INPLASY PROTOCOL

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None declared.

Efficacy and safety of contralateral C7 nerve transfer for cerebral injury induced upper limb spastic paralysis: a systematic review and meta-analysis

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Review question / Objective: **Contralateral C7 nerve transfer has proved its efficacy and safety for brachial plexus avulsion injury induced upper limb function reconstruction. Recently, the role of contralateral C7 nerve transfer for cerebral injury induced upper limb paralysis was studied. However, the results of those studies were inconsistent, and there had been no systematic review and meta-analysis till now. The aim of this paper is to investigate whether the application of contralateral C7 nerve transfer can lead to functional improvement in patients with upper limb spastic paralysis caused by cerebral injury.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 June 2022 and was last updated on 05 June 2022 (registration number INPLASY202260016).

INTRODUCTION

Review question / Objective: **Contralateral C7 nerve transfer has proved its efficacy and safety for brachial plexus avulsion injury induced upper limb function reconstruction. Recently, the role of contralateral C7 nerve transfer for cerebral injury induced upper limb paralysis was studied. However, the results of those studies were inconsistent, and there had been no systematic review and meta-analysis till now. The aim of this paper is to investigate whether the application of contralateral C7 nerve transfer can lead to functional improvement in patients with**

upper limb spastic paralysis caused by cerebral injury.

Condition being studied: Stroke, traumatic brain injury, or cerebral palsy can cause many serious sequelae, and one of the most common sequelae is long-term hemiparalysis. Many neuromodulatory strategies target upper limb paralysis caused by cerebral injury, including pharmacological interventions, physical therapy, and neurostimulation. Contralateral C7 nerve transfer was first used to treat brachial plexus avulsion injuries thirty years ago, and its efficacy and safety in restoring upper limb function in patients with brachial plexus injuries has been proven. Recently, this technique has been proposed to successfully improve upper limb function in patients with cerebral injuries by initiating the regeneration of peripheral nerves and initiating functional remodeling in the brain. Yet, systematic review and meta-analysis on the C7 nerve transfer for upper limb functional restoration after cerebral injury is still limited.

METHODS

Search strategy: Two investigators independently searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov to identify relevant studies published up to May 01, 2022. Additionally, reference lists of the relevant systematic reviews and meta-analyses were also screened to ensure a more comprehensive search. The following Medical Subject Headings (MeSH) terms and keywords (in the title/abstract) in multiple combinations were used: c-7, c7, seventh nerve, seventh cervical nerve, nerve transfer, neurotization. The search strategy was limited to English-language articles.

Participant or population: Participants had hemiplegia after cerebral injury, manifesting mainly as spasticity and weakness of the contralateral upper limb for at least 1 year.

Intervention: Contralateral C7 nerve transfer surgery.

Comparator: Rehabilitation only.

Study designs to be included: Prospective study, retrospective study, or randomized controlled trial (RCT) study design.

Eligibility criteria: The inclusion criteria were as follows: (1) study type: prospective study, retrospective study, or randomized controlled trial (RCT) study design; (2) language: published in English; (3) participants: Participants had hemiplegia after cerebral injury, manifesting mainly as spasticity and weakness of the contralateral upper limb for at least 1 year. (4) interventions: patients were categorized into the surgery (contralateral C7 nerve transfer surgery followed by rehabilitation) or the control (rehabilitation only) group. (5) outcomes: The primary outcome was the change in the upper-extremity Fugl-Meyer (UEFM) score from baseline to the end of follow-up. The secondary outcomes included changes in the Modified Ashworth Scale (MAS) score for elbow, forearm, wrist, thumb, and Fingers 2-5, and changes in range of motion for elbow, forearm rotation, and wrist. Safety outcomes included all adverse events and decrease in muscle strength of the bilateral upper limb at 6-month follow-up. Included studies were not requested to supply all the outcomes mentioned above.The exclusion criteria were as follows: (1) review, comment, letter, case report, or animal experiments; (2) lack of extractable data; (3) patients underwent contralateral C7 nerve transfer due to brachial plexus injury.

Information sources: MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov.

Main outcome(s): The primary outcome was the change in the upper-extremity Fugl-Meyer (UEFM) score from baseline to the end of follow-up.

Additional outcome(s): The secondary outcomes included changes in the

Modified Ashworth Scale (MAS) score for elbow, forearm, wrist, thumb, and fingers 2-5, and changes in range of motion for elbow, forearm rotation, and wrist. Safety outcomes included all adverse events and decrease in muscle strength of the bilateral upper limb at 6-month follow-up.

Quality assessment / Risk of bias analysis: The risk of bias for included RCTs was evaluated using the Cochrane Collaboration tool, including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. Each bias criterion was classified as "low", "high", or "unclear". The risk of bias for the included non-randomized study was assessed using the Methodological Index for Non-randomized Studies (MINORS). MINORS contained 12 items relating to potential areas of bias. Each item scored from 0 to 2, resulting in overall scores ranging from 0 to 24. Two investigators assessed the quality of the studies independently. Discrepancies were resolved by consensus or by another independent investigator.

Strategy of data synthesis: We used STATA software 12.0 (STATA Corp., College Station, Texas, USA) for the statistical analysis. The Meta-Analyses were based on random-effects models. Weighted mean difference (WMD) and 95% confidence interval (CI) were calculated for continuous outcomes. Risk ratio (RR) and 95% CI were calculated for dichotomous outcomes. Heterogeneity was assessed with Cochrane's Q test and I2. Sensitivity analysis was also performed to explore the stability of the consolidated results. For all the analyses, two-tailed tests were performed, and $P < 0.05$ was considered to be statistically significant.

Subgroup analysis: NA.

Sensitivity analysis: Sensitivity analysis was also performed to explore the stability of the consolidated results.

Language: English.

Country(ies) involved: China.

Keywords: C7; Cerebral injury; Meta analysis; Nerve Transfer; Spastic paralysis.

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