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Traumatic brain injury associated intracranial hemorrhage in the emergency department: Systematic review

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ABSTRACT

Background: A frequent reason for emergency department (ED) visits is mild traumatic brain injury (mTBI). A traumatic intracranial hemorrhage (ICH) will occur in a small percentage of these individuals, and even fewer may experience serious consequences. To improve current ED recommendations, this systematic study was conducted to describe known and novel risk factors that affect the risk of ICH in patients with mTBI. *Method*: This systematic review was conducted in accordance with the PRISMA guidelines. The terms "risk factor," "mild traumatic brain injury," and "traumatic intracranial hemorrhage" were used to search the Web of Science, MEDLINE, Scopus, and EMBASE databases. The search was limited to articles released between 2018 and 2024. Research involving general ED populations with head trauma is included, as is research on adult patients (≥18 years) with mTBI, which is defined as GCS 13–15; patients presenting with suspected or confirmed ICH following head trauma. *Result and conclusion*: Variations in ICH risk factors, the involvement of drugs, and changing epidemiology continue to complicate the diagnosis and treatment of mTBI patients. The biggest predictors of ICH are post-traumatic amnesia, skull fractures, older age, and GCS <15. The most reliable diagnostic method is the CT scan; biomarkers and machine learning approaches may potentially reduce unnecessary scans.

Keywords: Traumatic brain injury, intracranial hemorrhage, emergency department

1. INTRODUCTION

Accidental falls, car crashes, sports-related incidents, and violent crimes are the most frequent causes of traumatic brain injury (TBI), which is defined as an injury brought on by direct trauma or an acceleration-deceleration impact to the brain (Santiago et al., 2012). With more than 60 million cases annually, it is one of the primary causes of ED visits and a major contributor to morbidity and death worldwide (Maas et al., 2022).

Mild traumatic brain injury (mTBI), which is defined as individuals who report with an initial Glasgow Coma Scale (GCS) of 13–15, accounts for an estimated 70–90% of TBI (Maas et al., 2022; Steyerberg et al., 2019). Roughly 10% of these individuals will get a traumatic intracranial hemorrhage (tICH), according to earlier research (Fabbri et al., 2010; Smits et al., 2007). It has been demonstrated that the existence of a tICH increases the probability of a worsening that necessitates neurosurgical intervention and can lead to other problems, including traumatic cerebral vasospasm (Peng et al., 2024; Tourigny et al., 2021). Although there are a number of mTBI recommendations and management techniques, there is a great deal of heterogeneity in the risk variables that are taken into consideration by each guideline (Undén et al., 2013). Additionally, there have been documented problems with the overuse of computed tomography (CT) through the application of current guidelines, which increases the risk of needless radiation exposure to patients, lengthens ED wait times, raises healthcare costs, and burdens the environment with carbon dioxide emissions (Furlan et al., 2023; Saran et al., 2024). Additionally, since some of these guidelines were first put into effect, the prevalence of certain risk factors has changed, such as the introduction of direct oral anticoagulants (DOACs), and demographic trends have changed, such as the rise in the number of elderly patients with mTBI (Roozenbeek et al., 2013; Ruff et al., 2014).

To determine the current state of evidence regarding risk factors for ICH in mTBI patients in the emergency department, this systematic review and meta-analysis aimed to evaluate data from previously published research.

2. METHOD

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) criteria were followed in conducting this systematic review (Figure 1). Variants of "mild traumatic brain injury," "risk factor," and "traumatic intracranial hemorrhage" were used to search MEDLINE, Scopus, EMBASE, and Web of Science. Only papers published between 2018 and 2024 were included in the search. We include studies on adult patients (≥18 years) with mTBI (defined as GCS 13-15); Patients presenting with suspected or confirmed intracranial hemorrhage (ICH) following head trauma; Studies including general emergency department (ED) populations with head trauma. We exclude studies focusing solely on moderate-to-severe traumatic brain injury (TBI) (GCS <13) or pediatric populations (<18 years).

