

Severe Traumatic Brain Injury in Austria VI: Effects of guideline-based management

Martin Rusnak¹, Ivan Janciak¹, Marek Majdan¹, Ingrid Wilbacher¹, and Walter Mauritz²
for the Austrian Severe TBI Study Investigators

¹INRO (International Neurotrauma Research Organisation), Vienna, Austria

²Department of Anaesthesia and Critical Care Medicine, Trauma Hospital "Lorenz Boehler";
INRO Medical Advisory Board, Vienna, Austria

Austrian Severe TBI Study Investigators

Local study coordinators: Florin Botha (Linz), Franz Chmeliczek (Salzburg), Georg Clarici (Graz), Hilda-Dietlinde Gulle (Klagenfurt), Walter Moser (Klagenfurt), Ernst Tramitsch (Klagenfurt)

INRO team: Alexandra Brazinova, Katharina Erb, Johannes Leitgeb, Lucia Lenartova, Annalisa Rosso

Schweres Schädelhirntrauma in Österreich VI: Auswirkungen eines auf Richtlinien basierenden Managements

Zusammenfassung. Ziele: Das Ziel der vorliegenden Arbeit ist es, die Zusammenhänge zwischen den Ergebnissen der Behandlung und den einzelnen Empfehlungen der Richtlinien darzustellen.

Patienten und Methoden: Es standen Datensätze von 405 Patienten zur Verfügung, die von 5 österreichischen Zentren in die Studie inkludiert worden waren. Analysiert wurde, in welchem Ausmaß die Behandlung der Patienten den Richtlinien der „Brain Trauma Foundation“ folgte. Hierzu wurde ein Algorithmus entwickelt, mittels dessen sich die Compliance mit den Richtlinien für jeden Patienten Tag für Tag überprüfen ließ und der einen Score ergab, der dann für weitere Analysen herangezogen wurde. Mit diesem Score wurden die Beziehungen zwischen einzelnen Empfehlungen und dem Überleben der Intensivbehandlung, gutem Zustand nach einem Jahr, und der Dauer von Intensivbehandlung und Spitalsaufenthalt analysiert. Dies erfolgte mittels logistischer Regression, wobei für die Faktoren Alter, Injury Severity Score und Glasgow Coma Scale korrigiert wurde.

Ergebnisse: Die Option „Prähospitale Therapie“ wurde in 84% der Fälle angewandt, und die Richtlinie „Rasche Schocktherapie“ wurde bei 79% erfüllt. Am häufigsten wurde die Richtlinie befolgt, den intrakraniellen Druck ab einer Höhe von 25 mmHg zu therapieren (89%). Die Option, den zerebralen Perfusionsdruck über 70 mmHg zu halten, wurde nur selten befolgt (29%). Ein statistisch signifikanter positiver Einfluss der Befolgung von Empfehlungen auf das Überleben der Intensivbehandlung fand sich nur für die Richtlinie „Rasche Schocktherapie“ und

für die Option „Zerebraler Perfusionsdruck“. Für einige andere Empfehlungen (zu Technik der Hirndruckmessung, Hyperventilation, Antiepileptika) sowie für den Gesamtscore fand sich ebenfalls ein positiver Einfluss (nicht signifikant). Für die Befolgung der übrigen Empfehlungen fand sich ein (nicht signifikanter) negativer Einfluss auf das Überleben der Intensivbehandlung. Bei der Analyse der Beziehung von Compliance Scores und Dauer von Intensiv- und Spitalsaufenthalt von Überlebenden zeigte sich, dass die Implementierung der Empfehlungen zur Technik der Hirndruckmessung den Intensiv- und Spitalsaufenthalt verkürzte. Befolgte man die Richtlinie zur Hyperventilation, so resultierte eine Verkürzung des Intensiv- und eine Verlängerung des Spitalsaufenthalts, befolgte man jene zu Mannitol, so wurde der Spitals-, jedoch nicht der Intensivaufenthalt verkürzt. Unterlassung der Verwendung von Kortikosteroiden (Standard) resultierte in einer Verkürzung von Intensiv- und Spitalsaufenthalt. Vermeidung der prophylaktischen Anwendung von Antiepileptika (Standard) führte zu einer Verkürzung des Intensiv- und Spitalsaufenthalts. Würde man alle Richtlinien befolgen, so würde dies zu einer Verlängerung des Intensiv- und einer Verkürzung des Spitalsaufenthalts führen.

