CHAPTER 7

Update of the CHIP (CT in Head Injury Patients) decision rule for patients with minor head injury based on a multicenter consecutive case series

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ABSTRACT

Objective

To update the existing CHIP (CT in Head Injury Patients) decision rule for detection of (intra)cranial findings in adult patients following minor head injury (MHI).

Methods

The study is a prospective multicenter cohort study in the Netherlands. Consecutive MHI patients of 16 years and older were included. Primary outcome was any (intra)cranial traumatic finding on computed tomography (CT). Secondary outcomes were any potential neurosurgical lesion and neurosurgical intervention. The CHIP model was validated and subsequently updated and revised. Diagnostic performance was assessed by calculating the c-statistic.

Results

Among 4557 included patients 3742 received a CT (82%). In 383 patients (8.4%) a traumatic finding was present on CT. A potential neurosurgical lesion was found in 73 patients (1.6%) with 18 (0.4%) actually undergoing neurosurgery. The original CHIP underestimated the risk of traumatic (intra)cranial findings in low-predicted-risk groups, while in high-predicted-risk groups the risk was overestimated. The c-statistic of the original CHIP model was 0.72 (95% CI 0.69-0.74) and it would have missed two potential neurosurgical lesions and one patient that underwent neurosurgery. The updated model performed better over a wide range of predicted risks (c-statistic 0.77 95% CI 0.74-0.79). At the same CT rate as the original CHIP (75%), the updated CHIP would not have missed any (potential) neurosurgical lesions.

Conclusions

Use of the updated CHIP decision rule is a good alternative to current decision rules for patients with MHI. In contrast to the original CHIP the update identified all patients with (potential) neurosurgical lesions without increasing CT rate.

Introduction

Minor head injury (MHI) is a common and increasing cause of emergency department (ED) visits worldwide.[1-3] With ageing of the population it is expected that the burden caused by MHI will continue to rise in the next decades. The vast majority (>90%) of patients with MHI will have no (intra)cranial traumatic lesions.[4,5] Nonetheless, (intra)cranial traumatic lesions can result in severe disability or death and therefore require clinical observation and a small percentage needs neurosurgical intervention. This study aims to provide a method to improve selection of patients that require a head computed tomography (CT) to identify traumatic lesions.

Currently the most used technique to rule out traumatic findings after MHI is CT. CT is widely available and the fraction of patients receiving a CT for MHI has increased significantly in the last decades.[6,7] The use of CT has many advantages because it is fast and reliable. However, its increasing use in MHI also has several important disadvantages. First, a CT exposes the patient to radiation risks.[8] Second, a CT is costly and should, in the light of ever-expanding healthcare costs, only be used when necessary. Last but not least, performing more diagnostic procedures such as CT may lead to prolonged ED throughput times and thus result in ED-crowding.[9] With increasing ED visits for MHI it is more important than ever to identify those patients that will benefit from a CT.

To enhance selective use of head-CT several decision rules for MHI have been developed. Worldwide the most used decision rules are probably the Canadian CT Head Rule (CCHR) and the New Orleans Criteria (NOC).[10,11] Both CCHR as NOC are only applicable to patients with loss of consciousness, post traumatic amnesia or confusion. However, most patients with MHI do not experience any of these and (intra)cranial findings can be present even in the absence of these risk factors.[12,13] Therefore, another decision rule was developed in four level one trauma centers in the Netherlands in the beginning of this century. This rule is applicable to *all* ED patients with MHI, the CT in Head Injury Patients (CHIP) rule.[4] The ACEP (American College of Emergency Physicians) clinical policy for neuroimaging in MHI includes recommendations from the CHIP study for patients without loss of consciousness or posttraumatic amnesia.[14]

We recently validated the CHIP-rule and compared it to the NOC and the CCHR.[15] In line with an ageing population, the patient population in this validation-study differed substantially from the original CHIP, NOC and CCHR studies.[1,4,10,11,15] The population was older and trauma was more often caused by ground level falls. In

this validation-study sensitivity and specificity for any traumatic finding were 94% and 22% for the CHIP rule; 99% and 4% for the NOC and 80% and 44% for the CCHR. Based on these results we concluded that the CHIP rule performed well compared to several other prediction rules in terms of a proper balance between specificity and sensitivity. Nonetheless, we also conclude that there is room for improvement of the CHIP because the sensitivity for detecting (potential) neurosurgical lesions was less than 100%.[15]

Given the potential for improvement of the CHIP, the changing demographic characteristics of MHI patients and the fact that the CHIP was developed in level one trauma centers only, there seems to be need for an update of the CHIP. Therefore, the aim of the current study is to update and improve the CHIP decision rule for detection of (intra)cranial findings following MHI.

