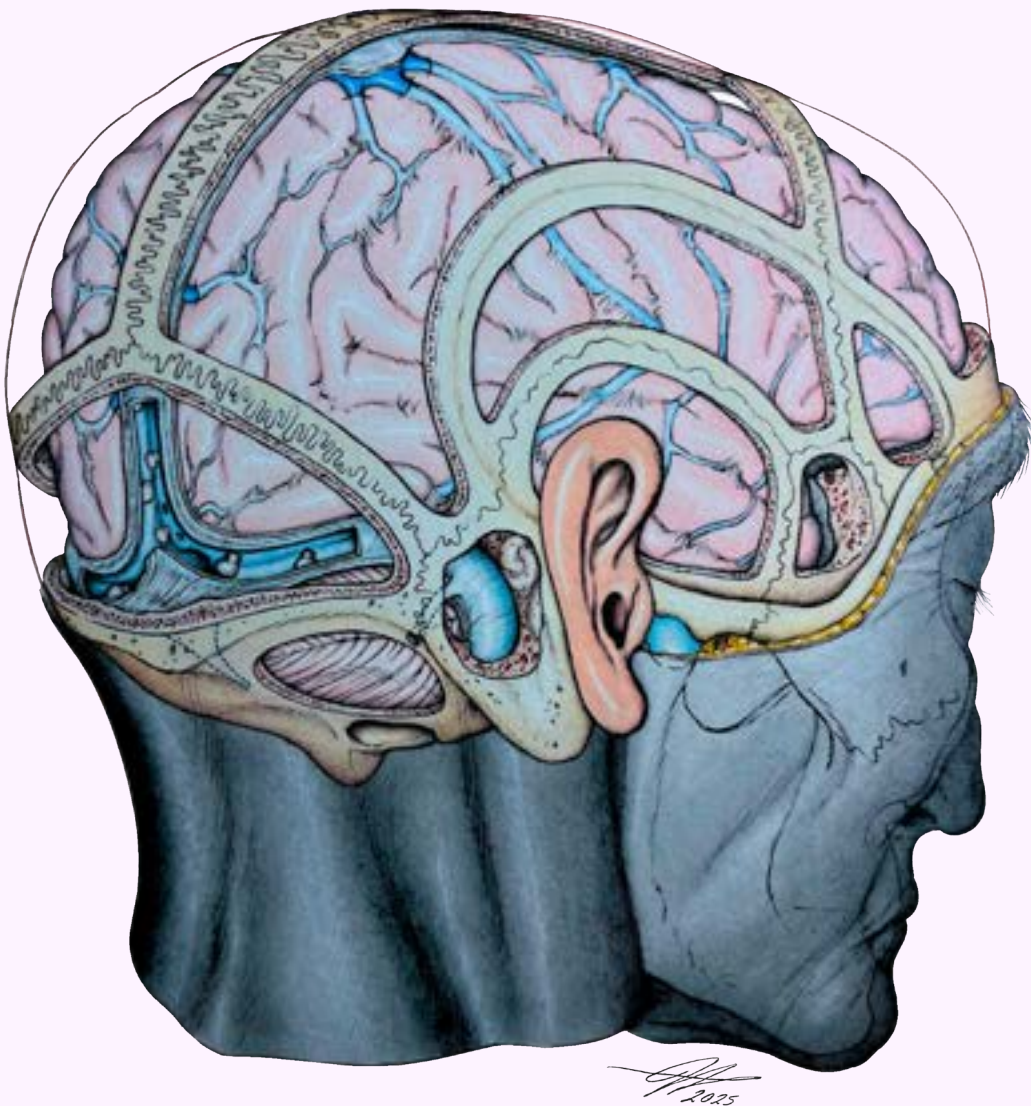


# JBNC

JORNAL BRASILEIRO DE NEUROCIRURGIA  
BRAZILIAN JOURNAL OF NEUROSURGERY



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# JBNC

Brazilian Journal of Neurosurgery

## Jornal Brasileiro de Neurocirurgia

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The editorial board's role is more focused on giving advice on strategic journal development matters, its members might be requested to assist both the executive and scientific editors, should their expertise in their respective academic fields be required. This can involve:

Advising on specific submissions, contributing to discussions on content areas, and providing insights that help maintain the journal's academic rigor. Provide operational support to the executive editor in implementing policies and procedures, or assisting the scientific editor in overseeing the scientific quality and integrity of the journal.

