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Abstract

The Scandinavian Guidelines for Initial Management of Minimal, Mild, and Moderate Head Injuries in Adults (Scandinavian guidelines) are the first to incorporate serum measurement of the S100 astroglial calcium-binding protein B (S100B) to emergency department (ED) triage of patients with head injury (HI). This prospective validation study was conducted in the ED of the Tampere University Hospital, Finland, between November 2015 to November 2016. All consecutive adult patients with HI presenting to the ED within 24 hours from injury were eligible for inclusion. Venous blood for S100B sampling was drawn from all patients and the result was available at the ED. Head CTs were performed according to the on-call physician's evaluation. Only the samples collected within 6 hours after injury were used. A one-week follow-up was conducted to identify possible HI-related complications. A total of 295 patients (median age=67.0 years, range=18-100; women=48.8%) were enrolled. Of those, 196 (66.4%) were scanned. Acute traumatic lesions were detected on 31 (15.8%) of the scans. Two of the CT-positive patients were scanned without a guidelines-based indication. These lesions did not require any specific treatment or repeated imaging. The guidelines-based sensitivity was 0.94 (95% CI=0.77-0.99) and specificity 0.19 (95% CI=0.13-0.26) for predicting traumatic intracranial CT abnormalities. The positive and negative predictive value for positive head CT was 0.18 (95% CI=0.12-0.25) and 0.94 (95% CI=0.78-0.99), respectively. In the mild-low risk group, no false negative S100B values were recorded. Thirteen patients (4.4%) were re-admitted to the ED and 2 patients (0.7%) died one week after the primary HI. The deaths were unrelated to the injury. None of these adverse events were directly caused by a primarily undiagnosed intracranial injury. The Scandinavian guidelines incorporated with S100B are a valid means of screening clinically significant acute traumatic lesions following HI and have the potential to reduce unnecessary CT scanning.

Introduction

Traumatic brain injury (TBI) is a major health issue, one of the most common reasons for seeking emergency department (ED) care, and a leading cause of morbidity and mortality globally.[1–3] Head computed tomography (CT) imaging is used in the ED to identify the subgroup of patients with intracranial pathology and those in need of neurosurgical intervention.[4–6] Although head CT is effective in detecting these patients, the majority of head CTs are negative for macroscopic structural brain injury.[7,8]

Several guidelines and CT criteria (e.g., Canadian CT Head Rule [CCHR],[9] New Orleans Criteria [NOC],[10] the CT in head injury patients [CHIP] rule,[11] and the National Institute for Health and Care Excellence [NICE][12]), have been developed to help a physician decide how to risk-stratify patients with TBI in the ED. The guidelines are usually based on certain risk factors from a patient's history, presenting symptoms, and physical examination that indicate the need for a head CT.[9–12] A recent multicenter study compared the four aforementioned guidelines' performances in patients with minor head injuries. The NICE guideline had the lowest sensitivity for an intracranial traumatic CT finding (0.73) of the four criteria but was also the most specific (0.61). Conversely, the NOC was the most sensitive (0.99) but had extremely low specificity (0.04). Sensitivity and specificity for a potential neurosurgically manageable lesions ranged from 0.85 (NICE) to 1.00 (NOC), and 0.04 (NOC) to 0.59 (NICE), respectively.[13]

The Scandinavian Guidelines for Initial Management of Minimal, Mild, and Moderate Head Injuries in Adults (hereafter: Scandinavian guidelines) stratifies head injury (HI) patient management based on the severity of injury and clinical risk factors for acute traumatic intracranial haemorrhage.[14] In 2013, the guidelines were updated and mild TBIs were categorized in low, medium, and high risk groups depending on certain risk factors. Different from other guidelines, Scandinavian Guidelines added the use of serum biomarker S100 astroglial calcium-binding protein B (S100B) to the management of the low risk group in hopes of reducing unnecessary CT imaging.[15] In a retrospective validation study conducted by Undén and colleagues,[16] the Scandinavian guidelines were 0.97 (95% CI, 0.84-1.00) sensitive and 0.34 (95% CI, 0.30–0.37) specific for the detection of acute

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traumatic intracranial lesions. The study showed that the use of the guidelines would have resulted in a 32% reduction in CT scans. The Scandinavian guidelines have also been shown to reduce the CT usage and costs after S100B has been added to the guidelines.[17]

The aim of this study was to clinically validate the Scandinavian guidelines in the Finnish healthcare system with a prospective ED cohort. We hypothesized that the guidelines would be sensitive for recognizing CT-positive intracranial lesions and that the use of S100B reduces the need for CT imaging in mild TBI.

