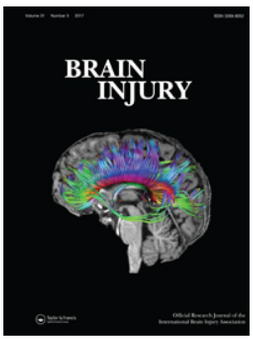

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ORIGINAL ARTICLE

Computed tomography and clinical outcome in patients with severe traumatic brain injury

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ABSTRACT

Objective: To study: (i) acute computed tomography (CT) characteristics and clinical outcome; (ii) clinical course and (iii) Corticosteroid Randomisation after Significant Head Injury acute calculator protocol (CRASH) model and clinical outcome in patients with severe traumatic brain injury (sTBI).

Methods: Initial CT (CT_i) and CT 24 hours post-trauma (CT_{24}) were evaluated according to Marshall and Rotterdam classifications. Rancho Los Amigos Cognitive Scale-Revised (RLAS-R) and Glasgow Outcome Scale Extended (GOSE) were assessed at three months and one year post-trauma. The prognostic value of the CRASH model was evaluated.

Results: Thirty-seven patients were included. Marshall CT_i and CT_{24} were significantly correlated with RLAS-R at three months. Rotterdam CT_{24} was significantly correlated with GOSE at three months. RLAS-R and the GOSE improved significantly from three months to one year. CRASH predicted unfavourable outcome at six months for 81% of patients with bad outcome and for 85% of patients with favourable outcome according to GOSE at one year.

Conclusion: Neither CT nor CRASH yielded clinically useful predictions of outcome at one year post-injury. The study showed encouragingly many instances of significant recovery in this population of sTBI. The combination of lack of reliable prognostic indicators and favourable outcomes supports the case for intensive acute management and rehabilitation as the default protocol in the cases of sTBI.

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Computed tomography; severe traumatic brain injury; outcome

Introduction

Traumatic brain injury (TBI) is a major cause of death and long-term disability [1], particularly among young people. The most widely used TBI severity classification is based on the level of consciousness (LOC) on admission, typically as defined by Glasgow Coma Scale (GCS) [2]. The annual incidence of all-severity TBI in Sweden is 250–350/100 000 [3,4], while severe TBI (sTBI) comprises 3–12/100 000 per year [3]. In the acute stage after TBI, brain CT is the most frequently used neuroimaging method. The brain injury maybe characterised based on its findings, e.g. presence of focal lesion, mass lesion or diffuse brain injury [5]. CT also yields signs of increased intracranial pressure (ICP), e.g. midline shift, obliteration of basal cisterns and diffuse hemispheric swelling [6]. In order to systematise such pathological changes after sTBI, imaging features have been combined into classification systems such as Marshall [7] and Rotterdam [8]. Both systems have been used for prognostication [9]. Although Marshall is the most widely used, a recent study reported that Rotterdam was superior in capturing the dynamics of intracranial pathology, thus making a case for the use of both methods [9].

Current state-of-the-art neurointensive care comprises standardised, protocol-driven therapies, such as the 'Lund' concept, an ICP targeted therapy [10]. This concept has been assessed in a number of outcome studies and has shown a reasonably high ratio of favourable results [11,12]. As a consequence of improved neurosurgical and neurointensive care, individuals with sTBI are more likely to survive, thus increasing the demands for rehabilitation [13].

As sTBI comprises injuries with wide variations as regards complexity of impairments and functional outcomes, further development of prognostic indicators are essential for rehabilitative resource allocation and prioritisation. Currently, the most commonly used outcome scale in patients with sTBI is Glasgow Outcome Scale (GOS) [14,15] and/or an extended version of this scale, Glasgow Outcome Scale Extended (GOSE) [16]. Moreover, Rancho Los Amigos Cognitive Scale-Revised (RLAS-R) [17] has been used both in clinical practice and in several studies to follow recovery after sTBI, as well as for designing appropriate rehabilitation protocols [18]. Yet another model for prediction of (unfavourable) outcome is Corticosteroid Randomisation after Significant Head Injury acute calculator protocol (CRASH) [19]. In CRASH, CT brain features are included. Initial assessment of patients with sTBI routinely includes an acute CT scan. However, most radiologically detectable pathology develops during the first 24–48 hours and may