Assist in strategic planning and development of the journal by evaluating and recommending best practices, organizing and suggesting calls for special or thematic issues, while ensuring that the journal's direction aligns with current trends and needs in the field.



## INSTRUCTIONS FOR AUTHORS

### 01. MISSION AND SCOPE

The Brazilian Journal of Neurosurgery – JBNC (ISSN print 0103-5118, ISSN online 2446-6786) is an online journal published by the Academia Brasileira de Neurocirurgia. The journal is fully open access, peer reviewed and accepts submissions written in English, Portuguese, or Spanish. Accepted contributions are published in a quarterly issue-based model with four issues per year, and licensed under the Creative Commons Attribution 4.0 International (CC BY 4.0) license. JBNC does not charge submission or publication fees.

#### Open Access Policy

The Jornal Brasileiro de Neurocirurgia (Brazilian Journal of Neurosurgery) is a peer-reviewed open-access journal, which means that all content is freely available without charge to the user or his/her institution.

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#### SECTION SPECIFIC REQUIREMENTS

Submissions must follow the limits and specific requirements outlined on the table below, according to their section.

Section	Abstract	Text sections	Text length	Tables & Figures	References (max)
Original article	structured not exceeding 200 word	introduction, methods, results, discussion, conclusion and references	4000 words	10	75
Review (preferably systematic review)	non-structured not exceeding 200 words	introduction, method, results, discussion, conclusion and references	4000 words	10	75
Case Report (preferably with systematic rev <<	non-structured not exceeding 200 words	introduction (with brief literature review), clinical case presentation, discussion, final comments and references	3500 words	8	45
Brief Note	non-structured not exceeding 200 words	no requirement	1500 words	3	30
Clinical Images	non-structured not exceeding 200 words	no requirement	1500 words	5	30

#### INTRODUCTION

In the Introduction section we state the motivation for the work presented in the manuscript. Its contents could be: 1) context (to orient readers who are less familiar with the topic and to establish the importance of the manuscript),

2) need (to state the need for the work, as an opposition between what the scientific community currently has and what it wants), 3) task (to indicate what was done in the effort to address the need), and 4) object of the document (to prepare the readers for its structure).

## **CLINICAL CASE PRESENTATION**

Patient's clinical data in comprehensive account of the presenting features, with medical, and social, family history, if needed are presented. All crucial investigations to the management of decisions should be discussed. Images of the case: Choose appropriate images being aware of removing any detail that can identify the patient. If relevant, describe the treatment or surgery. Outcomes and follow-up are described elsewhere.

## **METHODS**

In Materials and Methods section, the technical specifications and quantities and source or method of preparation are described. Attention to the use only scientific names of drugs; inclusion of the manufacturer in brackets when describing equipment. Discuss statistical methods if needed.

## **RESULTS**

In Results section, the results of the paper are presented in logical order, using tables and graphs as necessary. Remember that results must be presented and then explained. The results are explained showing how they help to answer the research questions (already cited in the Introduction section).

## **DISCUSSION**

In Discussion section, the principles, relationships and generalizations shown by the results are presented. Also, exceptions or lack of correlations are pointed out. The authors show how their results agree or disagree with previously published papers, and discuss the theoretical implications as well as practical applications of the paper, and the significance of their results.

## **CONCLUSIONS**

In Conclusions section the most important outcome of the work is stated, and interpretation of the findings also. If the authors have succeeded, or not, in addressing the need stated in the Introduction is reported here.

## **PRODUCT NAMES**

If any product is cited in the manuscript the usage of ® or ™, and manufacturer data are mandatory. Use only scientific names of drugs. Include the manufacturer in brackets when describing equipment.

## **UNITS OF MEASUREMENT**

Units of measurements should follow the primary language used (Portuguese/Spanish or English).



## ABBREVIATIONS AND SYMBOLS

Abbreviations should follow the first mention of the term in the manuscript. The list of abbreviations is waived.