Two writers independently examined all complete texts, abstracts, and titles. All full-text publications were examined by two impartial assessors to find pertinent information for the systematic review. A senior member of the review team was consulted to help develop an agreement in cases where the assessors' results disagreed. Data was extracted in a pre-designed Google sheet, information extracted includes (study aim, study design, main findings, outcome, and population characteristics)

The quality assessment of the included studies was performed using the Newcastle-Ottawa Scale (NOS) quality assessment tool (Table 1). Five studies show high-quality scores (Galliazzo et al., 2019; Haddadi et al., 2022; Isokuortti et al., 2018, 2022; Niklasson et al., 2024). It shows a strong selection method, controlled for confounding factors, and used well-defined outcome measures. Moderate-quality studies (Bonney et al., 2020; Hosseininejad et al., 2023) had limitations in selection and comparability, particularly in confounding control and follow-up.

Table 1: Quality assessment of the included studies according to the Newcastle-Ottawa Scale (NOS)

Study	Study Design	Selection (0-4)	Comparability (0-2)	Outcome (0-3)	Total Score (0-9)	Quality
Bonney et al., (2020)	Retrospective observational	3	1	2	6/9	Moderate
Galliazzo et al., (2019)	Retrospective cohort	4	2	2	8/9	High
Haddadi et al., (2022)	Prospective cohort	4	2	3	9/9	High
Hosseininejad et al., (2023)	Cross-sectional	3	1	2	6/9	Moderate
Isokuortti et al., (2022)	Prospective case-control	3	2	2	7/9	High
Niklasson et al., (2024)	Retrospective cohort	4	2	3	9/9	High
Isokuortti et al., (2018)	Retrospective cohort	4	2	2	8/9	High

