

## Management of Mild Brain Trauma in the Elderly: Literature Review

### Abstract

**Purpose:** The world population is aging. As direct consequence, geriatric trauma is increasing both in absolute number and in the proportion of annual admissions causing a challenge for the health-care system worldwide. The aim of this review is to delineate the specific and practice rules for the management of mild brain trauma in the elderly. **Methods:** Systematic review of the last 15 years literature on mild traumatic brain injury (mTBI) in elderly patients. **Results:** A total of 68 articles met all eligibility criteria and were selected for the systematic review. We collected 29% high-quality studies and 71% low-quality studies. **Conclusion:** Clinical advices for a comprehensive management are provided. Current outcome data from mTBIs in the elderly show a condition that cannot be sustained in the future by families, society, and health-care systems. There is a strong need for more research on geriatric mild brain trauma addressed to prevent falls, to reduce the impact of polypharmacy, and to define specific management strategies.

**Keywords:** Brain trauma, elderly, head injury, head trauma, mild brain trauma

### Introduction

The world population is aging. It is estimated that almost two billion people will be older than 60 years by 2050.<sup>[1]</sup> In the USA, in 2030, one in five residents is expected to be 65 years or older with a projection to doubling the current number in 2050.<sup>[2]</sup> A similar trend has been observed in Canada.<sup>[3]</sup>

As direct consequence, geriatric trauma is increasing both in absolute number and in the proportion of annual admissions,<sup>[4]</sup> causing a challenge for the health-care system worldwide.

Traumatic brain injury (TBI) represents a major cause of mortality and morbidity which involves globally more than 10 million individuals annually,<sup>[5]</sup> with no substantial differences in the incidence between low- and high-income countries.<sup>[6]</sup>

Since TBI used to be prevalent in young people, nowadays, we are witnessing in a shift in the epidemiology of TBI toward the elderly.<sup>[5]</sup> This is the result of mainly two factors: first, the aging of population as seen above; second, the decrease of traffic accidents due to the improvement of traffic safety which allowed falls to become the

most important cause of TBI. Moreover, falls account for over 65% of TBI-related hospital admissions in the elderly.<sup>[7]</sup>

Epidemiologic studies show that the majority of TBI in older patients is mild with an incidence ranging from 60% to 80%.<sup>[3,8,9]</sup>

Mild TBI (mTBI) is defined by the Neurotraumatology Committee of the World Federation of Neurosurgical Societies as a head injury presenting with Initial Glasgow Coma Score (GCS) of 14 or 15.<sup>[10]</sup> History of loss of consciousness (LoC) and posttraumatic amnesia may be or not be present. Consider 65 years as a cutoff for the elderly is widely accepted in the international literature, mostly after the report of Mosenthal *et al.* which demonstrates the age 65 and more to be a predictor of increased mortality after TBI.<sup>[11]</sup>

This cohort of patients represents a challenge for clinicians because of the unique physiologic and clinical factors, including frailty, chronic health diseases and polypharmacy, which make them more prone to primary and secondary injury following TBI, regardless of severity.

Frailty is defined as a syndrome of decreased reserves (energy, physical ability,

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cognition, and health) that gives rise to vulnerability in times of acute stress.<sup>[12]</sup> It has been calculated that about 7% of the people older than 65 years and 20% older than 80 years have frailty syndrome.<sup>[12]</sup>

Despite what was discussed above, the researcher in the last 15 years does not seem to have found interest in exploring a common address for the management of mTBI in the elderly.

