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Original Articles

Risk of Intracranial Complications in Minor Head Injury: The Role of Loss of Consciousness and Post-Traumatic Amnesia in a Multi-Center Observational Study

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Abstract

Various guidelines for minor head injury focus on patients with a Glasgow Coma Scale (GCS) score of 13–15 and loss of consciousness (LOC) or post-traumatic amnesia (PTA), while clinical management for patients without LOC or PTA is often unclear. We aimed to investigate the effect of presence and absence of LOC or PTA on intracranial complications in minor head injury. A prospective multi-center cohort study of all patients with blunt head injury and GCS score of 15 was conducted at six Dutch centers between 2015 and 2017. Five centers used the national guideline and one center used a local guideline—both based on the CT in Head Injury Patients (CHIP) prediction model—to identify patients in need of a computed tomography (CT) scan. We studied the presence of traumatic findings and neurosurgical interventions in patients with and without LOC or PTA. In addition, we assessed the association of LOC and PTA with traumatic findings with logistic regression analysis and the additional predictive value of LOC and PTA compared with other risk factors in the CHIP model. Of 3914 patients, 2249 (58%) experienced neither LOC nor PTA and in 305 (8%) LOC and PTA was unknown. Traumatic findings were present in 153 of 1360 patients (11%) with LOC or PTA and in 67 of 2249 patients (3%) without LOC and PTA. Five patients without LOC and PTA had potential neurosurgical lesions and one patient underwent a neurosurgical intervention. LOC and PTA were strongly associated with traumatic findings on CT, with adjusted odds ratios of 2.9 (95% confidence interval [CI] 2.2–3.8) and 3.5 (95% CI 2.7–4.6), respectively. To conclude, patients who had minor head injury with neither LOC nor PTA are at risk of intracranial complications. Clinical guidelines should include clinical management for patients without LOC and PTA, and they should include LOC and PTA as separate risk factors rather than as diagnostic selection criteria.

Keywords: clinical guidelines; loss of consciousness; mild traumatic brain injury; minor head injury; post-traumatic amnesia

Introduction

Head injury is a common injury seen at emergency departments, comprising mostly (~90%) patients with minor head injury.[1,2] Besides minor head injury, various other definitions are used, such as mild traumatic brain injury, minor traumatic brain injury, or mild head injury.[3] Key components of these definitions are blunt traumatic injury to the head, a Glasgow Coma Scale (GCS) score of 13–15 on admission, and often loss of consciousness (LOC) or post-traumatic amnesia (PTA).[4,5]

For minor head injury, several clinical guidelines and decision rules have been developed to help decide which patients are at higher risk of intracranial complications and need a computed tomography (CT) of the head.[6–9] Some of these clinical guidelines

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were only developed for patients with LOC or PTA, while for patients without LOC or PTA no scan recommendation was provided, or clinicians were simply advisd to discharge the patients to home without a CT (Table 1).[10–13] However, it is likely that the absence of LOC and PTA does not exclude the possibility of intracranial traumatic findings, including a subdural and epidural hematoma. In many emergency departments only guidelines for patients with LOC or PTA are used, which may lead to discharge of high-risk patients without CT.[14]

Moreover, LOC and PTA are known risk factors for intracranial traumatic findings, but have not been added as separate risk factors in some clinical guidelines (Table 1).[11,12,15,16]

We hypothesize that although LOC and PTA are important risk factors for intracranial complications, patients without LOC and PTA are still at risk of intracranial complications. Therefore, the aim of our study is to investigate the effect of absence and presence of LOC and PTA on intracranial complications in a prospective multi-center study in the Netherlands.

Methods

Study design and setting

Data were prospectively collected in six emergency departments in the Netherlands between 2015 and 2017.[17] The six centers included one university center (trauma Level 1) and five non-university centers (trauma Level 1 [two centers], trauma Level 2 [one center], trauma Level 3 [two centers]). All centers had an urban location. We obtained institutional ethics and research board approval and informed consent was waived.

