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Natural history of recovery after intracerebral haemorrhage: a scoping review protocol

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ABSTRACT

Introduction Clinical trials for intracerebral haemorrhage typically measure outcomes in the same way and at the same time points as trials for ischaemic stroke. However, there is growing evidence that the trajectory of recovery following intracerebral haemorrhage may differ significantly from that following ischaemic stroke. A better understanding of current approaches to outcome assessment is essential to ensure that future trials examining treatments for intracerebral haemorrhage are designed appropriately.

Objective To determine when and how outcomes are measured in patients with intracerebral haemorrhage.

Methods and analysis With the assistance of an information specialist, we will conduct a scoping review by searching MEDLINE, Embase, Cochrane Central Register of Controlled Trials and Web of Science for prospective studies of adults with primary intracerebral haemorrhage and documented outcomes with specified times. Two reviewers will independently collect data on included studies pertaining to publication data, study population information, timing of outcome and details of the outcome measurement tools used. The extracted data will be used to demonstrate the type and timing of outcome measures.

Ethics and dissemination Primary data will not be collected therefore formal ethics is not required. The findings of this study will be disseminated through peer-reviewed publications and through presentation at academic conferences.

Strengths and limitations of this study

- Addresses an important gap in knowledge about intracerebral haemorrhage recovery.
- This study uses a broad search strategy to ensure maximal coverage of the subject area.
- Limited to prospective studies.
- No quantitative data synthesis will be attempted.

INTRODUCTION

The increasing burden of stroke

Stroke is a global health burden.[1] In 2010, stroke was the second-leading cause of death[1] and third-leading cause of disability worldwide[2]; one in four deaths were caused by stroke.[1] About half of all stroke survivors are left with cognitive or physical impairment which contributes to the billions of dollars spent on stroke in the USA alone.[3] Between 1990 and 2010, stroke incidence increased by 68% with an 84% increase in stroke survivors.[4]

Intracerebral haemorrhage

Intracerebral haemorrhage (ICH) accounts for 10%–20% of all strokes,[5 6] and leads to high morbidity and mortality rates; mortality rates can exceed 40%, and 80% of survivors are disabled.[7] Despite poor outcomes, less is known about the natural history of this disease compared with ischaemic stroke.[8]

Stroke recovery

In ischaemic stroke, the rate of recovery is typically fastest in the first 3 months.[9] While recovery continues beyond this point, it does so at a slower pace and tends to plateau by 6 months.[9] Based on our understanding of ischaemic stroke recovery, rehabilitation efforts target this early time period,[10] and outcome assessments for clinical trials typically occur at 3 months.[11] Despite a relative absence of long-term outcome studies, ICH is managed in a similar fashion, with clinical trial outcomes measured at 3 months. Yet, there is mounting evidence that patients with ICH can demonstrate significant recovery well beyond 6 months.[12] Therefore, in order to see the full extent of recovery after ICH, outcome measures may need to be assessed beyond 3 months. However, it remains unclear what outcome measures, observed at what time points, would be ideal to capture recovery in patients with ICH. We believe this information will be crucial to inform the design of future clinical treatment trials for ICH.

Objectives

Our primary objective is to determine the timing of outcomes provided by prospective studies of patients with ICH. Outcomes of interest will include mortality, disability and quality of life. Our secondary objectives are to describe the assessment scales used to measure outcomes, and to determine if the existing data will allow for a subsequent systematic review with meta-analysis. To accomplish these goals, we will perform a scoping review of the ICH literature to better understand the natural history of recovery following ICH.

METHODS

Study registration

This study will be conducted based on the guidelines of the Johana Briggs Institute (JBI) Methodology for Scoping Reviews.[13] The findings of this study will be reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension statement for reporting of Scoping Reviews (PRISMA-SCR).[14] This protocol will be reported, using JBI guidelines,[13] and is registered and hosted at the University of Ottawa Research Repository (URL: https://ruor.uottawa.ca/).

Inclusion/exclusion criteria

Eligibility criteria were established using the Population, Concept, Context framework. Studies will be selected according to the following criteria.

