Clinical Impact of Hemorrhagic Lesion Progression Following Moderate-to-Severe Traumatic Brain Injury: An Observational Cohort Study

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Abstract

Background

Hemorrhage progression following traumatic brain injury (TBI) is not fully understood, and preventing it would be a potential therapeutic opportunity in TBI management. The aim of this study was to determine how non-operated hemorrhagic lesions progress following TBI, and how this affects outcome.

Methods

This was a retrospective observational cohort study of adult patients (≥ 15 years) with moderate-to-severe TBI. Hemorrhage volumes were calculated from computed tomography (CT) scans using semi-automated volumetric segmentation.

Results

In total, 643 patients were included, with a median Glasgow Coma Scale of 7. Contusions were the most common form of traumatic intracranial hemorrhage. The mean total lesion volume on the first CT scan was 4.29 ml, and the mean lesion progression volume (LPV), i.e. the increase in volume from first CT scan until the lesion had stopped progressing, was 3.85 ml. Contusions showed a significantly larger LPV than SDH and EDH ($p < 0.001$). The median lesion progression time (LPT), i.e. the time from injury until all lesions had stopped progressing, was 5.98 hours, with contusions progressing for a longer time than tSAH, SDH and EDH ($p < 0.001$). Hemorrhage progression also slowed exponentially over time, with almost no further expansion occurring 24 hours after trauma. In multivariable regression analysis, LPV was independently associated with 12-month Glasgow Outcome Score after adjusting for known TBI outcome predictors ($p < 0.001$).

Conclusions

Contusions were the most common form of traumatic intracranial hemorrhage, and exhibited both a larger LPV and longer LPT than extra-axial hematomas. Regression analysis indicated that LPV was independently related to, and possibly a driver of, unfavorable outcome. Interventions to prevent lesion progression are therefore likely to improve outcome in TBI patients. Moreover, this study suggests a wider window of opportunity to prevent lesion progression than what has previously been suggested.

Introduction

Background

In traumatic brain injury (TBI), the primary injury often initiates a sequence of events that leads to secondary brain damage [1]. Of the many potential secondary processes, hemorrhage progression

presents a potential therapeutic target, as it not only exacerbates an already grave situation, but often does so when patients are hospitalized. Thus, there is ample opportunity to intervene if proper treatment can be identified. While much is known about predictors of hemorrhage progression following TBI [2], surprisingly little has been written about the temporal progression of these lesions. Fundamental questions therefore remain unanswered, such as: When do traumatic intracranial lesions stop progressing? How are they expected to progress, and can this be affected? Does their progression affect outcome?

Several well-written studies have provided some answers. Among the various subtypes of intracranial bleeds, contusions seem to be the most likely to progress, and in the majority of cases this occurs within the first 24 hours after injury [2]. However, limitations to these studies have restricted their clinical applicability. The studies have typically been performed on small cohorts, and solely focused on identifying predictors of lesion progression [3,4,13–15,5–12]. Moreover, they have generally employed a binary definition of hemorrhage progression, without taking into account the time since injury or how much a lesion has progressed. With few exceptions [10,13,16], the studies have also utilized the ABC/2 formula to calculate lesion size [3,4,17,5–9,12,14,15], even though it is known to overestimate volume relative to volumetric segmentation [18]. Relative volume changes, ranging from 5 to 50 %, have also been used to define lesion progression, although these definitions were generally decided upon in a somewhat arbitrary manner [3,6,7,10,12–15,17]. Most studies have also primarily focused on traumatic contusions [2], ignoring the simultaneous progressions of traumatic subarachnoid (tSAH), subdural (SDH) and epidural hemorrhages (EDH).

The aim of this study was therefore to characterize hemorrhage progression in moderate-to-severe TBI, using semi-automated volumetric segmentation, in order to better understand how these lesions progress and how this relates to outcome.