Schlussfolgerungen: Die Empfehlungen zur Schocktherapie und zur Aufrechterhaltung des zerebralen Perfusionsdruck führten zu einer höheren Rate an Überlebenden und sollten deshalb immer umgesetzt werden. Da die Umsetzung der Richtlinien eine Verkürzung des Spitalsaufenthalts zu Folge haben könnte ist die Implementierung eines entsprechenden Programms aus ökonomischer Sicht ebenfalls zu befürworten.

Summary. Objectives: The goal of this paper is to report relations between health outcomes and implementation of individual recommendations of the guidelines.

Patients and methods: Data sets from 405 patients included by 5 Austrian hospitals were available. The analysis focused on the compliance of treatment modalities to TBI guidelines recommendations. Compliance was evaluated based on scores developed specifically for this purpose. To evaluate the relations between the TBI

guidelines compliance and outcomes the estimation of odds ratios was computed using multiple as well as logistic regression with age, ISS and initial GCS used to control confounding.

Results: The option on prehospital resuscitation was followed in 84%, the guideline on early resuscitation was followed in 79%. The guideline on intracranial pressure treatment threshold was the most closely followed one (89%). The option on cerebral perfusion pressure was followed in less than 30% of patients. Only the scores on resuscitation of blood pressure and oxygenation and on cerebral perfusion pressure were positively and statistically significantly related to ICU survival. Positive relations were also found for adherence to the recommendations on the type of monitoring, hyperventilation (guideline), prophylactic use of anti-seizure drugs, and the total of scores. The other recommendations were negatively related to ICU survival, but computed odds ratios were statistically not significant. Analysis of relations between compliance scores and length of ICU and hospital stay in survivors showed that adherence to the recommendations on type of monitoring was related to a reduction of length of stay in ICU and hospital, adherence to the hyperventilation guideline was related to shortened ICU, but increased hospital stay, and adherence to the guideline on mannitol was related to reduced days in hospital, but not to days in ICU. Implementing the standard on corticosteroid use was related to a reduction of days both in hospital and ICU. Using the standard on prophylactic use of anti-seizure drugs was related to a reduction in ICU days. If all the recommendations were closely followed an increase of days in ICU would be observed, while the length of stay in hospital would be reduced.

Conclusions: The relatively strong relation between initial resuscitation in the hospital and ICU survival provides a firm basis for future efforts of emergency teams. The positive influence of some of the recommendations on reduction of ICU or hospital days may provide economic incentives to promote guidelines implementation.

Key words: Brain injury, traumatic, guidelines, compliance, resuscitation, mannitol, ICP, barbiturates, corticosteroids, hyperventilation, lengths of stay, monitoring, outcome.

Introduction

The Austrian Severe Traumatic Brain Injury (TBI) Study was done in five participating Austrian hospitals and enrolled a total of 492 patients with severe TBI. Detailed information regarding background, goals, and methods of the study has been published in a previous paper [1]. Briefly, the goals of the study were to investigate the current management of patients with severe TBI in Austria and to assess the effects of introduction of guidelines for the management of severe TBI [2] upon the outcome of these patients. In principle, there is good reason to expect that TBI guidelines would provide cost effective improvement in the management of TBI patients. However, evidence to prove this does not exist for Austria. The goal of this paper is to report the effects of guidelines implementation on ICU survival, on long-term outcome, and on the duration of ICU and hospital stay.

Patients and methods

The methods of the Austrian Severe TBI Study have previously been described in detail [1]. All patients admitted to the participating hospitals were included if they fulfilled the criteria for severe brain trauma [3]. Patients who died at the scene, during transport to the hospital, or immediately after admission to the emergency room were excluded. Data on accident, prehospital treatment, hospital treatment, and patient status were collected using internet-based databases [4]. Patient data was entered daily for the first 10 days in hospital and then up to a year after discharge from intensive care. For this evaluation all data sets that included the required ICU data as well as outcome data ($n = 405$) were used. The data was extracted into Microsoft Excel files for analysis. The analysis focused on:

- *Process of guidelines implementation:* frequencies of the use of the recommendations in the treatment of TBI patients were analysed.
- *Health outcomes of TBI patients in relation to TBI guidelines compliance:* Intensive Care Unit (ICU) outcome (survived/died) and last available Glasgow Outcome Scale (GOS) [5] were correlated to the guideline compliance scores.
- *Treatment process indicators:* the total number of days spent on the ICU and in the hospital were correlated to the guideline compliance scores.

To evaluate the extent of compliance with the guidelines recommendations a scoring system was developed. The guidelines document has 13 chapters where one or more recommendations are formulated. The terminology used in the guidelines document (standards, guidelines, options) followed that used by the American Academy of Neurology [6, 7]. We scored implementation of the recommendations according to the level of evidence involved, so that (see Table 1)

- adherence to a "standard" (based on the strongest level of evidence) scored 5,
- adherence to a "guideline" (based on a moderate level of evidence) scored 3, and
- adherence to an "option" (based on the weakest level of evidence) scored 1 point.