Inclusion and exclusion criteria

Consecutive patients with blunt traumatic head injury were included if they met the following criteria: presentation within 24 h after blunt trauma to the head, a GCS score of 15 at presentation at the emergency department, and age 16 years and older. All patients with a GCS score of 13–14 were excluded because clinical guidelines will recommend the performance of a head CT regardless of the presence of other risk factors. Patients with and without a head CT were included. All patients transferred from other hospitals were excluded.

Definition of risk factors

Information about risk factors for intracranial complications included in the CT in Head Injury Patients (CHIP) prediction rule were collected as follows: LOC reported by the patient or witness, PTA reported by the patient, the witness or tested at neurological examination, age in years, trauma mechanism (pedestrian or cyclist versus vehicle, ejected from vehicle and fall from any elevation), vomiting, signs of a skull base fracture (for example: raccoon eyes, battle sign, cerebrospinal fluid otorrhea, palpable discontinuity, bleeding from ear), GCS score deterioration (1 or more points) within 1 h after presentation, use of pre-injury anticoagulants, post-traumatic seizure, visible injury to the head (excluding the face), neurological

Table 1. Guideline Recommendations for CT of Patients with and without LOC and PTA

Guideline/decision rule	*Patients with LOC*	*Patients with PTA*	*Patients without LOC*	*Patients without PTA*
American College of Emergency Physicians guideline for mild traumatic brain injury[9]	Other risk factor	Other risk factor	Other risk factor	Other risk factor
Canadian CT Head Rule (CCHR), 2001[10]	Other risk factor	Other risk factor	No recommendation*	No recommendation*
CT in Head Injury Patients (CHIP), 2007[7]	Other risk factor	- If PTA >4 h - If PTA 2–4 h: if other risk factor - If persistent amnesia: if other risk factor	Other risk factor	Other risk factor
European Federation of Neurological Societies (EFNS) guideline TBI, 2012[27]	Always CT	Always CT	Other risk factor	Other risk factor
National Institute for Health and Care Excellence (NICE): head injury, 2014[8]	Other risk factor	Other risk factor	Other risk factor	Other risk factor
National Emergency X-Radiography Utilization Study (NEXUS) head CT, 2005[16]	Other risk factor	Abnormal level of alertness including disorientation	Other risk factor	Other risk factor
NCWFNS guideline for mild head injury, 2001[13]	Always CT	Always CT	No CT	No CT
New Orleans Criteria (NOC), 2000[11]	Other risk factor	Deficits in short-term memory and LOC	No recommendation#	No recommendation
Ono, 2007[19]	LOC or PTA	LOC or PTA	Other risk factor	Other risk factor
Scandinavian guidelines TBI, 2013[12]	If LOC and abnormal S100B	No CT	Other risk factor	Other risk factor

Other risk factor: any other risk factor which will lead to performing a head CT, for example vomiting or use of anticoagulation.
*CCHR was only developed for patients with witnessed LOC, definite amnesia, or witnessed disorientation.
#NOC was only developed for patients with GCS 15 and LOC.
CT, computed tomography; LOC, loss of consciousness; PTA, post-traumatic amnesia; NCWFNS, Neurotraumatology Committee of the World Federation of Neurosurgical Societies; S100B, S100 calcium binding protein (biomarker for head injury); GCS, Glasgow Coma Scale.

deficit (paresis, dysphasia or other such as cranial nerve damage including diplopia, changes in sensibility, asymmetrical reflexes or pathological reflexes, coordination problems, and ataxia).[7] In addition, information about retrograde amnesia and intoxication with drugs or alcohol (history or suggestive findings on examination, such as symmetrical nystagmus, foetor) was collected.

Outcome measures

The primary outcome was any (intra)cranial traumatic finding on CT, including skull fractures, subdural hematomas, epidural hematomas, subarachnoid hemorrhages, cerebral contusions, suspicion of diffuse axonal injury (at least one petechial hemorrhage), and intraventricular hemorrhages. Secondary outcomes were a 1) neurosurgical intervention within 30 days after the injury and 2) any potential neurosurgical lesion, such as epidural hematomas, large acute subdural hematomas (or mass lesions), large contusions (or mass lesions), depressed skull fractures or any lesion with a midline shift or herniation.