Methods

Study design

This was a single-center, population-based, observational cohort study. Adults (≥ 15 years) with moderate-to-severe TBI (Glasgow Coma Scale (GCS) 3–13), who were admitted to the Karolinska University Hospital between 2006 and 2019, were eligible for inclusion. The study hospital is the only level 1 trauma center equivalent in the region and offers neurosurgical and neuro-intensive care to a population of approximately 2.3 million people. Exclusion criteria were; no hemorrhagic lesions detected, unknown time of injury, penetrating brain injury, or if the first or second computed tomography (CT) scan was performed more than 12 or 48 hours after injury, respectively. The study was approved by the Swedish Ethical Review Authority (Dnr: 2019–04476) who waived the need for informed consent.

Data collection

Patients were identified using the Karolinska Neurotrauma Database, which includes all patients admitted to the hospital with a TBI. Clinical data was retrospectively reviewed using the medical record software TakeCare (CompuGroup Medical Sweden AB, Farsta, Sweden), and imaging data was collected from the radiological management software Sectra Picture Archiving and Communication System (PACS) IDS7 (Sectra AB, Linköping, Sweden). Collected variables included demographics, comorbidities, injury mechanism, time of injury, clinical status on admission, radiographic data from all CT scans performed during hospitalization, lesion progression volume (LPV), lesion progression time (LPT), treatment and Glasgow Outcome Scale (GOS), which was collected at median 12 months follow-up for surviving patients. LPV was defined as the net increase in lesion volume from first CT scan until the lesion had stopped progressing, and was noted for each lesion individually as well as for all lesions together ("total LPV"). LPT was defined as the time that had elapsed from the time of injury until the lesion had stopped progressing, with the time noted for each lesion individually as well as until all lesions had stopped progressing ("total LPT"). Patients with extracranial Abbreviated Injury Scale (AIS) ≤ 2 were defined as isolated TBI. If a patient was intubated upon trauma center arrival, the last known GCS prior to intubation was used.

Semi-automated volumetric analyses

Lesion volumes were calculated from CT scans using the semi-automated volumetric segmentation tool built into the radiological management system PACS IDS7 Version 21.1.8. Using this tool, the lesions were manually identified and their volumes automatically calculated based on adjacent voxels of similar Hounsfield units. The automated lesion map was manually corrected if needed, for example if it included part of the skull when measuring the volume of an EDH. Final lesion volumes were then extracted from these corrected predictions. In the case of multiple lesions of the same type, the volumes were summed. Lesion progression was defined as any expansion of existing hemorrhagic lesions or the appearance of a new lesion, and a lesion was determined to have stopped progressing when two consecutive CT scans showed the same volume for the lesion in question. As this study only included patients with moderate-to-severe TBI, patients were generally followed with frequent CT scans until all lesions had stopped progressing. To reduce the influence that surgical treatment has on lesion progression, only non-operated lesions were assessed, and this was evaluated for each lesion individually. For example, if a patient had a surgically treated SDH and a conservatively managed contusion, the contusion was assessed for lesion progression. For tSAH, volume calculation was not possible and progression was instead dichotomized into progression vs no progression as determined by two independent neuroradiologists, in accordance with clinical practice. IVH progression was not evaluated due to uncertainty whether or not their increase was due to the redistribution of tSAH.

Statistics

Shapiro-Wilks test was used to evaluate the normality of continuous data. As all continuous data significantly deviated from a normal distribution pattern (Shapiro-Wilks test p value < 0.05), it is presented as median (range) and categorical data as numbers (proportion). LPV was also presented as mean (standard deviation) to illustrate significant differences. The Chi-square test and Kruskal-Wallis test

(including multiple pairwise comparisons between groups) were used to compare LPV and LPT between contusions, EDH, SDH and tSAH. Proportional odds logistic regression analysis was performed to determine how LPV and LPT affected 12-month GOS. Other variables included in the regression analysis were those from the core and CT IMPACT model previously shown to be major predictors for TBI outcome (including age, GCS, pupillary status, Marshall CT score, presence of tSAH and EDH, as well as oxygen saturation and blood pressure at the scene of accident [19]). In the step-down multivariable model, variables significant in the univariable analysis were sequentially omitted, based on the highest p-value, until all values in the model were significant. As only 0.3 % of the data in the multivariable regression model was missing, listwise deletion was used to handle missing data. Statistical significance was set at $p < 0.05$. All analyses were conducted using the statistical software program R (version 4.0.3).