Only two recommendations out of 13 are based on firm evidence and thus scored 5 points. For those recommendations where more than one day of procedure is envisaged we computed an average value of the scores achieved on each treatment day. Instances where a recommendation was not followed were fined by awarding negative score values. The total score for an individual patient was computed by summing up all scores.

Table 2 provides an overview of all recommendations scored. We scored only 11 of the 13 recommendations: the recommendation on the organization of trauma care (#1) was not scored because it was regarded as adequate in all areas, and the recommendation on nutrition (#12) was not scored because we felt that the definition was too complicated and that we had not enough data to base the algorithm on. Also, the assignment of 5 points to the recommendation to use an intraventricular catheter for intracranial pressure (ICP) monitoring (#6) is not based on evidence, but on previous experiences with this type of monitoring. The scores within a recommendation are hierarchical, only the highest one was accepted; if, for example, a patient had intraventricular as well as intraparenchymal ICP monitoring this was scored with the higher score only. Subse-

Table 1. Relation of clinical certainty to the evidence involved and scores assigned

	Definition	Evidence involved	Score assigned
Standards	Accepted principles of patient management that reflect a high degree of clinical certainty.	Generally based on Class I evidence. However, strong Class II evidence may form the basis for a standard, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I evidence may not be able to support a standard.	If YES: 5 If NO: -5
Guidelines	Represent a particular strategy or range of management strategies that reflect a moderate clinical certainty.	Usually based on Class II evidence or a preponderance of Class III evidence.	If YES: 3 If NO: -3
Options	Are the remaining strategies for patient management for which there is unclear clinical certainty.	Usually based on Class III evidence and are clearly much less useful except for educational purposes and in guiding future studies.	If YES: 1 If NO: -1

quently, we developed an algorithm which operated on the ITCP database data and produced a table of scores.

The XLSTAT add in for Microsoft Excel [8] and R statistics [9] were used for statistical processing of the data. To evaluate the relation between the TBI guidelines compliance and treatment health outcomes the estimation of odds ratios was computed using logistic regression. ICU outcome was coded as 1 in survivors and 0 in non-survivors; long-term outcome was coded as 1 if it was "favorable" (GOS score 5 or 4) or 0 if it was "unfavorable" (GOS score 3, 2, or 1). Each score was regressed individually against the outcome, using the variables age, ISS and initial GCS as confounders. The recommendation on hyperventilation was scored in two steps: one with the highest evidence (standard) and also with the moderate one (guideline). Multiple as well as logistic regressions were performed. Odds ratios were computed using logistic regression based on logit model using Wald Chi-Square to estimate goodness of fit for the equation coefficients. A $p < 0.05$ was considered significant.

Results

Guidelines implementation

The frequencies of achieved scores (Table 3) indicate that there was no significant correlation between strength of the recommendation (option vs. guideline vs. standard) and the level of implementation. The option on prehospital resuscitation (#2) was followed in most of the cases. The guideline on early resuscitation after admission to the hospital (#3) was followed in more than three quarters of all cases. The guideline on indications for intracranial pressure monitoring (#4) was followed in two thirds of cases. The guideline on intracranial pressure treatment threshold (#5) was the most closely followed recommendation (used in almost 90% of all cases). The recommendations on the technology to be used for intracranial pressure monitoring (#6) comprised all three levels. The one used most frequently was the guideline, as intraparenchymal monitors were used in 78%. Intraventricular catheters were used in 17%. One of the least frequently used recommendations was that on cerebral perfusion pressure (#7); for this option the frequency of adherence was less than 30%. There are two recommendations on the use of hyperventilation (#8): The guideline was followed in less

than 50% of patients while the standard was adhered to in 92%. The use of mannitol guideline (#9) was implemented in more than 50% of all cases. The recommendation on the use of barbiturates (#10), a guideline, was followed in more than 80%. The last two recommendations on the use of corticosteroids (#11) and on the use of anti-seizure prophylaxis (#13) are both standards, and compliance was very high (almost 90%).

Effects of compliance with the TBI guidelines on health outcomes

An overview of the effects of guideline compliance on ICU survival, adjusted for the confounders age, ISS, and first GCS, is given in Table 4. Only the scores on resuscitation of blood pressure and oxygenation (#3) and on cerebral perfusion pressure (#7) were positively and statistically significantly related to ICU survival. Positive relations were also found for the recommendations on the type of monitoring (#6), the hyperventilation guideline (#8B), the standard on prophylactic use of anti-seizure drugs (#13), and the total score (all not significant). The other recommendations were negatively related to ICU survival (i.e. following the recommendation impaired ICU outcome), but the computed odds ratios were statistically not significant.