Methods

Study design and setting
This prospective, multicenter cohort study was conducted in the Netherlands, data were collected between March 1st 2015 and January 1st 2017. Three level 1, one level 2 and two level three EDs participated in the study.[16]

Selection of participants
Consecutive patients of 16 years and older with MHI who arrived at one of the participating EDs within 24 hours after blunt trauma to the head were included. MHI was defined as:

Any trauma to the head, other than superficial injuries to the face and:
- *Glasgow Coma Scale (GCS) score 13-15 at first examination*
- *Loss of consciousness (not required): no more than 30 minutes*
- *Posttraumatic amnesia (not required): no more than 24 hours*

Patients who were transferred from another hospital were excluded. Clinical data concerning risk factors as used in the CHIP-rule and additional risk factors were collected (Supplementary Table 1).[17]

Outcomes
Similar to the original CHIP, the primary outcome was any (intra)cranial traumatic finding on CT, defined as: subdural hematoma, epidural hematoma, subarachnoid hemorrhage, hemorrhagic contusion, non-hemorrhagic contusion, diffuse axonal injury, intraventricular hemorrhage, and skull fracture. The secondary outcome was any potential neurosurgical lesion, which was defined as an (intra)cranial traumatic finding on CT which could lead to a neurosurgical intervention or death.[15] The following traumatic findings were labelled as potential neurosurgical lesions: epidural hematoma, large acute subdural hematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with midline shift or herniation. Another secondary outcome was neurosurgical intervention for traumatic skull or brain injury within 30 days. A prerequisite of the (updated) model was not to miss any potential neurosurgical findings.

Study procedures and analysis
We described study procedures and data management in detail elsewhere.[15] Sample size was based on 20 eligible variables in multivariable logistic regression. Per variable at least 10 events of the primary outcome measure were required. Based on earlier research the estimated incidence of traumatic findings on CT was 7.4%, hence at least 2703 scanned patients had to be included.[7]

In accordance to the original CHIP-study, we imputed loss of consciousness and posttraumatic amnesia as present if data was missing or unknown. Other missing data were assumed to be missing at random. We imputed missing data based on all risk factors mentioned above using "Multivariate Imputation by Chained Equations" (MICE) in R. Outcomes could not be observed in patients without CT. Therefore, we imputed the expected outcomes based on their risk factors with multiple imputation, acknowledging the uncertainty of imputations by performing the imputation multiple times (n=5).[18] Baseline and outcome are first reported without imputation mentioning any missing data. We used data with imputed outcomes for the primary analysis, similar to our previous study.[15] We performed a sensitivity analysis by including scanned patients only (without outcome imputation). Analyses were performed using IBM Statistical Package for Social Sciences version 24 and R foundation for statistical computing software, version 3.3.2.

Institutional ethics and research board approval was obtained, and informed consent was waived.

Validation and updating
Model validation, updating and revision were based on the methodology as described by Steyerberg.[19] First, we validated the original CHIP-rule. The predicted risk of any (intra)cranial traumatic finding was calculated for each patient using the original risk factors, regression coefficients and intercept. We calculated the observed frequency of any (intra)cranial traumatic finding in our dataset and present this in a calibration plot. A locally weighted regression curve (LOESS) was used in the calibration plot.

Updating of the CHIP decision model was performed based on the difference in fit of the CHIP-model and a newly fitted model in the current data.[19]

To update the CHIP we performed re-calibration as a first step. The intercept was updated to correct a potential deviation in 'calibration-in-the-large'. Calibration-in-the-large refers to whether the mean observed outcome is equal to the mean predicted outcome. The second step was to update both the intercept and the overall calibration slope. The third step was to re-estimate the intercept and the regression coefficients of the original CHIP predictors in the study data.

Model revision

In the next steps the model was extended with new predictors and existing predictors with limited predictive value were eliminated. We assessed performance by calculating the area under the receiver operating characteristic curve (c-statistic). Calibration was assessed by plotting the observed proportions versus predicted chances of the primary outcome (calibration plot). A locally weighted regression curve (LOESS) was used in the calibration plot.

To improve the performance of the model in future populations, we multiplied the regression coefficients by a shrinkage factor obtained using bootstrapping. The updated model (without shrinkage factor) was cross-validated six times by re-estimating the intercept and regression coefficients in five centers and testing it in the sixth center. We present the validated c-statistics in a forest plot.

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Results

We included 4557 consecutive eligible MHI patients during the study period. Patient characteristics are summarized in Table 1 and Supplementary Table 2. Compared to the original CHIP-study the current study population was older (53 versus 41 years) and more often female (42% versus 28%). Regarding trauma mechanism more injuries were the result of ground level falls (37% versus 22%) and less injuries were the result of assaults (15% versus 24%).[20]

Table 1. Baseline characteristics update study versus original CHIP study

	Update study (n=4557)	Missing	Original CHIP (n=3181)
Inclusion period	2015-2016		2002-2004
Age mean in years (range)	53.1 (16-101)	0	41.4 (16-102)
Sex, n male (%)	2656 (58.3%)	0	2246 (70.5%)
GCS score at presentation		0	
• GCS 13	143 (3.1%)		151 (4.7%)
• GCS 14	500 (11.0%)		568 (17.9%)
• GCS 15	3914 (85.8%)		2462 (77.4%)
Use of anticoagulation		29 (0.6%)	
• None	4045 (88.8%)		2963 (93.1%)
• Coumarin	418 (9.2%)		218 (6.9%)
• Direct oral anticoagulants	54 (1.2%)		NA
• Other	11 (0.2%)		0
Use of thrombocyte aggregation inhibitors (TAI)	615 (13.5%)	33 (0.7%)	
• None	3909 (85.9%)		unknown
• ASA monotherapy	405 (8.9%)		unknown
• Other TAI or combination	210 (4.6%)		unknown
Bleeding disorder	44 (1%)	33 (0.7%)	unknown
High Energy Trauma[a]	583 (12.7%)	3 (0.1%)	1457 (45.8%)
Mechanism of injury		0	
• Pedestrian or cyclist versus vehicle	226 (5.0%)		100 (3.1%)
• Road traffic accident other	1019 (22.4%)		unknown
• Ground level fall	1699 (37.3%)		691 (21.7%)
• Fall from height (>1 meter)	574 (12.6%)		513 (16.1%)
• Assaults or other violence	659 (14.5%)		771 (24.2%)
• Sports or recreational activitiy	158 (3.5%)		unknown
• Other[b]	222 (4.9%)		unknown