In 2004, the World Health Organization instituted a task force on mTBI with the scope of finding methodological issues and research recommendations.<sup>[13]</sup> After 10 years, the main research priorities included focus on the elderly and the development of validated clinical prediction rules for the prognosis.<sup>[14]</sup>

In 2015, the American Association for the Surgery of Trauma performed a member survey disclosing that 65% of the participants thought that geriatric trauma patients are undertriaged and not transferred appropriately to the higher levels of care. Reported concerns were the lack of uniformly accepted protocols, primarily for mTBI.<sup>[15]</sup>

More recently, a group from the University of Cambridge completed an extensive epidemiologic literature review with the conclusion that though increased admissions of elderly patients following TBI there was little or no evidence of corresponding increase of age of patients recruited for TBI in studies around the world.<sup>[16]</sup>

Finally, in a large cohort study including about 6000 mTBI older patients, Cheng *et al.* concluded that mTBI is an independent significant risk factor of death in the elderly and emphasized the need for head injury prevention and research.<sup>[17]</sup>

The aim of this review is to point out the state of the art of the literature focused on mTBI in the elderly with the scope of delineating specific and practice rules for the management and to define the lacking areas of research.

## Methods

This literature review study was conducted in accordance to the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement during the reporting of the current study's findings.<sup>[18]</sup> A literature search using PubMed was performed for English human studies published in the last 15 years using the following keywords: "traumatic brain injury AND elderly" and "head injury AND elderly." The literature search was conducted on March 6, 2019.

### Study selection

Studies were included if they met focus on mTBI in the elderly defined as people aged >65 years. The exclusion criteria were as follows: (1) animal studies and case reports, (2) studies focusing on severe and/or moderate TBI, (3) studies focusing on pediatric patients, (4) studies

that had reported data without distinction of age and trauma severity, (5) clinical trial still in progress, and (6) full-text reports unavailable on-line.

Each retrieved article was screened for eligibility by two independent reviewers (FM and GT) first at the title and abstract level, and then full-text level if potentially relevant. The references of the included articles had been also evaluated and articles that met our criteria had been comprised in the review [Figure 1].

## Results

A total of 388 studies were identified, and after duplicates exclusion, 359 unique abstracts were screened. Abstracts were evaluated by the first author (FM), and 148 potentially relevant articles were selected for full-text review and subsequently obtained and assessed for eligibility by two authors (FM and GT). Additional 15 full-text articles were identified through references. Finally, a total of 68 articles met all eligibility criteria and were selected for the review.

Quality assessment was achieved categorizing each study by level of evidence (LoE), according to the framework proposed by Sauer *et al.* for the surgical research.<sup>[19]</sup> We found 10 prospective prognostic and diagnostic studies (LoE I); 4 prospective therapeutic/care management studies (LoE II); 3 prospective prognostic and epidemiological studies (LoE II); 31 retrospective prognostic studies and 2 prognostic case-control studies (LoE III); one therapeutic case-control study and one retrospective epidemiological study (LoE III); 2 epidemiological studies (LoE IV-V) and 3 prognostic studies (LoE V). We collected three systematic