## FOOTNOTES

Footnotes are used only in Tables/Boxes

## 03. USE OF COLORS

Although the use of color is permitted, it is important that authors (or professionals hired for editing) make an effort to ensure that the use of color does not impair understanding for readers with some form of visual impairment. We recommend consulting the following resources before preparing figures or tables using colors:

- [How to make scientific figures accessible to readers with color-blindness](#) (2019, Science News, The American Society for Cell Biology)
- Wong, B. Points of view: Color blindness. Nat Methods 8, 441 (2011).  
<https://doi.org/10.1038/nmeth.1618>

## 04. FIGURES PREPARATION GUIDELINES

Graphs, photographs, diagrams, illustrations, and similar content should be referred to as figures (e.g., Figure 1, Figure 2, Figures 1, 2, 5-7) in ascending order according to their appearance in the text. Authors are strongly advised to adhere to the guidelines specified in the 'Use of Colors' and 'Preparation and Manipulation of Figures' sections below, in line with the [International Committee of Medical Journal Editors \(ICMJE\)](#) recommendations.

When using arrows, symbols, letters, or numbers to highlight specific parts of the figures, authors must clearly describe their purpose in the corresponding figure caption. Additionally, in compliance with privacy concerns and [ICMJE recommendations for the protection of research participants](#), images containing photographs of people must ensure that individuals cannot be identified unless their explicit permission for publication has been obtained. This ensures the protection of individual privacy and aligns with ethical standards in scholarly publication.

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- "What's in a picture? The temptation of image manipulation" (Mike Rossner, Kenneth M. Yamada. J Cell Biol 5 July 2004; 166 (1): 11–15. doi: <https://doi.org/10.1083/jcb.200406019>).
- Digital Images and Misconduct. (Council of Science Editors, White Paper on Publication Ethics)
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Never build tables using spaces or tabs. Tables and Boxes must be created using the text editor built-in table creation tool and follow the following guidelines:

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Every table must include an indication of the source and citations whenever relevant, and authors are responsible for obtaining the correct authorization for use (or adaptation of data) from other sources, as appropriate, directly from the copyright owner.

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References should adhere to the **Vancouver system**. List all references in consecutive order as they appear in the text. For publications with up to six authors, list all authors. For publications with more than six authors, list the first six followed by 'et al.'. Whenever available insert the PMIDs (PubMed identifier) and the full DOI URL (e.g., [https://doi.org/\[...\]](https://doi.org/[...])). Personal communications should not be included in the references list but may be mentioned in the text.

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- **Tables:** Make sure your tables are editable and designed using your text editor table tool.
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Please review each of these components carefully to ensure compliance with our standards. Complete and accurate submission of these documents is essential for the effective handling of your manuscript.

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As part of your submission to the Brazilian Journal of Neurosurgery (JBNC), you are required to upload various files. Each file serves a specific purpose in the submission and review process. Please refer to the table below for a detailed overview of the required files, their designations, filenames, and the necessity of each file.

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Original figure	figure1.jpg, figure2.jpg etc.	Yes, if images are used.
Disclosure forms	disclosurefiles.zip	Yes.
License agreement	agreement.pdf	Yes.
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Revision comments file	revisioncomments.pdf	Yes, when sending the revised version of your manuscript.

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The title page is a critical component of your submission and should include the following information, organized clearly and in order:

- **Submission Type (in English):** Indicate the manuscript type as per JBNC section policies.
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The cover letter should introduce your manuscript and explain its importance to the field of neurosurgery. It must include a declaration that the work is original, has not been published elsewhere, and is not under consideration by any other journal. The letter should briefly outline the major findings of your study and how they contribute to the existing knowledge. Additionally, any potential conflicts of interest or important points not covered in the manuscript or in other submission files should be disclosed. The cover letter is also an opportunity to suggest preferred or opposed reviewers and to provide any other information that may assist the editorial process.