Results

Baseline and outcome

A total of 936 patients were assessed, of whom 643 were included in the study (Fig. 1). Subjects were predominantly male ($n = 478$, 74.3 %) with a median age of 47 years (IQR 28–62). The median GCS score was 7 (IQR 3–11), and same-level falls were the major cause of injury ($n = 260$, 40.4 %) (Table 1). The median time from injury to admission was 1.02 hours, and the median time from injury to the first, second and third CT scan was 1.45, 7.98 and 35.2 hours, respectively (Fig. 2). Contusions were the most common type of hemorrhage ($n = 491$, 76.4 %), followed by tSAH ($n = 483$, 75.1 %) and SDH ($n = 458$, 71.2 %) (Table 2). Hematoma evacuation was performed in 285 patients (44.3 %), most often removal of a SDH ($n = 185$, 28.8 %). The median follow-up time was 11.9 months (IQR 10.7–12.9), at which point the median GOS was 4 (IQR 3–4) (Table 3).

Table 1
Patient characteristics

Variable	Patients (n = 643)
Age, median (IQR)	47.0 (28.0–62.0)
Male sex, n (%)	478 (74.3 %)
Alcohol use disorder, n (%)	87 (13.8 %), (12 missing)
Anticoagulant treatment, n (%)	20 (3.16 %), (10 missing)
Warfarin	16
DOAC	4
Antiplatelet treatment, n (%)	44 (6.95 %), (10 missing)
Aspirin	40
Clopidogrel	9
Other	6
Time from injury to admission (hours), median (IQR)	1.02 (0.67–3.75)
Injury mechanism, n (%)	
Fall (same level)	260 (40.4 %)
Fall (high level)	80 (12.4 %)
Traffic accident	206 (32.0 %)
Struck by blunt object	82 (12.8 %)
Unknown	15 (2.33 %)
Isolated TBI, n (%)	455 (70.8 %)
Glasgow Coma Scale, median (IQR)	7.0 (3.0–11)
Moderate TBI (GCS 9–13), n (%)	207 (32.2 %)
Severe TBI (GCS 3–8), n (%)	436 (67.8 %)
Pupils, n (%)	
Normal	487 (77.3 %)
Unilateral non-reactive	77 (12.2 %)
Bilateral non-reactive	66 (10.5 %)
Data missing	13

Abbreviations: DOAC = direct oral anticoagulants; GCS = Glasgow Coma Scale; IQR = interquartile range; n = number; TBI = traumatic brain injury

Table 2
Radiographic findings

Variable	Patients (n = 643)
Hours from injury to first CT scan, median (IQR)	1.45 (1.13–1.87)
Hours from injury to second CT scan, median (IQR)	7.98 (6.08–11.5)
Hours from injury to third CT scan, median (IQR)	35.2 (18.9–65.2)
Marshall CT score, median (IQR)	3 (2–5)
Contusion, n (%)	491 (76.4 %)
Left, n (%)	114 (23.2 %)
Right, n (%)	93 (18.9 %)
Bilateral, n (%)	284 (57.8 %)
Location, n (%)	
Frontal	431 (87.8 %)
Temporal	287 (58.5 %)
Parietal	70 (14.3 %)
Occipital	33 (6.72 %)
Central	54 (11.0 %)
Cerebellum	41 (8.35 %)
Brain stem	19 (3.87 %)
Subdural hemorrhage, n (%)	458 (71.2 %)
Left, n (%)	157 (34.3 %)
Right, n (%)	148 (32.3 %)
Bilateral, n (%)	153 (33.4 %)
Epidural hemorrhage, n (%)	157 (24.4 %)
Left, n (%)	73 (46.5 %)
Right, n (%)	71 (45.2 %)
Bilateral, n (%)	13 (8.28 %)
Subarachnoid hemorrhage, n (%)	483 (75.1 %)
Intraventricular hemorrhage, n (%)	194 (30.2 %)