Relation between the adherence to recommendations and favorable outcome, adjusted for the confounders, are shown in Table 5. As in the previous table, the only score positively and statistically significantly related to favorable outcome was Score #3. However, more scores than in the case of ICU outcome were positively related to favorable outcome, but none of these were statistically significant.

Treatment process indicators

Table 6 summarizes estimates of the relation between scores for adherence to guidelines recommendations and the length of stay in the ICU as well as days of hospital care. The estimation is based on multiple linear regression performed with the number of days as the dependent variable and the score (for each recommendation and total), age, ISS, and GCS used as independent variables.

Table 2. Recommendations used for scoring adherence to TBI guidelines

Recommendations
<p>2: <i>The Integration of Brain-Specific Treatments into The Initial Resuscitation of the Severe Head Injury Patient</i> <i>Option:</i> The first priority for the head -injured patient is complete and rapid physiologic resuscitation. No specific treatment should be directed at intracranial hypertension in the absence of signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial explanations. When either signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial explanations are present, however, the physician should assume that intracranial hypertension is present and treat it aggressively. Hyperventilation should be rapidly established. The administration of mannitol is desirable, but only under conditions of adequate volume resuscitation. Sedation and neuromuscular blockade can be useful in optimizing transport of the head injury patient. However, both treatments interfere with the neurological examination. In the absence of outcome-based studies, the choice of sedative is left to the physician. Neuromuscular blockade should be employed when sedation alone proves inadequate and short-acting agents should be used when possible</p>
<p>3: <i>Resuscitation of Blood Pressure and Oxygenation</i> <i>Guideline:</i> For Systolic Blood Pressure less than 90 mmHg, either i.v. started or Packed Red Cells administered; or for PaO₂ less than 60 mmHg and mechanical ventilation was started <i>Option:</i> If Mean Arterial Pressure is over 85 mmHg</p>
<p>4: <i>Indications for Intracranial Pressure Monitoring</i> <i>Guideline:</i> If ICP monitoring started and one of the following findings:</p> <ul style="list-style-type: none"> • Basal Cisterns closed on CT • Midline shift on CT • Hemorrhage or Multiple Lesions or Haematoma on CT • Or two of following conditions present: Systolic BP less than 90 mmHg; Patient's age is over 40 years; GCS at admission less than 9
<p>5: <i>Intracranial Pressure Treatment Threshold</i> <i>Guideline:</i> If value of ICP is over 25 mmHg for more than 2 hours and one of the following was satisfied:</p> <ul style="list-style-type: none"> • Craniotomy • Hypertonic Solutions Administered • Mannitol or Hypertonic NaCl Administered • Barbiturates over 200 mg/day • CSF Drainage
<p>6: <i>Recommendations for Intracranial Pressure Monitoring Technology</i> <i>Standard:</i> If ICP monitoring using Ventricular catheter <i>Guideline:</i> If ICP monitoring using Parenchymal catheter <i>Option:</i> If ICP monitoring using other method</p>
<p>7: <i>Guidelines for Cerebral Perfusion Pressure</i> <i>Option:</i> If CPP is kept over 70 mmHg or if not CPP less than 70 mmHg for more than 1 hour</p>
<p>8: <i>The Use of Hyperventilation in the Acute Management of Severe TBI</i> <i>Standard:</i> If ICP is higher than 25 mmHg for less than 2 hours and PCO₂ is higher than 25mmHg (= no hyperventilation for patients without elevated ICP) <i>Guideline:</i> If ICP is higher than 25 mmHg for less than 2 hours and PCO₂ is higher than 35 mmHg(= no hyperventilation for patients without elevated ICP)</p>
<p>9: <i>The Use of Mannitol in Severe Head Injury</i> <i>Guideline:</i> If ICP increased over 25 mmHg for more than 2 hours and mannitol administered</p>
<p>10: <i>The Use of Barbiturates in the Control of Intracranial Hypertension</i> <i>Guideline:</i> If ICP increased over 25 mmHg for more than 2 hours and if barbiturates administered in a dose higher than 200 mg/day</p>
<p>11: <i>The Role of Glucocorticoids in the Treatment of Severe Head Injury</i> <i>Standard:</i> If steroids were not administered</p>
<p>13: <i>The Role of Anti-Seizure Prophylaxis Following Head Injury</i> <i>Standard:</i> If no phenytoin, carbamazepine, or phenobarbital was used for prevention of late posttraumatic seizures (PTS) <i>Guideline:</i> If phenytoin and carbamazepine were used to treat seizures</p>