Data collection

All eligible patients were included by trained research physicians and the risk factors were collected by taking the patients' history or information from a witness or family member. The local guidelines were used to assess which patients needed a head CT.[17] Five centers used the national guideline and one center used a local guideline, both based on the CHIP prediction model, to identify patients in need of a CT (Appendix 1). Only the initial head CT was interpreted by (neuro)radiologists for traumatic findings. To ensure accuracy, a subset of CTs were over-read by neuroradiologists. Research physicians reviewed the electronic health records 30 days after the injury to assess information about neurosurgical interventions. All data were entered in the web-based application OpenClinica (LCC, Version 3.12.2).

Statistical analysis

Patients were categorized based on the LOC and PTA variables: all patients with LOC, with PTA, or both were selected for the group ''with LOC or PTA.'' All patients without LOC and PTA were selected for the group ''without LOC and PTA.'' All patients with unknown LOC and PTA were selected for the group ''unknown LOC and PTA.''

Demographic characteristics, risk factors, and outcome were described using frequencies and percentages for categorical variables, and median and interquartile range for continuous variables.

We performed univariable logistic regression analysis to quantify the relevance of LOC and PTA as individual risk factors for the presence of intracranial traumatic findings on CT and presented the odds ratios (ORs) and 95% confidence intervals (CIs). In addition, we performed multivariable logistic regression analysis to assess the incremental value of LOC and PTA in addition to other risk factors for intracranial traumatic CT findings present in the CHIP prediction model. The CHIP model consisted of the following variables: LOC, PTA, age, pedestrian or cyclist versus vehicle, ejected from vehicle, vomiting, signs of skull fracture, GCS score deterioration, use of anticoagulants, seizure, fall from any elevation, visible injury to the head and neurologic deficit. Four separate models were created: 1) CHIP model without LOC and PTA; 2) CHIP model with LOC; 3) CHIP model with PTA; and 4) complete CHIP model (including LOC and PTA as separate variables). We compared the variability in outcome explained by the variables by Nagelkerke R^2 values of the four models.[18]

For univariable and multivariable analysis, missing data (2.4%) were assumed to be missing at random and imputed based on the available data of all nine centers in the original study using multiple imputation (m = 5) with the mice package in R. For patients without a head CT, the expected outcomes (intracranial traumatic finding and potential neurosurgical lesion) were imputed based on their risk factors using multiple imputation.[17] All analyses were performed with R, version 3.3.2 (R foundation for statistical computing, Vienna, Austria).

