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Severe Traumatic Brain Injury in Austria III: Prehospital status and treatment

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Schweres Schädelhirntrauma in Österreich III: Präklinischer Status und Erstversorgung

Zusammenfassung. *Ziele:* Das Ziel der vorliegenden Arbeit ist es, präklinischen Status und präklinisches Management von Patienten mit schwerem Schädel-Hirn-Trauma (SHT) darzustellen.

Patienten und Methoden: Es standen Datensätze von 396 Patienten mit schwerem SHT (Glasgow Coma Scale < 9) zur Verfügung, die von 5 österreichischen Zentren in die Studie inkludiert worden waren. Analysiert wurden Inzidenz und Schweregrad typischer klinischer Symptome und die Häufigkeit der Verwendung verschiedener Behandlungsoptionen, und der Zusammenhang mit dem Behandlungsergebnis. Für Symptome und Behandlungsoptionen wurden ICU- und 90-Tage-Mortalität, Endzustand nach 6 oder 12 Monaten (gut = Normalzustand oder leichte Behinderung, schlecht = schwere Behinderung, vegetativer Zustand oder Tod), und die O/E ratio (Verhältnis von beobachteter zu erwarteter Mortalität) erhoben. Statistik: Es kamen Chi^2-test, t-test, Fisher's exact test, und logistische Regression zur Anwendung; ein p < 0,05 wurde als signifikant angesehen.

Ergebnisse: Die Mehrzahl (72%) der Patienten war männlich, das Alter betrug 49 ± 21 Jahre, der mittlere injury severity score (ISS) war 27 ± 17, die mittlere GCS betrug 5,6 ± 2,9, und die erwartete Überlebensrate lag bei 63 ± 30%. Die ICU-Mortalität lag bei 32%, und die 90-Tage-Mortalität bei 37%. Das Ergebnis war "gut" bei 35%, „schlecht" bei 53%, und unbekannt bei 12% der Patienten. Es fand sich, dass Alter > 60 a, ISS > 50, GCS score < 4, bilaterale Pupillenveränderungen, Atemfrequenz < 10/min, SBP < 90 mm Hg, und Herzfrequenz < 60/min mit signifikant erhöhter ICU- und 90-Tage-Mortalität und schlechtem Ergebnisses einhergingen. Zur Klassifikation von Patienten mit SHT können anstelle der gesamten Punktezahl der GCS auch nur die Punkte für die motorische Antwort verwendet werden. Die Gabe von > 1000 ml Volumen sowie Hubschraubertransport waren mit besserem Ergebnis als erwartet assoziiert, während die endotracheale Intubation weder einen positiven noch einen negativen Effekt hatte. Unterlassen der Volumentherapie oder Gabe von < 500 ml Volumen hatte ein schlechteres Ergebnis als erwartet zur Folge. Das Ergebnis war besser als erwartet bei den wenigen Patienten (5%) die hypertones NaCl erhalten hatten.

Schlussfolgerungen: Für das Behandlungsergebnisse dürften vor allem Alter, ISS und initialer neurologischer Zustand wesentlich sein. Hypotension muss vermieden werden. Es sollte rasch ausreichend Volumen gegeben werden, um einen SBP > 110 mm Hg zu erreichen oder zu halten. Für schwer verletzte Patienten mit SHT sollte ein Hubschraubertransport arrangiert werden.

Summary. *Objectives:* The goal of this paper is to describe prehospital status and treatment of patients with severe TBI in Austria.

Patients and methods: Data sets from 396 patients with severe TBI (Glasgow Coma Scale score < 9) included by 5 Austrian hospitals were available. The analysis focused on incidence and/or degree of severity of typical clinical signs, frequency of use of different management options, and association with outcomes for both. ICU mortality, 90-day mortality, final outcome (favorable = good recovery or moderate disability; unfavorable = severe disability, vegetative state, or death) after 6 or 12 months, and ratio of observed (90-day) to predicted mortality (O/E ratio) are reported for the selected parameters. Chi^2-test, t-test, Fisher's exact test, and logistic regression were used to identify significant ($p < 0.05$) differences for association with survival and favorable outcome (both coded as 1).

Results: The majority of patients were male (72%), mean age was 49 ± 21 years, mean injury severity score (ISS) was 27 ± 17, mean first GCS score was 5.6 ± 2.9,

and expected hospital survival was 63 ± 30%. ICU mortality was 32%, 90-day mortality was 37%, and final outcome was favorable in 35%, unfavorable in 53%, unknown in 12%. We found that age > 60 years, ISS > 50 points, GCS score < 4, bilateral changes in pupil size and reactivity, respiratory rate < 10/min, systolic blood pressure (SBP) < 90 mm Hg, and heart rate < 60/min were associated with significantly higher ICU and 90-day mortality rates, and lower rates of favorable outcome. With regard to prognostic value the GCS motor response score is identical to the full GCS score. Administration of > 1000 ml of fluid and helicopter transport were associated with better outcomes than expected, while endotracheal intubation in the field had neither a positive nor a negative effect on outcomes. Administration of no or < 500 ml of fluids was associated with worse outcomes than expected. Outcomes were better than expected in the few patients (5%) who received hypertonic saline.

