Cerebrospinal fluid and blood levels of neurofilament light chain in traumatic brain injury: a systematic review and meta-analysis

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Review question / Objective: Can neurofilament light chain levels in blood or CSF discriminate patients suffering from a traumatic brain injury from healthy controls?

Condition being studied: Traumatic brain injury (TBI) is one of the leading causes of disability in the United States and contributes approximately one-third of all injury-related deaths. Various biomarkers are currently studied for their efficacy in the early identification of patients with TBI and predicting the prognosis. Neurofilament light chain (NfL) is a protein, highly expressed in large myelinated axons. Increased levels are indicative of axonal damage and neuronal degeneration, and have been reported in various diseases, including traumatic brain injury. Nonetheless, the results have been inconsistent.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 October 2020 and was last updated on 09 October 2020 (registration number INPLASY2020100031).

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Support: None.

Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest: None.

INTRODUCTION

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predicting the prognosis. Neurofilament light chain (NfL) is a protein, highly expressed in large myelinated axons. Increased levels are indicative of axonal damage and neuronal degeneration, and have been reported in various diseases, including traumatic brain injury. Nonetheless, the results have been inconsistent.

METHODS

Search strategy: ((concussion OR traumatic brain injury OR TBI OR head trauma) AND (neurofilament light chain OR NFL)).

Participant or population: We will include studies with adult patients (18 years or older) suffering from TBI.

Intervention: Evaluation of NfL levels in blood and CSF.

Comparator: Healthy controls or the same patients at different time-points (ex. pre- and post-concussion).

Study designs to be included: All studies excluding case reports JC case series (number of participants≥10).

Eligibility criteria: Inclusion criteria: 1.Original article, 2.All studies excluding case reports JC case series, 3.Participants: adults ≥18 years old, diagnosis of TBI (any severity), 4.Examining the role of NfL in discriminating between patients and healthy controls or the same patients at different time-points, 5.Examining the role of NfL in discriminating between patients and healthy controls or the same patients at different time-points, 6.Specimen type, assay used, timing of collection, and NfL levels.

Quality assessment / Risk of bias analysis: Two authors will independently assess the risk of bias of each included study. Based on the Cochrane Handbook of Systematic Reviews, 7 aspects will be examined and they will be rated as High, Low, or Unclear risk of bias. Any arising disagreements between the two authors will be solved through discussion with the help of a third author.

Strategy of data synthesis: R studio, libraries meta, and mada software will be used to perform the final data combination and meta-analysis. Additional analyses will be performed, such as sensitivity analysis, subgroup analysis, analysis for the detection of potential publication bias, in order to assess the robustness of our results.

Subgroup analysis: Patients will be further categorized based on TBI severity and the NfL levels of each group will be compared to NfL levels of healthy controls.

Sensibility analysis: Sensitivity analysis will be conducted to assess the robustness of our results.
Country(ies) involved: Greece.

Keywords: traumatic brain injury; concussion; neurofilament light chain; biomarker.

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