Methods

We performed a prospective cohort study on adults (≥18 years) with acute (≤24 hours from injury) traumatic HI. Patients were enrolled from the ED of the Tampere University Hospital (Tampere, Finland) during a 1-year period from November 2015 to November 2016. The Tampere University Hospital is the only neurosurgical referral hospital in the hospital district and the ED provides health services for a total of approximately 470,000 residents from 22 municipalities, both urban and rural. Consecutive adult patients treated in the ED with acute HI were eligible for inclusion. A total of 3,067 adult head injured patients (mean age = 56.9 years, SD = 23.2, median = 58.0, range = 18-103; women = 50.2%) were seen in the ED during the study period. Minimum criteria for TBI were defined as follows: either blunt injury to the head or acceleration/deceleration type injury resulting in an initial Glasgow Coma Scale (GCS) score of 13-15, witnessed loss of consciousness, disorientation, or amnesia. An injury-ED admission delay of over 24 hours was considered an exclusion criterion. As shown in Figure 1, 295 patients (mean age = 61.1 years, SD = 22.7, median = 67.0, range = 18-100; women = 48.8%) were enrolled to the study. The patient enrollment was performed by on-call physicians working in the ED. Detailed reasons for patient exclusion/non-enrollment were not collected due to the pragmatic enrollment design. Subjects were classified into HI injury severity groups defined by the Scandinavian guidelines using clinical variables and S100B values (Figure 1). The study was approved by the Ethics Committee of Pirkanmaa Hospital District, Tampere, Finland (ethical code: R15045). All enrolled patients provided written informed consent according to the Declaration of Helsinki.

Clinical Variables

Patients were interviewed by the on-call physician to determine injury mechanism and initial symptoms. Medical history was determined by the interview and a medical record review. Systematic medical record review was later conducted to determine complete medical history for the purposes of this study. Initial GCS scores and witnessed signs and symptoms were derived from pre-hospital emergency charts and incorporated in the ED assessment. Physical examination and evaluation for the need of head CT was made by the on-call physician. Clinical variables were collected based on those included in the Scandinavian guidelines. GCS scores assessed in the ED were used for statistical analyses.

Outcome Measures

The primary outcome measure was an acute traumatic lesion on head CT. Delayed HI-related complications including hospital or ED re-admission, repeat head CT, or death within 1-week after injury were defined as the secondary outcome measures. One-week following injury, a phone call and medical record review was conducted by a research nurse to identify possible complications. The deaths were determined from medical records and death certificates.

CT Imaging

In the ED, a non-contrast head CT was performed with a 64-row CT scanner (GE, Lightspeed VCT, WI, USA). Referral criteria for acute head CT were based on the Scandinavian guidelines[15] and the physicians' evaluation. All CT findings were systematically coded by a radiologist based on the National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDE).[18]

S100B Measurement

The Scandinavian guidelines recommend S100B only with mild-low risk HI patients within 6 hours of injury. However, for this study venous blood was drawn from all patients with HI at ED admission, mostly before possible CT imaging. The result was available to the physician on call. For analyses that specifically test the Scandinavian guidelines, only the

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samples collected from mild-low risk HI patients within 6 hours after injury were used. Serum S100B was measured using the Elecsys S100B® assay (Roche Diagnostics, Penzberg, Germany). S100B levels of under 0.10 μg/L were considered normal.

Statistical Analyses

The statistical analyses were conducted with the Statistical Package for Social Sciences software program (IBM SPSS Statistics for Windows, Versions 22.0-24.0, Armonk, NY, USA). Descriptive statistics [frequency (n), percentage, median, interquartile range, range] were used to calculate variable and subgroup characteristics. The statistical significance level was set at 5%. The guideline sensitivity was calculated by dividing the number of patients with a guideline indication and positive head CT result by the total number of positive head CT results. The guideline specificity was calculated by dividing the number of patients without a guideline indication and negative head CT result by the total number of negative head CT results. The positive predictive value of the guideline indication was calculated as the proportion of patients with guideline indication and positive head CT result. The negative predictive value of no guideline indication was calculated as the proportion of patients without guideline indication and negative head CT result.