Table 1. Continued

	Update study [n=4557]	Missing	Original CHIP [n=3181]
Ejected from vehicle	150 (3.3%)	56 (1.2%)	65 (2.0%)
Focal high impact trauma	74 (1.6%)	5 (0.1%)	unknown
Loss of consciousness	1192 (26.2%)	651 (14.3%)	1951 (61.3)
Posttraumatic amnesia		502 (11%)	
• None	2951 (64.8%)		2181 (68.6%)
• Up to 2 hours	976 (21.4%)		916 (28.8%)
• 2-4 hours	69 (1.5%)		69 (2.2%)
• More than 4 hours	59 (1.3%)		15 (0.5%)
Intoxication with drugs or alcohol[c]	1031 (22.6%)	85 (1.9%)	1367 (43%)
Posttraumatic seizure	36 (0.8%)	68 (1.5%)	23 (0.7%)
Vomiting		50 (1.1%)	342 (10.8%)
• Once	158 (3.5%)		
• Twice or more	144 (3.2%)		
GCS deterioration[d]		23 (0.5%)	
• 1 point	38 (0.8%)		51 (1.6%)
• 2 or more points	12 (0.3%)		17 (0.5%)
Neurological deficit	130 (2.9%)	141 (3.1%)	304 (9.6%)
Signs of skull base fracture	144 (3.2%)	25 (0.5%)	66 (2.1%)
Visible injury of the head	2564 (56.3%)	19 (0.4%)	2861 (90%)

CT = computed tomography, GCS = Glasgow Coma Scale, NA = not applicable, ASA= Acetylsalicylic acid or carbasalate calcium

[a]In the update study this was defined as: High risk auto crash (intrusion >30cm to occupant site or >45cm to any other site, ejection from automobile, death in same passenger compartment, vehicle telemetry data consistent with high risk of injury); Auto versus pedestrian/bicyclist; motorcycle crash >32km/h (20 miles/h); fall from >6 meters (20 feet). The exact definition in the original CHIP is not known and may differ.

[b]Includes patients with mild head injury such as bump head against object.

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

[d]GCS deterioration 2 hrs after presentation

Of the 4557 included patients 3742 received a CT (82%). Compared to patients with CT, those without CT were on average younger (36 versus 57 years) and almost all of them had a GCS of 15 (99%). According to the CHIP-rule 3412 (75%) patients should have received a CT because of a predicted risk of ≥3% for traumatic (intra)cranial findings (Table 2).[4]

Table 2. CT rate in patients above and below the CHIP CT threshold (predicted risk ≥3%) (n=4557)

	CT performed, traumatic findings present (n=383)	CT performed, traumatic findings absent (n=3359)	CT *not* performed, imputed as traumatic findings present (n=23)	CT *not* performed, imputed as traumatic findings absent (n=792)
CHIP predicted risk ≥3% (n=3412)	367 (8.1%)	2841 (62.3%)	9 (0.2%)	195 (4.3%)
CHIP predicted risk <3% (n=1145)	16 (0.4%)	518 (11.4%)	14 (0.3%)	597 (13.1%)
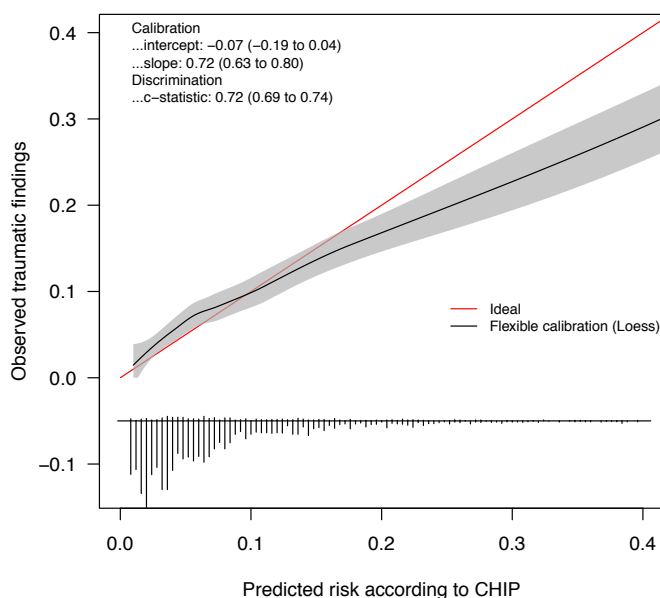
Figure 1. Calibration plot original CHIP

Calibration plot original CHIP, range 0 to 40% predicted and observed risk. A 95% confidence interval is given for intercept, slope and c-statistic.

In 383 of 4557 patients (8.4%) a traumatic (intra)cranial finding was present on CT (Supplementary Table 3). A potential neurosurgical lesion was found in 73 patients (1.6%) with 18 (0.4%) undergoing neurosurgery. In total 1511 patients (33%) were hospitalized for any cause. The vast majority of patients (n=340, 89%) with traumatic findings on head-CT were hospitalized. In total 32 patients (0.7%) died during their hospital admission, in 11 patients (0.2%) this was a result of their traumatic brain injury.