Table 3. Frequencies of achieved scores by value and TBI guidelines recommendation

Recommendation	Score											
	-5		-3		-1		1		3		5	
	n	%	n	%	n	%	n	%	n	%	n	%
#2: Prehospital resuscitation					67	16.1	348	83.9				
#3: Resuscitation of BP & O ₂			57	20.8					217	79.2		
#4: Indications for ICP Monit.			132	31.8					283	68.2		
#5: ICP Treatment Threshold			37	11.3					291	88.7		
#6: ICP Technology							12	4.5	206	78.0	46	17.4
#7: CPP					234	71.3	94	28.7				
#8: Hyperventilation	30	7.6	197	52.3					180	47.7	363	92.4
#9: Mannitol			142	39.9	28	7.9			186	52.2		
#10: Barbiturates			57	17.5					269	82.5		
#11: Glucocorticoids	47	11.5									362	88.5
#13: Anti-Seizure Prophylaxis	47	11.5									360	88.5

Results of the regression are reported as unit differences per a score of adherence to the guidelines recommendation. The value of the unit difference is interpreted as a change in days for a unit increase of a score value, when the confounders (age, ISS, and GCS) are kept constant. Thus, if adherence to a recommendation is scored 5, then the coefficient multiplied by the score value gives the increase (or reduction) of days. Of course, this analysis was performed for surviving patients only.

Overall, a statistically significant relation was found for all scores. Type of monitoring was related to a reduc-

tion of the number of days of both ICU and hospital stay. Adherence to the hyperventilation guideline (#8B) was related to reduced days in the ICU, while total length of stay in a hospital was slightly increased. Adherence to the recommendation on mannitol (#9) was related to reduced days in hospital, but not to days in ICU. Adherence to the standard on corticosteroids (#11) was related to the reduction of days both in hospital and ICU. Days in ICU were reduced when the standard on prophylactic use of anti-seizure drugs (#13) was followed. If all the recommendations were closely followed an increase of days in ICU

Table 4. Estimates of Odds Ratios for ICU survival, adjusted for age, Injury Severity Score (ISS) and Glasgow Coma Scale (GCS)

Recommendation	Coefficient estimate	Standard error	OR	OR_low (95%)	OR_up (95%)
Score #2 Prehospital resuscitation	-0.05	0.16	0.95	0.71	1.28
Score #3 Resuscitation of PB and O ₂	0.22	0.05	1.25 ^b	1.12	1.39
Score #4 Indication for ICP	-0.01	0.04	0.99	0.91	1.07
Score #5 ICP treatment threshold	-0.04	0.07	0.96	0.84	1.10
Score #6 Type of monitoring	0.05	0.16	1.05	0.77	1.43
Score #7 CPP	0.10	0.05	1.11 ^a	1.00	1.22
Score #8 Hyperventilation standard	-0.01	0.04	0.99	0.91	1.07
Score #8 Hyperventilation guideline	0.04	0.04	1.04	0.96	1.13
Score #9 Mannitol	-0.01	0.04	0.99	0.91	1.08
Score #10 Barbiturate use	-0.11	0.06	0.89	0.79	1.01
Score #11 Steroid use	-0.05	0.04	0.96	0.89	1.03
Score #13 Anti-seizure prophylaxis	0.01	0.04	1.01	0.94	1.09
Total scores	0.01	0.01	1.01	0.98	1.03

^ap < 0.05; ^bp < 0.0001.

Table 5. Estimates of Odds Ratios for favorable outcome, adjusted for age, Injury Severity Score (ISS) and Glasgow Coma Scale (GCS)

Recommendation	Coefficient estimate	Standard error	OR	OR_low (95%)	OR_up (95%)
Score #2 Prehospital resuscitation	-0.02	0.16	0.98	0.72	1.33
Score #3 Resuscitation of PB and O ₂	0.17	0.06	1.18 ^a	1.04	1.34
Score #4 Indication for ICP	0	0.04	1	0.92	1.09
Score #5 ICP treatment threshold	0.02	0.07	1.02	0.88	1.17
Score #6 Type of monitoring	-0.08	0.17	0.92	0.67	1.28
Score #7 CPP	0.02	0.05	1.02	0.93	1.11
Score #8 Hyperventilation standard	0.02	0.04	1.02	0.94	1.1
Score #8 Hyperventilation guideline	0.03	0.05	1.03	0.95	1.13
Score #9 Mannitol	-0.03	0.04	0.97	0.89	1.05
Score #10 Barbiturate use	-0.08	0.06	0.93	0.83	1.04
Score #11 Steroid use	0.04	0.04	1.04	0.96	1.12
Score #13 Anti-seizure prophylaxis	0.02	0.04	1.02	0.95	1.1
Total scores	0.01	0.01	1.02	0.99	1.04

^ap < 0.01.

would be observed, while the length of stay in hospital would be reduced.