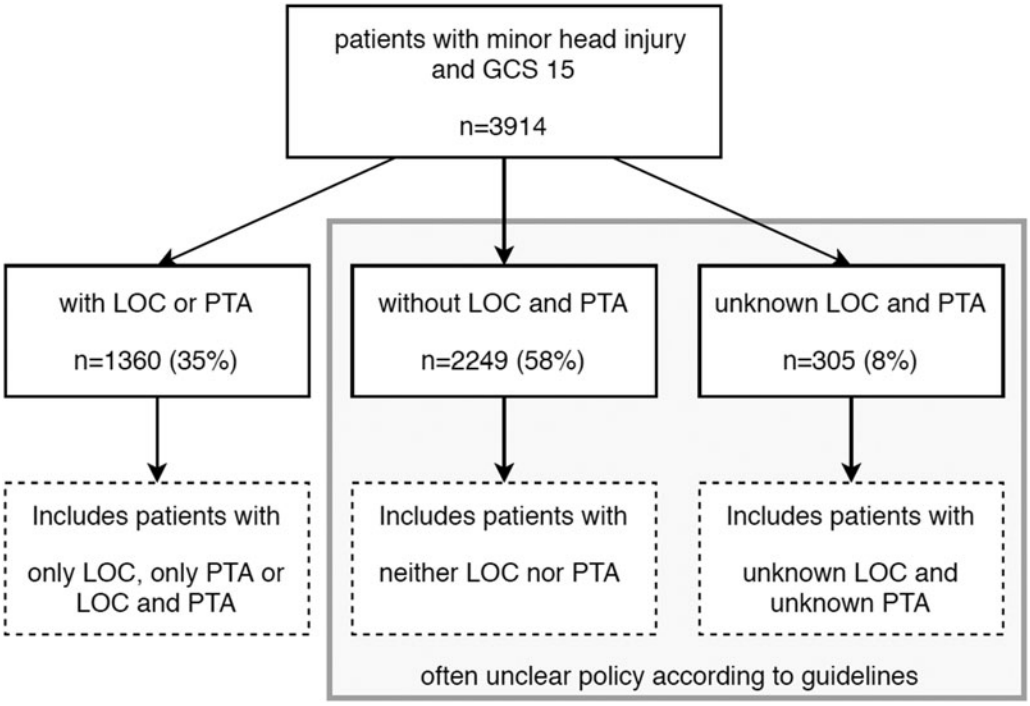

FIG. 1. Flowchart patient categorization. GCS, Glasgow Coma Scale; LOC, loss of consciousness; PTA, post-traumatic amnesia

Results

During the study period, 4557 consecutive patients with blunt traumatic head injury were seen at the six emergency departments. After excluding 643 patients with a GCS score of 13–14 at presentation, we analyzed 3914 minor head injury patients with a GCS score of 15.

LOC and PTA

LOC lasted less than 15 min in 962 patients ($n=962/3914$; 25%) and in 24 patients ($n=24/3914$; 1%) it lasted 15 min or more. LOC was not documented or unknown in 408 patients ($n=408/3914$; 10%). Most patients with PTA had post-traumatic amnesia for less than 2 h ($n=745/3914$; 19%), 40 patients ($n=40/3914$; 1%) between 2 and 4 h, and 31 patients ($n=31/3914$; 1%) for more than 4 h. The majority of patients did not experience LOC ($n=2520/3914$; 64%) or PTA ($n=2816/3914$; 72%). PTA was not documented or unknown in 282 patients ($n=282/3914$; 7%).

Baseline characteristics

Of all patients, 1360 ($n=1360/3914$; 35%) had LOC or PTA, 2249 ($n=2249/3914$; 58%) had no LOC and PTA, and 305 patients ($n=305/3914$; 8%) had unknown LOC and PTA (Fig. 1).

The patients with LOC or PTA were slightly younger than the patients without LOC and PTA (median 50.5 vs. median 53 years; Table 2). More patients without LOC and PTA used anticoagulants before the injury than patients with LOC or PTA ($n=227/2249$; 12% vs. $n=105/1360$; 8%). Patients with LOC or PTA were more often intoxicated with alcohol or drugs ($n=351/1360$; 26% vs. $n=284/2249$; 13%) and vomited ($n=133/1360$; 10% vs. $n=82/2249$; 4%) more often than patients without LOC and PTA.

Outcome

Most patients underwent a head CT ($n=3109/3914$; 79%) and 246 patients ($n=246/3914$; 6%) had a traumatic intracranial finding on CT, mostly traumatic subarachnoid hemorrhage ($n=111/3914$; 3%) or an acute subdural hematoma ($n=91/3914$; 2%; Table 3). A potential neurosurgical lesion was found in 32 patients ($n=32/3914$; 1%) and eight patients ($n=8/3914$; 0.2%) underwent a neurosurgical intervention.

Almost 70% of the patients without LOC and PTA ($n=1531/2249$; 68%) underwent a head CT and 67 patients ($n=67/2249$; 3%) had intracranial traumatic findings (Table 3). These 67 patients had a median age of 74 years (interquartile range 44.5–84.0 years), 12 patients ($n=12/67$; 18%) used anticoagulation and 10 patients ($n=10/67$; 15%) were intoxicated with drugs or alcohol. Two patients vomited twice or more (2/67; 3%) and one patient had a post-traumatic seizure. Three patients had signs of a skull base fracture ($n=3/67$; 5%), two patients had a new neurological deficit ($n=2/67$; 3%), and 45 patients had a visible injury to the head (45/67; 67%). Five patients ($n=5/2249$; 0.2%) had a potential neurosurgical lesion; all had a small epidural hematoma, and one patient also had a depressed skull fracture. One patient ($n=1/2249$; 0.0%) underwent a neurosurgical intervention because of a depression fracture and a small epidural hematoma.

