Severe traumatic brain injury - consequences of early adverse events.

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Abstract

Background: Several factors associated with unfavourable outcome after severe traumatic brain injury (TBI) have been described: prolonged pre-hospital time, secondary referral to a level 1 trauma centre, the occurrence of secondary insults such as hypoxia, hypotension or low end-tidal carbon dioxide ($ETCO_2$). To determine whether adverse events were linked to outcome, patients with severe TBI were studied before arrival at a level 1 trauma centre.

Methods Prospective, observational study design. Patients with severe TBI (*n*=48), admitted to Umeå University Hospital between January 2002 to December 2005 were included. All medical records from the site of the accident to arrival at the level 1 trauma centre were collected and evaluated.

Results: A pre-hospital time of >60 min, secondary referral to a level 1 trauma centre, documented hypoxia (oxygen saturation <95%) , hypotension (systolic blood pressure <90mmHg), hyperventilation ($ETCO_2$ <4.5kPa) or tachycardia (heart rate >100 beats/min) at any time before arrival at a level 1 trauma centre were not significantly related to an unfavourable outcome (Glasgow Outcome Scale 1-3).

Conclusion: Early adverse events before arrival at a level 1 trauma centre were without significance for outcome after severe TBI in the trauma system studied.

Introduction

Severe traumatic brain injury (TBI) is a major cause of death and disability. Of all deaths related to TBI, approximately 50% is assumed to occur within 2h after the injury. 1

The concept of the "golden hour" of trauma is defined as the time period when a critically injured trauma patient can be saved if appropriate care is provided. 2 It is therefore considered important for a trauma victim to reach a hospital as fast as possible. For patients with TBI, it is recommended to transport directly to a level 1 trauma centre, where intracranial pressure (ICP) can be measured, rather than to the closest hospital, if possible .1

Solely the occurrence (most common with no definition of duration) of secondary insults such as hypoxia/hypotension and hyperventilation in TBI patients, before, on admission to or in hospital, have been reported to be strongly related to a poor outcome. 3-7

The present study examined the pre-level 1 trauma centre care in patients with severe TBI. All patients were finally treated at Umeå University Hospital, a level 1 trauma centre. This hospital is situated in northern Sweden and has the regional responsibility over a vast rural area, covering half the area of Sweden (225.000 km2), with a population of approximately one million people. It is the only hospital in this region with a neurosurgical department. This implies that all patients with severe TBI in the region are primarily transported to, or transferred here.

The aim of this study was to describe the occurrence of adverse events: prolonged pre-hospital time defined as >60 min, secondary referral to a level 1 trauma centre, hypoxia defined as oxygen saturation (SaO2) <95%, hypotension defined as systolic blood pressure (SBP) <90mmHg, and hyperventilation defined as end-tidal carbon dioxide (ETCO2) <4.5kPa before arrival at a level 1 trauma centre, and relate them to outcome.

We hypothesized that adverse events would influence outcome.

Methods

This observational study of pre-level 1 trauma centre care in severe TBI is part of a prospective blinded randomized placebo-controlled study primarily designed to evaluate the effect of prostacyclin (epoprostenol, Flolan®, Glaxo, Solna, Sweden) vs. placebo in patients with severe TBI. [8]

Patients were included from January 2002 until December 2005.

Inclusion criteria were age 15–70 years, blunt head trauma, Glasgow Coma Scale (GCS) ≤8 by the time of sedation and intubation, arrival at the level 1 trauma centre within 24 h after the accident and cerebral perfusion pressure >10 mmHg at arrival. Patients with GCS 3 and non-reactive dilated pupils at admittance were included. Exclusion criteria were lactating or breastfeeding women.

There are 11 referral hospitals in the region, all with their own organization of ground ambulances, staffed with at least one registered nurse. There are three ambulance helicopters staffed with a nurse anaesthetist only or both a nurse anaesthetist and physician (always an anaesthesiologist). In addition, there is a fixed-wing transportation system (staffed with an anaesthesiologist and nurse anaesthetist/intensive care nurse). Ground ambulances have a response time to alarm of 2 min, ambulance helicopters of 20 min and fixed-wing "as soon as possible" (maximum 60 min). At arrival at the emergency department in every hospital, the patients were examined and treated according to the principles of advanced trauma life support (ATLS®).