Discussion

Clinical guidelines are recommendations for the care of individuals by healthcare professionals. Guidelines assist the practice of healthcare professionals, but do not replace their knowledge and skills [10]. It is generally believed that if there is evidence of variation in practice which affects patient outcomes and a strong research base providing evidence of effective practice, guidelines can assist doctors and other health care professionals in making decisions about appropriate and effective care for their patients [11]. But is this statement really valid in the management of a patient with severe TBI?

The TBI guidelines used during the Austrian project were published in 1996. Authors from Brain Trauma Foundation measured the proportion of recommendations used in US trauma centers in 1999 and 2000 by contacting the staff managing severe TBI patients before the guidelines were published [12] and several years later [13]. They found that full guideline compliance was rare (about 16% of those contacted), and that general treatment patterns were not significantly influenced by availability of the guidelines. A similar study was conducted in Austria: the authors concluded that treatment was not homogeneous, and that significant interdisciplinary (trauma surgeons versus neurosurgeons) differences in management existed [14]. The studies mentioned were based on a collection of data through interviews with the staff of departments providing the care. In our approach we tried to combine a procedure of automatic evaluation of the treatment process as described in the ITCP database with assigning a weight to individual recommendations according to the evidence used during the process of guidelines formulation. We expected that this approach would pro-

vide more detailed insight into process of TBI guidelines implementation and would allow for assessing the relative contribution of individual recommendations to patient's outcome as well as to performance indicators. Positive scores indicate that the recommendation was followed, negative scores indicate that a recommendation was not followed. Therefore, the frequency distribution of positive and negative values provides first hand information how closely recommendations from the TBI guidelines were followed.

Those recommendations which are based on the highest available evidence (i.e. the standards on hyperventilation, corticosteroids and anti-seizure prophylaxis) were implemented in more than 75% of all patients. The recommendation on intracranial pressure monitoring technology of the level of standard was followed in less than 20% of cases. This was outweighed by the frequent use of technology recommendation of level of guideline. The only recommendation which was most frequently neglected was the option on cerebral perfusion pressure. This indicates a rather high level of adherence to the TBI guidelines, and it also helps to understand why guideline compliance had only few statistically significant effects – the group of patient where guidelines were not followed was rather small. Originally, we hypothesized that in patients who were admitted in more serious condition the guidelines would be followed less strictly. However, even if those patients who died within 48 hours after admission were excluded from the analysis the general picture was not significantly modified.

Assessment of the influence of recommendations on health outcomes was based on the notion that there are strong confounders to be taken into an account. The first one is age, as demonstrated in a meta analysis of several studies [15]. The extent of general injury was measured by the Injury Severity Score, an anatomical scoring sys-

Table 6. Days in ICU and the length of stay in hospital in relation to the unit difference in a score, while controlled for age, ISS and GCS

Recommendation	Days in ICU		Days in hospital	
	Unit difference	Overall significance of the regression	Unit difference	Overall significance of the regression
Score #2 Prehospital resuscitation	1.12	0.009	2.76	0.003
Score #3 Resuscitation of PB and O ₂	0.90 ^a	0.022	1.39 ^b	0.025
Score #4 Indication for ICP	0.12	0.013	0.45	0.005
Score #5 ICP treatment threshold	0.43	0.025	1.68	0.003
Score #6 Type of monitoring	-1.41	0.013	-0.27	0.021
Score #7 CPP	0.16	0.031	0.20	0.010
Score #8 Hyperventilation Standard	0.14	0.014	0.07	0.010
Score #8 Hyperventilation Guideline	-0.16	0.013	0.04	0.007
Score #9 Mannitol	0.16	0.020	-0.15	0.017
Score #10 Barbiturate use	0.36	0.028	-0.69	0.008
Score #11 Steroid use	-0.21	0.007	-0.98	0.001
Score #13 Anti-seizure prophylaxis	-0.02	0.120	0.27	0.004
Total of scores	0.05	0.012	-0.04	0.006

^ap < 0.01; ^bp < 0.05.

tem which correlates linearly with mortality, morbidity, hospital stay and other measures of severity [16]. The third confounder was GCS, since it is generally recognized to be a powerful predictor of outcome [17, 18]. Originally we considered using the TRISS (Trauma Score – Injury Severity Score [19]) instead of ISS, but as TRISS is a score that also includes GCS we finally decided against its use. The relation between recommendations and ICU outcome was statistically significantly positive for the guideline on resuscitation of blood pressure and oxygenation, and the estimate of OR suggests, that those who underwent effective resuscitation had a 1.25 times higher chance of ICU survival. The positive and significant relation between adherence to the option on cerebral perfusion pressure and ICU survival seems to be supported by a study by Juul et al. [20]; the authors demonstrated that a low cerebral perfusion pressure was the most powerful predictor of neurological deterioration. With regard to long term outcome only adherence to guideline #3 (resuscitation) improved the rate of favorable outcome statistically significantly.