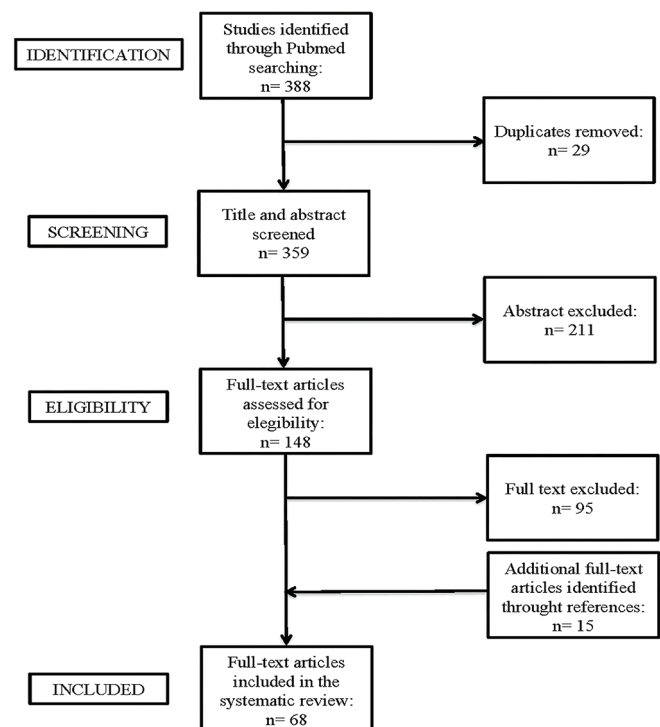


Figure 1: Flow diagram for studies identification and selection process

reviews of predominantly level II studies with no negative criteria (LoE II); 4 systematic reviews with up to two negative criteria (LoE III); 4 reviews (LoE IV). Overall, we collected 29% high-quality studies (LoE I or II) and 71% low-quality studies (LoE III or V). Studies were published between 1997 and 2018.

Extensive reading of the selected articles permitted to identify the major concerns of the recent literature about mTBI in the elderly to be discussed on. A total of 8 focused on epidemiology. Risk factors were reported in six articles. Thirty-five addressed the management of mTBI whom a total of 25 focusing patients on anticoagulation/antiplatelet (AP) therapy, and one described seizure therapy. Outcome and mortality were analyzed by 19 papers. All studies and their main characteristics are presented in Table 1 [Appendix A].

Only 8 studies (11,76%) were designed to assess exclusively elder mTBI patients, with the rest presenting mixed cohorts for age and severity. Due to the high heterogeneity of the topics found, statistical analysis was not performed.

## Discussion

The aging of the world population and the increase in life expectancy subject both emergency and neurosurgery departments to everyday challenges related to the management of TBI in the elderly. This is especially true for those with a mild trauma because it is estimated that 82% of older patients hospitalized for mTBI return to independent living after completing the medical, surgical, and physical treatments.<sup>[11]</sup> Triage and appropriate treatment should be uniformed to obtain the better results in terms of outcome for patients and cost-effectiveness for health-care system. As most of the international literature is focused on younger patients or severe TBI, and nonspecific guidelines exist, older mTBI patients are often undertriaged and the entity of trauma may be underestimated.

The results of our literature review were grouped and evaluated according to the major concerns emerged.

### Risk factors for traumatic brain injury and prevention

Mechanisms accounting for TBI in the elderly may be the same of younger people. Nonetheless, most of TBI in the elderly are attributable to falls either from standing or from heights,<sup>[9,20-23]</sup> accounting for over 80% of TBI hospitalizations and in-hospital mortality.<sup>[21]</sup>

Mild cognitive impairment or dementias, comorbidities, ambulation with assistance, and polypharmacy have been demonstrated as the risk factors for falls in older adults and subsequent admission for fall-related TBI (fr-TBI).<sup>[9,20,21]</sup>

However, even in the absence of comorbidities, older age is associated with an increased risk of falls due to physiologic age-related deterioration of physical functions

in balance, vision and hearing, physical strength, gait, and dexterity.<sup>[21,22]</sup>

Finally, older adults are particularly susceptible to suffering iatrogenic effects of medications because of the increased risk of polypharmacy, defined as the simultaneous use of multiple medications such as anticoagulants (ACs), psychotropics, and sedatives, defined as “fall risk-increasing drugs.”<sup>[22,24]</sup> Polypharmacy represents a relevant problem as it has been shown that more than 20% of older Americans receive at least one inappropriate drug.<sup>[25]</sup> Physicians must carefully weigh the risk-benefit ratio when making decisions to prescribe medication such as AC therapy to patients who are at a high risk of falling.<sup>[26]</sup> The Prevention of Falls in the Elderly Trial demonstrated the fundamental role of falls prevention with appropriate interventions, including the following: exercise programs aimed at improving strength and balance; vision assessments to correct poor eyesight; educational programs to encourage safer behavior among patients and families; periodic medication review to eliminate unnecessary medications or mitigate iatrogenic effects.<sup>[27]</sup>

However, there is some controversy in the literature regarding the optimal combination of these interventions, and the best prevention strategy for fr-TBI in the elderly has still to be elucidated.<sup>[21,26]</sup>

### Admission versus observation

The overall assessment of a geriatric mTBI patient requests an interdisciplinary collaboration to improve diagnosis and treatment of underlying comorbidities, management of medications, and to address the most appropriate care setting.<sup>[4]</sup>

It is estimated that 65% of annually visited TBI elderly patients in the emergency departments require admission,<sup>[28]</sup> thus establishing the guidelines to define the criteria for observation and discharge is mandatory.