At the level 1 trauma centre, an ICP-targeted therapy was used. This treatment protocol has been described in previous publications, and is based on the physiological principles of the Lund concept.[8-11]

Data collection

Data were collected from the site of the accident until arrival at Umeå University Hospital, Sweden.

The cause of the TBI was documented. GCS was used for the assessment of consciousness and the severity of trauma was evaluated according to the injury severity score (ISS).12,13

The number of documented data for every parameter is given in the results.

Hypotension was defined as SBP <90mmHg, hypoxia as SaO2 <95%, hyperventilation as ETCO2 <4.5kPa, and tachycardia as heart rate (HR) >100 beats/min (b.p.m.).

Pre-hospital data include estimated (as exact as possible) or exact accident time, alarm-time, time for arrival of pre-hospital staff at the scene of the accident, time spent at the accident site, duration of transportation to hospital and physician present at scene or not. The type of primary transportation was noted. The pre-hospital clinical condition of the patient, physiological parameters and all medical treatment were recorded.

Primary hospital data include physiological parameters, diagnostic procedures and all medical treatment.

Secondary transportation data include duration of transportation, type of secondary transportation, physiological parameters and all medical treatment.

At all times, vital parameters, SBP, SaO2, HR, and ETCO2, were measured using accessible equipment.

Outcome is given 3 months after trauma, assessed using the Glasgow Outcome Scale (GOS) by independent staff. 8,14

Ethics

The local ethics committee at Umeå University Hospital approved the study. Written informed consent to participate in the study was obtained by the next of kin when the patient arrived at the university hospital.

Statistics

Statistics were calculated using PRISM Graph Pad version 5.0b. Data are given as median (range), or percentage. Fisher's exact test was used to compare unfavourable (GOS 1-3) vs. favourable (GOS 4-5) outcome, or dead vs. alive, with, more or less than 60 min of pre-hospital time , intubation or not at scene, pre-hospital fluid administration or not, SaO_2 more or less than 95%, SBP more or less than 90 mmHg, HR more or less than 100 b.p.m. and $ETCO_2$ more or less than 4.5 kPa.The non-parametric Mann-Whitney U-test was used to compare time spent on scene with or without a physician, time spent on scene regarding intubation or not, the primary transportation time between patients intubated or not at scene, GCS at scene in intubated or not intubated patients, GCS and more or less than 60 min spent on scene, GCS and intubation before or after computerized tomography (CT), GCS with or without hypoxia, GCS with or without hypotension, ISS with or without hypoxia, ISS with or without hypotension, GOS and primary or secondary transportation to Umeå University Hospital. In order to evaluate the prognostic values of the results, a logistic regression model was used for pre-hospital data. A p-value of ≤ 0.05 was regarded as statistically significant.

Results

Forty-eight patients were included in the study. The basic characteristics of the study population are given in Table 1. There were no statistically significant differences in the basic characteristics (age, gender, GCS, ISS) or outcome (GOS) at 3 months between the two treatment groups: prostacyclin (n=23) and placebo (n=25).[8] The study population can thus be considered as one group for this study.

Table 1. Basic characteristics of the study population

Age (years)	
Median (range), mean ± SD	30 (15–63), 35 ± 15
Sex number (%)	M 31 (65%), F 17 (35%)
ISS	
Median (range)	29 (9–50)
GCS (accident site)	
Median (range)	5 (3–13)
GCS (intubation)	
Median (range)	6 (3–8)
Cause of accident (%)	
Motor vehicle	64%
Fall	21%
Other	15%
Multiple injuries* number (%)	
	33/48 (69%)
Thoracic injuries	23/48 (48%)
Long bone fractures	3/48 (6%)
Abdominal injuries	4/48 (8%)
Spinal fractures	16/48 (33%)

* One patient can have more than one injury.