Validation

Figure 1 shows observed frequency of traumatic (intra)cranial findings in our population compared with the predictions according to the CHIP-model. In the low-predicted-risk patients, the original CHIP slightly underestimated the risk, while in the high-predicted-risk patients the model overestimated the risk. By applying the original CHIP-rule 30 traumatic findings would have been missed, including two potential neurosurgical lesions and one neurosurgical intervention. In total 1145 patients (25%) had no indication for CT according to the original CHIP (at a cut-off value of 3% predicted-risk). The sensitivity of the original CHIP for any traumatic lesion was 93% (95% CI 90-95%) and the specificity was 27% (95% CI 26-28%). Sensitivity and specificity for potential neurosurgical lesions were 97% (95% CI 90-100%) and 25% (95% CI 24-27%) respectively. Sensitivity and specificity for neurosurgical intervention were 94% (95% CI 73-100%) and 25% (95% CI 24-26%).

The c-statistic for any traumatic finding was 0.72 (95% CI 0.69-0.74). For potential neurosurgical lesions and for actual neurosurgical interventions the c-statistic was 0.82 (95% CI 0.77-0.87) and 0.84 (95% CI 0.73-0.94) respectively.

Updating

The overall observed frequency of traumatic (intra)cranial findings was slightly lower in our population (8.9%[1]) compared to the CHIP predicted frequency (9.4%) ($P < 0.001$). To correct for this "calibration in the large" the intercept was adjusted.

After that, we refitted the regression slope, the new calibration slope ($b_{overall}$) was significantly steeper in the updated model compared to the original model ($P < 0.001$). This adjustment would increase sensitivity to 97%, but at the cost of a decline in specificity to 11% (at a cut-off value of 3% predicted-risk).

Next, we re-estimated regression coefficients of original risk factors in the current dataset. Some regression coefficients were similar in the validation data and the CHIP-model, others differed and two (use of anticoagulants and ejection from vehicle) had a negative regression coefficient in our dataset. Because we consider a protective effect of risk factors clinically implausible we omit these predictors from the updated model. (Supplementary Table 4)

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1   The observed frequency of traumatic findings of 8.9% includes imputed data, hence the discrepancy with the earlier mentioned 8.4%.

Model revision

Several updated models have been considered of which the model in Table 3 showed the best performance in terms of c-statistic and calibration (Table 3 and Figure 2). All selected variables showed significant effects ($P < 0.05$). The c-statistic for any traumatic finding was 0.77 (95% CI 0.74-0.79). For potential neurosurgical lesions and for neurosurgical intervention lesions the c-statistic was 0.87 (95% CI 0.84-0.91) and 0.92 (95% CI 0.86-0.98) respectively.

Table 3. Variables included in updated CHIP with regression coefficients

Risk factor	Odds ratio	Beta-coefficient	*P* value	Penalized beta-coefficient
Signs of skullbase fracture	4.6	1.53	<0.01	1.48
GCS 13	2.5	0.90	<0.01	0.88
GCS 14	1.6	0.48	<0.01	0.46
Contusion skull	1.8	0.59	<0.01	0.57
Vomiting more than once	1.7	0.52	0.05	0.50
Age (per year over 16)	1.0	0.01	<0.01	0.01
Post traumatic amnesia 0 to 2h (or unknown)	2.0	0.70	<0.01	0.67
Post traumatic amnesia 2 to 4h	2.6	0.96	<0.01	0.93
Post traumatic amnesia >4h	5.7	1.73	<0.01	1.68
Loss of consciousness (or unknown)	1.9	0.62	<0.01	0.61
Neurologic deficit	2.5	0.90	<0.01	0.87
Fall from any elevation	1.6	0.49	<0.01	0.47
Use of antiplatelet therapy[a]	1.7	0.51	<0.01	0.49
Dangerous trauma mechanism[b]	1.9	0.64	<0.01	0.62
Focal high impact trauma	2.4	0.87	<0.01	0.84

To determine the need for a CT scan the beta-coefficients of present risk factors have to be added (for age multiplied by age in years over 16). The intercept is -4.34 and the intercept for the penalized estimation is -4.27. The predicted probability of a traumatic intracranial finding equals: $1/(1+e^{-(-4.27+\text{penalized beta score})})$. A penalized beta score of 0.79 equals a predicted probability of a traumatic intracranial finding of 3.0%

[a]Acetylsalicylic acid monotherapy or carbasalate calcium monotherapy should not be regarded as risk factor.

[b]Definition: High risk auto crash (intrusion >30cm to occupant site or >45cm to any other site, ejection from automobile, death in same passenger compartment, vehicle telemetry data consistent with high risk of injury); Auto versus pedestrian/bicyclist; motorcycle crash >32km/h (20 miles/h); fall from >6 meters (20 feet)