Conclusions: Age, ISS, and initial neuro status are the factors most closely associated with outcome. Hypotension must be avoided. Fluids should be given to restore and/or maintain SBP > 110 mm Hg. Helicopter transport should be arranged for more seriously injured patients.

Key words: Brain injury, traumatic, outcome, prehospital, Glasgow Coma Scale, vital signs, fluid administration, transport.

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 have been published in a previous paper [1]. The goal of this paper is to describe prehospital status and management, and how these may affect outcome.

Patients and methods

The methods of the Austrian Severe TBI Study have previously been described in detail [1]. In brief, data on accident, prehospital treatment, hospital treatment, and patient status was collected using internet-based databases. All patients admitted to the participating hospitals were included if they fulfilled the criteria for severe brain trauma [2]. Patients who died at the scene, during transport to the hospital, or immediately after admission to the emergency room were excluded. For this paper only data sets that included all relevant prehospital data and TRISS (Trauma and Injury Severity Score) were used. Thus, data sets from 396 patients were available for analysis. Relevant data was extracted into Microsoft Excel files for analysis. The analysis focused on:

- Status of the patients immediately after TBI: incidence of typical findings, relationship between degree of severity of typical symptoms and outcomes;
- Prehospital management: incidence of typical treatment options, indications for the use of these treatment options, and relationship between treatment options and outcomes.

Physiologic variables recorded during the prehospital phase were analyzed to describe the incidence and degree of severity of typical symptoms. For all typical symptoms as well as treatment options, correlations between these and ICU outcome (survival or death), 90-day outcome (survival or death) and final outcome (see [1]) were performed. Final outcome is reported as "favorable" (good recovery, moderate disability) or "unfavorable" (severe disability, persistent vegetative state, death). The mortality prediction made possible by TRISS [3] was used to calculate the Observed vs. Expected mortality ratio (O/E ratio) at day 90; a detailed discussion is provided in the first paper of this series [1].

The XLSTAT add in for Microsoft Excel [4] was used for statistical processing of the data. The analyses were done using standard descriptive statistics and univariate correlation, and the significances of differences between variables were tested by means of Chi^2-test and Fisher's exact test for nominal variables, and t-test for numeric variables. Association of variables to outcome was tested using logistic regression to correct for age, injury severity score (ISS), and first Glasgow Coma Scale (GCS) score. A $p < 0.05$ was considered significant.

Results

The majority of patients were male (284; 72%), mean age was 48.9 ± 20.8 years, mean ISS was 27.0 ± 12.7 points, mean first GCS score was 5.6 ± 2.9 points, and expected hospital survival was 62.9 ± 29.9%. Overall ICU mortality was 31.8% (126/396), and 90-day mortality was 37.1% (147/396). The final outcome was favorable in 35.4% (140/396), unfavorable in 52.5% (208/396), and unknown in 12.1% (48/396) of the cases.

Demographic data

An overview is given in Table 1. There was no influence of gender upon outcomes; ICU and 90-day mortality, rates of favorable outcome, and O/E ratios were quite similar. Age had a significant effect upon outcomes: after age 60, ICU and 90-day mortality rates were significantly higher, and the rates of favorable outcome decreased significantly with age. Injury severity also had some effects on outcomes, but only in patients with an ISS of >50 points; these patients had significantly higher mortality rates, and a significantly lower rate of favorable outcome.

Patient status after TBI

With regard to patient status at the site of the accident, neither differences between the centers nor between genders were found. An overview of the relevant parameters is given in Table 2.

First GCS: Patients with a score of 3 had the worst outcome; almost half of them died within 90 days, and only 25% had a favorable outcome. This outcome, however, was still better than expected, as the O/E ratio was only 0.82. Significantly lower mortality rates were observed in patients with GCS scores of 7 or 8, and more than half of these patients had a favorable outcome. Patients with the highest GCS scores (> 8), however, had higher mortality rates and an extremely high O/E ratio, and only one third of these patients had a favorable outcome. This was due to the fact that in many of these patients the symptoms of the injury developed more slowly, and the GCS deteriorated later (otherwise, the patients would not have been included into this study), while

Table 1. Demographic data. Abbreviations: *O/E ratio* ratio of observed mortality (= 90-day mortality) to expected mortality (= mortality predicted by TRISS)

Parameter	Patients (n/%)	Mortality ICU (%)	Mortality 90-days (%)	Favorable outcome (%)	O/E ratio
Gender					
Female	112 (28.3)	30.4	37.5	34.8	0.93
Male	284 (71.7)	32.4	37.0	35.6	1.03
Differences		n.s.	n.s.	n.s.	
Age					
0–20	36 (9.1)	25.0	27.8	52.8	0.72
21–40	121 (30.6)	21.5	25.6	47.1	0.82
41–60	107 (27.0)	29.9	32.7	40.2	1.10
61–80	108 (27.3)	41.7	50.9	17.6	1.08
81–99	24 (6.1)	58.3	66.7	8.3	1.30
Differences		$p < 0.001$ (21–40) vs (61–80) (21–40) vs (81–99)	$p < 0.0001$ (0–20) vs (81–99) (21–40) vs (61–80) (21–40) vs (81–99) (41–60) vs (81–99)	$p < 0.0001$ (0–20) vs (61–80) (0–20) vs (81–99) (21–40) vs (61–80) (21–40) vs (81–99) (41–60) vs (61–80) (41–60) vs (81–99)	
Injury Severity Score					
9–16	121 (30.6)	28.1	34.7	27.3	1.42
17–25	123 (31.1)	33.3	37.4	41.5	1.08
26–50	131 (33.1)	26.7	31.3	40.5	0.74
51–75	21 (5.3)	76.2	85.7	14.3	0.93
Differences		$p < 0.0001$ (9–16) vs (51–75) (17–25) vs (51–75) (26–50) vs (51–75)	$p < 0.0001$ (9–16) vs (51–75) (17–25) vs (51–75) (26–50) vs (51–75)	$p < 0.05$ (26–50) vs (51–75)	

TRISS is calculated with the first available values after trauma. To classify these patients correctly, one would have to use the GCS at the time of enrollment into this study.