It is also interesting to see which of the recommendations did not significantly relate to health outcomes. One unexpected result was the lack of relation to the total scores. This seems to be contradictory to findings from other studies [21–25] where implementation of TBI guidelines had dramatic effects on patients' health outcome. One major difference between these studies and our own project was the monitoring of guideline compliance: while most authors just report that "guidelines were followed" our compliance score measured the level of evidence involved as well as "fined" those instances where the recommendation was not implemented. Another difference may be the use of logistic regression and the controlling for confounders in our study. Lastly, it is worth to notice that

the clinical importance of the various guideline recommendations is clearly different: it may be more important to perform effective prehospital resuscitation (option) and use only intraparenchymal ICP monitoring (guideline), which gives a total of 4 points, than to forego prehospital resuscitation and use intraventricular ICP monitoring, which gives a total of 5 points. Our system of scoring guideline compliance needs some further refinements, but we need more data to calculate "weights" for each score.

When investigating the length of stay in ICU and hospital several recommendations were found to be related to either reduction or prolongation of these. Implementing the recommendations on type of monitoring, hyperventilation guideline, steroid use, and anti-seizure prophylaxis was associated with a reduction of days in ICU. The length of stay in hospital was reduced by implementing the guidelines on mannitol and barbiturate use, while using the standard on anti-seizure prophylaxis was related to more days in hospital. Total scores were related to increased ICU days and the reduction of the length of stay in hospital. This may challenge the finding from the study of Fakhry et al. [21] who reported a reduction of ICU stay by 1.8 days (p = 0.021) and total hospital stay by 5.4 days (p < 0.001). On the other hand our results also do not support the statement of Clayton et al. [24] that the median ICU and hospital length of stay remained constant over the study period.

The high variation of treatment approaches, the relatively small sample size, and the limited information about the time after the first 10 days at ICU represent major limitations of this study. The authors are also aware of the limitations of the scoring procedure, where no weighting was introduced and the differences in duration of the condition were not taken into an account. All of those made it difficult to interpret relation between scores

and favorable outcome, since apart from the time spent in the hospital and in the rehabilitation centre the treatment a patient received after discharge from the ICU was not documented. This represents a real challenge to our team and we plan to make further improvements and refinements into the scoring mechanism.

Conclusions

The results revealed a number of open questions for further investigation as well as created a firm ground to target development of new TBI guidelines for Austria. This innovative approach could be used not only for research but also predominantly for reducing treatment variance as well as for improving the quality of care. The relatively strong relation between initial resuscitation in the hospital and ICU survival provides a firm basis for future efforts of emergency teams. The positive influence of some of the recommendations on reduction of ICU or hospital days may provide economic incentives to promote guidelines implementation.

Acknowledgements

We have to thank Prim. Dr. Walter Löffler (Linz), Prim. Prof. Dr. Gernot Pauser (Salzburg), Prim. Dr. Volker Schalk (Klagenfurt) and Prof. Dr. Hans Tritthart (Graz), for their active support of the study in their departments.

Funding: The study was supported by a grant from the Jubiläumsfonds of the Österreichische Nationalbank (grant reference Jubiläumsfonds-Projekt Nr. 8987) which covered the costs of the meeting, the development, programming, distribution, and maintenance of the ITCP database, and fees for researchers. An additional grant was received from the Allgemeine Unfallversicherungsanstalt (AUVA), which covered the costs of the participation of Trauma Hospital "Lorenz Boehler". Prof. Dr. Rusnak's salary as study manager was paid partly by a grant from Mrs. Ala Auersperg-Isham and Mr. Ralph Isham. The costs of translating, printing, and distributing the guidelines were supported by a grant from Fresenius Kabi Ges.m.b.H.