At a cut-off value for CT of *3% predicted-risk of any traumatic finding*, similar to original CHIP, the sensitivity of the updated CHIP was 92% (95% CI 89-94%) and the specificity was 27% (95% CI 26-28%). Sensitivity and specificity over a range of cut-off

values are shown in supplementary Table 5. Sensitivity and specificity for potential neurosurgical lesions at a cut-off value for CT of *3% predicted-risk of any traumatic finding* were 100% [95% CI 95-100%] and 26% [95% CI 25-27%] respectively. At this cut-off value sensitivity and specificity for neurosurgical intervention were 100% [95% CI 82-100%] and 26% [95% CI 24-27%].
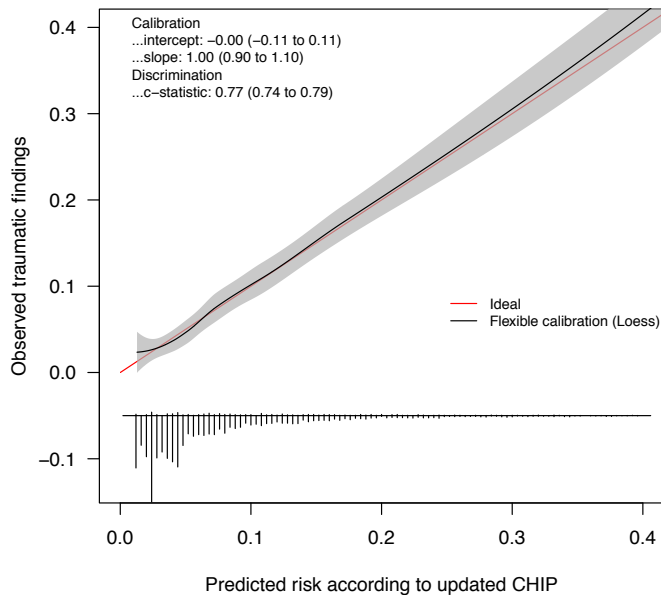

Figure 2. Calibration plot updated CHIP

Calibration plot updated CHIP, range 0 to 40% predicted and observed risk. A 95% confidence interval is given for intercept, slope and c-statistic.

Internal validation of the updated model using bootstrapping indicated optimism for the c-statistic, which we expected to decrease from 0.77 to 0.76 for any traumatic (intra)cranial finding. Internal validation using crossvalidation per center would decrease the c-statistic from 0.77 to 0.73 [Supplementary Figures 1 and 2]. To correct for optimism penalized beta-coefficients were calculated [Table 3].

A sensitivity analysis only including scanned patients showed similar results for the updated CHIP. The c-statistic for any traumatic finding was 0.76 [95% CI 0.73-0.78]. The c-statistic for potential neurosurgical lesions and neurosurgical intervention was 0.85 [0.81-0.89] and 0.90 [0.84-0.97] respectively. At a cut-off of *3% predicted-risk* 16 traumatic (intra)cranial findings were missed of which none was a potential neurosurgical lesion or needed neurosurgical intervention (sensitivity 96%; specificity 34%).

Discussion

The aim of this study was to update the CHIP decision rule, this was done in a large multicenter study in a contemporary Dutch cohort. The original CHIP-model underestimated the risk of traumatic (intra)cranial findings in low-predicted-risk patients, while in high-predicted-risk patients the risk was overestimated. The updated model performed better over a wide range of predicted risks.

The updated model uses three variables less than the original CHIP-model (12 versus 15) which makes it easier to use. The c-statistic for any traumatic finding would improve from 0.72 to 0.77. From the calibration plot it can be concluded that especially in the low-predicted-risk groups the updated model performs better than the original. Performance in these low-predicted-risk groups is most important because the high-predicted-risk groups will be scanned regardless of the exact predicted risk. Probably even more important, in contrast to the original CHIP, the updated CHIP would not miss any potential neurosurgical lesions or patients that actually underwent neurosurgery. Compared to the original CHIP-study potential neurosurgical lesions have been added as secondary outcome measure besides actual neurosurgical intervention. Neurosurgical intervention is rare in MHI patients and the decision to operate a patient is surgeon and country dependent.[21] Nonetheless nobody wants to miss a traumatic epidural hematoma or a large acute subdural hematoma, therefore the term potential neurosurgical lesion was introduced to more objectively identify the traumatic findings that definitely should not be missed. Hence, the largest gain of the updated model compared to the original CHIP is better identification of patients with (potential) neurosurgical lesions.

In the original CHIP-study a cut-off value of *3% predicted-risk for any traumatic finding* for performing a CT is used. This rather arbitrary threshold is used in this update study as well. Nevertheless, one could argue that a different cut-off value can be more suitable depending on setting and preferences. For cut-off levels up to *3.5%* and 6.0% *predicted risk for any traumatic finding* sensitivity for respectively potential neurosurgical lesions and actual neurosurgical intervention remained 100% in our study sample.

A striking difference between the original CHIP and this update is that the use of anticoagulants is no longer found to be a predictor of traumatic (intra)cranial findings, neither in univariable nor in multivariable analysis. Although it is impossible to establish the exact cause of this surprising change there are some possible explanations. First anticoagulants may be a smaller risk factor than previously thought. There are only

few studies that have established the risk of anticoagulant therapy for traumatic intracranial hemorrhage in MHI.[22,23] A recent systematic review found a pooled incidence of traumatic findings in MHI patients that used anticoagulants of 8.9%. [22] However, there was a large variation and in the two largest studies in the review this incidence was only 4%. A second reason for the difference could be that referral patterns have changed. Possibly patients on anticoagulant therapy are referred to the ED for less severe trauma than patients without anticoagulant therapy. This potential difference was nonetheless not reflected in the multivariable analysis. Finally we do not know how well anticoagulants were used, it is known that patients on anticoagulants frequently have a sub-therapeutic INR.[24] However, although anticoagulant use was not a risk factor for traumatic findings in the current study, a low threshold for scanning these patients should be considered in our opinion because traumatic findings may have a worse outcome in the presence of anticoagulant use. [25-27] Scanning all patients on anticoagulant therapy would (at a 3% *predicted-risk* scanning-threshold) lead to 81 extra CTs and a reduction of two patients with missed traumatic findings (sensitivity 92%; specificity 25%).