First GCS motor response score: Using only the motor response score of the GCS achieved results similar to those obtained by using the full GCS scores. Again, the worst outcomes were seen with the lowest score of 1, and there was a significant improvement in mortality rates and rates of favorable outcome at higher scores. The patients with the highest score of 6 had outcomes comparable to those seen at scores of 3 or 4, and their O/E ratio was extremely high, for the reason explained above.

Pupil size and reactivity: Pupil sizes and reactivity were normal in more than two thirds of the patients, and these patients had the best outcomes. One fifth of the patients had abnormal pupil size and/or reactivity; mortality was higher, and a favorable outcome was observed in only 27% of these patients. The worst outcomes were seen in patients with bilateral fixed and dilated pupils; mortality was significantly higher, and favorable outcome was observed in only 11% of these patients. Of the 45 patients with bilateral fixed and dilated pupils, 38 (84%) had a GCS score of 3, and only 3 of these (8%) had a favorable outcome.

Respiratory rate: Most patients had a normal respiratory rate (10–15/min); these patients had the lowest mortality and the highest rate of favorable outcome. An abnormally low respiratory rate was associated with significantly higher ICU and 90-day mortality and a significantly lower rate of favorable outcome. Of the 50 patients with a respiratory rate below 10/min, 38 (76%) had a GCS score of 3, and only 4 of these (11%) had a favorable outcome. Only few patients had an abnormally high respiratory rate; in these patients, mortality was slightly lower, but the rate of favorable outcome was also lower.

Oxygen saturation: About half of the patients had a normal oxygen saturation (98–100%); these patients had the lowest mortality and the highest rate of favorable outcome. With decreasing oxygen saturation, ICU and 90-day mortality increased, and the rates of favorable outcome decreased significantly.. There was no correlation between the level of oxygen saturation and GCS score, respiratory rate, or trauma severity (ISS).

Lowest systolic blood pressure (SBP): About half of the patients had a SBP in the low normal range (between 90 and 109 mm Hg). Mortality rates were slightly lower, without significant changes in the rates of favorable outcome, in patients with higher levels of SBP. Mortality rates were higher in those few patients who had a lowest

Table 2. Prehospital status. Abbreviations: *GCS* Glasgow Coma Scale; *SBP* systolic blood pressure; *O/E ratio* ratio of observed mortality (= 90-day mortality) to expected mortality (= mortality predicted by TRISS)

Parameter		Patients (n/%)	Mortality ICU (%)	Mortality 90-days (%)	Favorable outcome (%)	O/E ratio
First GCS Score	3	163 (41.2)	44.8	48.5	25.2	0.82
	4	34 (8.6)	29.4	38.2	26.5	1.13
	5–6	50 (12.6)	30.0	40.0	40.0	1.40
	7–8	75 (18.9)	13.3	18.7	57.3	0.84
	> 8	74 (18.7)	24.3	28.4	36.5	2.69
Differences			$p < 0.0001$ (3) vs (07–08) (3) vs (> 8)	$p < 0.0001$ (3) vs (07–08)	$p < 0.0001$ (3) vs (07–08) (4) vs (07–08)	
GCS Motor Score	1	184 (46.5)	41.3	44.6	28.3	0.80
	2	43 (10.9)	32.6	39.5	37.2	1.33
	3	54 (13.6)	16.7	29.6	38.9	1.21
	4	74 (18.7)	23.0	28.4	47.3	1.46
	5	7 (1.8)	0.0	14.3	57.1	2.38
	6	34 (8.6)	29.4	29.4	35.3	2.87
Differences			$p < 0.005$ (1) vs (3) (1) vs (5) (2) vs (5) (4) vs (5) (5) vs (6)	$p < 0.05$ (1) vs (5) (2) vs (5)	*n.s.*	
Pupils	Normal (N)	267 (67.9)	24.0	28.8	42.3	0.92
	Abnormal (A)	81 (20.6)	30.9	38.3	27.2	1.04
	Bilateral fixed & dilated (B)	45 (11.5)	80.0	84.4	11.1	1.23
Differences			$p < 0.0001$ (N) vs (B) (A) vs (B)	$p < 0.0001$ (N) vs (B) (A) vs (B)	$p < 0.0001$ (N) vs (A) (N) vs (B) (A) vs (B)	
Respiratory rate	0–9	50 (12.6)	64.0	66.0	10.0	1.01
	10–15	321 (81.1)	27.4	33.3	40.2	1.00
	16–30	25 (6.3)	24.0	28.0	24.0	0.99
Differences			$p < 0.0001$ (0–9) vs (10–15); (0–9) vs (16–30)	$p < 0.0001$ (0–9) vs (10–15); (0–9) vs (16–30)	$p < 0.0001$ (0–9) vs (10–15)	
Oxygen saturation	< 90	27 (7.2)	37.0	44.4	33.3	1.04
	90–95	51 (13.6)	45.1	51.0	19.6	1.13
	96–97	118 (31.5)	33.9	39.8	35.6	1.05
	98–100	179 (47.7)	25.7	30.7	40.8	0.94
Differences			*n.s.*	$p < 0.05$ (90–95) vs (98–100)	$p < 0.05$ (90–95) vs (98–100)	
Lowest SBP	< 90	37 (9.6)	48.6	56.8	29.7	0.82
	90–109	212 (55.1)	31.1	36.3	35.4	1.08
	110–130	62 (16.1)	30.6	35.5	41.9	0.90
	>130	74 (19.2)	27.0	31.1	35.1	1.05
Differences			*n.s.*	*n.s.*	*n.s.*	
First heart rate	< 60	18 (4.6)	50.0	55.6	27.8	1.12
	60–79	95 (24.4)	30.5	36.8	35.8	1.06
	80–100	238 (61.2)	29.4	33.6	36.6	0.97
	> 100	38 (9.8)	42.1	52.6	31.6	1.08
Differences			n.s.	n.s.	n.s.	

