Always (90-100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>53. How often is DVT prophylaxis used?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>54. If you use DVT prophylaxis, when is DVT prophylaxis initiated?</td>
<td>&lt; 24 hrs</td>
<td>24-72 hrs</td>
<td>&lt; 72 hrs</td>
<td>Never</td>
<td></td>
</tr>
<tr>
<td>In the absence of hemorrhagic lesions</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>In the presence of hemorrhagic lesion</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>After intracranial surgery</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>55. In patients who receive DVT prophylaxis, what medication is given?</td>
<td>☐</td>
<td>Subcutaneous unfractioned heparin</td>
<td>☐</td>
<td>Low-molecular weight heparin</td>
<td>☐</td>
</tr>
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This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

56. Coagulopathy related to the trauma is treated with:

<table>
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<tr>
<th>Compartment</th>
<th>Never (0-10%)</th>
<th>Rarely (10-30%)</th>
<th>Sometimes (30-70%)</th>
<th>Frequently (70-90%)</th>
<th>Always (90-100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh Frozen Plasma (FFP)</td>
<td>□</td>
<td>□</td>
<td>□</td>
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</tr>
<tr>
<td>Platelets</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Fibrinogen</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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</tr>
<tr>
<td>Novo 7 (recombinant factor VII)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>PCC (Prothrombin Complex Concentrate)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Other, please specify…</td>
<td>□</td>
<td>□</td>
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### General ICU treatments / protocols

#### Red blood cell policy

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