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thus not be detectable on the initial scan [5]. In this study we therefore decided to evaluate post-traumatic CT scans at two time points (the first available CT scan and CT 24 hours post-trauma). Many prognostic studies of TBI include patients with mixed severity grades of TBI and outcomes assessed up to six months after injury [37]. Fewer studies have focused on long time recovery of the most severely injured group of TBI. Furthermore, since a key goal of rehabilitation is for the patient to regain as much independence as possible, outcome assessment should ideally also include clinical screening measures of cognitive and behavioural functioning. This, however, have less often been the case. Based on these considerations, the aim of this study was to correlate an initial and a subsequent CT scan, as assessed according to Marshall and Rotterdam protocols, with GOSE and RLAS-R clinical outcomes at three months and one year post sTBI, as well as by CRASH prognostic model.

Methods

This prospective cohort study was conducted at the Neurotrauma Center (NC) at Umeå University Hospital, covering the North Health Region (NHR). The geographical area of NHR comprises almost half of the total area of Sweden (136, 373 km^2). It is divided into four counties and has approximately 900,000 habitants, thus comprising only 10% of the total national population. Patients sustaining a sTBI in the NHR are admitted to a county hospital or a local hospital for initial assessment and stabilisation prior to further transportation to the NC. In accordance with the clinical protocol during the study period, all subjects with sTBI, regardless of severity, complicating illness or concomitant injuries, were admitted to the NC. The study comprised part of a prospective multicentre observational study of patients with sTBI, the PROBRAIN study.

Patients

Patients were included from January 2010 to December 2011. Inclusion criteria were: acute, severe, non-penetrating TBI, with a lowest non-sedated GCS [2] score of 3–8 (or, on the Swedish Reaction Level Scale (RLS) score of 8–4) [20,21] within 24 hours post-trauma, age 18–65 years and requiring neurosurgical intensive care (or collaborative care with a neurosurgeon in a general intensive care unit). The exclusion criterion was death within three weeks post-trauma (in accordance with the PROBRAIN study protocol). Patients were evaluated at three weeks, three months and one year after injury. The patients gave written consent in cases where he or she had the capacity to do so. In the majority of cases, however, the patients lacked this capacity, and the patient's nearest relative gave consent to inclusion.

Clinical protocol

Enrolled patients were treated at the NC according to the 'Lund' concept, which is standard protocol at this centre [10]. Briefly, this concept involves rapid and aggressive neurosurgical interventions, including evacuation of hematomas and an ICP targeted care protocol. Hourly mean ICP were calculated by using all the minute-to-minute ICP values during the first five days. ICP_{Max} was defined as the mean ICP of the hour with the highest ICP during the first five days and was measured with the intention to assess the potential secondary damage of the brain. Patients were sedated, received continuous analgesia, were mechanically ventilated and were initially nursed supine with no head elevation. Midazolam is the drug of choice used for sedation and fentanyl for analgesia. An initial (CT_i) scan of the brain was performed as soon as possible after arrival at the primary receiving hospital. CT_i scans were evaluated against subsequent scanning approximately 24 hours after the trauma (CT_{24}) to capture dynamic changes of the primary injury.

Scans were also subsequently classified according to the Marshall [7] and Rotterdam [8] protocols by two of the authors, one a senior neuroradiologist, the other a senior neurorehabilitationist. Clinical outcome assessment at three months and one year post-injury were obtained by one of the authors (MS), who also gathered information on relevant patient descriptors through interviews with patients and/or significant others. Additional information pertinent to this study was retrieved from medical records.

Level of consciousness and post-traumatic amnesia

GCS [2] rates LOC by assessing the patient's responses as recorded verbally, by eye opening and by motor responses, summing responses on a scale from 3 to 15 whereby higher scores indicate better responses. In Sweden, the 8-point RLS [20] is the most commonly used scale. Conversion studies of these scales have been carried out [21,27], so that RLS 8 = GCS 3, RLS 7 = GCS 4, RLS 6 = GCS 5, RLS 5 = GCS 6 and RLS 4 = GCS 7 [27].

Rivermead Post-traumatic Amnesia Protocol documents the duration of post-traumatic amnesia (PTA) [28] and comprises four categories: Mild <1 hours, Moderate 1–24 hours, Severe 1–7 days and Very severe PTA >7 days.