SBP below 90 mm Hg, and the rate of favorable outcome was also lower in these patients (n.s.). There was no correlation between lowest SBP and either GCS score or pupil size and reactivity. Eight patients had the combination of lowest SBP < 90 mm Hg, a GCS score of 3, and bilateral fixed and dilated pupils; 6 of these patients died, one became vegetative, but one had a good outcome (GOS 5)!

First heart rate: Most patients had normal heart rates between 60/min and 100/min. Bradycardia as well as tachycardia were associated with higher mortality rates and lower rates of favorable outcome; however, the differences were not significant. There was no correlation between heart rate and either GCS score or pupil size and reactivity.

Prehospital management

With regard to prehospital management we found some significant differences between the participating centers: the center in Vienna received significantly ($p < 0.05$) more patients (51%) by helicopter than all other centers (27–37%), while the Wagner-Jauregg Hospital received significantly ($p < 0.001$) more patients (70%) as secondary transfers than all the other centers (3–16%). There were no differences in the incidence of use of various treatment options (e.g. intubation, ventilation, hypertonic saline) between the centers. There was one significant ($p < 0.01$) difference between genders: women were much less likely (8/112; 7.1%) to be admitted during the night shift (22.00–06.00) than men (57/284; 20.1%). There were no differences in the incidence of use of various treatment options (e.g. intubation, ventilation, hypertonic saline) between genders. Almost all patients (381/396; 96.2%) were treated by teams that included an emergency physician. Patients that were treated by paramedic teams were significantly ($p < 0.001$) less likely to be intubated, and none of these patients was hyperventilated, or received hypertonic saline. An overview of the relevant parameters is given in Table 3.

Airway management: Most patients were intubated in the field; they had significantly higher ICU and 90-day mortality rates than patients who were not intubated, and their rate of favorable outcome was lower. This was probably due to a significant ($p < 0.0001$) difference in GCS: only 8/69 patients (11.6%) who were not intubated had a GCS score of 6 or less, while 237/324 (73.1%) of the intubated patients had a GCS score in that range. This may explain the high O/E ratio in the group of patients who were not intubated: in many of these patients the symptoms of the injury developed more slowly, with the consequences as discussed above. Hemodynamic status might have been an additional factor. More than one value for SBP was available in 146 patients; of these, 22 were not intubated, and 124 were intubated in the field. The first value for SBP was significantly lower in the patients who were intubated (115 ± 33 vs. 149 ± 33 mm Hg; $p < 0.0001$), and the lowest SBP was also significantly lower (105 ± 29 vs. 137 ± 36 mm Hg; $p < 0.0001$). Quite surprisingly, alternative airway devices (e.g. laryngeal mask airway, supraglottic airway) were not at all used; all patients who were not intubated had no airway device in place.

Ventilation: All patients who were not intubated were breathing spontaneously, and they had the best outcomes. Most of the intubated patients were normoventilated, and their ICU and 90-day mortality rates were higher. Hyperventilation was done in 6% of the intubated patients; these patients had slightly lower ICU and 90-day mortality rates, but their rate of favorable outcome was also lower. Neither of these differences was significant.

Fluid administration: About 12% of the patients received more than 1000 ml of fluids; these patients had the best outcomes. Administration of less fluids was associated with slightly higher mortality rates and lower rates of favorable outcome. Patients who received no fluids had significantly better GCS scores (score 6 or less in 23%, $p < 0.05$) than patients who received fluids (score 6 or less in 56–73%). It seems that the SBP of the patients was an important factor for the decision to use more fluids; 50% of the patients who received more than 1000 ml of fluids had an SBP below 110 mm Hg, while that rate was significantly lower (0–28%) in patients who received no or less fluids ($p < 0.01$). Another important factor may have been trauma severity; patients who received more than 1000 ml of fluids had an ISS of 37.9 ± 15.6, whereas patients who received no fluids had an ISS of 21.2 ± 9.7; those who received 100–500 ml of fluids had an ISS of 22.6 ± 9.7, and those who received 500–1000 ml had an ISS of 28.0 ± 12.2. The difference in ISS between patients who received more than 1000 ml of fluids and all other patients was significant ($p < 0.0001$). Patients who received more than 1000 ml of fluids had an expected mortality rate of 54%, and their outcomes were remarkably better than that (O/E ratio 0.58!) while the outcome was not better or even worse than expected in all other patients.