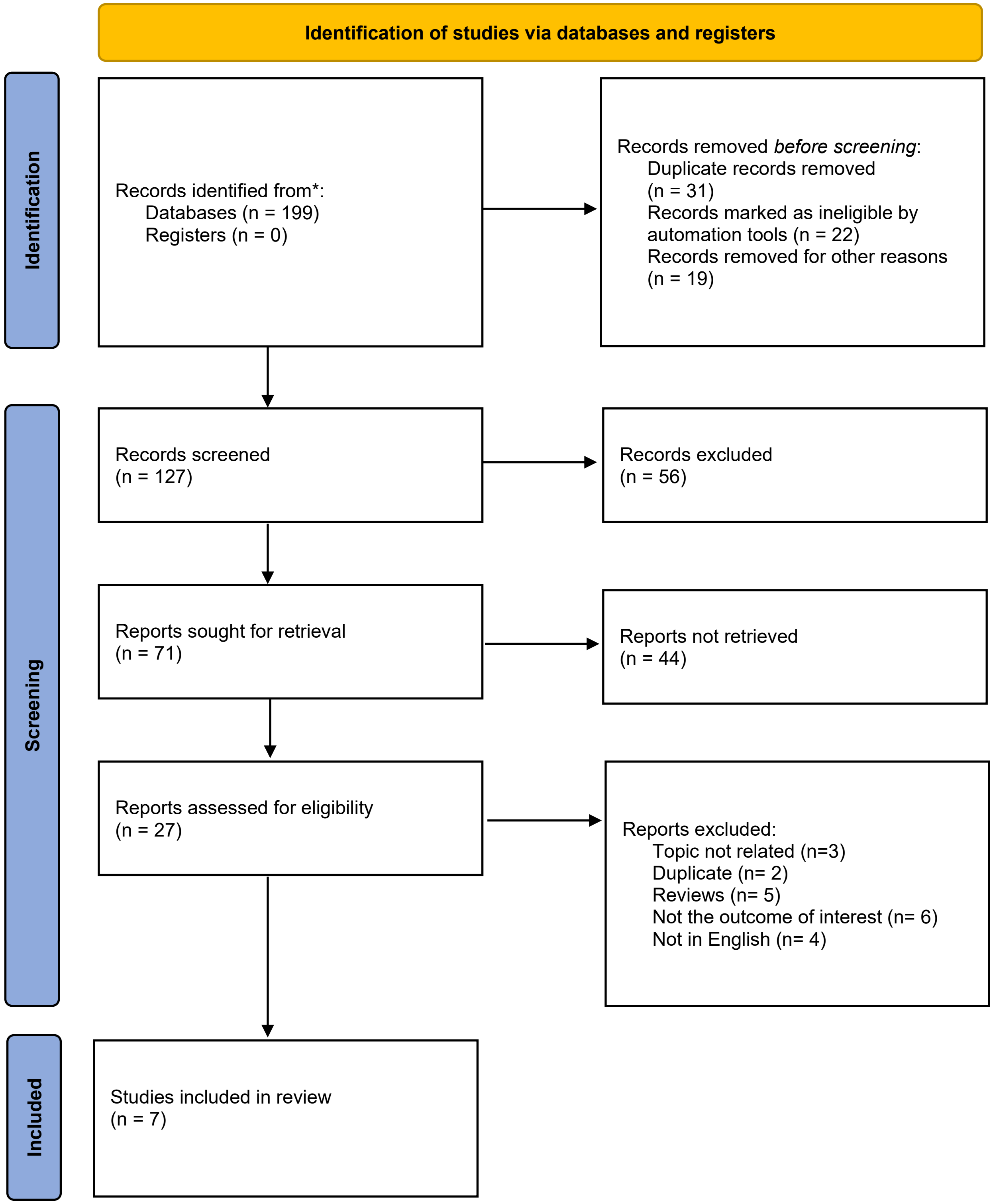

Fig 1: PRISMA consort chart of studies selection

3. RESULTS

In this systematic review study, we included 7 articles (Fig. 1). The reviewed studies discussed risk factors, diagnostic tools, and management strategies for mTBI, in relation to intracranial hemorrhage (ICH) and predictive biomarkers. Bonney et al., (2020) tested the incidence of ICH in patients with mTBI at a Level I trauma center; 8.5% of patients had positive CT findings, mainly subdural hematomas and subarachnoid hemorrhages. Older age and male sex were significantly associated with a higher likelihood of intracranial bleeding. According to Isokuortti et al., (2018), 16.1% of mTBI patients complain of intracranial abnormalities, risk factors include, older age, male sex, alcohol abuse, and preexisting brain lesions.

Multiple studies examined the impact of medications on ICH risk. According to Niklasson et al., (2024), patients on antiplatelet therapy had a significantly higher risk of traumatic ICH than patients on oral anticoagulation. Their study suggested that antiplatelet therapy should be given equal or greater consideration in clinical guidelines. Antithrombotic therapy and serotonergic antidepressants did not increase the risk of ICH according to Galliazzo et al., (2019) and Isokuortti et al., (2022) studies. GCS less than 15, post-traumatic amnesia, vomiting, and skull fractures were associated with ICH (Isokuortti et al., 2022).

Biomarker studies offer a valuable alternative diagnostic tool to reduce the need for CT scans. Aldolase C (ALDOC) serum levels correlated strongly with CT findings in mTBI cases, with a cutoff of 6.95 ng/mL providing 100% sensitivity and 98% specificity for diagnosing brain abnormalities (Haddadi et al., 2022). C-reactive protein (CRP) and D-dimer levels were effective prognostic markers, with D-dimer showing a 100% sensitivity and 98.5% specificity for detecting pathological lesions (Hosseininejad et al., 2023). The main findings and outcomes of the included studies are presented in Tables 2 and 3.

Table 2: Main Findings of the included studies

Study	Study Duration	Demographic Characteristics	Investigations Used	Main Findings
Haddadi et al., (2022)	2018-2019	89 patients with mTBI (GCS 13-15), age range unspecified	Blood samples for ALDOC levels, Brain CT scan	ALDOC serum levels were significantly higher in patients with positive CT findings. A cutoff of 6.95 ng/mL had 100% sensitivity and 98% specificity for detecting brain abnormalities.
Hosseininejad et al., (2023)	2018-2019	74 patients with mTBI, mean age 36.92 years	CRP and D-dimer blood tests, Brain CT scan	CRP >11.50 had 75% sensitivity and 95.5% specificity; D-dimer >0.90 had 100% sensitivity and 98.5% specificity for detecting pathological lesions on CT. These markers may help reduce unnecessary CT scans.
Isokuortti et al., (2022)	2015-2016	218 patients with mTBI, median age 70 years	Head CT scan, Medical history from Finnish national prescription registry	No significant association between serotonergic antidepressant use and traumatic ICH after mTBI.
Niklasson et al., (2024)	2017 & 2020-2021	4,850 patients with head trauma, median age 70 years	Head CT scan, Medication records, Logistic regression analysis	Patients on antiplatelet therapy had a higher risk of traumatic ICH than those on anticoagulation therapy. Antiplatelets should be given more consideration in head trauma guidelines.
Isokuortti et al., (2018)	2010-2012	3,023 patients with head trauma, majority with mTBI	Head CT scan, Alcohol use assessment, Medical history	16.1% of mTBI cases had intracranial lesions. Older age, male sex, alcohol abuse, and falls were associated with higher risk.