Severity of trauma evaluated by the Injurity Severity Score (ISS). Assessment of consciousness by the Glasgow Coma Scale (GCS). Motor vehicle accidents includes cars, motorcycles, snowmobiles and pedestrians hit by a motor vehicle. Other causes includes bicycle, ski-accidents and abuse. Regarding multiple injuries, one patient can have more than one injury.

M, male; F, female; ISS, injury severity score

Data from the scene of the accident and primary transportation

The estimated median time from accident to alarm, median time from alarm to arrival, time spent on scene, duration of primary transportation (from the scene of the accident to primary hospital/level 1 trauma centre) and total pre-hospital time are given in Fig. 1.

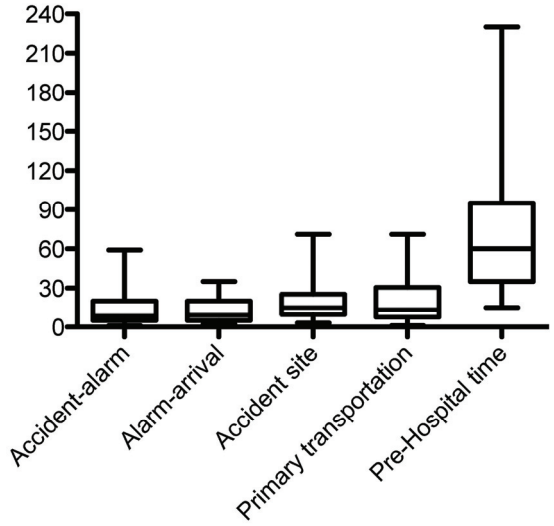

Fig. 1. Pre-hospital time intervals. Box plots show the medians and 25th–75th percentiles. Time is given in minutes. Accident to alarm; 8.5 (0–59) n546. Alarm to arrival at the scene; 9 (2–35) n547. Time spent on scene 15 (3–71) n546. Primary transportation 13.5 (1–71) n546. Total pre-hospital time 60 (15–230) n547

A physician was present at the accident site with 13/48 (27%) patients. The median time spent on scene with a physician present was 24 (5-60) min, and that with no physician present was 14 (3-71) minutes, non-significant (NS). The median GCS at scene (*n*=48) was 5 (3-13). In the group with pre-hospital time < 60 minutes (*n*=24), the median GCS at scene was 4 (3-8), and in the group with pre-hospital time > 60 minutes (*n*=24), the median GCS was 6 (3-13) (NS).

Patients who were not intubated before arrival at the primary hospital (*n*=36, including one unsuccessful attempt) had a median on scene time of 12.5 (3-44) min, compared with intubated patients (*n*=10), where the median on scene time was 34.5 (18-71) min ($p<0.0001$). Two patients intubated at community centres were excluded from this comparison because they were neither intubated at scene nor at primary hospital. Staff accustomed to the pre-hospital setting carried out all intubations. There was a statistically significant difference in the primary transportation time (from the scene of the accident to primary hospital or directly to the level 1 trauma centre) between patients intubated at scene (*n*=10), median 35 (8-57) min, and patients not intubated at scene (*n*=36), median 10 (1-98) min ($p <0.0005$).

The median GCS for the ten patients intubated at scene was 5 (3-8) and the median GCS for patients who were not intubated (*n*=36) at scene was also 5 (3-13) (NS). Intravenous access was established in 33/48 (69%) patients, and intravenous fluids were administered to 26/48 (54%) patients. Ringer-Acetat® solution (Fresenius Kabi, Uppsala, Sweden) was given to 22/26 (85%) patients; four patients received other fluids i.e. RescueFlow® (BioPhausia, Stockholm Sweden), Plasmodex® (Meda, Solna, Sweden), isotonic saline (Fresenius Kabi, Uppsala, Sweden) or combinations thereof.