Participants

We will include prospective observational and interventional studies of adult patients (≥18 years of age) presenting with spontaneous ICH, confirmed with either CT or MRI. Eighteen is the threshold age for adulthood used in haemorrhage trials. Paediatric ICH is more often secondary to intravascular lesions and malignancy and hence, will not be included in this review. Patients presenting with isolated non-parenchymal haemorrhage (subarachnoid, subdural, epidural, intraventricular) will be excluded, as will parenchymal haemorrhage with a known secondary aetiology (tumour, vascular malformation, trauma, aneurysms, neoplasm or other causes).

Concept

The major concept we will explore in this scoping review is to determine the timing of outcomes across studies and understand the range of assessment tools used to measure these outcomes in ICH patients. We will include all prospective observational and interventional studies that clearly document the timing of outcome assessment, irrespective of the type of outcome collected. Studies in which ICH is the sole outcome will be excluded. Retrospective studies will be excluded as they do not have planned repeated measurement of outcomes.

Context

There is no restriction on healthcare locations (emergency room, intensive care unit or neurological/neurosurgical ward, etc). We also have no restrictions on country of study, ethnicity, gender or socioeconomic status.

Information sources and search strategy

Our search strategy will include the following four databases from the date of inception to November 2019: MEDLINE, Embase, Cochrane Central Register of Controlled Trials and Web of Science. A search strategy was developed (see online supplementary appendix), with the assistance of an information specialist, using search terms specific to the database being searched. Supplemental searches will include scanning the reference list of included studies. We will only include studies presented in the English due to constraints in translational resources. No other restrictions were placed on search results.

Study records

Data management

Database search results will be uploaded to Covidence Systematic Review Software (Covidence, Melbourne, VIC, Australia). After removal of duplicate results, citation titles and abstracts will be screened.

Selection process

Two reviewers will independently screen the articles in a two-step manner. Initially, screening will be concerned with a review of titles and abstracts (step 1). All studies deemed potentially relevant studies will proceed to screening of the full journal article (step 2). Full-text screening will be performed using a standardised screening form. Should there be a disagreement between the two reviewers in either step, a senior third reviewer (DD) will resolve discrepancies. The process of study selection will be described using a PRISMA flow diagram.

Data extraction process and outcomes selected

Reviewers will independently extract data from the included studies using an a priori designed data extraction form. We will collect information on publication data (eg, journal of publication, authorship list, funding), study population information (demographic, radiological and medical history), and details of the outcome measurement tools used. Potential outcomes to be collected will include, but are not limited to: mortality, modified Rankin Scale, National Institute of Health Stroke Scale, Functional Independence Measure, Quality of Life Measures scores (ie, General Health Questionnaire, Severity of Alcohol Dependence Questionnaire, Five level EQ-5D and the time periods where datawere collected. The time points at which these outcomes are assessed (eg, 1 month, 3 months, 6 months, 1 year, etc) will also be collected. The data extracted will be compared in a tabular form with side-by-side comparisons of the outcome measures. Where possible and relevant, the reliability and validity of outcome measures will be presented.

Data synthesis and risk of bias assessment

The analysis of ICH outcome is ultimately dependent on the data that can be extracted from each study. Since one of the goals of our scoping review is to determine if the existing data will allow for a subsequent systematic review with meta-analysis, formal quantitative analysis is not planned as part of this review. Instead, we will focus on assessing the appropriateness of potential meta-analysis by assessing heterogeneity in outcome measures, data paucity and timing in outcome ascertainment. As data synthesis is not the primary aim of a scoping review, a formal assessment of methodological quality of the included studies will not be performed.

PATIENT AND PUBLIC INVOLVEMENT

The data collected within this scoping review is derived from previously published studies. As a result, neither patients nor the general public were involved in the development of the research question or assessment methods.

ETHICS AND DISSEMINATION

The findings of this scoping review will inform future clinical trial design. We intend to publish and present our findings around timing and methods of ICH outcome assessment in relevant journals and stroke/ICH conferences.

Contributors SM and DD were responsible for the concept, design, search strategy, review, first draft and final draft of the manuscript. AD was responsible for developing the search strategy and for revisions. BD, RL and VY were involved in the design, search strategy, review and revisions. MS and DAF were involved in the concept, design and revisions.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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