CT evaluation

Marshall [7] is a descriptive classification of morphological abnormalities as depicted on CT scanning. Marshall CT I–IV comprise a diffuse injury severity rating scale and V–VI reflect a mass lesion. This classification is commonly used for prediction of clinical outcome after TBI. In this study, we also dichotomised Marshall scores into two groups: 'less severe brain injury' as defined as Marshall scores I–II, and 'more severe brain injury' defined as Marshall scores III–VI [31].

Rotterdam [8] includes six points consistent with the motor score of the GCS and also with Marshall. Rotterdam includes presence or absence of traumatic subarachnoid haemorrhage (tSAH) [22–26], intraventricular haemorrhage, mass lesions and status of the basal cisterns.

Outcome assessment

Outcome variables were patient survival/death, GOSE [16] and RLAS-R [17] at three months and one year after trauma.

Rancho Los Amigos Cognitive Scale Revised, levels of cognitive functioning

The RLAS-R [17] is a descriptive clinical screening scale comprising ten levels. Scores reflect cognitive and behavioural recovery. Higher scores indicate superior functioning. For the purposes of this study, the RLAS-R scale was further dichotomised into I–VI representing 'unfavourable outcome' (I–III total assistance and IV–VI maximal to moderate assistance) and VII–X 'favourable outcome' (minimal assistance for daily living to modified independent).

Glasgow Outcome Scale Extended

The GOSE [16] extends the five categories of the previously developed GOS [14,15] to eight, thereby increasing its sensitivity. With a structured interview, identifying specific criteria, with good inter-rater reliability and validity, GOSE has been developed for a more detailed categorisation of impairment and measure of global outcome after TBI. For the purposes of this study, results were also summarised and dichotomised into 'unfavourable outcome', (1–4) and 'favourable outcome', (5–8). Furthermore, 'good recovery' was defined as 7–8.

The CRASH acute prognostic model

CRASH [19] is used for prediction of mortality at 14 days and at six months and severe disability at six months in adult patients with TBI. It incorporates acute variables: GCS, pupillary reaction, presence of major extracranial injury, age and five CT-brain features within 8 hours. Since this model was used for prognostication in previous PROBRAIN multicentre studies [38,39] we decided to also use CRASH in this study. CRASH is intended to predict risk for unfavourable outcome at six months (cutoff ≥50%). For this study, we used the online calculator of CRASH (calculator/index.html).

Statistical analysis

Data were analysed with Statistical Package for the Social Sciences (SPSS), version 22.0 for Windows. Data are reported as mean, median and range. Non-parametric tests were applied as samples were small and/or not normally distributed. The Mann–Whitney *U* test was used for comparisons of continuous variables, and Wilcoxon signed-rank test for study of paired observations. For analysis of bivariate correlation, the Spearman's rank correlation coefficient was used. A χ^2 test was used for comparison of proportions. A *P*-value <0.05 was considered to be statistically significant.

Ethics

This study is part of a multicentre study that was approved by the Regional Ethics Committee of Stockholm, Sweden (number 2009/1644/31/3).

Results

Patient and clinical characteristics

A total of 37 patients with acute sTBI were consecutively included in the study. One of these patients (GCS 3) was included shortly before the patient's 18th birthday due to minor protocol violation. The median GCS was 5 (3–8). For patient characteristics, see Table I.

Falls were the most frequent (54%) cause of injury. Motor vehicle accidents were seen in 30%. Hospital deaths occurred in six patients (four men and two women). One of these patients died at the NC due to respiratory complications. One of the fatalities suffered from multiple illnesses at the time of injury, two patients with very severe brain injury (GCS 3) died because of respiratory complications, one died because of inoperable traumatic intracranial aneurysm and one patient died from intracerebral bleeding after transportation from NC to the local hospital.

Fatalities (16%) had more severe injuries, GCS median 3, (3–6) compared with survivors, GCS median 5, (3–8) and a significantly higher mean age in comparison with patients who survived (52.8 ± 17.8 vs. 41.3 ± 15.1, $P = 0.048$). GCS 3 was seen in 24% ($n = 9$) of the included patients and hospital deaths occurred in 44% ($n = 4$) of these patients.

A review at the NC to identify possibly missed patients revealed an additional six patients, all males, mean age 49.8

Table I. Patients' characteristics ($n = 37$).