SBP was recorded in 38/48 (79%) patients (Fig. 2a). SaO_2 was documented in 41/48 (85%) patients, (Fig. 2b). SBP <90 mmHg in combination with SaO_2 <95% was present in 6/38 (16%) patients (one ambulance record missing, counted as no interventions). Three of the

patients with both hypoxia and hypotension had a cardiac arrest at the scene of the accident. They all regained adequate circulation at scene and arrived alive at the level 1 trauma centre. There was no statistically significant difference in GCS or ISS between patients who were hypoxic or hypotensive pre-hospitally compared to patients who were not.

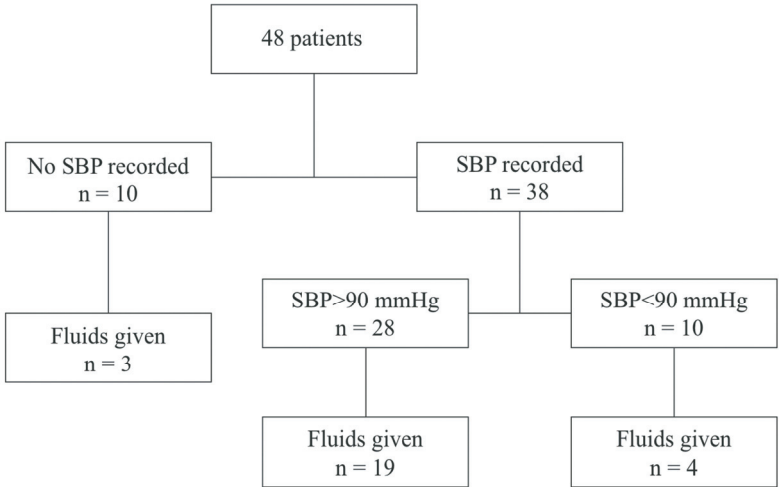

Fig 2A. Pre-hospital systolic bloodpressure (SBP) and fluids administered.

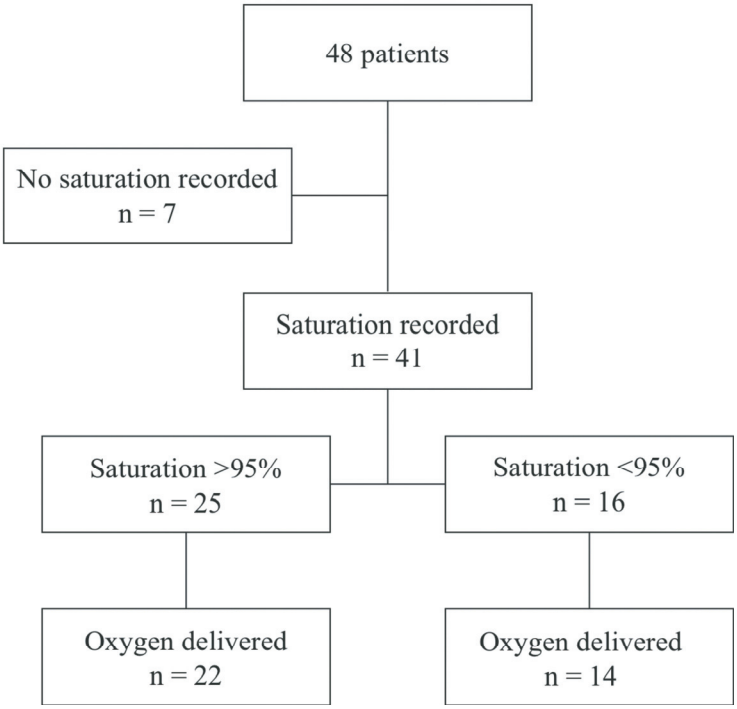

Fig 2B. Pre-hospital saturation and oxygen delivered.

Data from primary receiving hospital

The level 1 trauma centre was the primary hospital for 13/48 (27%) patients and 35/48 (73%) patients were referred. A schematic presentation from the accident site to the level 1 trauma centre for all 48 patients included in the study is given in Fig. 3.