Hypertonic saline: About 5% of the patients received hypertonic saline; there was no difference in outcomes between these and patients who did not receive hypertonic saline. There were no significant differences regarding SBP, ISS, or GCS, but patients who received hypertonic saline had abnormal pupil size and/or reactivity significantly more frequently ($p < 0.05$), and still had a better than expected outcome (O/E ratio 0.79).

Mode of transport: One third of the patients were transported by helicopter; these patients had a slightly lower mortality, and a significantly higher rate of favorable outcome. All helicopter patients had the standard monitoring of ECG and pulse oximetry, while EGC was not used in 5, and pulse oximetry was not used in 7 patients transported by ambulances. Capnography was used in only 5 patients, who were all transported by helicopter. Helicopter patients were more likely to be intubated (93 vs. 76%; $p < 0.0001$) and to receive more fluids (1074 ± 617 vs. 883 ± 454 ml; $p < 0.001$). Helicopter patients were more seriously injured; 71% had a GCS score of 6 or less, while only 57% of the ambulance patients had a score in that range ($p < 0.01$), and ISS was significantly higher (30.9 ± 14.1 vs. 24.7 ± 11.2; $p < 0.0001$). There were no other differences between the groups. Expected mortality was 40% for helicopter patients, and 35% for ambulance patients, but the outcomes were exactly the opposite.

Secondary transfer: The few patients (15%) who underwent secondary transfer had significantly lower mortal-

Table 3. Prehospital treatment. Abbreviations: O/E ratio = ratio of observed mortality (= 90-day mortality) to expected mortality (= mortality predicted by TRISS)

Parameter	Patients (n/%)	Mortality ICU (%)	Mortality 90-days (%)	Favorable outcome (%)	O/E ratio
Airway management					
No endotracheal intubation	69 (17.6)	21.7	26.1	40.6	1.70
Endotracheal intubation	324 (82.4)	34.0	39.5	34.6	0.95
		p < 0.05	*p < 0.05*	*n.s.*	
Ventilation					
Spontaneous breathing	69 (17.6)	21.7	26.1	40.6	1.70
No hyperventilation	304 (77.6)	34.2	39.8	34.9	0.97
Hyperventilation	19 (4.8)	31.6	36.8	26.3	0.81
		n.s.	*n.s.*	*n.s.*	
Fluid administration					
No fluids	26 (6.6)	30.8	34.6	19.2	1.44
100–500 ml	126 (31.8)	32.5	37.3	32.5	1.17
500–1000 ml	196 (49.5)	33.7	38.8	37.2	1.02
> 1000 ml	48 (12.1)	22.9	31.3	43.8	0.58
		n.s.	*n.s.*	*n.s.*	
Hypertonic saline					
No	375 (94.7)	31.5	37.1	35.5	1.02
Yes	21 (5.3)	38.1	38.1	33.3	0.79
		n.s.	*n.s.*	*n.s.*	
Mode of transport					
Air	148 (37.6)	29.7	35.1	41.9	0.87
Ground	246 (62.4)	32.9	38.2	31.7	1.10
		n.s.	*n.s.*	*p < 0.05*	
Secondary transfer					
No	338 (85.4)	33.7	39.6	34.6	1.05
Yes	58 (14.6)	20.7	22.4	39.7	0.69
		n.s.	*p < 0.01*	*n.s.*	
Time of hospital admission					
06.00–14.00	168 (42.4)	33.3	40.5	34.5	1.01
14.00–22.00	163 (41.2)	29.4	33.7	34.4	0.97
22.00–06.00	65 (16.4)	33.8	36.9	40.0	1.07
		n.s.	*n.s.*	*n.s.*	

ity than those who were admitted directly from the scene of accident. This was at least partly due to lower trauma severity (ISS 27.7 ± 13.1 vs. 23.0 ± 9.2; p < 0.001) and better hemodynamic status (SBP < 110 mmHg in 7.3% vs. 28.9%; p < 0.01).

Time of hospital admission: Only few patients (16%) were admitted during the night shift (22.00–06.00). Outcomes were marginally better in patients who were admitted during the morning shift (06.00–14.00), but none of the differences were significant. Helicopter transport was less frequently used during the night shift (18% vs. 40% during the other shifts; p < 0.01). There were no differences in GCS scores, trauma severity, or SBP, but patients admitted during the night shift had a higher rate of abnormal pupils (44.6% vs. 30%; p < 0.05).