Results

The sample characteristics of the 295 eligible patients are summarized in Table 1. The enrolled patients (n = 295) did not significantly differ from all the ED-treated adult patients with HI (n = 3,067, mean age = 56.9 years, SD = 23.2, median = 58.0, range = 18-103, women = 46.8% [n = 1,435]) in relation to age or gender (both, p > 0.05). Figure 1 presents the study process and the main characteristics of patients in all subgroups stratified according to the Scandinavian guidelines. The main clinical findings and outcome measures of the subgroups are presented in Table 2. One patient with a GCS score due to a pre-existing medical condition (severe alcohol-related dementia, unable to communicate orally and totally dependent of the nursing home facilities) was recruited because of an acute head injury. The patient had a negative head CT and was classified as having a

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moderate TBI despite a GCS score of 8. She was discharged back to a nursing home after follow-up.

A total of 196 patients underwent head CT imaging. Acute traumatic CT findings were found in 31 (15.8%) of the scans. The most common findings were subdural hematomas (7.1%, n = 17) and traumatic subarachnoid hemorrhages (7.1%, n = 17). The findings according to the NINDS CDEs are shown in Table 3.

According to the Scandinavian guidelines, 187 patients required a head CT, and 108 would have been discharged without CT scanning. The overall compliance to the guideline was 80.7% (n = 238) and a head CT was performed on 196 patients. Details of the performance of the guidelines are presented in Figure 2. The guideline sensitivity was 0.94 (95% CI = 0.77-0.99) and specificity 0.19 (95% CI = 0.13-0.26) for predicting traumatic CT abnormalities. The guidelines' positive and negative predictive values for positive head CT were 0.18 (95% CI = 0.12-0.25) and 0.94 (95% CI = 0.78-0.99), respectively. There were no delayed HI-related complications for the non-CT-imaged subgroup of patients.

The performance of S100B in the low risk mild TBI group is presented in Figure 3. Compliance to the negative S100B values would have resulted in 29.0% (n = 18) reduction of CT imaging in the group. When compared to all the mild TBI patients, the reduction would have been 9.1%.

According to the guidelines, 24 patients who did not undergo CT imaging should have had a head CT, and 33 had a CT done without a guidelines-based indication. None of the 24 patients who were not scanned developed a HI-related complication within one week after injury. Two patients (6.0% of 33 patients) without a guidelines-based indication for imaging had traumatic lesions on their CTs. Both were categorized in the minimal TBI group, and both patients had an acute subdural hematoma on their CT scans. First, an 88-year-old woman (acute subdural hematoma, 2 mm thick, right temporal convexity) sustained a ground-level fall with post-traumatic amnesia and external injuries above the clavicles, and second, a 68-year-old woman (acute subdural hematoma, 1 mm thick, over the left tentorium) who fell, had external injuries above the clavicles, and had headache in the ED. They were discharged home after 6 and 17 hours of observation in the ED,

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respectively. Neither of the two patients were readmitted to the ED within 1-week after the injury. Neither of them required neurosurgery.

Two patients (0.7%) died during the one-week follow-up time period, one from the minimal TBI group and the other from high risk mild TBI group. Neither showed traumatic lesions on head CTs. The patient from the minimal TBI group was originally discharged home and the other transferred to a central hospital ward. The former died of a spinal injury caused by a new trauma and the latter due to a cardiogenic cause. Both deaths were unrelated to the primary HI.

Discussion

Head injury is among the most common causes for seeking emergency medical care, and patients present to the ED with vast clinical heterogeneity.[2,3] Given increasing health care costs, unnecessary ED resource utilization, and non-trivial iatrogenic risk associated with CT scanning (mainly for radiation-induced neoplasia), eliminating unnecessary CT scanning is desired.[16,17]