Mild head trauma in older population is not as mild as in younger patients. Several studies showed a discrepancy of observed GCS between the elderly and young patients with similar anatomic severity of TBI, with geriatric TBI having better GCS than younger patients.<sup>[29,30]</sup> This creates a false idea that the elderly could tolerate equivalent injuries better, leading to underestimate the entity of TBI. The mechanisms behind this phenomenon are unknown, but they are certainly related to comorbidities and differences in physiological response to injury.

Although LoC has a strong predictive value for intracranial hemorrhage (ICH),<sup>[31]</sup> most older patients with mTBI who require surgical intervention do not have a history of LoC.<sup>[32]</sup> These data suggest that GCS and neurology examination alone cannot reliably exclude significant intracranial pathology in the elderly with mTBI. Given the lack of validated clinical evidence for identifying mTBI older patients who can be managed without cranial

**Table 1: Characteristics of selected studies**

	<b>Number of studies</b>	<b>Type of studies</b>	<b>Authors and year</b>	<b>LoE</b>		
Epidemiology	8	2 prospective prognostic	Jiang J <i>et al.</i> 2013 de Guise <i>et al.</i> 2015	I		
		1 prospective epidemiological	Stocchetti N <i>et al.</i> 2014	II		
		1 systematic review	Gaastra B <i>et al.</i> 2016	II		
		1 epidemiological retrospective	Van den Brand CL <i>et al.</i> 2018	III		
		1 epidemiological retrospective	Cetty L <i>et al.</i> 2017	IV		
		1 review	Adams SD <i>et al.</i> 2015	IV		
		1 epidemiological	Kristman VL <i>et al.</i> 2014	V		
		1 prospective prognostic	Fu WW <i>et al.</i> 2017	I		
Risk factors	6	2 retrospective prognostic	Evans D <i>et al.</i> 2015 Teo DB <i>et al.</i> 2018	III		
		3 prognostic	Filler W <i>et al.</i> 2015 Karibe H <i>et al.</i> 2017 Krishnamoorthy V <i>et al.</i> 2015	V		
		3 prospective prognostic	Batey M <i>et al.</i> 2018 Chenoweth JA <i>et al.</i> 2018 Nishijima DK <i>et al.</i> 2012	I		
		2 diagnostic	Clement CM <i>et al.</i> 2006 Haydel M <i>et al.</i> 2000	I		
		2 prospective therapeutic/ management	Ivascu FA <i>et al.</i> 2005 Menditto VG <i>et al.</i> 2012	II		
		2 prospective prognostic	Kaen A <i>et al.</i> 2010* Riccardi A <i>et al.</i> 2017*	II		
Management, imaging and complication	35	1 systematic review	Jagoda AS <i>et al.</i> 2008	II		
		20 retro prognostic	Beynon C <i>et al.</i> 2015 Campiglio L <i>et al.</i> 2017 Cohen D.B. <i>et al.</i> 2006 Collins CE <i>et al.</i> 2014 Franko J <i>et al.</i> 2006 Gangavati A.S. <i>et al.</i> 2009 Grandhi R. <i>et al.</i> 2015 Helmes E <i>et al.</i> 2011 Howard J.L. <i>et al.</i> 2009 Julien J <i>et al.</i> 2017 Kim DY <i>et al.</i> 2012 Lavoie A <i>et al.</i> 2004 Li J <i>et al.</i> 2001 Mann N <i>et al.</i> 2018* Moore MM <i>et al.</i> 2012 Parra MW <i>et al.</i> 2013 Pieracci M <i>et al.</i> 2007 Riccardi A <i>et al.</i> 2013* Scantling D <i>et al.</i> 2017 Swap C <i>et al.</i> 2016*	III		
		2 case-control prognostic	Mahler B <i>et al.</i> 2015 Tseng JH <i>et al.</i> 2014*	III		
		2 systematic reviews	Callaway DW <i>et al.</i> 2007 Miller J <i>et al.</i> 2015	III		
		1 review	Haydel M <i>et al.</i> 2012	IV		
		Outcome and rehabilitation	19	2 prospective prognostic	Brousseau AA <i>et al.</i> 2016* Mosenthal AC <i>et al.</i> 2004	I
				1 prospective therapeutic	Pedersen A <i>et al.</i> 2015	II