Discussion

Almost 30 years ago, Teasdale and Jennett [5] showed that their new "Glasgow Coma Scale" scores correlated well with prognosis of patients with severe brain trauma. Since then, numerous studies have been done, and most have confirmed that result. A recent study from Great Britain [6] found that until 1996, GCS had correlated well with GOS after 6 months, while after 1996, no such correlation could be found. A clear association between first

GCS score and outcome has also been found in our study. Assessment of GCS is even part of the guidelines for treatment of patients with severe TBI [7]. The guidelines state that patients with the lowest GCS score of 3 have a mortality rate of approximately 80%, and an 8–10% rate of favorable outcome [7]. Compared to these predictions, outcomes for patients with a GCS score of 3 were much better in our study, as 90-day mortality was 49%, and the rate of favorable outcome was 25%. One major problem with low GCS scores is their lack of precision for prediction of a good outcome. High GCS scores may, as in our study, lead to incorrect predictions because some patients may develop their clinical symptoms more slowly. Not surprisingly, research has focused on additional factors that might improve the prognostic value of the GCS.

In 1988, Choi et al. [8] proposed a score that included the patient's age, the best motor response of the GCS, and the pupil response. With these three parameters, which were obtained in the emergency room, they were able to correctly predict the GOS score at 6 months after trauma in 78% of their 523 patients. This was confirmed in our study: age, pupil size and reactivity, and GCS score had significant effects upon outcomes. Our study also confirmed that the use of the motor response score, instead of the full GCS score, allows for a classification of patients that correlates well with outcomes. Their model, however, did not perform well when used to classify our patients. For example, the model predicts unfavorable outcome for patients with normal pupils, a GCS motor response score of 4, and age over 50 years. In our study 25 patients fulfilled these criteria, and 8 of these (32%) had a favorable outcome. The model also predicts unfavorable outcome for patients with unilateral abnormal pupils, a GCS motor response score of 4, and age over 20 years. In our study 10 patients fulfilled these criteria, and 7 of these (70%) had a favorable outcome. These disappointing results might be explained by improvements in treatment of TBI during the last 20 years. A recent study [9] investigated the outcomes of 173 patients with a GCS score of 3 and bilateral fixed and dilated pupils and found not a single survivor. But even with that combination, 3/38 patients (8%) had a favorable outcome in our study.

Other authors [10] studied the predictive value of the Revised Trauma Score (RTS; weighted values for GCS, respiratory rate, and systolic blood pressure are multiplied with fixed coefficients and added to obtain a single number) and found no correlation to functional outcomes. The RTS reliably predicts probability of death for trauma patients, and performs better than each of the components alone, but cannot predict functional outcome after severe TBI. Our study confirms these results; abnormal respiratory rates were associated with worse outcomes, but even in the subgroup of 38 patients with a low respiratory rate and a GCS score of 3 there were some survivors with favorable outcomes. Hypotension is well known as a major risk factor for bad outcome; in the landmark study by Chesnut et al. [11] early hypotension (i.e. SBP < 90 mm Hg occurring from injury through resuscitation) was associated with a mortality rate of 55%. A similar mortality rate for hypotensive patients (57%) was found in our study.

A reliable prognostic index, based on prehospitally available symptoms like GCS score, GCS motor response score, pupil size and reactivity, breathing rate, or SBP, would allow for more precise decisions than at present possible. The clinical signs are useful for triage, as it is well known that more seriously injured patients should be transported to the most appropriate center as fast as possible [12]. The clinical signs, obviously, are relevant for monitoring of the course of the patient and of the effects of treatment. The clinical signs are also useful for research, as they allow for classification of patients. At present, however, the clinical signs available to prehospital care providers cannot be used to reliably predict outcome.

All available guidelines [7, 13, 14] recommend that patients with severe TBI (defined as patients with a GCS score of 8 or less) should at least receive supplemental oxygen, and should be intubated and ventilated, if possible. The rationale behind that recommendation is the well known fact that hypoxia is a serious secondary injury which may worsen outcome. Chesnut et al. [15] demonstrated that patients who had hypoxia (defined as pO_2 < 60 mm Hg or apnea or cyanosis) had a higher hospital mortality (33 vs. 27%) and a lower rate of favorable outcome (45 vs. 51%) compared to patients who did not. A more recent study [16] found that hypoxia was not associated with increased mortality, but led to prolonged ICU and hospital stay. In our own study, lower rates of oxygen saturation were associated with higher mortality and lower rates of favorable outcome. Thus, it seems rational to intubate and ventilate patients with severe TBI. Winchell & Hoyt [17] compared the outcomes of patients who had been intubated in the field to those from patients who had not been intubated. Almost all patients (92%) fulfilled the field intubation criteria then used by aeromedical teams, but due to different criteria used by ambulance teams, only about 50% of these patients were actually intubated. Of the 1092 patients, 671 had severe TBI, and 351 had isolated severe TBI. Mortality rates were significantly lower for those patients that had been intubated: 36% vs. 57% for patients with severe TBI, and 23% vs. 50% for patients with isolated severe TBI.