Age at injury	
Median (range)	45 (17–64)
Mean (SD)	41.3 (±15.1)
Age at injury, male ($n = 26$)	
Mean (SD)	40.1 (±15.3)
Age at injury, female ($n = 11$)	
Mean (SD)	44.0 (±14.9)
Gender, male/female, *n* (%)	26/11 (70/30)
Employment and livelihood	
Part-time or fulltime worker or as a student (%)	(65)
Sick leave full or part-time *n* (%)	(24)
Social care *n* (%)	(11)
Other *n* (%)	(8)
Education	
≥12 years *n* (%)	(38)
<12 years *n* (%)	(62)
Marital status	
Single	(35)
Living with someone	(65)
Worst unsedated GCS first 24 hours, median (range)	5 (3–8)
Age according to CRASH prognostic model	
17–40, *n* (%)	14 (38)
41–65, *n* (%)	23 (62)
Cause of injury	
Transport accident, *n* (%)	13 (35)
Fall, *n* (%)	20 (54)
Other, *n* (%)	3 (8)
Data not available, *n* (%)	1 (3)
Known drug or alcohol misuse at time of injury (none missing) *n* (%)	11 (30)
Influence of alcohol or drugs at time of injury (none missing) *n* (%)	18 (49)
Previous brain injury requiring hospitalization (missing = 1) *n* (%)	12 (32)
Previous brain injury (none missing) *n* (%)	14 (38)

(±9.6) age, GCS median 6.5 (4–7). These patients could not be included in the study, as they were identified later than three weeks post-injury (which is the latest time of inclusion as stipulated by the study protocol). For clinical characteristics, see Table II. Two of these patients died within three months. Both suffered very severe comorbidities at the time of trauma.

CT evaluation

CT_i was assessed in all patients. A subsequent CT_{24}, according to the study protocol, was assessed in 34 patients. In this study, 81% of the patients performed CT_i within 4 hours post-trauma and 41% within 2 hours. The mean time from trauma to CT_i was 2.7 ± 1.6 hours (n = 31). One patient was excluded because of delayed admission to the hospital (15.2 hours). For five patients, the exact elapsed time post-trauma could not be established, but was deduced to be within 22 hours. The mean time from trauma to CT_{24} was 25.4 ± 12.4 hours (n = 30). Two patients were investigated by CT_{24} after 60 hours due to clinical reasons. For CT characteristics, see Table III.

The median (range) score of CT_i according to Marshall was 3 (1–6) and the corresponding results of CT_{24} was 5 (1–6). The median (range) Rotterdam score of CT_i was 4 (2–6) and of CT_{24} 3 (1–6). See Figures 1, 2 and Table IV.

Table II. Clinical characteristics (n = 37).

Additional injury (none missing) n (%)	13 (35)
Posttraumatic amnesia (PTA), n (%)	
Severe 1–7 days	1 (3)
Very severe >7 days	36 (97)
Pupils react to light n (%)	
Both	10 (27)
One or both pupils react slowly	9 (24)
One non-reacting	3 (8)
Both non-reacting	9 (24)
No assessment analogue	1 (3)
Data not available	5 (14)
ICP was monitored, number of days (n = 31*)	
Mean (SD)	10 (±5.1)
ICP_{Max} first five days (n = 31*)	
Mean (SD)	29.5 (±12.0)
Hourly mean ICP first five days (n = 31*)	
Mean (SD)	16.8 (±4.7)
ICP_{Max} hospital death (n = 6)	
Mean (SD)	25.4 (±9.4)
Length of stay forintensive care, total days for all patients, (n = 37)	648
Mean (SD)	17.7 (±11.3)
Median (range)	16 (2–54)
Length of stay for intensive care, total days for all patients with hospital death, (n = 6)	145
Mean, (SD)	24.2 (±10.4)
Median (range)	26.5 (9–37)
Length of stay for in-hospital rehabilitation, total days (n = 29)	1664
Mean (SD)	45.0 (±52.9)
Median (range)	31 (0–247)
Out-hospital rehabilitation n (%)	3 (8)
Length of stay for in-hospital rehabilitation patients with intra-parenchymal pressure measuring, total days (n = 25)	1392
Mean (SD)	62 (±55.1)
Median (range)	43 (3–247)
Length of stay for in-hospital total days for all patients, (n = 37)	3020
Mean (SD)	81.6 (±70.7)
Median (range)	59 (16–283)

*ICP data were not available for six patients (three patients were initially treated at hospitals outside the NHR, two were operated on immediately because of epidural hemorrhage (EDH), mass lesion, and one patient did not get intracranial pressure monitoring. All of these six patients had favourable outcome.

Table III. CT characteristics.

