UPDATES ON CAUSES, PSYCHOLOGICAL IMPACT AND MANAGEMENT OF INTRACRANIAL HEMORRHAGE: A SYSTEMATIC REVIEW

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Abstract

Objectives: To assemble the results of the research and provide insight into the causes, risk factors, and treatment of ICH.

Methods: A comprehensive exploration of relevant databases was conducted to find studies satisfying the inclusion requirements. An extensive search of PubMed, SCOPUS, Web of Science, and Science Direct was done to find pertinent material.

Results: We included data from 10 trials with 47,654 total participants, of which 24,312 (51%) were male. Anticoagulation, intravenous drug users (IVDU), and thrombolytic therapy, along with old age, were reported as independent significant risk factors for ICH. Medication for female hormones has been associated with a higher incidence of ICH. In individuals suffering from acute ischemic stroke, endovascular and revascularization treatments are independent indicators of ICH. Excellent hemostasis was attained with 4-factor prothrombin complex concentrate (4F-PCC) and tranexamic acid, which were also linked to a lower risk of death in patients with ICH. Decompressive hemicraniectomy may be beneficial in the management of large hematoma.

Conclusion: It was found to be of multifactorial causes. Although the evaluation examined a range of ICH therapy options, the impact of treatments differs depending on the type of damage being treated. This review is restricted to the analysis of treatments since certain studies did not report the study of a particular injury type by each discussed medicinal. A sufficiently large sample size will allow for an analysis of each therapy in future prospective studies.

Keywords: Intracranial hemorrhage; Risk factors; Causes; Management; Systematic review.

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Introduction

Intracranial hemorrhage (ICH) refers to any bleeding that occurs inside the intracranial vault. The anatomic site of the bleeding further defines ICH subgroups. In the US, there are between 40,000 and 67,000 instances of spontaneous ICH occur annually, accounting for 24.6 incidences per 100,000 person-years worldwide. After six months, between 35% and 52% of survivors are expected to die within 30 days, and only 20% of survivors are expected to have fully recovered functionally.3. During the first 24 hours, around half of these fatalities occur, which emphasizes how crucial it is for emergency departments (EDs) to provide prompt, efficient care [1-3].

A small vascular disease that is present at baseline usually manifests as primary ICH. Chronic hypertension initially generates hypertensive vasculopathy, which is a minor degenerative alteration in the walls of small to medium-sized penetrating capillaries known as lipo hyalinosis. [4]. Second, one characteristic of CAA is the accumulation of amyloid-b peptide in the walls of tiny cortical and leptomeningeal capillaries. [5]. The end consequence is degenerative changes in the vascular wall, which include smooth muscle cell loss, thickening of the wall, narrowing of the lumina, formation of microaneurysms, and microhemorrhages, even if the underlying process causing the buildup of amyloid is still unknown [6].

Based on the patient's medical history and physical examination, the diagnosis of ICH is confirmed by a brain CT scan that pinpoints the site of anatomic bleeding. An extensive medical history, if available, ought to be the initial step in the ICH diagnosis procedure [7, 8].

For each ICH subtype to get specific therapy, an accurate diagnosis is necessary. Indications for surgical intervention are EDH volume greater than 30 cm3, hydrocephalus, SDH or EDH with anisocoria in comatose individuals, and a Glasgow Coma Score of less than 8 in potentially recoverable individuals with either traumatic ICH or IPH with herniation. Optimizing cerebral perfusion pressure will improve the prognosis of patients with ICH [9]. This systematic review aimed to identify knowledge gaps, synthesize recent literature, and provide ideas for future research and clinical practice to shed light on the etiology, risk factors, and management of ICH.

Methods

Search Strategy

For the systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [10]. A PubMed, SCOPUS, Web of Science, and Science Direct electronic search was conducted with the language restriction set to English. For these situations, relevant keywords were incorporated into the search strategy; "Intracranial hemorrhage", "Intracerebral hemorrhage", "Risk factors", "Causes" and "Management". Reviewers independently sorted through the search results, selected relevant publications, gathered information, and applied appropriate evaluation techniques to ascertain the caliber of the included research.

Study Selection

Articles reporting the causes, risk factors, and management of ICH in adults over eighteen years old with a design of Randomized controlled trials, cohort, cross-sectional and case studies of at least five patients, published between 2023 and 2024 were included. However, studies with insufficient data or vague methodology; studies with overlapping data; animal studies, or review articles, were excluded.