Other studies, however, came to different conclusions. Davis et al. [18] compared 209 prospectively collected patients with moderate to severe TBI (definition: abbreviated injury score [AIS] for head/neck > 2) who had had rapid sequence intubation (RSI, with midazolam, succhinyl choline, and rocuronium) in the field to 629 hand-matched historical controls who had not had RSI. The groups were similar with regard to all matching parameters (e.g. age, GCS score, frequency of specific brain trauma diagnoses, incidence of invasive procedures). Mortality was higher (41 vs. 30%), and the rate of good outcome was lower (46 vs. 58%) in the patients who had been intubated in the field. The authors then used another approach [19]: they analyzed the outcomes of 13625 patients with moderate to severe TBI (definition: AIS for head/neck > 2) from five trauma centers, using logistic regression to control for age, trauma mechanism, gender, GCS score, AIS for head/neck, ISS, and hypotension. About one fifth (19.3%) of the patients had been intubated in the field, and their mortality rate was signifi-

cantly higher (55% vs. 15%). This was also true for the patients with severe TBI (definition: AIS for head/neck > 3 and GCS score < 9), but not for the patients who were treated by aeromedical teams; this latter group included patients who had had RSI, while all other intubated patients had been given no drugs to facilitate intubation. This analysis also identified a subgroup of patients who might benefit from prehospital intubation; the main parameters were higher trauma severity, GCS score < 8, and presence of hypotension. They concluded that prehospital intubation is associated with a decrease in survival among patients with moderate to severe TBI, while more critically injured patients might benefit from prehospital intubation. Wang et al. [20] compared outcomes for 4098 patients with an AIS for head/neck > 2 who had had either prehospital (44%) or emergency department intubation (56%). They used logistic regression to control for the usual risk factors, and found that the patients who had had prehospital intubation had a higher mortality rate (49 vs. 28%) and a lower rate of favorable outcome (41 vs. 58%). As before, patients treated by aeromedical teams which used RSI fared significantly better than patients treated by ambulance crews which did not use RSI.

The implications for clinical care are not fully clear. Neither of the three studies can be considered Class I evidence, but the total number of patients included (> 18000 patients!) is impressive. It is possible that there were significant differences between the groups that remained undetected: a patient who can be intubated without the use of drugs is clearly more seriously injured than a patient with similar characteristics who will not tolerate endotracheal intubation without RSI. One indication that this may be a serious limitation of these studies are the published mortality rates: hospital mortality rates for the patients who had had intubation in the field were 49% [20] and 55% [19]; these rates were much higher than those found in our study. But still, it is reasonable to conclude that prehospital intubation may be an additional risk for patients with severe TBI. A large prospective study to prove or refute this hypothesis should be done, but should include only patients treated by teams that are using drugs to facilitate intubation.

Assuming that prehospital intubation may worsen outcomes for patients with TBI, what could be the possible mechanisms? Prehospital intubation usually requires anesthesia, and anesthesia may lead to hypotension. In our study, we found a significantly lower SBP in those patients who were intubated; this might have been an effect of anesthesia. Patients who were intubated later in the emergency room had significantly higher values for SBP during their prehospital phase. The quality of ventilation might be another significant factor. Helm et al. [21] investigated 122 patients with severe TBI who had been intubated in the field. Optimal oxygenation (defined as $pO_2 > 100$ mm Hg) was achieved in 85%, and optimal ventilation (defined as pCO_2 between 35 and 45 mm Hg) was achieved in 43% of the patients. Hyperventilation was common (41%), hypoventilation (16%) and hypoxaemia (3%) were less frequently observed. In only 38% of the study patients were oxygenation as well as ventilation considered adequate. In another study [22] of 40 patients with severe TBI, 28 (70%) had been unintentionally hyperventilated. The rate of unfavorable outcome was higher in the hyperventilated group (39 vs. 25%). Davis et al. [23] studied the quality of prehospital ventilation in 76 patients where end-tidal pCO_2 had been monitored. Hyperventilation (defined as end-tidal $pCO_2 < 30$ mm Hg) was observed in 79% of the patients, and the mean duration of hyperventilation was 8 minutes (range 6–10 minutes). In a recent paper [24] from the same group, the association between hyperventilation and increased mortality after severe TBI was confirmed. Obviously, inadvertent hyperventilation is common during prehospital ventilation. It is well known that hyperventilation should be used with caution in patients with severe TBI [25], and all guidelines [7, 13, 14] state that hyperventilation during the first 24 hours after TBI should be avoided because of the risk of cerebral hypoperfusion. Thus, prehospital intubation frequently leads to a combination of hyperventilation and low SBP, which in turn may cause critical cerebral hypoperfusion in patients with severe TBI, and that could be the reason for the worse outcomes reported for patients who were intubated in the field.

What are the implications for clinical care? Firstly, drugs that do not lower blood pressure (i.e ketamine) should be preferred for anesthesia; ketamine has no deleterious effects upon intracranial pressure (ICP) as long as the patient is adequately ventilated [26]. Secondly, monitoring of patients with severe TBI who are intubated in the field should include capnography to limit incidence as well as duration of inadvertent hyperventilation.

Prehospital fluid administration after trauma is another hotly debated topic. In 1994, Bickell et al. [27] published their landmark paper which showed that delayed fluid resuscitation (i.e. less than 500 ml of fluids given prior to surgery) improved survival in patients with penetrating torso injuries. This may be due to a number of reasons: loss of valuable time while securing venous access, increase in blood pressure that may cause increased bleeding, and a decrease in haematocrit and clotting factors caused by the volume of fluid. The main conclusion from this study is that in patients with penetrating trauma, the first priority is control of hemorrhage, and not normalization of blood pressure. The implications of this study for patients with blunt trauma, and especially patients with TBI, are far from clear. An excellent review of the present knowledge has been presented by Soreide and Deakin [28] in 2005. For patients with blunt trauma and suspected severe TBI they recommend that the minimal amount needed to restore and/or maintain a SBP > 110 mm Hg should be given in rapidly infused aliquots of 500 ml. The results of our study seem to confirm that concept: patients who received > 1000 ml of fluids had the best outcomes although these patients were significantly more severely injured and had lower GCS scores. Outcomes were worse for patients who received less or no fluids although these patients were less severely injured and had higher GCS scores. However, only 8/396 patients (2%) had penetrating TBI, and none had penetrating torso injuries. The outcomes might be different for patients with penetrating torso injuries and TBI.