Time from trauma to CT_i (hours)	n	% of total
<4	30	81
≥4 or unknown	7	19
	CT_i n (%)	CT_{24} n (%)
tSAH	29 (78)	21 (62)
EDH	5 (14)	6 (18)
Basal cisterns		
Normal	15 (40)	16 (43)
Compressed	11 (30)	15 (40)
Absent	11 (30)	3 (8)
Midline shift		
No shift or shift <5 mm	24 (65)	25 (68)
Shift >5 mm	13 (35)	9 (24)
Data not available	0 (0)	3 (8)

Non-evacuated mass lesion on the CT_i was seen in 19% (n = 7/37) compared with 9% (n = 3/34) on CT_{24}. Out of 27 patients with available CT_i and CT_{24} and with detectable diffuse injury (Marshall I–IV) on the initial scan, 48% subsequently developed a mass lesion on CT_{24}, which was then evacuated. One patient who sustained high-energy trauma displayed findings of no pathological according to Marshall CT_i and CT_{24}. Nevertheless, the patient presented GCS 6 at admission and diffuse axonal injury on magnetic resonance imaging and GOSE 5 at one year. According to Rotterdam, 16 patients out of 34 (47%) showed improvement from CT_i to CT_{24}, whereas four patients (12%) deteriorated.

There was a positive correlation between Marshall CT_i and Rotterdam CT_i (r = 0.716, P < 0.001) but no significant correlation between Marshall CT_{24} and Rotterdam CT_{24} (r = 0.077, P = 0.667). Rotterdam CT_{24} showed a negative correlation to GOSE at three months (r = −0.421, P = 0.015). There were negative correlations between Marshall CT_i and CT_{24} and RLAS-R at three months (CT_i r = −0.364, P = 0.044; CT_{24} r = −0.425, P = 0.024). However, Marshall and Rotterdam scores of CT_i and CT_{24} did not correlate with the GOSE and RLAS-R scores at one year, this being the study endpoint as regards outcome.

Clinical outcomes

- GOSE improved significantly from three months (median 4.5 (1–8), mean 4.4 ± 2.3) to one year (median 7 (1–8); mean 5.5 ± 2.7, P = 0.003). At thee months, GOSE 1–4 was seen in 50% and GOSE 5–8 in 50%. At one year, GOSE 1–4 was seen in 36% and GOSE 5–8 in 64%. One patient was in a vegetative state at one year. Good recovery (GOSE 7–8) was seen in 59% at one year.
- RLAS-R also improved significantly from three months (median 9 (2–1); mean 8.0 ± 2.4) to one year (median 10 (3–10); mean 8.9 ± 1.9, P = 0.003). At one year, RLAS-R 1–6 was seen in 10% and RLAS-R 7–10 in 90% and 77% reached the highest level, i.e. 'Stand-by assistance on request' and 'Modified independent' (RLAS-R 9–10). One patient who was classified on CT_i as Marshall I (i.e. no visible intracranial pathologic change) had an initial score of GCS 6 and was classified as GOSE 5 at one year due to diffuse axonal injury.
- GCS on admission correlated with GOSE at one year (r = 0.366, P = 0.026). There were negative correlations

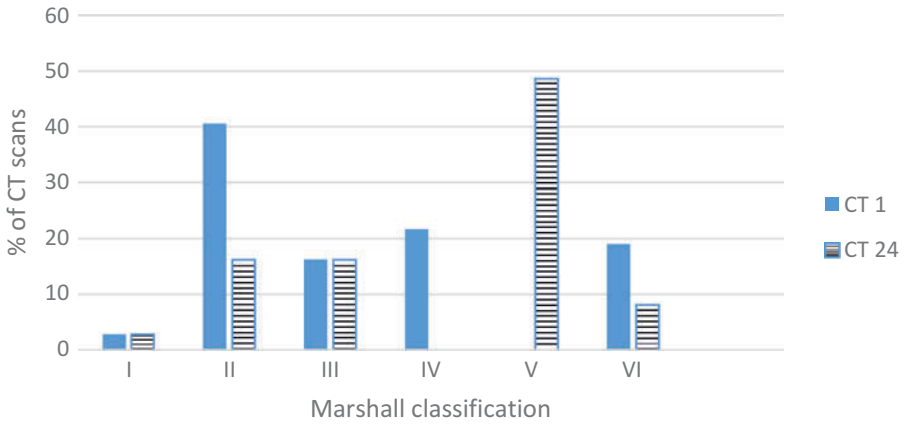

Figure 1. Marshall classification CT_i and CT_{24}.