Table 2. Baseline Characteristics

	All patients (n = *3914*)	*With LOC or PTA* (n = *1360*)	*Without LOC and PTA* (n = *2249*)	*Unknown LOC and PTA* (n = *305*)
Demographics				
Age in years, median (IQR)	53 (30–73)	50.5 (29–68)	53 (31–75)	62 (38–79)
Sex, *n* male	2241 (57%)	814 (60%)	1247 (55%)	180 (59%)
Use of anticoagulants[a]	421 (11%)	105 (8%)	277 (12%)	39 (13%)
Injury descriptives				
Mechanism of injury[b]				
- Pedestrian or cyclist vs. vehicle	106 (3%)	38 (3%)	50 (2%)	18 (6%)
- Road traffic accident vehicle or motor	410 (11%)	125 (9%)	250 (11%)	35 (12%)
- Fall from height	574 (15%)	220 (16%)	302 (13%)	52 (17%)
- Fall from standing	1574 (40%)	584 (43%)	905 (40%)	85 (28%)
- Assault	432 (11%)	154 (11%)	238 (11%)	40 (13%)
- Other*	790 (20%)	219 (16%)	503 (22%)	68 (22%)
Ejected from vehicle[c]	127 (3%)	48 (4%)	69 (3%)	10 (3%)
Fall from any elevation[d]	743 (19%)	310 (23%)	384 (17%)	49 (16%)
Intoxication with drugs or alcohol[e]	758 (19%)	351 (26%)	284 (13%)	123 (40%)
Symptoms				
Retrograde amnesia[f]	339 (9%)	300 (22%)	15 (1%)	24 (8%)
Vomiting[g]	240 (6%)	133 (10%)	82 (4%)	25 (8%)
Neurological deficit[h]**	94 (2%)	40 (3%)	49 (2%)	5 (2%)
Seizure[i]	27 (1%)	22 (2%)	4 (0.2%)	1 (0.3%)
Visible injury of the head[j]	2202 (56%)	756 (56%)	1267 (56%)	179 (59%)
Signs of skull fracture[k]	102 (3%)	49 (4%)	45 (2%)	8 (3%)
GCS score deterioration[l #]	11 (0.3%)	9 (1%)	2 (0.1%)	-

[a]Missing $n=13$, 0.3%; [b]missing $n=28$, 1%; [c]missing $n=42$; 1%; [d]missing $n=22$, 1%, [e] missing $n=66$, 2%; [f] missing $n=386$, 10%; [g] missing $n=38$, 1%; [h] missing $n=128$, 3%; [i] missing $n=42$, 1%; [j] missing $n=19$, 1%; [k] missing $n=20$, 1%; [l] missing $n=15$, 0.4%.

*Includes patients with mild head injury such as bump head against object.

**History or suggestive findings on examination (for example nystagmus, abnormal walking, etc.).

[#]GCS deterioration (1 or more points) 1 h after presentation at the emergency department.

LOC, loss of consciousness; PTA, post-traumatic amnesia; IQR, interquartile range; GCS, Glasgow Coma Scale.

Table 3. Primary and Secondary Outcomes

Outcome	*All patients (n = 3914)*	*With LOC or PTA (n = 1360)*	*Without LOC and PTA (n = 2249)*	*Unknown LOC and PTA (n = 305)*
CT performed	3109 (79%)	1285 (95%)	1531 (68%)	293 (96%)
Traumatic findings on CT	246 (6%)	153 (11%)	67 (3%)	26 (9%)
Skull fracture	82 (2%)	51 (4%)	25 (1%)	6 (2%)
- Linear skull fracture	46 (1%)	31 (2%)	12 (1%)	3 (1%)
Epidural hematoma	18 (1%)	13 (1%)	5 (0.2%)	-
Acute subdural hematoma	91 (2%)	56 (4%)	23 (1%)	12 (4%)
Contusion	68 (2%)	46 (3%)	14 (1%)	8 (3%)
Subarachnoid hemorrhage	111 (3%)	82 (6%)	20 (1%)	9 (3%)
Potential neurosurgical lesion	32 (1%)	26 (2%)	5 (0.2%)	1 (0.3%)
Neurosurgical intervention	8 (0.2%)	7 (1%)	1 (0.0%)	-

LOC, loss of consciousness; PTA, post-traumatic amnesia; CT, computed tomography.