Many studies have confirmed that the use of S100B in TBI patient management safely reduces CT imaging and management costs.[16,17,19,20] There are several published CT decision rules for managing patients with head injuries, but the Scandinavian guidelines are the first to incorporate S100B as a negative predictor for the need of head CT.[19] To our knowledge, this is the first prospective study that examines the clinical validity of the Scandinavian guidelines. Our study showed that the guideline can be safely used in head CT imaging decision making within 24 hours of head injury. The sensitivity and specificity of the guideline was 0.94 and 0.19, respectively. The positive and negative predictive value for acute traumatic lesions on head CT was 0.18 and 0.94, respectively. The sensitivity of the guideline was lower, but the specificity was higher than the recent reports on the NOC criteria.[13] Recently published results from the ALERT-TBI study demonstrated that a blood test combining serum levels of glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase-L1 (UCH-L1) in predicting traumatic intracranial injuries yielded better sensitivity and specificity than the Scandinavian Guidelines in this validation study.[21] However, those biomarkers are not currently incorporated into any guideline and the test does not take

into account clinical covariates such as extracranial injuries or factors predisposing for intracranial hemorrhage. Currently, the analytics of GFAP and UCH-L1 demands several hours, thus limiting the applicability of these blood-based biomarkers to an ED setting. S100B results can be attained generally within one hour.

In our study, the Scandinavian guidelines did not detect two CT-positive lesions. The two false negative cases that were missed were elderly patients with isolated thin acute subdural hematomas. These hematomas did not have mass effect and they were managed conservatively without complications. In retrospect, unrecorded or unrecognized pre-injury medical problems in these two missed cases could have distorted medical judgment in the ED in relation to guidelines-based risk factors. Furthermore, acetylsalicylic acid is available prescription-free in Finland, and many elderly patients may be using this by their own choice and without medical documentation.

With a 100% adherence to the Scandinavian guidelines, the use of S100B would have decreased the need of head CT by 9%. Among the low risk mild TBI subgroup, none of the cases with a S100B level of under 0.1 µg/L had a positive head CT or suffered from HI-related complication. Therefore, a negative S100B result was reliable in excluding CT-positive findings in the context of the Scandinavian guidelines. In the low risk mild subgroup, the majority of the patients with a positive S100B result had a negative head CT, and none of these patients experienced a HI-related complication. Our study cohort was mostly elderly, and the patients had numerous long-term illnesses. Most likely these factors, especially the diseases of the central nervous system, partly explain the large number of false positive S100B findings and the overall low guideline specificity. Age has been shown to have an effect on S100B levels.[22,23] Nevertheless, excellent accuracy for S100B in discriminating CT-positive lesions among elderly patients has been reported.[24] In addition to head trauma, serum S100B levels have been shown to increase after conservatively treated extracranial injuries without head trauma,[25–28] and in several other medical conditions, such as stroke,[29] depression,[30] and dementia.[31]

Based on the validation results, 267 out of 3,067 patients with HI (9%) could have been treated without a head CT scan. The cost of a head CT scan at the Tampere University

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Hospital ED is currently 184 USD (163 €), and the average cost for S100B assessment is 45 USD (40 €). Consequently, a saving per one patient is 139 USD. At the Tampere University Hospital, annual savings of approximately 37,000 USD could have been achieved with the Scandinavian guidelines. However, 4% (n=8) of the mild TBI patients would have required a head CT against the physician's clinical decision due to a false positive S100B result, lowering the actual financial savings. The false positive results could also lead to additional stress and worry in some patients.

Acute traumatic lesions were found in 15.8% (n=31) of the CT-imaged patients. The prevalence of traumatic lesions on CT was highest in the medium risk mild TBI group (23.3%) and lowest in the minimal TBI group (8.3%). The prevalence of traumatic lesions was higher than in similar studies conducted recently, their prevalence varying from 4.7% to 8.5%.[16,17,20] The difference is likely to be partly affected by the age distribution in this study, as well as the study's higher compliance to the Scandinavian guidelines, because the patients undergoing CT imaging are presumably more likely to have traumatic CT findings. In addition, the study population was inclined to more severe injuries. The mild-low risk and minimal TBI subgroups constituted up to 55.9% of our study sample. In the Undén et al. (2015) validation study, the same figure was 79.0%. In our study, the most common traumatic intracranial findings were subdural hematomas (7.1%, n=17) and traumatic subarachnoid hemorrhages (7.1%, n=17). Whereas in the studies by Undén et al. (2015) and Calcagnile et al. (2016), the most common finding was a contusion.