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In contrast to the original CHIP-rule we choose to present the detailed results only, the updated decision rule will be integrated into an easy to use app. A simplified decision rule is less reliable and not necessary anymore because everybody uses smart phones and electronic patient records are widespread.

Future research is needed to externally validate this updated CHIP decision rule. Until now the CHIP-model has only been validated in The Netherlands. To increase generalizability validation data should preferably also be collected in other countries.

A limitation of this study is that not all consecutive MHI patients received a CT. This is a result of the current Dutch guidelines for patients with MHI[28]. Patients that were not scanned could possibly have had traumatic findings that would have been missed. To anticipate these possible false negatives, the outcomes of these patients were imputed. Because of different scanning rates in hospitals all different risk profiles of patients were present in the non imputed dataset. Nonetheless, differential patterns of missing data may introduce unknown biases despite multiple imputation.

The CHIP-rule predicts the presence or absence of traumatic findings on CT. Nonetheless, the real outcome of interest is the long-term clinical outcome which was not assessed in the current study.

Because there was no follow-up for discharged patients with a negative CT (or without CT) it is possible that some of these patients would have developed traumatic findings on consecutive scans. However development of an intracranial lesion after a normal CT is rare.[29]

In summary use of the updated CHIP decision rule should be considered in patients with MHI. Compared to the original CHIP the updated rule seems to be better able to identify patients with (potential) neurosurgical lesions without increasing the CT rate. In the current study anticoagulant use was not identified as independent risk factor for traumatic findings. Nonetheless a low threshold for scanning these patients is advised because of potentially worse outcome of traumatic intracranial hemorrhage in the presence of anticoagulant use. Future research is needed to externally validate the updated CHIP decision rule.

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Supplementary Material

Supplementary Table 1. Definition of potential risk factors

Risk factor	Explanation (if necessary)
Age	Age in years
GCS score on presentation	GCS score on presentation to the ED
Change in GCS	One hour after presentation to the ED
Clinical signs of skull fracture	Raccoon eyes, battle sign, hemotympanum, CSF otorrhea, CSF rhinorrhea, palpable discontinuity, bleeding from ear
Contusion of skull	Any injury above the eyebrows other than an abrasion or superficial cut
Vomiting	As reported or observed, presence and frequency
Posttraumatic amnesia (PTA)	As reported or observed, presence and duration (PTA unknown is considered to be PTA in the 'up to two hours' category)
Loss of consciousness (LOC)	As reported or observed, presence and duration (LOC unknown is considered to be present)
Neurologic deficit	Any deficit not known to be pre-existent such as: paresis, dysphasia or other such as cranial nerve damage including diplopia, changes in sensibility, asymmetrical reflexes or pathological reflexes, coordination problems and ataxia
Headache	At presentation to the ED, generalized or local
Use of anticoagulant therapy	Known or reported use of: vitamin K antagonists, NOACs, therapeutic (low molecular weight) heparin
Use of antiplatelet therapy	Known or reported use of antiplatelet medication including type. In the final decision model acetylsalicylic acid monotherapy or carbasalate calcium monotherapy is not regarded as risk factor[a]
Fall from any elevation	As reported or observed (standing height is not considered any elevation)
Pedestrian or cyclist versus motorized vehicle	As reported or observed
Ejected from vehicle	As reported or observed
Posttraumatic seizure	As reported or observed
Dangerous trauma mechanism	As reported or observed. Definition according to CDC guidelines for field triage[1]: High risk auto crash (intrusion >30cm to occupant site or >45cm to any other site, ejection from automobile, death in same passenger compartment, vehicle telemetry data consistent with high risk of injury); Auto versus pedestrian/bicyclist; motorcycle crash >32km/h (20 miles/h); fall from >6 meter (20 feet)

Supplementary Table 1. Continued

Risk factor	Explanation (if necessary)
Fall from elevation	As reported or observed. Fall from more than 1 meter or 5 stairs
Intoxication with alcohol or drugs	History or suggestive findings on examination
Focal high impact injury	As reported or observed. Suspicion of intracranial injury after focal high impact injury (e.g. struck with a baton, golf or hockey ball)

[a] The decision not to consider acetylsalicylic acid or carbasalate calcium monotherapy was based on our data and a recent systematic review[2].