Contd...

Table 1: Contd...

Number of studies	Type of studies	Authors and year	LoE
	1 retrospective therapeutic	Susman M <i>et al.</i> 2002	II
	1 systematic review	Werman HA <i>et al.</i> 2011	II
	9 retrospective prognostic	Bouras T <i>et al.</i> 2007	III
		Cheng PL <i>et al.</i> 2014*	
		Depreitere B <i>et al.</i> 2012	
		Flaada JT <i>et al.</i> 2007	
		Haring RS <i>et al.</i> 2015	
		Herou E <i>et al.</i> 2015	
		LeBlanc J <i>et al.</i> 2006	
		Salotto K <i>et al.</i> 2014	
		Shimoda K <i>et al.</i> 2014	
	1 case-control therapeutic	Stapert S <i>et al.</i> 2006	III
	2 systematic reviews	Levin HS <i>et al.</i> 1997	III
		Menzel JC <i>et al.</i> 2008	
	2 reviews	Cruise CM <i>et al.</i> 2006	IV
		Flanagan SR <i>et al.</i> 2005	

\*Exclusively elder mTBI patients. Complete references are available as supplemental material (Appendix A). LoE – Level of evidence; mTBI – Mild traumatic brain injury

computed tomography (CT), radiological evaluation is always needed.<sup>[33-35]</sup>

Clinical observation is also often involved because it has been showed that 80% of patients in need of neurosurgical intervention can be identified by worsening of symptoms during the first 6 h.<sup>[36]</sup>

Admission criteria to a trauma center are strongly correlated with the presence of co-injuries, clotting disorders, and preexistent diseases. The role of anticoagulation/AP therapy is discussed further in this section. Certainly, elderly patients on anticoagulation and documented intracranial pathology should be admitted to the neurosurgical department.<sup>[28]</sup> In case of normal CT and elevated international normalized ratio (INR), mTBI patients should be observed for 12–24 h,<sup>[37]</sup> and those with normal INR and CT, and no other associated injury, may be discharged and followed-up at home by a care provider.<sup>[28]</sup>

Several authors suggested that most of observed patients can be safely discharged without a second CT scan, in the absence of clinical impairment, due to the low rates of delayed ICH occurring after 24 h from trauma.<sup>[38-43]</sup>

Finally, coinjuries and chronic diseases are considered the positive predictors of worse outcome and mortality when associated to mTBI in the elderly, claiming admission to a trauma center.<sup>[1]</sup>

A comprehensive flow chart for the management is provided in Figure 2.