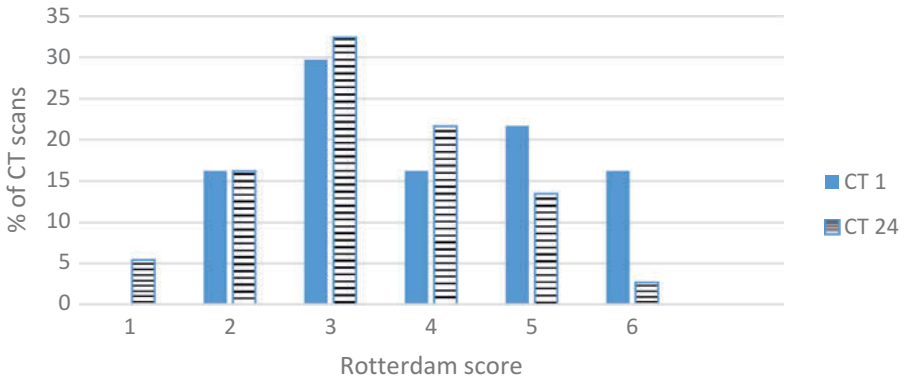

Figure 2. Rotterdam score CT_i and CT_{24}.

Table IV. CT_i and CT_{24} according to the Marshall classification and Rotterdam score.

	Marshall classification	*n* (%)
	CT_i	CT_{24}
Less severe injury		
I	1 (3)	1 (3)
II	15 (40)	6 (16)
More severe injury		
III (swelling)	6 (16)	6 (16)
IV (shift)	8 (22)	0 (0)
V evacuated mass lesion (EML)	0 (0)	18 (49)
VI non-evacuated mass lesion (NEML)	7 (19)	3 (8)
Total	37 (100)	34 (92)
Data not available	0 (0)	3 (8)
	Rotterdam score	*n* (%)
	CT_i	CT_{24}
Score 1	0 (0)	2 (5)
Score 2	6 (16)	6 (16)
Score 3	11 (30)	12 (32)
Score 4	6 (16)	8 (22)
Score 5	8 (22)	5 (14)
Score 6	6 (16)	1 (3)
Total	37 (100)	34 (92)
Data not available	0 (0)	3 (8)

between in-hospital total days and GOSE at three months and one year ($r = -0.419$, $P = 0.011$ and $r = -0.429$, $P = 0.008$) and between in-hospital total days and RLAS-R at three months and one year ($r = -0.738$, $P < 0.001$ and $r = -0.713$, $P < 0.001$).

- The proportion of unfavourable outcome (GOSE 1–4) at one year was 31% for men and 46% for women.

CRASH

In this study, CRASH predicted risk of unfavourable outcome (≥50% risk) for 9 patients of 11 (81%) with unfavourable outcome (GOSE 1–4) at one year. CRASH also predicted risk of unfavourable outcome for 17 patients of 20 (85%), although they, in fact, had favourable outcome (GOSE 5–8) at one year. Two patients with unfavourable outcome and four patients with favourable outcome were not included in CRASH calculations because the first CT_i was done more than 8 hours after trauma or unknown. There were four patients with hospital death (GCS 3, GOSE 1) and unfavourable outcome (>95%) according to CRASH, see Table V.

Discussion

To our knowledge, there are no previous studies using both Rotterdam and Marshall for study of outcome of comprehensive management and rehabilitation of sTBI. In previous prognostic studies on mortality and outcome in TBI, Marshall or Rotterdam were utilised with a main focus on neurointensive care [9].

In this study, we found a negative correlation between Marshall and Rotterdam and the clinical outcome according to GOSE and RLAS-R at three months. However, there was no correlation between CT scores and GOSE or RLAS-R at one year post-injury, indicating that analysis of CT acutely

Table V. CRASH prognostic model compared with initial GCS score, Marshall classification and Rotterdam score CT_i, CT_{24}, and length of stay at intensive care, and length of stay at inpatient rehabilitation with GOSE and RLAS-R at one year.

