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Clinical Review

RISK OF DELAYED INTRACRANIAL HEMORRHAGE IN ANTICOAGULATED PATIENTS WITH MILD TRAUMATIC BRAIN INJURY: SYSTEMATIC REVIEW AND META-ANALYSIS

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□ **Abstract—Background: Delayed intracranial hemorrhage is a potential complication of head trauma in anticoagulated patients. Objective: Our aim was to use a systematic review and meta-analysis to determine the risk of delayed intracranial hemorrhage 24 h after head trauma in patients who have a normal initial brain computed tomography (CT) scan but took vitamin K antagonist before injury. Methods: EMBASE, Medline, and Cochrane Library were searched using controlled vocabulary and keywords. Retrospective and prospective observational studies were included. Outcomes included positive CT scan 24 h post-trauma, need for surgical intervention, or death. Pooled risk was estimated with logit proportion in a random effect model with 95% confidence intervals (CIs). Results: Seven publications were identified encompassing 1,594 patients that were rescanned after a normal first head scan. For these patients, the pooled estimate of the incidence of intracranial hemorrhage on the second CT scan 24 h later was 0.60% (95% CI 0–1.2%) and the resulting risk of neurosurgical intervention or death was 0.13% (95% CI 0.02–0.45%). Conclusions: The present study is the first published meta-analysis estimating the risk of delayed intracranial hemorrhage 24 h after head trauma in patients anticoagulated with vitamin K antagonist and normal initial CT scan. In most situations, a repeat CT scan in the emergency department 24 h later is not necessary if the first CT scan is normal. Special care may be required for patients with serious mechanism of injury, patients showing signs of neurologic deterioration, and patients presenting with excessive anticoagulation or receiving antiplatelet co-medication.**

□ **Keywords—traumatic brain injury; delayed intracranial hemorrhage; anticoagulation therapy; coagulopathy; vitamin K antagonist**

INTRODUCTION

Traumatic brain injury represents a major health and socioeconomic problem in high-income countries, where it is the leading cause of morbidity and mortality among young individuals, with an incidence of 100–300 per 100,000 (1,2). These commonly seen injuries in the emergency department (ED) require rapid diagnosis and proper management in order to improve patient outcomes (3). The initial evaluation of patients includes computed tomography (CT) scans of the brain to quickly

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determine the type and extent of injury as well as to select the optimal management strategy (4,5). The role of the first CT scan, as well as supplemental ones in cases of rapid neurologic deterioration, is well accepted (6). However, the importance of repeated scans for anticoagulated patients suffering from a mild traumatic brain injury with a normal initial head CT scan is not clearly established in current guidelines.

Several studies suggest that anticoagulated patients are exposed to an increased risk of intracranial hemorrhage (ICH) after head trauma (7–10). In addition, usage of oral anticoagulants is rapidly increasing in the elderly population (11,12). With the anticipated growth of this population and the increasing number of head injury patients seen in the ED, the clinical dilemmas surrounding these patients become increasingly relevant. Among elderly patients suffering a fall, long-term anticoagulation has been shown to not only increase the incidence of ICH when compared to those not taking anticoagulant, but also to increase the mortality of those suffering an ICH (13,14).

Delayed ICH is a potential complication of head trauma in anticoagulated patients after an initial normal head CT scan. Although clinical decision rules exist to help determine which patients suffering from a head injury require a head CT scan, these rules do not apply to anticoagulated patients. Some guidelines suggest that all anticoagulated patients with head injury should undergo strict observation during the first 24 h and have a control CT before discharge (15–18). Recent National Institute for Health and Care Excellence guidelines now propose secondary scans at delays ranging from 7 days up to 1 month (19). However, these recommendations are not based on studies looking at the prevalence of delayed ICH. Other guidelines rather propose to proceed with community follow-up in cases of mild traumatic brain injury (20).

The aim of this study was to conduct a systematic review and meta-analysis to estimate the 24-h risk of delayed ICH in anticoagulated patients with mild traumatic brain injury and normal initial brain CT, considering the wide range of reported incidence of delayed ICH (0–11% using confidence interval [CI]) and that no meta-analysis has ever been published on this specific topic.

METHODS

The methodological approach followed for this systematic review and meta-analysis was based upon the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) methodology and the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) 2015 statement (21,22).

Search Strategy

EMBASE, MEDLINE, and Cochrane Library were searched using controlled vocabulary and keywords without language or date limitations. Search terms were as follows for our MEDLINE strategy: ((((hemorrhage [MeSH Terms] OR intracranial hemorrhage[MeSH Terms] OR brain hemorrhage[MeSH Terms] OR delayed bleeding[Title/Abstract] OR delayed hemorrha*[Title/Abstract])) AND ((tbi[Title/Abstract] OR traumatic brain injury[Title/Abstract] OR craniocerebral trauma [MeSH Terms] OR brain injury, chronic[MeSH Terms] OR brain injuries[MeSH Terms]))) AND ((coumadins [MeSH Terms] OR warfarin[MeSH Terms] OR anticoagulants[MeSH Terms])). A similar but specific strategy was used for EMBASE. We also searched the grey literature with the following databases using the same keywords: OpenSIGLE, New York Academy of Medicine (Grey Literature Collection), Greylit.org, and Google Scholar. All database searches were done under the guidance of an information specialist. Attempts were made to contact authors of all selected manuscripts to ensure data content and complete cases of missing information. References from eligible studies were also screened for other relevant publications.

Identification of Studies

Studies retained for our systematic review were: randomized controlled trials, prospective or retrospective cohort studies, case-control studies, or cross-sectional studies. To be included, studies had to focus mainly on patients with mild traumatic brain injury (see Figure 1 for definition by Carroll et al.), who used vitamin K antagonist before injury, who were scanned on hospital presentation, and whose initial scan was normal (23). Delayed ICH was

> **"MTBI is an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include: (i) 1 or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; (ii) Glasgow Coma Scale score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare. These manifestations of MTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries (e.g. systemic injuries, facial injuries or intubation), caused by other problems (e.g. psychological trauma, language barrier or coexisting medical conditions) or caused by penetrating craniocerebral injury."**

Figure 1. Operational definition of mild traumatic brain injury (MTBI) as recommended by The World Health Organization (WHO) Collaborating Centre Task Force on Mild Traumatic Brain Injury in Carroll et al. (23).