Of the 305 patients with unknown LOC and PTA, the majority underwent a head CT ($n = 293/305$; 96%). In 26 patients ($n = 26/305$; 9%) intracranial traumatic findings were found and one patient ($n = 1/305$; 0.3%) had a potential neurosurgical lesion, a large acute subdural hematoma (Table 3).

No other risk factors

There were 42 ($n = 42/1360$; 3%) patients with LOC or PTA who did not have other risk factors of the CHIP model for intracranial abnormalities and none of these patients had intracranial traumatic findings on CT. There were 69 ($n = 69/2249$; 3%) patients without LOC and PTA who did not have other risk factors of the CHIP model. Of these, one patient ($n = 1/2249$; 0.04%) had an intracranial traumatic finding on CT (a small contusion), and none had potential neurosurgical lesions or underwent a neurosurgical intervention. Eight patients ($n = 8/305$; 3%) with unknown LOC and PTA had no other risk factors of the CHIP model, and none of these patients had intracranial traumatic findings on CT.

Predictive value of LOC and PTA

Univariable logistic regression analysis for the association between LOC and an intracranial traumatic finding on CT yielded an OR of 3.0 (95% CI 2.4–3.9; Table 4). For PTA, the OR was 3.8 (95% CI 2.9–4.9). For LOC and PTA, the OR was 4.1 (95% CI 3.1–5.3). Multivariable logistic regression analysis for the association between LOC and an intracranial traumatic finding on CT yielded an adjusted OR of 2.9 (95% CI 2.2–3.8). For PTA, the adjusted OR was 3.5 (95% CI 2.7–4.6).

In multivariable logistic regression analysis, the CHIP prediction model without LOC and PTA had a R^2 of 6%. The CHIP model with addition of LOC as a predictor had a R^2 of 10% and with the addition of PTA as a predictor a R^2 of 12% (Fig. 2). After adding both LOC and PTA as predictors, the R^2 increased to 13% (Fig. 2).

Discussion

In this study of patients with blunt traumatic head injury and a GCS score of 15, we confirmed that both LOC and PTA are important risk factors for identifying traumatic intracranial findings on CT. Nevertheless, among more than half of the patients who did not experience LOC and PTA, a small proportion had traumatic intracranial findings on CT and one patient underwent a neurosurgical intervention. Almost all patients with unknown LOC and PTA underwent a head CT and in a small portion, traumatic intracranial findings were found.

Our study shows a strong association of LOC and PTA with traumatic findings on CT. In previous studies, univariable logistic regression analyses yielded ORs for LOC between 1.9 and 6.5 and for PTA between 1.7 and 6.3.[7,15,19–21] Because these studies all used different inclusion criteria and definitions of outcome and variables, the associations are difficult to compare head to head. However, these studies all show that LOC and PTA should be included as risk factors in guidelines for minor head injury. This is confirmed in our study.

Patients with LOC or PTA are at higher risk of intracranial complications than patients without LOC and PTA, but the risk in patients without LOC and PTA should not be ignored. In the past, the risk of intracranial complications in patients without LOC or PTA was estimated to be low and a head CT did not seem necessary.[22] This resulted in still widely used guidelines that exclude patients without LOC and PTA for imaging. However, in a few studies, the occurrence of traumatic lesions in patients without LOC and PTA was described and ranged between 2.9–10%.[15,21,23,24] This is similar to our results and confirms our hypothesis that the risk of complications in patients without LOC and PTA is not always negligible. It should be noted that in our study, where centers used the CHIP rule, the majority of patients without LOC and PTA were scanned because they had other risk factors. Only a small portion of the patients without LOC and PTA had no other risk factors.