Abbreviations: CT = computed tomography; IQR = interquartile range; n = number

Table 3
Treatment and outcome

Variable	Patients (n = 643)
Tranexamic acid within 3 hours, n (%)	46 (7.15 %)
Intubation, n (%)	580 (90.2 %)
Surgery, n (%)	505 (78.5 %)
Neuromonitoring	421 (65.5 %)
ICP-monitor	303 (47.1 %)
Microdialysis	204 (31.7 %)
External ventricular drain	194 (30.2 %)
Hematoma evacuation	285 (44.3 %)
Contusion evacuation	51 (7.93 %)
SDH evacuation	185 (28.8 %)
EDH evacuation	95 (14.8 %)
Outcome	
GOS at discharge, median (IQR)	3 (3–3)
Months to follow-up, median (IQR)	11.9 (10.7–12.9)
GOS at follow-up, median (IQR)	4 (3–4)
30-day mortality, n (%)	74 (11.5 %)
12-month mortality, n (%)	114 (17.7 %)

Abbreviations: GOS = Glasgow Outcome Scale; ICP = intracranial pressure; IQR = interquartile range; n = number

Lesion progression

The mean lesion volume on the admission CT scan was 4.29 ($\pm$ 10.7) ml. Overall, 61.3 % (n = 394) of patients showed lesion progression between the first and second CT scan, and 10.1 % (n = 64) between the second and third CT scan. The mean total LPV for all lesions combined was 3.85 ($\pm$ 9.27) ml, with contusions exhibiting a significantly larger LPV (4.72 $\pm$ 10.0 ml) than SDH (1.31 $\pm$ 4.28 ml) and EDH (1.50 $\pm$ 5.18 ml) (p < 0.001) (Table 4, Fig. 3). The median total LPT was 5.98 hours (IQR 1.76–9.97), and contusions had a significantly longer LPT (6.27 hours) compared to tSAH (1.76 hours), SDH (1.68 hours)

and EDH (1.58 hours) ($p < 0.001$) (Table 4, Table 5, Fig. 4). Lesion progression also slowed over time exponentially, with almost no expansion 24 hours after trauma (Fig. 5).

Table 4
Hemorrhagic lesion progression

Variable	Patients (n = 643)
Lesion progression between first and second CT scan, n (%)	394 (61.3 %)
Lesion progression between second and third CT scan, n (%)	65 (10.1 %)
Initial lesion volume (ml), mean (SD) / median (IQR)	4.29 ($\pm$ 10.7) / 1 (1–4)
Contusion	3.96 ($\pm$ 9.08) / 1 (1–2)
SDH	18.9 ($\pm$ 31.7) / 5 (1–20)
EDH	27.5 ($\pm$ 47.7) / 1 (6–36)
Total LPV (ml), mean (SD) / median (IQR)	3.85 ($\pm$ 9.27) / 0 (0–3)
Contusion LPV	4.72 ($\pm$ 10.0) / 1 (0–4)
SDH LPV	1.31 ($\pm$ 4.28) / 0 (0–1)
EDH LPV	1.50 ($\pm$ 5.18) / 0 (0–1)
Total LPT (hours), median (IQR)	5.98 (1.76–9.97)
Contusion LPT	6.27 (1.78–10.1)
SDH LPT	1.68 (1.20–5.53)
EDH LPT	1.58 (1.17–5.71)
tSAH LPT	1.76 (1.23–5.09)