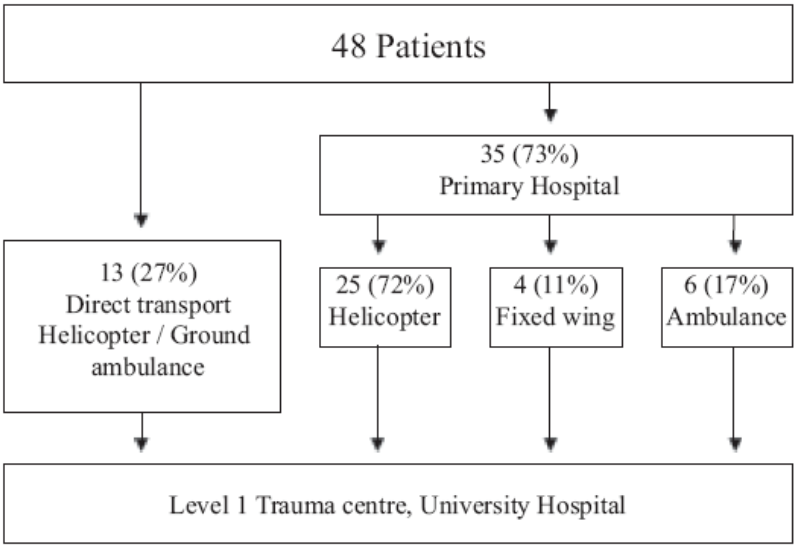

Fig 3. Flow chart for patients from accident site to level 1 trauma centre

A CT-scan of the brain was performed in all 48 patients. The median time from arrival at any hospital to the CT-scan was 42.5 (10-201) min. There was a statistically significant difference in the median GCS for patients intubated before a CT-scan, median 6 (range 3-8), compared with patients intubated after a CT-scan, median 7 (3-8), ($p < 0.05$).

Of the 10 patients with hypotension pre-hospitally, six were still hypotensive at arrival. Of the 16 hypoxic patients, only five were still hypoxic at arrival.

The total median time spent at primary receiving hospital for patients later transferred was 224 (54-990) minutes, (n=34, one missing value). Two patients were in need of acute surgical intervention and spent >16 h at the primary hospital.

All patients were intubated before secondary transportation. The median distance from the primary hospital to the level 1 trauma centre was 138 (114-215) km if ground ambulances were used, 321 (135-598) km if ambulance helicopters were used and 400 (265-598) km when fixed wing transportation was used.

The median time from accident to arrival at the level 1 trauma centre for all patients, directly transported or transferred, is given in Fig. 4.

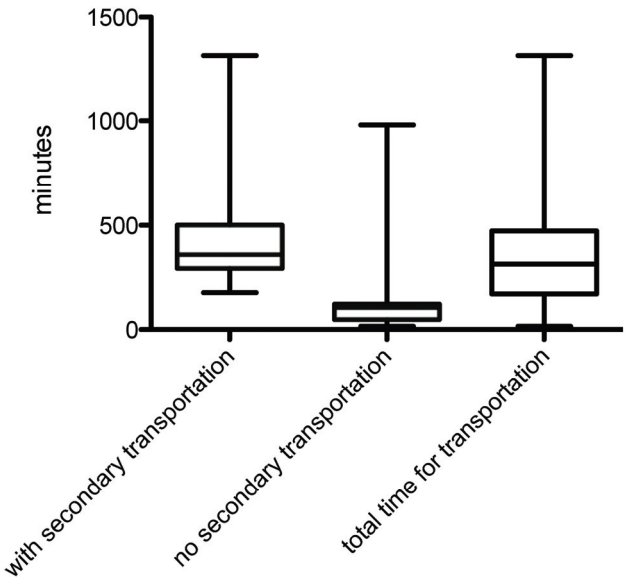

Fig 4. Time from accident to arrival to a level 1 trauma centre. Boxplots show the median and 25th-75th percentile. Time is given in minutes. With secondary transportation (n=35), 360 (175-1315). With no secondary transportation (n=13), 104 (16-981) Total time for transportation, all patients (n=48), 315 (16-1315).