With regard to the type of fluids, colloids, isotonic and hypertonic crystalloids, and combinations of colloids and hypertonic crystalloids have been studied in TBI patients.

Hypotonic crystalloids (e.g. Ringer's lactate) are clearly not indicated as they might increase brain edema. Isotonic crystalloids (e.g. Ringer's solution, NaCl) seem to be safe. Recently, Cooper et al. [29] published the results of a study where 229 hypotensive (SBP < 110 mm Hg) patients with severe TBI (GCS score < 9) received a bolus of either 250 ml 7.5% saline or 250 ml Ringer's lactate (controls) as the first infusion after trauma, followed by standard treatment as required. Mortality rates were higher in the control group (50 vs 45% at hospital discharge, and 53 vs. 45% after 6 months), but this was statistically not significant ($p = 0.23$). The rates of favorable outcome were equal. The authors concluded that hypertonic saline had no benefits for patients with severe TBI; however, due to the small number of patients, a beta-type error cannot be ruled out. Unfortunately, the number of patients in our study who received hypertonic saline was too small to make any conclusions. Another recent study [30] compared 4% albumine to normal saline for fluid resuscitation, and found no differences between the groups. A subgroup analysis of 492 patients with TBI, however, revealed significantly increased mortality in the albumin group (25 vs. 15%, $p = 0.009$). Hydroxyethyl starch (HES) seems to be a more promising colloid, either alone or in combination with hypertonic saline. Neff et al. [31] found that HES 130/0.4 can be safely used in patients with severe TBI. The combination of HES 200/0.5 plus 7.2% saline (Hyperhes®) has been shown to be more effective than mannitol in decreasing elevated ICP [32], and has been found to be safe for prehospital use in another study [33]. Wade et al. [34] did a meta-analysis of previous studies on the effects of a combination of 7.5% saline/dextran (HSD) vs. standard treatment in trauma patients. They found that patients with hypotension (SBP < 90 mm Hg) and severe TBI who had received HSD were about twice as likely to survive (OR 2.12; $p = 0.048$). Thus, if all these studies are taken into account, it can be concluded that patients with severe TBI should be given fluids if SBP is < 110 mm Hg, that an initial bolus of hypertonic saline (in combination with a colloid) might be beneficial, and that HES and/or normal saline and/or Ringer's solution may be used to maintain blood pressure.

In our study helicopter transport was associated with better outcomes although these patients were significantly more severely injured and had lower GCS scores. As there were no significant differences with regard to known risk factors (e.g. age, pupils, lowest SBP) it has to be assumed that this was due to faster arrival at the hospital and/or differences in treatment (higher rates of intubation, more fluids). Unfortunately, we do not have reliable data on the time of accident, and cannot investigate this further. Better outcomes for TBI patients who had been treated by aeromedical teams have been reported by other authors, too [19, 20, 35]. Faster transport as well as more advanced treatment have been discussed as possible reasons. The most unexpected finding in our study was the fact that outcomes were better for patients who had had treatment at another hospital, and had then been transported to one of the study centers. Most experts recommend that TBI patients should be transported directly to the most appropriate hospital [12]; this is also part of the guidelines [7, 13, 14]. Considering the fact that the patients who had had a secondary transport were less severely injured, it must be concluded that probably only the more stable patients were selected for secondary transport to one of our study centers. The rationale behind that strategy must remain unclear, as these decisions were made at the primary hospitals, and not at the admitting centers.

Conclusions

Our study investigated prehospital status and treatment of patients with severe TBI. We found that age > 60 years, ISS > 50 points, GCS score < 4, bilateral changes in pupil size and reactivity, respiratory rate < 10/min, SBP < 90 mm Hg, and heart rate < 60/min were associated with significantly increased ICU and 90-day mortality rates, and lower rates of favorable outcome. With regard to prognostic value, the GCS motor response score is identical to the full GCS score. No parameter or combination of parameters allowed for reliable outcome predictions. Administration of > 1000 ml of fluid and helicopter transport were associated with better outcomes than expected, while endotracheal intubation in the field had neither a positive nor a negative effect on outcomes. Outcomes were better than expected in the few patients who received hypertonic saline. Based on these results, and the review of the literature, our recommendations are:

- As there are no parameters that allow for reliable prediction of unfavorable outcome all patients should have the appropriate treatment, even if the odds for favorable outcome seem to be poor;
- hypotension and hyperventilation due to intubation must be avoided; end-tidal pCO_2 should be monitored;
- bag mask ventilation may be an acceptable alternative for less seriously injured patients;
- the minimal amount of fluids needed to restore and/or maintain a SBP > 110 mm Hg should be given in rapidly infused aliquots of 500 ml;
- HES, normal saline, and Ringer's solution have been used, and are considered safe for patients with severe TBI;
- Helicopter transport should be arranged for more seriously injured patients.

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