Abbreviations: CT = computed tomography; EDH = epidural hemorrhage; GOS = Glasgow Outcome Scale; IQR = interquartile range; LPT = lesion progression time; LPV = lesion progression volume; ml = milliliters; tSAH = traumatic subarachnoid hemorrhage; SDH = subdural hemorrhage; SD = standard deviation

Table 5
Comparison of LPT and LPV between the different forms of traumatic intracranial lesions

Variable	Contusion	SDH	EDH	tSAH	p-value
Total LPT (hours), median (IQR)	6.27 (1.8–10)	1.68 (1.2–5.5)	1.58 (1.2–5.7)	1.76 (1.2–5.1)	< 0.001
Total LPV (ml), mean (SD)	4.72 ($\pm$ 10.0)	1.31 ($\pm$ 4.28)	1.50 ($\pm$ 5.18)	-	< 0.001

Abbreviations: EDH = epidural hemorrhage; IQR = interquartile range; LPT = lesion progression time; LPV = lesion progression volume; tSAH = traumatic subarachnoid hemorrhage; SDH = subdural hemorrhage; SD = standard deviation

Bold text in the p-value column indicates a statistically significant correlation ($p < 0.05$)

Predictors of outcome

Both total LPV ($p < 0.001$, Nagelkerke's pseudo- $R^2 = 0.082$, OR 0.94), total LPT ($p < 0.001$, pseudo- $R^2 = 0.039$, OR 0.96) and final lesion volume ($p < 0.001$, pseudo- $R^2 = 0.082$, OR 0.96) were significantly associated with 12-month GOS in univariable analyses (Table 6, Fig. 6). They all had an OR < 1 , i.e. an increase in their values led to a decrease in GOS (= more unfavorable outcome). After adjusting for known TBI outcome predictors, LPV remained independently associated with 12-month GOS ($p < 0.001$) in multivariable analysis. The other significant predictors of GOS in the multivariable analysis were age (pseudo- $R^2 = 0.094$, OR 0.97), admission GCS (pseudo- $R^2 = 0.130$, OR 1.21), bilateral dilated pupils (pseudo- $R^2 = 0.094$, OR 0.16) and EDH (pseudo- $R^2 = 0.057$, OR 2.72) (Table 7).

Table 6
Univariable proportional odds regression model predicting 12-month GOS

Variable	p-value	Nagelkerke's pseudo- R^2	OR (95 % CI)
IMPACT model			
Age (years)	< 0.001	0.094	0.97 (0.96–0.98)
GCS at admission	< 0.001	0.130	1.21 (1.16–1.26)
Unilateral pupil dilation	0.002	0.017	0.52 (0.34–0.79)
Bilateral pupil dilation	< 0.001	0.094	0.16 (0.10–0.26)
Marshall CT score	0.005	0.014	0.87 (0.79–0.96)
Subarachnoid hemorrhage	0.014	0.010	0.67 (0.49–0.92)
Epidural hemorrhage	< 0.001	0.057	2.72 (1.93–3.84)
Oxygen saturation at SoA (%)	< 0.001	0.028	1.05 (1.02–1.08)
Blood pressure at SoA (mmHg)	< 0.001	0.053	0.99 (0.98–0.99)
New variables			
Total LPV (ml)	< 0.001	0.082	0.94 (0.93–0.96)
Total LPT (hours)	< 0.001	0.039	0.96 (0.95–0.98)
Final lesion volume (ml)	< 0.001	0.082	0.96 (0.95–0.97)

Abbreviations: CI = confidence interval; CT = computed tomography; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; LPT = lesion progression time; LPV = lesion progression volume; ml = milliliters; mmHg = millimeters of mercury; OR = odds ratio; SoA = scene of accident

Bold text in the p-value column indicates a statistically significant correlation ($p < 0.05$).

OR < 1 means that the presence of, or increase in, the explanatory variable leads to decreased GOS (i.e. a more unfavorable outcome).