Outcome

Outcome was evaluated 3 months after trauma. The overall mortality of the 48 patients included in this study was 13% and the favourable outcome (GOS 4-5) was 52%.

There was no statistical significant difference in favourable (GOS 4-5) vs. unfavourable (GOS 1-3) outcome, or dead vs. alive, related to the total prehospital time more or less than 60 min, fluids administered pre-hospitally or not, or persistent hypoxia or hypotension at arrival at hospital or not. Six patients were both hypoxic and hypotensive at scene; three of these had a cardiac arrest but regained spontaneous circulation at scene. In the three patients who had a cardiac arrest at scene, GOS was 1(dead day 4), 1(dead day 9), and 4, respectively. GOS in the remaining three patients was 4,4, and 5, respectively.

SBP, SaO2, HR and $ETCO_2$ in the pre-hospital setting, at the primary hospital and during secondary transportation related to unfavourable/favourable outcome are given in Table 2. There was no statistically significant difference at any time between favourable or unfavourable outcome and SBP more or less than 90mmHg, SaO_2 more or less than 95%, $ETCO_2$ more or less than 4.5 kPa and HR more or less than 100 b.p.m.

There was no statistically significant difference in outcome if the patients were pre-hospitally intubated or not. There was also no statistically significant difference in outcome if the patients were transported directly to the level 1 trauma centre or referred. No statistically significant prognostic values were found when using pre-hospital hypoxia, hypotension, >60-min at scene, and referral as independent variables and GOS, unfavourable/favourable outcome and dead/alive at 3 months as dependent variables in a logistic regression model.

Table 2. Vital parameters in the pre-hospital setting, at the primary hospital and during secondary transportation related to GOS 1–3 (unfavourable outcome) and GOS 4–5 (favourable outcome).

Vital parameter	Pre-hospital setting GOS 1–3 GOS 4–5	Primary hospital GOS 1–3 GOS 4–5	Secondary transportation GOS 1–3 GOS 4–5
SBP < 90 mmHg (numbers)	1/16 NS 4/18	5/17 NS 5/18	3/17 NS 2/17
SaO_2 < 95% (numbers)	4/16 NS 9/20	7/16 NS 4/18	1/16 NS 1/17
HR > 100/min (numbers)	3/17 NS 7/22	6/17 NS 8/18	6/17 NS 4/17
$ETCO_2$ < 4.5 kPa (numbers)	1/2 NS 1/2	10/11 NS 6/8	12/13 NS 6/11

Figures given are the number of patients with abnormal vital parameter/total number of patients with notations – divided into outcome categories.
GOS, Glasgow Outcome Scale; NS, non-significant; SBP, systolic blood pressure; HR, heart rate; $ETCO_2$, end-tidal carbon dioxide; SaO_2, oxygen saturation.

Discussion

The concepts of "scoop and run" or "stay and play" and the "golden hour" have been discussed extensively in the pre-hospital literature. The actual effect, if any, of prolonged pre-hospital time on outcome from TBI is unknown and what pre-hospital time is used for must be taken into account. [15,16]

In the present study, 24/48 (50%) patients had > 60 min of pre-hospital time.

The patients with severe TBI in this study did not seem to be harmed by a prolonged "golden hour". However, the median time from accident to arrival of ambulance staff at scene was only 9 (2-35) min, indicating that early care of the patients was established.

Pre-hospital hypotension (defined as a single notation of SBP <90 mmHg) and hypoxia (defined as a single notation of apnoea, cyanosis SaO_2<90-92%) have been reported as strong predictors of an unfavourable outcome after TBI, independent of age, GCS and pupillary status. [1, 3-6]

In this study, we could not relate unfavourable outcome (GOS 1-3) to single episodes of hypoxia (SaO_2<95%) or hypotension (SBP<90mmHg) before arrival at a level 1 trauma centre. Hypoxia was corrected in the majority of the patients (69%) at arrival to hospital; hypotension was corrected in 40% of the patients. Oxygen was more frequently delivered to hypoxic patients than fluids were given to hypotensive patients, which can explain this difference.