GCS first 24 hours	GOSE one year	GOSE U/F one year	RLAS-R U/F one year	CRASH prognostic model		Marshall		Rotterdam		Length of stay-intensive care (days)	Length of stay-inpatient rehabilitation unit (days)
				Risk of 14 day mortality (95% CI)	Risk of unfavourable outcome at six months	CT_i	CT_{24}	CT_i	CT_{24}		
3	1	U	HD+	80.5% (69.5–88.2)	95.1% (91.7–97.1)	2	2	4	4	27	0
3	7	F	F	81.5% (70.2–89.1)	91.5% (85.5–95.1)	2	3	4	3	22	34
3	7	F	F	94.5% (90.5–96.9)	97.1% (94.8–98.4)	6	5	6	4	17	82
3	1	U	HD+	94.3% (89.2–97.0)	97.9% (96.2–98.9)	4	5	5	4	37	156
3	8	F	F	63.8% (50.1–75.6)	81.6% (72.4–88.3)	4	5	3	1	5	0
3	8	F	F	CT_i >8 hours or unknown	CT_i >8 hours or unknown	6	5	6	5	9	45
3	1	U	HD+	97.0% (94.6–98.4)	98.4% (97.1–99.1)	6	5	6	5	9	0
3	2	U	U	37.0% (25.3–50.4)	73.0% (62.2–81.6)	3	3	4	3	54	30
3	1	U	HD+	87.3% (77.8–93.1)	95.6% (91.9–97.6)	4	5	6	4	15	0
4	7	F	F	44.7% (31.6–58.7)	73.8% (63.1–82.3)	3	5	5	3	28	127
4	3	U	U	CT_i >8 hours or unknown	CT_i >8 hours or unknown	6	6	2	2	10	64
4	7	F	F	79.7% (68.3–87.7)	91.8% (86.6–95.1)	4	5	5	5	18	108
4	3	U	F	25.3% (16.2–37.3)	58.4% (46.0–69.8)	2	2	2	2	9	35
4	8	F	F	CT_i >8 hours or unknown	CT_{in} >8 hours or unknown	3	x	5	x	23	8
4	3	U	F	6.9% (4.5–10.7)	39.7% (31.9–48.1)	2	2	3	3	30	52
5	8	F	F	7.8% (5.1–11.6)	42.6% (34.8–50.7)	2	2	3	3	7	7
5	7	F	F	61.4% (45.3–75.4)	80.6% (69.7–88.3)	4	5	4	3	13	43
5	5	F	F	81.6% (70.2–89.3)	92.7% (87.7–95.8)	6	5	5	5	23	89
5	8	F	F	CT_i >8 hours or unknown	CT_i >8 hours or unknown	2	2	3	3	23	20
5	1	U	HD+	35.4% (23.3–49.7)	72.2% (60.4–81.6)	2	3	3	4	31	0
5	7	F	F	50.5% (35.2–65.7)	78.9% (67.5–87.1)	2	5	4	2	6	18
5	8	F	F	76.2% (64.1–85.2)	90.1% (84.0–94.0)	2	x	3	x	20	22
6	1	U	HD+	47.4% (35.6–59.4)	85.8% (79.9–90.2)	3	5	3	4	26	0
6	8	F	F	96.4% (93.1–98.1)	98.1% (96.5–99.0)	6	5	6	3	11	3
6	3	U	F	CT_i >8 hours or unknown	CT_i >8 hours or unknown	6	6	5	3	39	117
6	3	U	F	10.4% (6.6–16.0)	43.9% (35.0–53.3)	2	5	2	2	18	49
6	8	F	F	17.0% (11.3–24.6)	57.9% (48.8–66.4)	2	5	3	1	5	6
6	4	U	F	41.7% (27.9–56.8)	77.3% (66.1–85.6)	2	5	2	2	22	0
6	5	F	F	8.7% (5.3–14.1)	44.7% (33.8–56.1)	1	1	2	2	16	43
6	8	F	F	62.4% (49.3–73.9)	80.6% (71.2–87.4)	4	5	5	3	2	0
6	7	F	F	25.1% (17.2–35.2)	69.4% (60.5–77.1)	2	6	3	4	23	77
7	8	F	F	CT_i >8 hours or unknown	CT_i >8 hours or unknown	4	3	5	6	6	0
7	8	F	F	30.2% (19.9–42.9)	60.0% (47.8–71.0)	3	3	3	3	14	28
7	7	F	F	30.2% (19.9–42.9)	60.0% (47.8–71.0)	3	3	4	4	14	31
7	8	F	F	76.2% (64.1–85.2)	90.1% (84.0–94.0)	4	5	6	5	3	15
8	7	F	F	4.2% (2.7–6.4)	25.8% (20.2–32.3)	2	x	2	x	13	74
8	8	F	F	26.9% (17.4–39.1)	56.0 (43.7–67.6)	2	2	3	3	7	34