Data Extraction and Quality Assessment

Rayyan (QCRI) was used to check the search results to make sure they were accurate [11]. The inclusion and exclusion criteria were applied to assess the relevancy of the titles and abstracts that the search produced. The research team thoroughly reviewed the publications that met the criteria for inclusion. Conflicts were resolved by reaching a consensus. Key research data was recorded using a pre-established data extraction form. To analyze the potential for bias, an unbiased evaluation tool was developed.

Risk of Bias Assessment

The quality was assessed using critical assessment criteria for studies providing prevalence data from The Joanna Briggs Institute (JBI) [12]. There were nine questions in the tool. A score of one was assigned to a positive response and a score of zero to a negative one. A score below 4 was categorized as low, 5-7 as moderate and over 7 as high. Researchers assessed the studies' quality on their own, and disagreements were resolved through dialogue.

Results

Systematic search outcomes

A thorough search turned up a total of 961 study articles after 506 duplicates were eliminated. 388 papers were eliminated after the titles and abstracts of 455 research were assessed. Of the 67 reports that needed to be obtained, only 4 items could not be found. 63 papers made it through the screening

procedure to be evaluated in full text; Eight were rejected due to the inappropriate population type, two were editor's letters, and forty-three were denied due to incorrect study results. In this systematic review, ten research papers met the qualifying standards. An outline of the process by which the research was selected is provided in (Figure 1).

Sociodemographic features of the comprised studies

Table 1 displays the publications' sociodemographic information**.** Our data includes ten trials with a total of 47,654 individuals, of which 24,312 (51%) were male. Five investigations used prospective cohorts [13, 15, 16, 17, 18] and five of them were retrospective cohorts [14, 19, 20, 21, 22]. In the USA, three investigations were carried out [14, 19, 21], one in Germany [13], one in Hungary [15], one in France [16], one in China [17], one in Sweden [18], one in Viet Nam [20], and one in Taiwan [22].

Clinical outcomes

Seven studies discussed the possible risk factors and causes of the incidence of ICH. Anticoagulation, IVDU, and thrombolytic therapy, along with old age, were reported as independent significant risk factors for ICH [14, 15, 18, 19]. The use of female hormone medications has been associated with a higher risk of cerebral bleeding caused by cerebral cavernous malformations [13]. In individuals suffering from acute ischemic stroke, endovascular and revascularization treatments are independent indicators of ICH [16, 17].

Excellent hemostasis was obtained with tranexamic acid and 4-factor prothrombin complex concentrate (4F-PCC), which were also linked to a lower risk of death in patients with ICH [21, 22]. In patients with large hematoma, decompressive hemicraniectomy may be beneficial in the management of significant intracerebral bleeding [20].

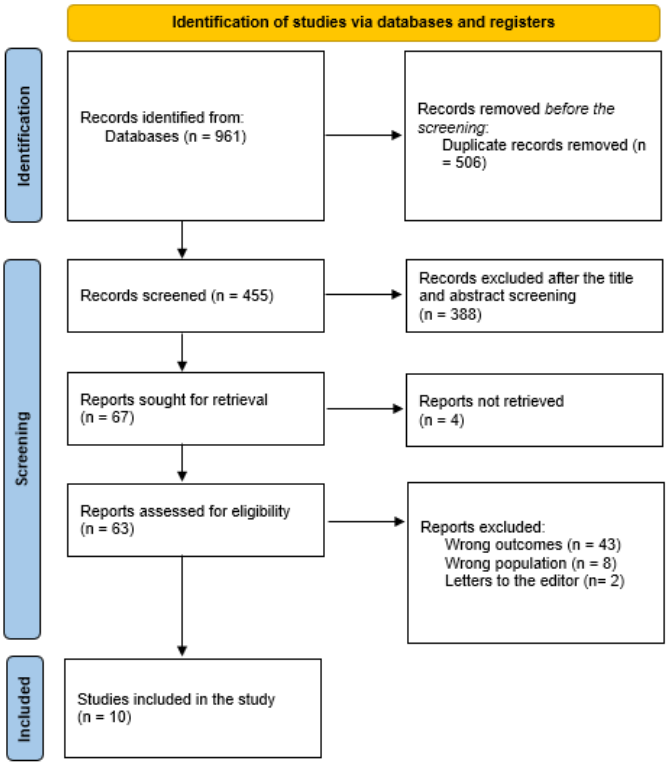

Figure 1. PRISMA diagram.