It is usually recommended that patients with a severe TBI, who demonstrate hypoxia not corrected by supplemental oxygen and who lack the ability to maintain their own airway with oropharyngeal or nasopharyngeal airway support devices, should be intubated. [1,17] In this study, intubation or not in the pre-hospital setting was not related to outcome, and expected long transportation time seemed to be the most important factor for the decision to intubate.

Trauma patients can suffer from hypovolemia that leads to decreased organ perfusion and impaired oxygen delivery. Fluid administration is needed to restore circulating plasma volume and optimize oxygen delivery. Crystalloid fluids are most often used in the pre-hospital resuscitation of TBI patients, even though the superiority of these fluids has never has been evaluated in studies. No evidence of the possible benefit of fluid administration in the pre-hospital setting for trauma patients exists. [18-20] In this study, intravenous fluids were administered to 60% of the patients pre-hospitally. The majority of our patients received crystalloids. The administration of fluids in the pre-hospital setting did not influence the

outcome. Further studies to determine the most effective fluid for resuscitation in TBI patients are needed. [1,20-22]

In the Brain Trauma Foundation guidelines (2007), it is recommended that patients with severe TBI should be transported directly to a hospital with neurosurgical care, with the ability to monitor ICP and treat intracranial hypertension. The mortality rate has been reported to be significantly lower at trauma centers than at non-trauma centers. [23-26]

In this study, there was no statistically significant difference in outcome between patients who were directly transported to the level 1 trauma centre compared with those who were referred. The time spent in primary hospitals was used for resuscitation, CT-scan, contact with the level 1 trauma centre, and booking of secondary transportation. In two cases, life-saving surgical procedures were performed. In rural areas, transport to the nearest hospital, with the ambition to refer as soon as possible, may be better than a direct transportation to the level 1 trauma centre.

Other studies have reported worse outcome and increased mortality in patients hyperventilated before arrival at hospital, probably due to vasoconstriction causing cerebral ischemia.[27,28]In this study, we could not relate the occurrence of $ETCO_2$<4.5 at any time before arrival at a level 1 trauma centre to an unfavourable outcome.

The median time from accident to the level 1 trauma centre in this study was 6 h, a short time considering the vast area, and probably of importance for the non-significant result regarding primary or secondary transport to a level 1 trauma centre. Primary transportation from the site of the accident directly to the level 1 trauma centre took place in 13/48 patients. Helicopters were used in 46% (6/13) of those cases. However, helicopter was used for 71% (25/35) of the secondary transports between the primary hospital and the level 1 trauma centre, decreasing the time for secondary transportation.

The limitations in this study are that the numbers of patients studied are low and that only the patients who arrived alive at the level 1 trauma centre were included. Nonetheless, the patients included were severely traumatized and made a good recovery in spite of, in the majority of cases, a long chain of events before reaching the level 1 trauma centre. The lack of significance both statistically and clinically regarding the outcome in this study may be explained by the fact that early care was established and patients arrived relatively fast to the level 1 trauma centre. Further, it is plausible that the level 1 trauma centre care has strongly influenced the outcome.

Patient survival and outcome after severe TBI is dependent on all the components in the chain of care, the pre-hospital care, the transportation systems, the initial care at the receiving hospital and the level 1 trauma centre care, as well as the knowledge and skills of the staff in different parts of the chain.

Conclusion

Unfavourable outcome in severely traumatized TBI patients were not related to adverse events such as prolonged “golden hour”, secondary referral, hypoxia (SaO_2<95%), hypotension (SBP<90%), hyperventilation ($ETCO_2$<4.5kPa) or tachycardia (HR>100/min) at any time before arrival at a level 1 trauma centre in the trauma system studied.

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