U = unfavourable, (GOSE 1–4, RLAS-R 1–6), F = favourable (GOSE 5–8, RLAS-R 7–10), HD+ = Hospital death.

and within 24–48 hours lack predictive ability as regards long-term clinical outcome in sTBI. Likewise, CRASH failed to predict outcome in this sTBI population. Similar findings were reported by Olivecrona and Olivecrona [29], who also used CRASH for prediction after sTBI at six months. In previous research from our hospital, Marshall and Rotterdam CT_i and Marshall CT_{24} correlated with the disability outcome Glasgow Outcome Scale (GOS) both at three months and at one year [9]. However, since GOSE is an extended version of GOS, these instruments are not completely comparable; it might be that a prognostic prediction based on CT protocols lack sufficient sensitivity to provide more fine grained outcome assessments, particularly within a TBI subgroup comprising the most severe injuries. Another possible reason may be related to the inclusion criteria. The PROBRAIN study included patients who survived at three weeks, this was not a criterion in the previous study [9].

It is of particular clinical relevance that overall outcome among patients with severe TBI in our study was encouragingly favourable (GOSE 5–8, 64%) (GOSE 7–8, 59%), while instruments for prognostication failed to predict favourable/unfavourable outcome at one year. When interpreting data from this study, some distinguishing factors pertaining to this study population and design should be emphasised.

First, patients were somewhat older (mean age +6 years) than in some previous studies [5,9] on this topic. Second, in comparison with a prior study from our centre [9], patients on average had lower GCS score (5 vs 6), indicating more severe injury. Patients who died (16%) suffered more severe injuries (GCS 3) compared with survivors (GCS 5) and were also older (approximately +10 years). Third, this study was limited by the relatively small study population. However, sTBI is rare in comparison with mild and moderate TBI. Also, the included patients in fact comprised a near-total population of incident cases of sTBI fulfilling selection criteria during two years. Furthermore, all data were collected by one of the authors, who also personally examined all patients during the course of the study, minimising the amount of

missing or secondary data. One fourth of the patients were initially classified as severely injured and with a minimal GCS score (3). Nevertheless, at one year, 44% of this subgroup was classified as 'good recovery' on the GOSE (7–8), pointing to the importance of providing active care for all patients with sTBI [36,40,41].

Both a history of previous brain injury and indications of alcohol use at the time of injury have been shown to be risk factors for TBI [34,35]. Over one third of patients in our study had been hospitalised previously for TBI, and almost half were under the influence of alcohol and/or drugs at the time of injury. This is a much higher rate of alcohol use in patients with sTBI than that recently reported in a Norwegian study (32%) [30]. These findings highlight the concept of high-risk populations and high-risk situations in conjunction with sTBI, and thus the need and potential for preventative measures.

CT scan of the brain remains a standard diagnostic tool for assessing TBI, and it is also used for prediction of outcome. Since studies have shown that pathological intracranial changes in the brain often progress during the first 24 and even 48 hours, routine, repeated CT scans have been proposed to capture intracranial dynamics [33]. In this study, the proportion of 'less severely injured' patients based on Marshall CT_i was higher than in some previous studies [9,31]. However, when comparing our results on CT_{24}, the percentage of severely injured patients was similar to these studies, as the severely injured group increased by more than 50% from CT_i to CT_{24}. Thus, it should be emphasised that intracranial pathology after sTBI commonly progress, therefore repeated CT scans in the early stage may often be implicated.

The majority of patients in our study experienced good recovery as regards disability and cognitive and behavioural functioning, and about two thirds were assessed as having good outcomes on both GOSE and RLAS-R. Those patients were independent as regards activities of daily living and did not need another person's assistance at one year post-injury.

Conclusion

In conclusion, the findings of this study proved negative as regards the predictive ability of CT and CRASH protocol on outcome prognostication at one year post-injury in sTBI. At the same time, good outcomes were found in about two thirds of survivors. Patients with sTBI should be offered a combination of active and intensive neurosurgical care and neurorehabilitation as a majority of the patients showed favourable outcome by such management and as our possibilities for early prognostication failed to identify who will benefit or not.

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Declarations of interest

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