# **INPLASY PROTOCOL**

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**Conflicts of interest:** None declared.

## **Systematic Review of Spinal Glial Tumors**

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Review question / Objective: Does the extent of resection of intramedullary spinal cord astrocytomas affect oncologic and neurologic outcomes?

Condition being studied: Intramedullary spinal cord tumors, which are a class of tumors arising from the cells from within the spinal cord.

Study designs to be included: Randomized clinical trials, clinical and observational studies, and case series with available abstracts and published as full-scale original articles, brief reports in peer-reviewed academic journals or descriptive publications on surgical techniques with no restriction on language or time of publication.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 April 2023 and was last updated on 25 April 2023 (registration number INPLASY202340085).

### INTRODUCTION

Review question / Objective: Does the extent of resection of intramedullary spinal cord astrocytomas affect oncologic and neurologic outcomes?

Rationale: Although intramedullary spinal cord tumors (IMSCTs) comprise a relatively small proportion of spinal cord tumors (2-5%), they possess significant treatment dilemmas. A majority of IMSCTs are gliomas, which are subdivided into astrocytomas and ependymomas. Ependymomas are the most common IMSCT in adults whereas astrocytomas are the most common in children. While gross total resection (GTR) is possible in most low grade intramedullary gliomas, higher grade gliomas are typically only partially resected or biopsied which may lead to more worse outcomes.

Ependymomas typically have more welldefined borders and GTR is possible in up to 90% of cases. However, GTR of astrocytomas pose a greater challenge. The margins of astrocytomas, particularly those of high grade, are ill-defined often leading surgeons to only pursue debulking or biopsy. However, it has been observed that GTR of astrocytomas may lead to improved prognosis and better outcomes compared to those only undergoing biopsy alone. We aim to survey and summarize the existing literature by performing a systematic review and meta-analysis of the literature to inform management of IMSCTs and the use of total resection.

Condition being studied: Intramedullary spinal cord tumors, which are a class of tumors arising from the cells from within the spinal cord.

#### **METHODS**

Search strategy: Pubmed MeSH Search Clause: ("Spinal Cord/Surgery" [Mesh] OR "spinal cord"[tiab]) AND ("Neurosurgical Procedures" [Mesh] AND ("Spinal Cord Neoplasms/Surgery"[Mesh] OR "Glioma/ Surgery" [Mesh] OR "Astrocytoma/Surgery" [Mesh] OR "Ependymoma/Surgery" OR Glioma[tiab] OR Astrocytoma[tiab] OR Ependymoma[tiab]).

Other databases will be searched with a similar search strategy. The exact search query will be made available in the publication along with results.

Participant or population: Adult patients (>18) who underwent surgical (biopsy, partial, or gross total resection) of IMSCTs.

Intervention: Total resection of IMSCT.

Comparator: Sub-total resection or biopsy of IMSCT.

Study designs to be included: Randomized clinical trials, clinical and observational studies, and case series with available abstracts and published as full-scale original articles, brief reports in peerreviewed academic journals or descriptive publications on surgical techniques with no restriction on language or time of publication.

Eligibility criteria: Including studies reporting outcomes following surgical resection of intramedullary ependymomas and astrocytomas. Excluding patients with history of previous intramedullary surgery, patients with extramedullary spinal cord tumors, patients with no follow-up data, and studies that did not specify extent of resection.

Information sources: Medline, Embase, Scopus, Cochrane Central, Cinahl, Google Scholar, and PubMed.

Main outcome(s): Primary outcome is overall survival adjusting for follow up time.

Additional outcome(s): Quality of life; Mortality; Need for re-operation; Periprocedural complications.

Data management: Two databases will be created for this study. One database will be for selected studies (study design, sample size, year of publications, PMID, database, etc.) and the second database will be for data extraction with preselected variables.

Quality assessment / Risk of bias analysis: Risk of bias will be determined at the study level:

- Should there be randomized control trials, we plan on employing the Risk of Bias in randomized trials (RoB 2) tool.12
- For observational studies we plan on employing the Risk Of Bias in Nonrandomized Studies - of Interventions (ROBINS I) tool
- In case series it will be noted if greater than 50% of cases were treated primarily by surgical versus non-surgical treatment to note potential treatment bias.
- It will be noted if the study is missing primary outcome data on all or greater than 50% patients included.
- In any study competing interests in each study will be noted if any author had ties to industry, particularly those funded by an industry sponsor, have the potential for bias in favor of the sponsor's product or if such information was not disclosed.
- Studies will be assessed on quality based on compliance to EQUATOR network guidelines.

We plan on using a funnel plot using Egger tests to assess the possibility of publication bias.

Strategy of data synthesis: Given the rare nature of this condition and expected low reports in the literature, we plan on including data from observational studies and case series for data extraction and data synthesis.

We expect variability in patient selection among the included studies and several uncontrolled variables. Therefore, we plan on using a random-effect model to perform a proportional meta-analysis. We plan on using an inconsistency index (I2) to assess for heterogeneity and significance will be assumed if and significance was assumed when  $I^2$  was >50%.

Subgroup analysis: We plan on exploratory subgroup analysis by tumor type.

Sensitivity analysis: We plan on sensitivity analysis by introducing variations in the between-group variance. Depending on individual study contributions to the overall effect size, sensitivity analysis will also be preformed by leave-one-out method.

Language restriction: English only.

Country(ies) involved: United States of America.

Keywords: intramedullary tumors; spinal cord tumor; Spinal Astrocytoma; Spinal Ependymoma; Spinal Glioma.

Dissemination plans: We plan to submit the results from our study to a peer review journal with the possibility of a pre-print access. The manuscript will follow PRISMA reporting guidelines.

#### Contributions of each author:

Author 1 - Dagoberto Estevez-Ordonez -Study design, data analysis, guarantors of review, independent screening, and oversight of design, review, and supervision.

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