References

- Rusnak M, Janciak I, Majdan M, Wilbacher I, Mauritz W; for the Austrian Severe TBI Study Investigators (2007) Severe traumatic brain injury in Austria I: introduction to the study. *Wien Klin Wochenschr* 119: 23–28
- Bullock R, Chesnut RM, Clifton G, Ghajar J, Marion D, Narayan R, Newell D, Pitts LH, Rosner M, Wilberger J (1996) Guidelines for the management of severe head injury. Brain Trauma Foundation, *Eur J Emerg Med* 3: 109–127
- Marshall LF, Becker DP, Bowers SA, et al (1983) The National Traumatic Coma Data Bank. Part 1: design, purpose, goals, and results. *J Neurosurg* 59: 276–284
- Mauritz W, Rusnak M, Janciak I (2003) Implementing scientific evidence-based guidelines: case study of severe traumatic brain injuries. *Clinical Research and Regulatory Affairs* 20: 81–87
- Jennett B, Bond M (1975) Assessment of outcome after severe brain damage. *Lancet* 1; 1 (7905): 480–484
- Rosenberg J, Greenberg MK (1992) Practice parameters: strategies for survival into the nineties. *Neurology* 42: 1110–1115
- Walters BC (1998) Clinical practice parameter development. In: Bean JR (ed) *Neurosurgery in transition*. Williams & Wilkins, Baltimore, pp 99–111
- Downloaded from www.xlstat.com/, 1.1.2006
- Downloaded from www.r-project.org/, 1.3.2006
- Hurwitz B (1999) Clinical guidelines: legal and political considerations of clinical practice guidelines. *BMJ* 318: 661–664
- SIGN 50: a guideline developers' handbook. www.sign.ac.uk/guidelines/fulltext/50/index.html
- Ghajar J, Hariri RJ, Narayan RK, Iacono LA, Firlik K, Patterson RH (1995) Survey of critical care management of comatose, head-injured patients in the United States. *Crit Care Med* 23: 560–567
- Hesdorffer DC, Ghajar J, Iacono L (2002) Predictors of compliance with the evidence-based guidelines for traumatic brain injury care: a survey of United States trauma centers. *J Trauma* 52: 1202–1209
- Drobetz H, Freudenschuss B, Kutscha-Lissberg E, Buchinger W, Mauritz W (2000) The treatment of severe head-brain injuries in Austria. *AINS* 35: 630–634
- Hukkelhoven CWPM, Steyerberg EW, Rampen AJJ, Farace E, Habbema JDF, Marshall LF, Murray GD, Maas AIR (2003) Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. *J Neurosurg* 99: 666–673
- Baker SP, O'Neill B, Haddon W Jr, Long WB (1974) The Injury Severity Score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 14: 187–196
- King JT Jr, Carlier PM, Marion DW (2005) Early Glasgow Outcome Scale scores predict long-term functional outcome in patients with severe traumatic brain injury. *J Neurotrauma* 22: 947–954
- Miller KJ, Schwab KA, Warden DL (2005) Predictive value of an early Glasgow Outcome Scale score: 15-month score changes. *J Neurosurg* 103: 239–245
- Boyd CR, Tolson MA, Copes WS (1987) Evaluating Trauma Care: The TRISS Method. *J Trauma* 27: 370–378
- Juul N, Morris GF, Marshall SB, Marshall LF (2000) Intracranial hypertension and cerebral perfusion pressure: Influence on neurological deterioration and outcome in severe head injury. The Executive Committee of the International Selfotel Trial. *J Neurosurg* 92: 1–6
- Fakhry SM, Trask AL, Waller MA, Watts DD, IRTC Neurotrauma Task Force (2004) Management of brain-injured patients by an evidence-based medicine protocol improves outcomes and decreases hospital charges. *J Trauma* 56: 492–499
- McIlvoy L, Spain DA, Raque G, Vitaz T, Boaz P, Meyer K (2001) Successful incorporation of the Severe Head Injury Guidelines into a phased-outcome clinical pathway. *J Neurosci Nurs* 33: 72–82
- Palmer S, Bader MK, Qureshi A, Palmer J, Shaver T, Borzatta M, Stalcup C (2001) The impact on outcomes in a community hospital setting of using the AANS traumatic brain injury guidelines. *American Association for Neurologic Surgeons. J Trauma* 50: 657–664
- Clayton TJ, Nelson RJ, Manara AR (2004) Reduction in mortality from severe head injury following introduction of a protocol for intensive care management. *Br J Anaesth* 93: 761–767
- Vukic M, Negovetic L, Kovac D, Ghajar J, Glavic Z, Gopcevic A (1999) The effect of implementation of guidelines for the management of severe head injury on patient treatment and outcome. *Acta Neurochirurgica* 141: 1203–1208

Correspondence: Prof. Walter Mauritz, INRO, Mölkgasse 4/3, 1080 Vienna, Austria, E-mail: walter.mauritz@igeh.org