With the increasing prevalence of patients with minor head injury presenting at the emergency departments, it is important that adequate guidelines are used to help decide if patients need a head

Table 4. Univariable Analysis of LOC and PTA for Identification of Traumatic Findings on CT

Variable	*Number of patients*	*Number of patients with traumatic finding*	*Odds ratio (95% CI)*
LOC	1184	147	3.0 (2.4–3.9)
PTA	904	135	3.8 (2.9–4.9)
LOC or PTA	1449	172	3.3 (2.5–4.3)
LOC and PTA	639	110	4.1 (3.1–5.3)
No LOC, no PTA	2465	97	0.3 (0.2–0.4)

Calculated after imputation of missing data.

LOC, loss of consciousness; PTA, post-traumatic amnesia; CT, computed tomography; CI, confidence interval.

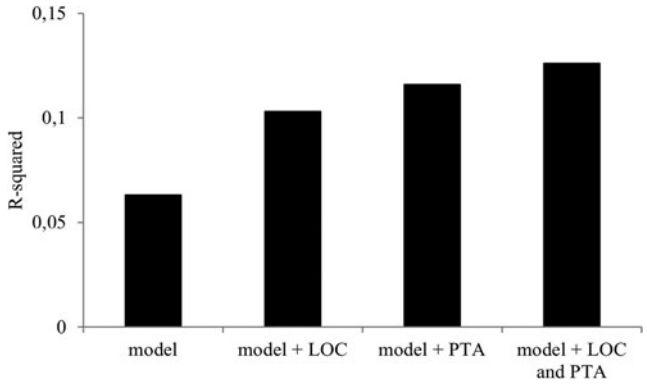

FIG. 2. Cumulative prognostic value of LOC and PTA in multivariable logistic regression analysis for identification of traumatic findings on computed tomography (CT). Model: traumatic findings on CT ~ age + pedestrian or cyclist versus vehicle + ejected from vehicle + vomiting + signs of skull fracture + Glasgow Coma Scale score deterioration + use of anticoagulants + seizure + fall from any elevation + visible injury to the head + neurologic deficit. Model +LOC and PTA is the CT in Head Injury Patients (CHIP) prediction rule. R-squared = the proportion of variability in outcome explained by the variables. Calculated after imputation of missing data. PTA, post-traumatic amnesia, LOC, loss of consciousness.

CT.[2,25] If guidelines only apply to a subgroup of patients, such as patients with LOC or PTA, clinical management for the patients without LOC and PTA is not clear. This results in practice variation with unnecessary scanning or discharge of patients at risk. Further, clinical management is unclear not only for patients without LOC and PTA, but also for patients with unknown LOC or PTA. After sustaining a head injury, it is not uncommon that patients do not know whether or not they experienced LOC or PTA, especially when there was no relative or witness present. In our study we found that in 8% of the patients LOC and PTA was unknown and that 9% of these patients had a traumatic finding on CT. Patients with unknown LOC and PTA were older and more often intoxicated with alcohol or drugs, which could lead to performing a CT regardless of presence of any other risk factors.

Two other studies described the proportion of patients with unknown LOC or PTA; 18–32% for LOC and 10–24% for PTA.[7,26] However, in most other studies the proportion of patients with missing or unknown LOC and PTA was never mentioned. Our results suggest that clinical guidelines for minor head injury should not only include LOC and PTA as separate risk factors, but they should also be made applicable to patients without and unknown LOC and PTA. Examples of guidelines that comply with these requisites are the National Institute for Health and Care Excellence (NICE) head injury guideline, the CHIP prediction rule, and the American College of Emergency Physicians (ACEP) guideline for mild traumatic brain injury.[7–9] In the future, clinical guidelines might be improved by incorporating blood-based biomarkers to predict intracranial traumatic findings on CT, although the additional diagnostic value of these biomarkers over clinical characteristics remains to be established.[27,28] For instance, the opportunities for improvement of the CHIP prediction model are reflected by the relatively small R^2 values of the full model (< 15%; Fig. 2). Substantial variability may be explained by risk factors that have not (yet) been included in the CHIP prediction model.