Overall, the compliance to the Scandinavian guidelines was relatively high (i.e., 80.7%). Compliance to the guideline was lowest in the minimal TBI and low risk mild TBI groups (i.e., 73.3% in both). This might reflect the physicians' general insecurity in relying on the Scandinavian guidelines to exclude CT-positive TBI lesions. Partly supporting the on-call physicians' lack of trust in the guideline, the two missed cases belonged to the minimal TBI group. However, none of these patients required neurosurgery, specific medical treatment, or suffered from delayed head injury-related complications. A recent partly prospective study on the Scandinavian guidelines reported a lower compliance (i.e., 63.0%) to the guidelines and did not further asses the guidelines' ability to detect intracranial findings, thus making our study more informative on the validity of the guidelines in

clinical use.[32] This study by Ananthaharan et al. (2018) was conducted during the introduction period of the guidelines and provided the physicians with a study form partly dictating the guidelines pathway. Our study is more representative of the routine use of the guideline in clinical practice.

Compared to previous studies on the Scandinavian guidelines, our strength was the pragmatic and prospective study design. We did not apply any exclusion criteria, and the enrolled patients were comparable to all the adult head injury patients seen in the ED during the study period in relation to age and gender; thus, minimizing potential selection bias. The study results are widely generalizable and applicable to similar ED settings as ours, especially to cohorts with an over-representation of older adults. Head CT scans were systematically interpreted and coded according to the NINDS CDEs.

There were limitations in our study. The variable "significant external injury" was determined only based on whether the patient needed a surgery other than neurosurgery. The more minor orthopaedic injuries were not noted. Although the guidelines were used in the ED with good compliance, it is possible that some of the patients who were classified as being in the mild low risk group and considered suitable for S100B assessment had minor orthopedic injuries resulting in elevated S100B levels. This could have led to false positive S100B results in the CT-negative patients, lowering the specificity of the guideline. Our sample represents a rather elderly cohort, and therefore caution should be taken when applying these results more widely. The updated guidelines are mostly used in Scandinavian EDs, but also in some other European countries.[33] Studies have shown its potential in reducing CT imaging in different health care systems, but the introduction of the guidelines to clinical use is still in process and additional research is needed.[16,17,32] Finally, we used the NINDS CDEs to characterize acute traumatic intracranial lesions, and therefore included skull fractures as positive CT lesions. This should be noted when comparing our results to other studies that might have used other strategies to define trauma lesions (e.g., excluding skull fractures as TBI lesions).

Our cohort was relatively small and had only three patients that needed a neurosurgical intervention. Future studies on the Scandinavian guidelines should be

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conducted with larger cohorts to determine the guideline's ability to detect lesions resulting in neurosurgery or specific medical interventions.

Conclusions

The Scandinavian guidelines are a valid means of screening for clinically significant acute traumatic lesions in patients with mild TBIs. The guideline can potentially reduce unnecessary head CT scanning.

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Declaration of interest statement

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Table 1. Sample characteristics.

Variable	Md	IQR
Age (years)	67.0	38.0
Time between injury and blood sampling (hours)	3.2	3.2
Time between injury and ED admission (hours)	1.3	1.8
Time between injury and head CT (hours)	4.5	4.3
Time between injury and hospital discharge (hours)	69	74
Time between injury and ED discharge (hours)	6.8	5.4
Time of ED stay (hours)	4.8	3.4
	N	**%**
Men	151	51.2
Women	144	48.8
Health Problems Documented in Medical Records		
Diseases of the circulatory system (I00-99)	175	59.3
Diseases of the respiratory system (J00-99)	55	18.6
Mental and behavioral disorders (F01-99)	139	47.1
Diseases of the nervous system (G00-99)	101	34.2
Endocrine, nutritional, and metabolic diseases (E00-90)	117	39.7
Diseases of the digestive system (K00-93)	60	20.3
Diseases of the genitourinary system (N00-99)	71	24.1
Diseases of the musculoskeletal system and connective tissue (M00-99)	100	33.9
Neoplasms (C00-D48)	76	25.8
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-89)	17	5.8
Diseases of the eye and adnexa (H00-59)	79	26.8
Diseases of the ear and mastoid process (H60-95)	45	15.3
Diseases of the skin and subcutaneous tissue (L00-99)	26	8.8