### The role of anticoagulation/antiplatelet therapy

Anticoagulants (ACs), APs, and the more recent direct oral anticoagulants (DOACs) are frequently used among the elderly. This trend, together with the high risk of falling,

determines a difficult dilemma for clinicians who have to balance the risk of ICH with thromboembolic complications. Therefore, benefits may not always outweigh the risks. Even though an ICH may also occur in patients not taking any ACs or APs medications,<sup>[44]</sup> it is well known that long-term oral anticoagulation is an independent risk factor for both immediate and delayed ICH, and it is significantly associated with worse outcome and higher mortality.<sup>[45,46]</sup> Risk's classification for ICH requiring surgery according with GCS score and clinical manifestations is resumed in Table 2.<sup>[44]</sup> The management of these older mTBI patients is still largely debated in the literature and a common strategy has not yet been achieved. ACs drugs like warfarin are associated with the higher increased risk for ICH in the setting of TBI<sup>[47]</sup> and with elevated chances of ICH progression in the follow-up period.<sup>[48]</sup> Conversely, DOACs have a considerably lower rate of development of ICH compared to warfarin<sup>[49,50]</sup> and lesser chances of ICH progression.<sup>[48]</sup> These data support the safer profile of DOACs than ACs, suggesting that they should be used as first choice in older patients with high risk of falling. However, warfarin and DOACs users have similar mortality rates,<sup>[48]</sup> reflecting the fact that every effort to prevent falls should be accomplished in patients who need ACs or DOACs therapy. APs use also confer a slight increase rate of ICH,<sup>[47,51]</sup> particularly clopidogrel more than aspirin,<sup>[41]</sup> but they are not associated with higher mortality if not used in combination.<sup>[48]</sup> Part of the management of mTBI elderly patients on ACs or APs therapy involves the need of discontinuation and/or reversal of these drugs. In case of ICH at the initial CT scan, prompt reversal of warfarin with fresh frozen plasma demonstrated to be effective in decreasing ICH progression and mortality.<sup>[52]</sup> Furthermore, APs and DOACs should be discontinued in this setting, but potential drawbacks are the inability to rapidly reverse DOACs, as an antidote is not always available,

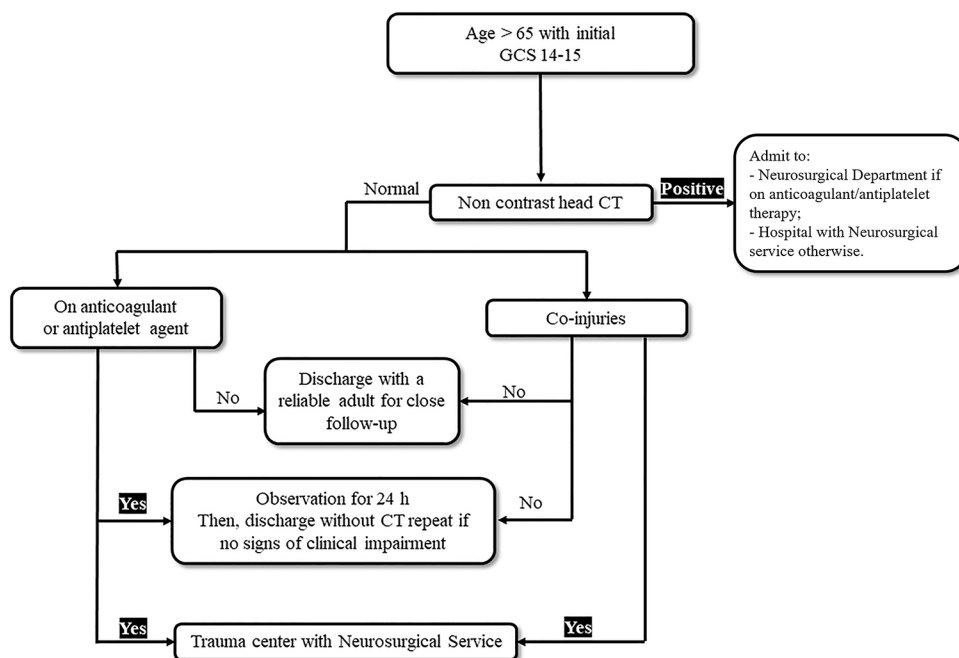


Figure 2: Flowchart for management of mild traumatic brain injury in elderly patients. Co-injuries and anticoagulant therapy must be combined (GCS: Glasgow Coma Score; CT: Computed tomography; LoE: Level of evidence)