Discussion

It is crucial to comprehend the risk factors and management techniques to enhance patient outcomes and lower the death rates linked to ICH. This comprehensive review reported that anticoagulation, IVDU, and thrombolytic therapy, along with old age, were reported as independent significant risk factors for ICH [14, 15, 18, 19]. ICH is a potentially fatal side effect of long-term anticoagulant medication. Anticoagulation for individuals with clear treatment indications, including atrial fibrillation, has long been restricted due to the risk of ICH. The older adult population most at risk of cerebral bleeding from falls is also a vulnerable group for thrombotic complications in the absence of anticoagulant medication. Zeng *et al.* also predicted the risk of cerebral bleeding linked with anticoagulants in their meta-analysis, and they also influenced future research and guidelines for preventing intracranial hemorrhage [23]. Shoamanesh *et al.* stated that patients with cerebral microbleeds are more likely to experience ICH after thrombolysis, especially if their load of cerebral microbleeds is larger. Nonetheless, there is no evidence to warrant withholding tissue plasminogen activator, a staple of treatment, from acute ischemic stroke patients based only on the presence of cerebral microbleeds. [24].

According to this review, endovascular and revascularization treatments are independent predictors of ICH in individuals with acute ischemic stroke. [16, 17]. Similarly, after endovascular therapy, there is a higher risk of ICH, according to Hao et al. [25]. Hemorrhagic tendency linked to thrombolytic agents or heparinization [27, 28], mechanical lesion of the vessel wall, reperfusion lesion, increased permeability of the blood-brain barrier, [26], and hemodynamic lesion as a result of blood pressure fluctuations [29] can all cause intracerebral hemorrhage during or after endovascular therapy to treat acute ischemic stroke. Patients undergoing endovascular treatment are the only ones who can experience intracranial hemorrhage from mechanical vessel lesions; patients receiving medicinal treatment are not at risk.

This study found that the use of female hormone medication has been associated with a higher risk of cerebral cavernous malformations-induced cerebral hemorrhage [13]. The hypothesis that thrombus formation in the dilated caverns of these malformations, where blood flow is slow, or in a related developmental venous anomaly, may be the cause of intracranial hemorrhage is supported by the finding that female hormone therapy is associated with an increased risk of cerebral cavernous malformation-related intracranial hemorrhage. [30, 31]. Those with cerebral venous thrombosis also have hemorrhagic infarcts, which are caused by a similar pathophysiologic mechanism. Cerebral venous thrombosis is another risk factor for women using oral contraceptives. [32].

Regarding the management, we discovered that tranexamic acid and 4-factor prothrombin complex concentrate (4F-PCC) achieved excellent hemostasis and were linked to a lower risk of mortality in ICH patients. [21, 22] 4F-PCCs contain almost 25 times as many vitamin K-dependent clotting factors (such as factors II, VII, IX, and Xa). 4F-PCCs were chosen over FFP due to their leukocyte-free product, rapid administration, small volume, minimal risk of lung damage from transfusions, and heart failure safety. Before the approval of certain DOAC reversal medications, 4F-PCCs were utilized for FXaI-related bleeding reversal [33].

In patients with large hematoma, decompressive hemicraniectomy may be beneficial in the management of significant intracerebral bleeding [20]. Hematoma-induced damage and the mass effect are successfully reduced by surgically removing the clot mass. For this reason, decompressive craniectomy combined with evacuation of hematoma is a rapid and efficient way to reduce ICP in patients of significant ICH. [34].

Table 1. Demography of the research population

Study	Study design	Country	Participants	Mean age/ range	Males (%)
Zuurbier et al., 2023 [13]	Prospective cohort	Germany	722	23.7-54	0
Hoang et al., 2023 [14]	Retrospective cohort	USA	351	NM	203 (57.8%)
Fekete et al., 2023 [15]	Prospective cohort	Hungary	1252	67.7 ± 12.9	702 (56%)
Amaral et al., 2023 [16]	Prospective cohort	France	176	70.7 ± 8.5	84 (47.7%)
Zuo et al., 2023 [17]	Prospective cohort	China	215	66.9 ± 12.2	121 (56.3%)
Niklasson et al., 2024 [18]	Prospective cohort	Sweden	4850	70	2466 (50.8%)
Mac Grory et al., 2023 [19]	Retrospective cohort	USA	32,715	72	16128 (49.3%)
Trong et al., 2024 [20]	Retrospective cohort	Viet Nam	55	55 ± 11	45 (81.8%)
Whaley et al., 2024 [21]	Retrospective cohort	USA	76	NM	37 (48.7%)
Chiu et al., 2024 [22]	Retrospective cohort	Taiwan	7242	19 to > 80	4526 (62.5%)

Table 2. Conclusion of the included research.