Table 7
Final multivariable step-down
proportional odds regression model
predicting 12-month GOS

Variable	p-value
Age (years)	< 0.001
GCS at admission	< 0.001
Total LPV (ml)	< 0.001
Bilateral dilated pupils	< 0.001
Epidural hemorrhage	0.018

Nagelkerke's pseudo- $R^2 = 0.341$

Abbreviations: CT = computed tomography; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; ml = milliliters; LPT = lesion progression time

Bold text in the p-value column indicates a statistically significant correlation ($p < 0.05$)

Discussion

In this paper we assessed how traumatic hemorrhagic lesions progressed following moderate-to-severe TBI, and how this progression is related to neurological outcome. Contusions were the most common lesion type, and progressed more, and for a longer period of time, than SDH, EDH and tSAH. Total LPV was also independently associated with 12-month GOS. To the best of our knowledge, this is the first study to arrive at these conclusions by combining volumetric lesion analysis with temporal data in TBI patients.

This study confirms previous observations that lesion progression is more common in contusions than EDH, SDH and tSAH [2, 4, 5, 20]. In addition, we found that the mean total LPV was 3.85 ml, with contusions expanding the most of any lesion type. Our mean contusion progression volume of 4.72 ml is comparable to the 6.0 ml seen in the control group of a recent CENTER-TBI study on the effects of antiplatelet therapy on contusion expansion [20]. We also found that lesions stopped progressing within

a median of 5.98 hours, with contusions progressing the longest of any lesion type. These findings shed light on a potential time-window for interventions that target hematoma expansion. The differences in LPV and LPT between contusions and extra-axial hematomas may be due to their underlying pathophysiology; while the growth of extra-axial hematomas can be credited to bleeding from damaged vessels, contusion progression has also been attributed to the effects of a traumatic penumbra surrounding the lesion, where molecular processes may lead to delayed microvessel structural failure and bleeding progression, even in regions that appear to be unaffected on the first CT scan [21]. Our identification of a trend towards decreasing lesion volume change over time (Fig. 5), also indicates that treatment delay will reduce the potential for hemostatic agents to prevent intracranial bleeding. This is supported by results from the CRASH-3 trial of tranexamic acid in TBI [22], which found that early treatment conferred the greatest mortality benefit. However, while the CRASH-3 study employed a time window for eligibility of 3 hours, our finding that many lesions progress beyond this limit might enable future studies of other hemostatic agents to expand this window, especially in contusion subgroups, as long as the risk of progression outweighs that of thrombotic complications.

Although some studies have reported that lesion progression is associated with neurological outcome, this has not consistently been observed [2]. Juratli and colleagues showed that patients with contusion progression were more likely to show a modified Rankin Scale score ≥ 4 at follow-up [11], and Cepeda et al found that both the presence and volume of progression were associated with 6-month unfavorable GOS [10]. Similarly, Qureshi et al reported a higher proportion of patients with favorable 6-month Extended GOS (GOSE) in those without lesion progression [23]. While these studies demonstrated univariate associations between lesion progression and neurological outcome, the associations did not remain significant in multivariate analyses, leading to a belief that lesion progression might represent severe TBI rather than have a direct impact on outcome [2]. It is therefore interesting that total LPV was independently associated with 12-month GOS in our study, even after adjusting for other known TBI outcome predictors [19]. This is consistent with a hypothesis that lesion expansion is a driver, and not simply a marker, of severe injury and poor outcome. Total LPV had an explanatory power (pseudo- R^2) of 0.082 – lower than GCS (pseudo- $R^2 = 0.130$), age (pseudo- $R^2 = 0.094$) and bilateral dilated pupils (pseudo- $R^2 = 0.094$), but higher than the explanatory power of EDH (pseudo- $R^2 = 0.057$). It was also the only independent outcome predictor that is potentially preventable, highlighting its role as a potential therapeutic opportunity to improve outcome in TBI patients.