**Table 2: Stratification of risk of hematoma requiring neurosurgical intervention**

Categories	Characteristic	Risk of neurosurgical intervention (%)
Low risk	GCS 15 No LOC No amnesia No vomiting No HA	<0.1
Medium risk	GCS 15 with one or more of the following LOC Amnesia Vomiting HA	1-3
High risk	GCS 14-15 or neurologic deficits or Drug induced coagulopathies Alcoholism Drug abuse Epilepsy Previous neurologic treatment Disabled elderly patients	10

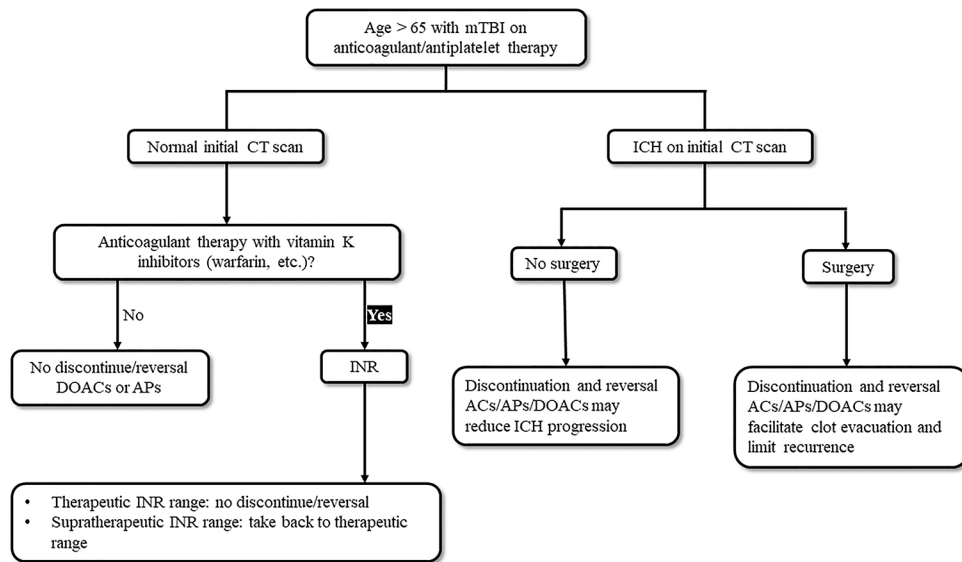
LOC – Loss of consciousness; GCS – Glasgow Coma Score; HA – Headache

and that platelet transfusion is not associated with benefit in mortality and outcome in case of aspirin or clopidogrel usage.<sup>[53]</sup> Patients on ACs or APs therapy with initial normal CT scan have a cumulative incidence of delayed ICH very low (<1%), and there is no evidence that their therapy must be reversed or discontinued.<sup>[41]</sup> Nevertheless, supratherapeutic INR levels should be taken back to therapeutic range in all mTBI patients. When neurosurgical intervention for ICH is needed, ACs or DOACs reversal may facilitate clot evacuation and limit recurrences. A flowchart for a proposed management based on our review is provided

in Figure 3. Despite this extensive literature search, no clear indications are emerged on when to restart ACs or APs medications if discontinued after a mTBI.