Study ID	Population	Risk factors/ causes	Management approach	Follow-up (years)	Conclusions	JBI
Risk factors/ causes						
Zuurbier et al., 2023 [13]	Females on hormonal therapy	Hormonal therapy	NM	5	A higher risk of cerebral bleeding caused by cerebral cavernous malformations has been associated with the use of female hormone medications.	Moderate
Hoang et al., 2023 [14]	Drug abusers	IVDU	NM	NM	higher hemorrhagic stroke and higher neurodiagnostic imaging frequency are linked to IVDU-associated endocarditis.	Moderate
Fekete et al., 2023 [15]	Patients with acute ischemic stroke	Thrombolytic therapy	NM	1	Major vascular blockage, intra-arterial thrombolysis, advanced age, and a higher National Institute of Health Stroke Scale (NIHSS) score are all potential risk factors for ICH.	Moderate
Amaral et al., 2023 [16]	Patients with acute ischemic stroke	Bridging revascularization therapy	NM	0.5	ICH occurred in one out of every twelve ischemic patients receiving bridging treatment. Upon initial clinical examination, these individuals had a more severe stroke; upon admission, they had higher blood pressure; on imaging, their blood inflammatory profiles were greater, and they had increased leukoaraiosis, cerebral calcifications, and intracranial atheroma.	High
Zuo et al., 2023 [17]	Patients with acute ischemic stroke	Endovascular treatment	NM	NM	A predictor of ICH in patients undergoing endovascular treatment for acute anterior circulation stroke is higher neuron-specific enolase (NSE) levels.	Moderate
Niklasson et al., 2024 [18]	Patients on oral anticoagulation	Anticoagulation therapy	NM	60.5	Compared to oral anticoagulation, antiplatelet treatment is linked to an increased risk of catastrophic cerebral hemorrhage.	Moderate
Mac Grory et al., 2023 [19]	Patients on oral anticoagulation	Anticoagulation therapy	NM	NM	The use of vitamin K antagonists over the seven days prior to the study did not significantly raise the risk of ICH overall.	Moderate
Management						
Trong et al., 2024 [20]	ICH patients	NM	Decompressive hemicraniectomy	6 m	In certain patient populations, decompressive hemicraniectomy may be beneficial in the management of significant intracerebral bleeding. Positive outcomes are more likely to occur in younger patients with lower hematoma volumes and higher preoperative GCS scores.	Moderate
Whaley et al., 2024 [21]	ICH patients	NM	4F-PCC	NM	In 80.3% of cases, good or excellent hemostasis was attained. A thrombotic event occurred in five of the individuals. For ICH linked to factor Xa inhibitors, 4F-PCC is both safe and efficacious.	Moderate
Chiu et al., 2024 [22]	ICH patients	NM	Tranexamic Acid	180 d	Tranexamic acid-treated individuals with nontraumatic ICH had a decreased death rate over the first seven days.	Moderate

Long-term anxiety is a prevalent issue among survivors of intracranial hemorrhage (ICH), with studies indicating that approximately 17% to 40% of patients experience significant anxiety symptoms years after the event. Research shows that anxiety often coexists with depressive symptoms, affecting around 48% to 61% of those with anxiety at various follow-up intervals post-ICH. Notably, the location of the hemorrhage specifically lobar ICH—has been identified as a significant predictor of anxiety, while other factors such as cognitive impairment and functional disability do not show a strong correlation with anxiety levels. This suggests that the psychological impact of ICH may not solely stem from physical limitations but also from the trauma associated with the event itself [35].

Effective management of anxiety in ICH survivors necessitates a comprehensive approach that integrates psychological support with medical care. Early identification of anxiety symptoms through standardized assessments, such as the Hospital Anxiety and Depression Scale (HADS), is crucial for timely intervention. Cognitive Behavioral Therapy (CBT) has emerged as a beneficial treatment modality, equipping patients with coping strategies to manage their anxiety. Additionally, rehabilitation programs should incorporate psychological components to address emotional well-being alongside physical recovery. Medication may also be considered for severe cases, although careful monitoring is essential to mitigate potential side effects [36].

A holistic approach to care is vital for ICH survivors, recognizing that mental health is as important as physical recovery. Rehabilitation programs should not only focus on restoring physical abilities but also include components that address emotional well-being. Support groups or peer counseling can provide valuable social support, helping survivors feel less isolated in their experiences. Furthermore, involving family members in the recovery process can create a supportive environment that fosters open communication about fears and anxieties related to recovery [37,38].

Conclusion

Because of its high 1-month mortality rate, ICH is considered a neurologic emergency and may necessitate neurosurgical intervention. It was found to be of multifactorial causes. Although the evaluation examined a range of ICH therapy options, the impact of treatments differs depending on the type of damage being treated. This review is restricted to the analysis of treatments since certain studies did not report the study of a particular injury type by each discussed medicinal. A sufficiently large sample size will allow for an analysis of each therapy in future prospective studies.

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