Limitations

Our omission of non-operated lesions tended to exclude large extra-axial hematomas, as they were more likely to be surgically treated. For example, 40 % (185/458) of SDHs and 61 % (95/157) of EDHs were evacuated, as compared to 10 % of contusions (51/491), with evacuated lesions being significantly larger than those managed conservatively (Supplementary table 1). This likely contributed to the fact that contusions appeared to progress for longer periods of time and to a greater extent than EDH or SDH. Requiring at least 2 CT scans within 48 hours also excluded the most severely injured patients who

passed away before a second CT scan could be performed, as well as the less injured patients who did not receive a second CT scan within this time frame. Highlighting this, out of the 21 patients excluded due to only 1 CT scan performed, 17 (81 %) passed away during hospitalization. LPT was also highly dependent on the timing of the second and third CT scans, and we can therefore only conclude that a lesion stopped progressing *within* a certain time frame, rather than at a certain time point. Lastly, we deliberately refrained from identifying predictors of lesion progression, as we considered it to be beyond the scope of this manuscript. Instead, we plan on doing so in a more detailed manner in future studies. Despite these limitations, our study draws strength from the large study population, volumetric calculation of lesion sizes, consideration of the time of injury, and continuous rather than binary measurement of lesion progression. For this reason, we believe that this study provides important information on the progression of traumatic intracranial lesions and how this may affect outcome.

Conclusions

We present a study of hemorrhage lesion progression in TBI using semi-automated volumetric lesion measurement. Contusions were the most common form of hemorrhage, and showed both a larger LPV and LPT compared to extra-axial hematomas. Total LPV was independently associated with 12-month GOS – highlighting its role as a potential therapeutic target in TBI management. This study also indicates a wider window of opportunity to prevent lesion progression than what has been previously suggested.

Abbreviations

AIS Abbreviated Injury Scale

CT Computed tomography

EDH Epidural hemorrhage

GCS Glasgow Coma Scale

GOS Glasgow Outcome Scale

GOSE Extended Glasgow Outcome Scale

LPT Lesion progression time

LPV Lesion progression volume

PACS Picture Archiving and Communication System

SAH Subarachnoid hemorrhage

SDH Subdural hemorrhage

Declarations

Ethics approval and consent to participate: The study was approved by the Swedish Ethical Review Authority (Dnr: 2019-04476) who waived the need for informed consent.

Consent for publication: N/A

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Study design: AFS. Data collection: AFS, CT, JT. Statistical analysis: AFS. Data interpretation: All authors. Draft of manuscript: AFS. Critical revision of manuscript: All authors. Approval of final manuscript: All authors. Study supervision: ET, BMB.

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Figures

Figure 1

Flowchart illustrating the patient selection process.

Figure 2

Density plot illustrating when the first, second and third computed tomography (CT) scans were performed in relation to the time of injury. The x-axis was logarithmized due to its non-parametric distribution.

Figure 3

Box plot showing the first and final lesion volumes for contusions, epidural hematomas (EDH), subdural hematomas (SDH), and all lesions combined.

Figure 4

Kaplan Meier curve showing lesion progression time for contusions, epidural hematomas (EDH), subdural hematomas (SDH), and subarachnoid hematomas (tSAH). The shaded areas indicate 95% confidence intervals. Lesion progression was defined as any expansion of existing hemorrhagic lesions or the appearance of a new lesion, and a lesion was determined to have stopped progressing when two consecutive CT scans showed the same volume for the lesion in question.

Figure 5

Scatterplot of percentage increase in lesion volume in relation to time since injury. Each dot represents a patients' change in lesion volume compared to their prior CT scan. A value of 0 % indicates unchanged lesion volume, 100 % indicates that the lesion volume had doubled, and negative values indicate that the lesion volume decreased. The line is a LOWESS curve and the shaded area surrounding it indicates 95% confidence intervals.

Figure 6

Conditional density (CD) plot of lesion progression volume, lesion progression time and final lesion volume versus Glasgow Outcome Scale (GOS). The x-axis' have been logarithmized due to their non-parametric data distribution. The red line in both graphs illustrates data distribution.

Supplementary Files

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