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Pregnancy, childbirth, and the puerperium (O00-99)	3	1.0
Certain conditions originating in the perinatal period (P00-96)	1	0.3
Congenital malformations, deformations and chromosomal abnormalities (Q00-99)	9	3.1
Injury, poisoning and certain other consequences of external causes (S00-T98)	289	98.0
Prior cranial neurosurgery in general	2	0.7
Prior cranial neurosurgery due to a trauma	8	2.7
Injury mechanism		
Unknown	3	1.0
Car accident	5	1.7
Ground-level fall	207	70.3
Motorcycle accindent	1	0.3
Bicycle accident	7	2.4
Fall from a distance	29	9.8
Sports	12	4.1
Violence	18	6.1
Pedestrian struck by a motor vehicle	0	0.0
Other, not specified	13	4.4
Anticoagulant medication	64	21.7
Warfarin	59	20.0
Apixaban	1	0.3
Dabigatran	3	1.0
Antiplatelet medication	49	16.6
Acetylsalicylic acid	40	13.6
Acetylsalicylic acid-dipyridamol	6	2.0
Clopidogrel	2	0.7
Ticagrelor	0	0.0
Acetylsalicylic acid and clopidogrel	1	0.3
Coagulopathy	3	1.0

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Intracranial shunt	0	0.0
Glasgow Coma Scale score	Md=15	Range 8-15
Loss of consciousness, witnessed or suspected	111	37.6
Post-traumatic amnesia	107	36.3
Focal neurological deficit	21	7.1
Clinical signs of a skull fracture	7	2.4
Post-traumatic seizure	4	1.4
External injury above the clavicle level	227	76.9
Vomiting ≥2 times	12	4.1
Headache	128	43.4
Alcohol intoxication	95	32.2
Neurosurgery due to acute head injury	3	1.0
Acute extracranial surgery	4	1.4
Place of follow-up treatment after the emergency department visit		
Home	198	67.1
University hospital ward	12	4.1
University hospital intensive care unit	2	0.7
Non-university hospital ward	35	11.9
Health center	26	8.8
Other healthcare facility	6	2.0
Detoxification center	15	5.1
Police station	1	0.3
Death	0	0.0

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Table 2. Clinical findings and outcome measures of the study sample stratified by Scandinavian guideline subgroups.

	Minimal TBI n=90		MTBI-Low Risk n=75		MTBI-Moderate Risk n=36		MTBI-High Risk n=88		Moderate TBI n=6	
	n	%	n	%	n	%	n	%	n	%
Underwent Head CT Scan	24	26.7	55	73.3	30	83.3	82	93.2	5	83.3
GCS 8	--	--	--	--	--	--	--	--	1	16.7
GCS 9-11	--	--	--	--	--	--	--	--	0	0
GCS 12	--	--	--	--	--	--	--	--	4	66.7
GCS 13	--	--	--	--	--	--	--	--	1	16.7
GCS 14	--	--	6	8.0	1	2.8	6	6.8	--	--
GCS 15	90	100	69	92.0	35	97.2	82	93.2	--	--
Witnessed or suspected LOC	--	--	64	85.3	13	36.1	31	35.2	1	16.7
Repeated vomiting	--	--	6	8.0	0	0.0	4	4.5	0	0.0
LOC AND vomiting	--	--	2	2.7	0	0.0	0	0.0	0	0.0
Post-traumatic seizures	--	--	--	--	--	--	4	4.5	0	0.0
Focal neurological findings	--	--	--	--	--	--	19	21.6	2	33.3
Clinical signs of skull fracture	--	--	--	--	--	--	7	8.0	0	0.0
Intracranial shunt	--	--	--	--	--	--	0	0.0	0	0.0
Anticoagulant medication	--	--	--	--	--	--	62	70.5	2	33.3