Supplementary Table 2. Univariable analysis of potential risk factors

Variable	Total n=4557	Patients tICH[a] (n=406)	Odds Ratio	95% CI lower	95% CI upper	P value
age (years)	53.1	57.5	1.09	1.04	1.14	0.00
trauma mechanism, n (%)						
pedestrian or cyclist vs vehicle	230 (5.0)	37 (9.1)	2.06	1.42	2.97	0.00
fall from any elevation	940 (20.6)	138 (34.0)	2.15	1.73	2.68	0.00
ejected from vehicle	154 (3.4)	16 (3.9)	1.19	0.70	2.02	0.51
high energy trauma	588 (12.9)	92 (22.7)	2.16	1.68	2.77	0.00
symptoms						
(any) vomiting, n (%)	311 (6.8)	40 (9.9)	1.57	1.10	2.22	0.01
vomiting > once, n (%)	147 (3.2)	23 (5.7)	1.95	1.24	3.08	0.00
PTA[b]						
PTA 0-2h, n (%)	976 (21.4)	173 (42.8)	4.43	3.49	5.61	0.00
PTA 2-4h, n (%)	69 (1.5)	14 (3.5)	5.23	2.84	9.64	0.00
PTA > 4h, n (%)	59 (1.3)	21 (5.2)	11.35	6.49	19.87	0.00
PTA unknown	498 (10.9)	59 (14.6)	2.76	2.00	3.81	0.00
LOC[c]						
LOC 0-15min, n (%)	1160 (25.5)	166 (41.0)	3.24	2.55	4.12	0.00
LOC 15-30min, n (%)	32 (0.7)	10 (2.5)	8.82	4.09	19.00	0.00
LOC unknown, n (%)	648 (14.2)	96 (23.7)	3.38	2.56	4.46	0.00
headache, n(%)	1650 (36.2)	165 (40.6%)	1.23	1.00	1.51	0.05
posttraumatic seizure	38 (0.8)	8 (2.0)	2.76	1.26	6.06	0.01

Supplementary Table 2. Continued

Variable	Total n=4557	Patients tICH[a] (n=406)	Odds Ratio	95% CI lower	95% CI upper	*P* value
external evidence of injury						
signs of skull base fracture, n (%)	148 (3.2)	52 (12.8)	6.21	4.35	8.85	0.00
contusion of the skull, n (%)	2574 (56.5)	276 (68.0)	1.71	1.38	2.13	0.00
injury to the face, n (%)	1631 (36.0)	142 (34.5)	0.93	0.75	1.15	0.51
neurologic examination						
GCS[d] (15=reference)						
GCS 15, n (%)	3914 (85.9)	267 (65.8)				
GCS 14, n (%)	500 (11.0)	91 (22.4)	3.04	2.35	3.94	0.00
GCS 13, n (%)	143 (3.1)	48 (11.8)	6.90	4.77	9.98	0.00
GCS deterioration (after 1h), n (%)						
1 point deterioration	38 (0.8)	5 (1.2)	1.58	0.61	4.06	0.35
2 points deterioration	12 (0.3)	6 (1.5)	10.41	3.34	32.43	0.00
neurologic deficit, n (%)	134 (2.9)	28 (6.9)	2.83	1.84	4.34	0.00
use of anticoagulant therapy, n (%)	486 (10.7)	34 (8.4)	0.75	0.52	1.08	0.12
use of antiplatelet therapy[e], n (%)	211 (4.6)	33 (8.1)	1.98	1.34	2.91	0.00
intoxication, n (%)	1057 (23.2)	90 (22.2)	0.94	0.73	1.20	0.61

[a]tICH: traumatic intracranial hemorrhage/any traumatic finding

[b]PTA: posttraumatic amnesia

[c]LOC: Loss of consciousness

[d]GCS: Glasgow Coma Scale score

[e]Excluding acetylsalicylic acid or carbasalate calcium monotherapy

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Supplementary Table 3. Traumatic CT findings in 3742 patients with a head computed tomography (CT)

CT finding	N (%)[a,b]
Any traumatic CT finding	383 (8.4%)
Skull fracture	150 (3.3%)
Depressed fracture	19 (0.5%)
Linear fracture	66 (1.4%)
Skull base fracture	68 (1.5%)
Subarachnoid hemorrhage	182 (4.0%)
Contusion	
Small	115 (2.5%)
Large (mass)	10 (0.2%)
Subdural hematoma	
Small	126 (2.8%)
Large (mass)	22 (0.5%)
Epidural hematoma	
Small	30 (0.7%)
Large (mass)	5 (0.1%)
Suspicion of diffuse axonal injury on CT	13 (0.3%)
Basal cisterns compressed or obliterated	10 (0.2%)
CT shift	
• 0-4mm	16 (0.4%)
• 5mm or more	9 (0.2%)

[a] Some patients had more than 1 CT finding

[b] Percentage of the total number of patients (n=4557)