An important strength of this study is that all consecutive blunt head injury presenting at the emergency department were included. Studies in minor head injury patients often only include patients with a CT or patients with specific risk factors and a CT, causing the analysis to be limited to a subgroup of all patients with minor head injury presenting at the emergency department. However, this strength is also associated with a limitation of our study, being that the outcome of all patients without a CT (21%) was imputed for the univariable and multivariable analyses. In the participating centers, assessment whether or not patients with minor head injury needed a CT was based on national or local guidelines, and it was not feasible to acquire a CT in all patients for the purpose of this study. Therefore, we collected all possible risk factors and imputed the outcome based on these risk factors and patients with known outcome using multiple imputation. This resulted in an estimate of 18 more patients with a traumatic intracranial finding on CT and no patients with potential neurosurgical lesions. Further, variability in local guideline adherence may have influenced CT use. Unfortunately, information on guideline adherence was not available in our study.

Other limitations should also be acknowledged. For instance, no gold standard for PTA assessment exists and there is controversy about the preferred method to measure the presence and duration of PTA. Most centers in this study assessed PTA by asking the patients a few orientation questions, which could lead to discrepancies of the PTA duration. Additionally, patients undergoing a neurosurgical intervention in a different hospital might have been missed. However, we believe this is unlikely because the participating centers were all primary neurosurgery centers in the area. Nevertheless, we used potential neurosurgical lesion as a secondary outcome, and those findings were not affected by missing neurosurgical interventions.

To conclude, patients with neither LOC nor PTA are at risk of intracranial complications if other risk factors are present. This risk is low, but a low risk of a potential neurosurgical lesion or neurosurgical intervention is not negligible. Further, identification of intracranial traumatic findings causes a change in management, such as admission to the hospital for observation, temporary stop of oral anticoagulation, and a different follow-up policy. Clinicians should be aware of the risk of intracranial complications in patients without LOC and PTA, and clinical guidelines should include patients without LOC and PTA, such as the NICE head injury guideline, the CHIP rule, and the ACEP mild traumatic brain injury guideline. In addition, we confirmed that LOC and PTA are important risk factors in blunt traumatic head injury and we recommend that guidelines should include LOC and PTA as separate risk factors rather than as diagnostic selection criteria.

Collaborators

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Author Disclosure Statement

MGMH and DWJD were the principle investigators of the CHIP development study.

No competing financial interests exist.

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(*Appendix follows* →)

Appendix 1. Overview of CT Guidelines used in the Participating Centers

	National guideline	*Local guideline*
Number of centers	5	1
One or more major criteria	GCS <15 (including persisting PTA)	GCS <15
	2 or more points deterioration in GCS (1 h after presentation)	2 or more points deterioration in GCS (1 h after presentation)
	Vomiting	Vomiting
	Post-traumatic seizure	Post-traumatic seizure
	Signs of skull fracture	Age ≥60 years
	Pedestrian or cyclist versus vehicle	Signs of skull fracture
	Ejected from motor vehicle	Dangerous mechanism (pedestrian or cyclist versus vehicle; ejected from motor vehicle; Fall from more than 1 m or five stairs; or equivalent mechanism)
	Post-traumatic amnesia ≥4 h	Post-traumatic amnesia ≥4 h
	Use of anticoagulants	Coagulopathy, e.g., use of coumarin derivate (INR >1.7), NOACs, or chronic alcohol abuse
	Focal neurologic deficit	Focal neurologic deficit
	Suspicion of intracranial injury after focal ''high impact'' injury	Intoxication that impairs neurological examination
Two or more minor criteria	Fall from any elevation	Fall from <1 m
	Loss of consciousness	Loss of consciousness
	Post-traumatic amnesia 2-4 h	Post-traumatic amnesia 2-4 h
	Visible injury to the head, excluding the face (without signs of fracture)	Persisting post-traumatic amnesia (recall deficit)
		Traumatic injury above the clavicles
	1 point deterioration in GCS (1 h post-presentation)	1 point deterioration in GCS (1 h post-presentation)
	Age >40 years	Age 40–60 years

CT, computed tomography; GCS, Glasgow Coma Scale; PTA, post-traumatic amnesia; INR, international normalized ratio; NOACs, new oral anticoagulants.