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Coagulopathy	--	--	--	--	--	--	3	3.4	0	0.0
More than one of the aforementioned risk factors	--	--	--	--	--	--	7	8.9	1	16.7
S100B < 0.1 µg/L (within 6h after injury)	24	35.3	18	29.0	9	30.0	15	22.4	0	0.0
S100B ≥ 0.1 µg/L (within 6h after injury)	44	64.7	44	71.0	21	70.0	52	77.6	4	100
Significant extracranial injury	0	0.0	2	2.7	1	2.8	1	1.1	0	0.0
Traumatic lesion on head CT	2	8.3	6	10.9	7	23.3	15	18.3	1	20.0
Skull fracture	0	0.0	2	3.6	1	3.3	3	3.7	1	20.0
Acute subdural hematoma	2	8.3	1	1.8	5	16.7	6	7.3	0	0.0
Subacute or chronic subdural hematoma	0	0.0	0	0.0	0	0.0	4	4.9	0	0.0
Subarachnoid hemorrhage	0	0.0	3	5.5	1	3.3	9	11.0	1	20.0
Supratentorial midline shift	0	0.0	0	0.0	1	3.3	2	2.4	0	0.0
Intracerebral hemorrhage	0	0.0	0	0.0	0	0.0	2	2.4	0	0.0
Intraventricular hemorrhage	0	0.0	0	0.0	0	0.0	1	1.2	0	0.0
Edema	0	0.0	0	0.0	0	0.0	1	1.2	0	0.0
Contusion	0	0.0	0	0.0	1	3.3	6	7.3	0	0.0
Traumatic axonal injury	0	0.0	1	1.8	1	3.3	1	1.2	0	0.0
S100B < 0.1 µg/L AND traumatic lesion on head CT	1	5.9	0	0.0	2	7.7	1	1.6	0	0.0
S100B ≥ 0.1 µg/L AND traumatic lesion on head CT	1	5.9	5	13.9	4	15.4	12	18.8	0	0.0
Neurosurgery due to head trauma	0	0.0	0	0.0	1	2.8	2	2.3	0	0.0
Discharged home from the ED	7	80.	5	76.	2	58.	4	52.	2	33.

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	2	0	7	0	1	3	6	3		3
Admitted to a ward from the ED	8	8.9	14	18.7	11	30.6	40	50.0	2	33.3
Within 1-week following injury										
Re-admitted to ED	4	4.4	3	4.0	0	0.0	6	6.8	0	0
Reason for re-admission										
Post-injury symptoms	1	1.1	1	1.3	0	0.0	2	2.3	0	0.0
Post-injury symptoms, cSDH on a new CT	0	0.0	1	1.3	0	0.0	0	0.0	0	0.0
Invited back due to a missed intracranial hematoma	0	0.0	0	0.0	0	0.0	1	1.1	0	0.0
New unrelated illness	2	2.2	1	1.3	0	0.0	1	1.1	0	0.0
New head injury	0	0.0	0	0.0	0	0.0	2	2.3	0	0.0
Death	1	1.1	0	0.0	0	0.0	1	1.1	0	0.0

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Table 3. Head CT findings according to the NINDS Common Data Elements.

Finding	n	%
Normal Head CT Scan	165	84.2
Abnormal Head CT Scan	31	15.8
Skull Fracture	7	3.4
Epidural Hematoma (EDH)	0	0.0
Extraaxial Hematoma	25	12.8
Subdural Hematoma (SDH), Acute	14	7.1
Subdural Hematoma, Subacute or Chronic	4	2.0
Subdural Hematoma / Mixed Density Subdural Collection / CSF-like Collections	0	0.0
Subarachnoid Hemorrhage (SAH)	14	7.1
Vascular Dissection	0	0.0
Traumatic Aneurysm	0	0.0
Venous Sinus Injury	0	0.0
Midline Shift (Supratentorial)	3	1.5
Cisternal Compression	0	0.0
Fourth Ventricle Shift / Effacement	0	0.0
Contusion	7	3.4
Intracerebral Hemorrhage	2	1.0

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Intraventricular Hemorrhage	1	0.5
Diffuse Axonal Injury (DAI) (more than 3 foci of signal abnormality)	0	0.0
Traumatic Axonal Injury (TAI) (1-3 foci of signal abnormality)	3	1.5
Penetrating Injuries	0	0.0
Cervicomedullary Junction / Brainstem Injury	0	0.0
Edema	1	0.5
Brain Swelling	0	0.0
Ischemia / Infarction / Hypoxic-ischemic Injury	0	0.0