				Preexisting brain lesions increased risk for acute lesions.
Galliazzo et al., (2019)	2015-2017	1,846 patients with mTBI, mean age 71 years	Brain CT scan, Medical history, Antithrombotic medication use	No significant difference in intracranial bleeding risk between patients on and off antithrombotics. Key predictors of bleeding included GCS <15, amnesia, vomiting, and skull fractures.
Bonney et al., (2020)	2010-2011	5,634 patients with mTBI (GCS 13-15)	Brain CT scan, Trauma registry data analysis	8.5% had positive CT findings (subdural hematomas, subarachnoid hemorrhages). Older age and male sex were associated with higher risk. Clinical decision rules for CT use remain difficult to implement.

Table 3: Outcomes of the included studies

Study	Study Design	Aim	Population Characteristics	Outcome
Haddadi et al., (2022)	Prospective cohort study	To evaluate Aldolase C (ALDOC) as a biomarker for early detection of brain damage in mTBI patients	89 patients with mTBI (GCS 13-15)	ALDOC levels were significantly higher in patients with positive CT findings. A cutoff of 6.95 ng/mL had 100% sensitivity and 98% specificity for detecting brain abnormalities.
Hosseininejad et al., (2023)	Cross-sectional study	To assess CRP and D-dimer as prognostic markers in mTBI patients	74 patients with mTBI, mean age 36.92 years	CRP >11.50 had 75% sensitivity and 95.5% specificity; D-dimer >0.90 had 100% sensitivity and 98.5% specificity for detecting pathological lesions on CT. These markers may help reduce unnecessary CT scans.
Isokuortti et al., (2022)	Prospective case-control study	To investigate the risk of traumatic ICH in patients on serotonergic antidepressants after mTBI	218 patients with mTBI, median age 70 years	No significant association between serotonergic antidepressant use and increased risk of intracranial hemorrhage.
Niklasson et al., (2024)	Retrospective cohort study	To compare the risk of traumatic ICH in patients on antiplatelet vs.	4,850 patients with head trauma, median age 70 years	Patients on antiplatelet therapy had a higher risk of intracranial hemorrhage than those on anticoagulation.

		anticoagulation therapy		Antiplatelets should be given more consideration in head trauma guidelines.
Isokuortti et al., (2018)	Retrospective cohort study	To characterize the type and location of intracranial abnormalities in mTBI	3,023 patients with mTBI	16.1% had intracranial lesions. Older age, male sex, alcohol abuse, and falls were associated with a higher risk. Preexisting brain lesions increased risk for acute lesions.
Galliazzo et al., (2019)	Retrospective cohort study	To assess the risk of intracranial bleeding in mTBI patients on antithrombotic therapy	1,846 patients with mTBI, mean age 71 years	No significant difference in intracranial bleeding risk between patients on and off antithrombotics. Key predictors of bleeding included GCS <15, amnesia, vomiting, and skull fractures.
Bonney et al., (2020)	Retrospective observational study	To evaluate the incidence of intracranial hemorrhage in mTBI patients and discuss the use of clinical decision rules for CT use	5,634 patients with mTBI (GCS 13-15)	8.5% had positive CT findings (subdural hematomas, subarachnoid hemorrhages). Older age and male sex were associated with a higher risk. Clinical decision rules for CT use remain difficult to implement.