Supplementary Table 4. Re-estimation of regression coefficients CHIP

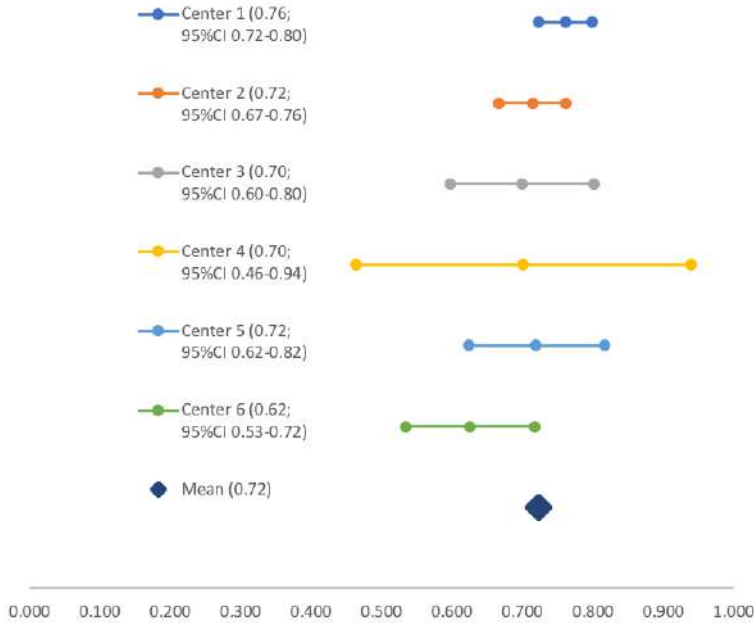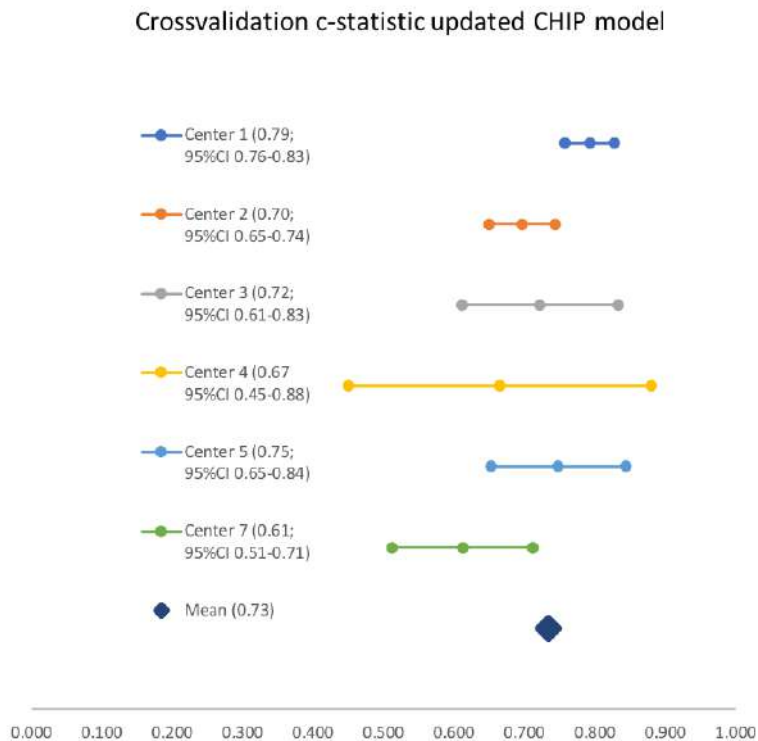| Risk factor	Odds ratio	Beta-coefficient	*P* value
Signs of skullbase fracture	4.7	1.55	<0.01
GCS 13	3.2	1.20	<0.01
GCS 14	2.0	0.68	<0.01
Contusion skull	1.8	0.59	<0.01
Vomiting	1.2	0.19	0.33
Age (per year over 16)	1.0	0.01	<0.01
Post traumatic amnesia 2 to 4h	1.5	0.42	0.21
Post traumatic amnesia > 4h	3.7	1.52	<0.01
Loss of consciousness (or unknown)	2.5	0.91	<0.01
Neurologic deficit	2.6	0.95	<0.01
Fall from any elevation	1.8	0.59	<0.01
Use of anticoagulant therapy	0.7	-0.42	0.04
GCS deterioration	1.1	0.08	0.78
Pedestrian or cyclist versus vehicle	1.9	0.62	<0.01
Ejected from vehicle	0.9	-0.11	0.72
Posttraumatic seizure	1.6	0.48	0.29
Intercept -4.12			

To determine the need for a CT scan the beta-coefficients of present risk factors have to be added (for age multiplied by age in years over 16). The predicted probability of a traumatic intracranial finding equals: $1/(1+e^{-(-4.12+\text{beta score})})$.

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Supplementary Table 5. Performance of updated CHIP at different cut-off levels (n=4557)

Cut-off (predicted risk)	CT scans prevented (%)	Traumatic findings missed (total n=406)	Potential neuro-surgical findings missed (total n=73)	Neuro-surgical inter-ventions missed (total n=18)	Sensitivity (any traumatic finding)	Specificity (any traumatic finding)
1.5%	211 (4.6%)	6	0	0	99%	4.9%
2.0%	409 (9.0%)	8	0	0	98%	9.7%
2.5%	764 (17%)	18	0	0	96%	18%
3.0%	1155 (25%)	33	0	0	92%	27%
3.5%	1397 (31%)	36	0	0	91%	33%
4.0%	1663 (37%)	45	2	0	89%	39%
4.5%	1965 (43%)	59	4	0	86%	46%
5.0%	2249 (49%)	72	4	0	82%	52%
5.5%	2388 (52%)	77	4	0	81%	56%
6.0%	2512 (55%)	81	4	0	80%	58%
6.5%	2640 (58%)	88	5	1	78%	62%

Crossvalidation c-statistic original CHIP model

- Center 1 (0.76; 95%CI 0.72-0.80)
- Center 2 (0.72; 95%CI 0.67-0.76)
- Center 3 (0.70; 95%CI 0.60-0.80)
- Center 4 (0.70; 95%CI 0.46-0.94)
- Center 5 (0.72; 95%CI 0.62-0.82)
- Center 6 (0.62; 95%CI 0.53-0.72)
- Mean (0.72)

0.000 0.100 0.200 0.300 0.400 0.500 0.600 0.700 0.800 0.900 1.000

Supplementary Figure 1. Crossvalidation c-statistic original CHIP model per center

Supplementary Figure 2. Crossvalidation c-statistic updated CHIP model per center

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