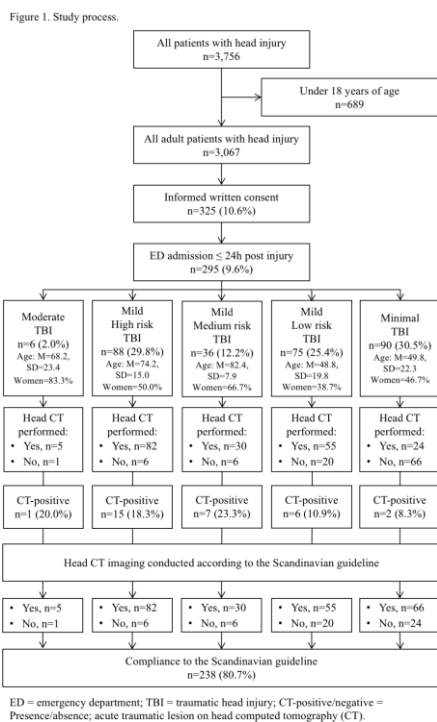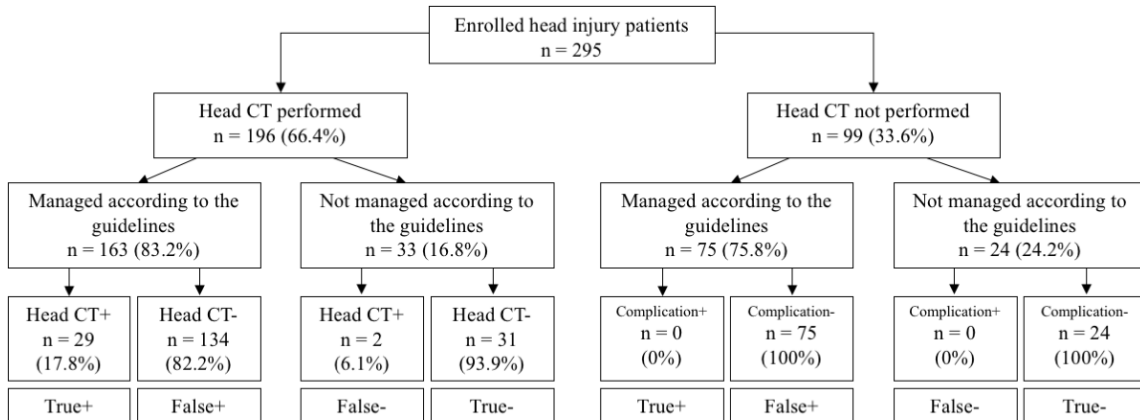# Figure legends

Figure 1. Study process.

Figure 1. Study process.

ED = emergency department; TBI = traumatic head injury; CT-positive/negative = Presence/absence; acute traumatic lesion on head computed tomography (CT).

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Figure 2. Performance of the Scandinavian guidelines.

CT+/- = Presence/absence; acute traumatic lesion on head computed tomography (CT); Complication+/- = Presence/absence; hospital or ED re-admission, repeat head CT, or death within 1-week after injury; the True/False ratings refer to the performance of the guidelines.

Figure 2. Performance of the Scandinavian guidelines.

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Figure 3. Performance of S100B in the mild-low risk group.

Blood sampling done within 6 hours after injury and no significant extracranial injury. CT+/- = Presence/absence; acute traumatic lesion on head computed tomography (CT); Complication+/- = Presence/absence; hospital or ED re-admission, repeat head CT, or death within 1-week after injury.
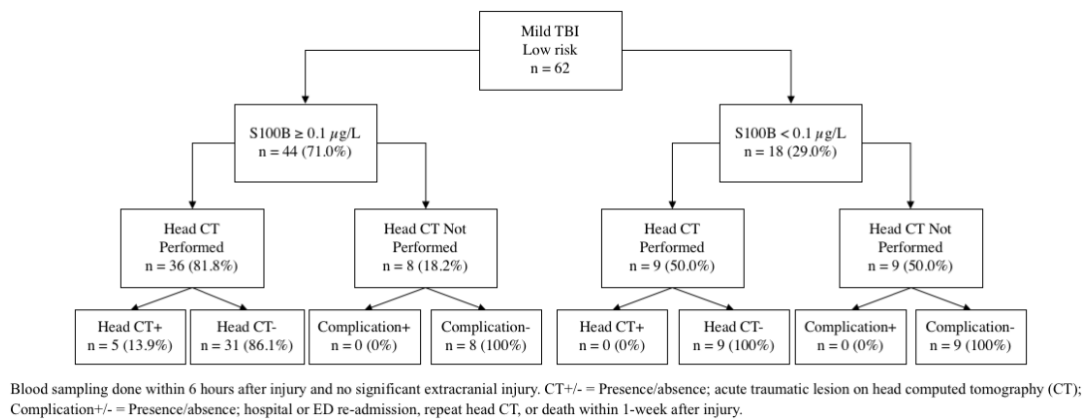
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