4. DISCUSSION

mTBI is a significant clinical challenge in determining the risk of ICH and the use of diagnostic tools. The reviewed studies examined diagnostic approaches, risk factors, and clinical decision-making in mTBI patients. Regarding important predictors that increase the risk of ICH in patients with mTBI. Yang et al., (2024) systematic review found that skull base fractures (OR 11.71), GCS <15 (OR 4.69), loss of consciousness (OR 2.57), and post-traumatic amnesia (OR 2.13) were the strongest predictors of ICH. These findings are supported by Smits et al., (2007), who developed the CHIP prediction rule, demonstrated that age, post-traumatic seizure, vomiting, and anticoagulant use significantly increase the risk of ICH. Stiell et al. (2001) examined the Canadian CT Head Rule and found that age >65, skull fractures, vomiting, and high-risk mechanisms of injury were major contributors to ICH risk.

Some of the included studies discussed the effect of antithrombotic medications on ICH risk. Patients on antiplatelets have a higher risk of ICH than those on anticoagulants, challenging current clinical guidelines that primarily focus on anticoagulation risks (Niklasson et al., 2024). Galliazzo et al., (2019) reported no significant increase in ICH risk associated with anticoagulant or antiplatelet therapy. Fiorelli et al., (2020), a systematic review and meta-analysis, revealed that patients on antiplatelet therapy have a 1.51 times greater risk of ICH compared to those who don't use blood thinners.

CT scans is the gold standard to diagnose ICH in mTBI patients. However, there is a developing interest in alternative diagnostic methods to reduce unnecessary use of CT scans. Aldolase C (ALDOC) levels were highly sensitive (100%) and specific (98%) for detecting brain abnormalities, which are considered a potential biomarker for mTBI assessment (Haddadi et al., 2022). C-reactive protein (CRP) and D-dimer were found to be effective prognostic markers, with D-dimer showing 100% sensitivity and 98.5% specificity (Hosseininejad et al., 2023). These biomarkers will help clinicians reduce unnecessary radiation exposure by limiting CT use to high-risk patients. Additionally, decision rules and machine-learning models were employed to improve risk stratification. Turcato et al., (2022) used a decision tree analysis to categorized mTBI patients on oral anticoagulants, found that GCS <15, post-traumatic amnesia, and trauma above the clavicles were key predictors of ICH. The CHIP prediction rule (Smits et al., 2007) show 94–96% sensitivity for detecting ICH and could reduce unnecessary CT scans by 23–30%. The epidemiology of mTBI changed over time, falls replaced road accidents as the leading cause of head injuries, mainly among the elderly. mTBI incidence is rising in older populations, likely due to an increase in fall-related injuries (Lefevre-Dognin et al., 2021). This shift is important, making older adults are at higher risk for ICH, mainly when they use antithrombotic medications.

Recent guidelines for mTBI management, have been widely adopted but have limitations (Stiell et al., 2001; Undén et al., 2013). Yang et al., (2024) show that existing guidelines overuse CT scans, leading to unnecessary radiation exposure and healthcare costs. Many guidelines fail to adequately address antiplatelet therapy as a bleeding risk adequately (Fiorelli et al., 2020). It's necessary to incorporate biomarker-based risk assessment, decision tree models, and targeted risk stratification for antithrombotic therapy to enhance the accuracy of mTBI diagnosis while minimizing unnecessary CT use.

5. CONCLUSIONS

The diagnosis and management of mTBI patients still complex due to variations in ICH risk factors, the role of medications, and evolving epidemiology. Older age, GCS <15, skull fractures, and post-traumatic amnesia are among the strongest predictors of ICH. The CT scan is the most accurate diagnostic technique; biomarkers and machine learning techniques may also help reduce unnecessary scans. It is necessary to revise clinical recommendations to incorporate these results by adding alternative diagnostic methods and a specific risk assessment for antiplatelet medication. To improve clinical decision-making in the management of mTBI, future research should focus on biomarker-based screening and validation of prediction models.

List of abbreviations

mTBI, Mild Traumatic Brain Injury
TBI, Traumatic Brain Injury
ICH, Traumatic Intracranial Hemorrhage
GCS, Glasgow Coma Scale
CT, Computed Tomography
ED, Emergency Department
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses
NOS, Newcastle-Ottawa Scale
DOACs, Direct Oral Anticoagulants
CRP, C-Reactive Protein
ALDOC, Aldolase C
CCHR, Canadian CT Head Rule
CHIP, CT in Head Injury Patients Prediction Rule
OAT, Oral Anticoagulant Therapy
CART, Classification and Regression Tree
MRI, Magnetic Resonance Imaging

Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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