### Seizure risk and prophylaxis

TBI is known to contribute to 4%–9% of all epilepsy cases, particularly mTBI is associated to a double risk for seizures in the general population.<sup>[54]</sup> Related TBI epilepsy is defined as at least one seizure occurring 7 days or later after the trauma; isolated seizure occurring in the first 7 days is considered as acute symptom.<sup>[54]</sup>



**Figure 3: Flowchart for management of anticoagulant/antiplatelet therapy in mild traumatic brain injury elderly patients (ACs: Anticoagulants; APs: Antiplatelets; DOACs: Direct oral anticoagulants; INR: International normalized ratio; ICH: Intracranial hemorrhage; mTBI: Mild traumatic brain injury; CT: Computed tomography; LoE: Level of evidence)**

New onset seizures in older patients are often focal and can differ for semiology from younger patients. Subtle and noncharacteristic symptoms lead to delayed diagnosis and include syncope, memory problems, confusional episodes, or mental status changes.<sup>[55]</sup> Only one report matches our inclusion criteria. In this large prospective case–control study, Mahler *et al.* assessed a cumulative relative risk of 2.5 in mTBI patients older than 65 years, which increased six times with a brain contusion. Conversely, an isolated skull fracture was not associated with an increased risk.<sup>[54]</sup> Based on these few data, seizure prophylaxis cannot be recommended in all cases, but physicians should be aware of the subtle and noncharacteristic symptoms to promptly confirm the diagnosis with an electroencephalogram and to start therapy if needed.

### Outcome

Long-term impact of mTBI on the patient, their family and society cannot be underestimated. It is mainly associated with loss of independence and cognitive decline secondary to the trauma. The high impact for the health-care systems is also reflected by the prolonged hospitalization and the needing for rehabilitative therapy. In the acute settings at the time of hospitalization, literature data showed that 45% of mTBI elderly patients could be discharged at home, 38% need physical or cognitive rehabilitation, and 8% need a long-term placement.<sup>[56]</sup> Mortality is still high, reported as about 8%,<sup>[46,56-58]</sup> and it has a strong and linear correlation with age. Moreover, 23% of discharged mTBI elderly patients have severe disability.<sup>[11]</sup> It is possible that these discouraging reports may have led to an undertreatment for these patients in the last years. However, there are suggestions that outcome may be improved with more invasive monitoring and aggressive care.<sup>[58,59]</sup> Furthermore,

a recent prospective study demonstrates that elderly TBI patients benefit from highly specialized rehabilitation, and it fails to prove inferiority regarding the younger age group.<sup>[60]</sup> Furthermore, for patients who need neurosurgical intervention, evidence that craniotomy will negatively affect outcome is lacking. When operated, mTBI elderly patients show a more favorable outcome than who do not undergo surgery.<sup>[56,61]</sup> Our review supports the idea that age should not be the sole factor for limiting care in mTBI patients. Physicians should be aware that older patients with mTBI deserve prompt and aggressive care and rehabilitation, as they can respond similarly to younger patients. However, the retrospective nature of this supporting data must be reinforced by more prospective studies.

### Limitations

This study is mainly subject to the classical limitation of all reviews: the overall quality of the studies included. The majority of studies presented level II or less, and only 6 studies (8%) were LoE I. Moreover, there is a high heterogeneity in the literature focused on elderly TBI patients, and very few articles consider primarily mTBI. This made it necessary to carry out a research work oriented in extracting data that could involve some bias in patients' selection and outcome results. Finally, the obtained data were not suitable for meta-analysis to reach the evidence of a systematic review and the given recommendations are only based directly on the LoE of the studies selected.

### Conclusion

Assuming that life expectancy is constantly increasing as well as the world population over the age of 65 years, reduction in mortality and morbidity should be the aim of managing patients with TBI in this cohort. Since severe

TBI still represents a challenge in both young and older people, current outcome data from mTBI in elderly show a condition that cannot be sustained in the future by families, society, and health-care systems.

There is a strong need for more research on geriatric mTBI addressed to prevent falls, to reduce the impact of polypharmacy, and to define specific management strategies based on the identification of patients who have chance of unfavorable outcome despite mild trauma.

Age alone should not limit care in these patients because they can have a good outcome if properly treated.

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### Conflicts of interest

There are no conflicts of interest.

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## Appendix A

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