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- Keywords and Palavras-chave/Palabras-clave
- Full text and references

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# Machine Learning Models for Six-Month Mortality Prediction After Ischemic Stroke: insights from the International Stroke Trial

*Modelos de Aprendizado de Máquina para Predição de Mortalidade em Seis Meses Após Acidente Vascular Cerebral Isquêmico: insights do International Stroke Trial*

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## ABSTRACT

**Introduction:** Accurate prediction of post-stroke mortality is essential for guiding treatment and resource allocation. Machine learning approaches may improve prognostic accuracy using routine admission data. **Objective:** To compare the performance of different ML algorithms, evaluate model discrimination and calibration, and assess the prognostic importance of key baseline variables in predicting six-month mortality after ischemic stroke. **Methods:** We analyzed 12,936 patients from the International Stroke Trial using nineteen baseline clinical variables. Seven supervised ML algorithms—logistic regression, SGD, SVM, MLP, random forest, gradient boosting, and XGBoost—were trained with and without resampling techniques (SMOTE, ADASYN, Tomek Links, ENN, hybrids). Nested cross-validation ensured unbiased evaluation using AUC-ROC, AUC-PR, calibration, and clinical metrics. **Results:** Logistic regression and SGD achieved the best performance (AUC-ROC  $\approx 0.76$ - $0.77$ ) with strong calibration and negative predictive value  $>92\%$ . Complex models showed no systematic advantage. Resampling strategies did not improve performance. SHAP analysis confirmed age, consciousness, and stroke subtype as dominant predictors. **Conclusion:** Parsimonious linear models provide robust and interpretable prediction of six-month mortality after ischemic stroke, supporting clinical decision-making. External validation and recalibration in contemporary cohorts remain essential.

**Keywords:** Stroke; Brain ischemia; Prognosis; Machine learning; Logistic models

## RESUMO

**Introdução:** A predição acurada da mortalidade pós-AVC orienta condutas clínicas e alocação de recursos. Modelos de aprendizado de máquina (ML) podem aprimorar o prognóstico usando dados clínicos rotineiros da admissão. **Objetivo:** Comparar o desempenho de diferentes algoritmos de ML, avaliar discriminação e calibração dos modelos, e determinar a importância das principais variáveis na previsão da mortalidade a seis meses após AVCi. **Métodos:** Analisaram-se 12.936 pacientes do International Stroke Trial (IST). Dezenove variáveis basais (demografia, consciência, subtipo de AVC, déficits neurológicos, fibrilação atrial e tratamentos precoces) foram incluídas. Sete algoritmos supervisionados — regressão logística, SGD, SVM, MLP, random forest, gradient boosting e XGBoost — foram treinados com e sem reamostragem (SMOTE, ADASYN, Tomek Links, ENN). Validação cruzada aninhada garantiu avaliação imparcial. **Resultados:** Regressão logística e SGD apresentaram melhor desempenho (AUC-ROC  $\approx 0,76$ - $0,77$ ), com valor preditivo negativo  $>92\%$ . Modelos complexos não mostraram vantagem consistente. A análise SHAP confirmou idade, consciência e subtipo de AVC como principais preditores. **Conclusão:** Modelos lineares parcimoniosos oferecem predição robusta e interpretável da mortalidade pós-AVC, com potencial apoio clínico.

**Palavras-Chave:** AVC; Isquemia cerebral; Prognóstico; Aprendizagem automática; Modelos logísticos

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## INTRODUCTION

Stroke remains the second leading cause of death worldwide, accounting for an estimated 7.3 million deaths (10.7% of all deaths) in 2021, and it continues to be a major contributor to long-term disability and global health burden. Beyond its clinical impact, stroke imposes substantial economic and social costs, particularly in low- and middle-income countries where access to specialized care and rehabilitation services is limited. Despite advances in acute management and rehabilitation, the ability to predict medium-term mortality—particularly at six months—remains limited. Reliable prognostic estimates at this stage are essential for guiding clinical decisions, tailoring rehabilitation strategies, allocating healthcare resources, and supporting informed communication with patients and families<sup>1</sup>.

Among historical cohorts, the International Stroke Trial (IST) stands out as one of the largest randomized controlled trials in acute ischemic stroke, conducted prior to the widespread adoption of reperfusion therapies. The trial enrolled 19,435 patients, evaluated the effects of aspirin and heparin, and systematically reported outcomes at both 14 days and six months (death or dependency, with vital status available). Importantly, IST collected only readily available baseline clinical variables—such as age, level of consciousness, blood pressure, atrial fibrillation, and neurological deficits—making it a uniquely valuable resource for prognostic modeling in both high- and low-resource settings<sup>2</sup>.

In recent years, machine learning (ML) approaches have gained increasing attention in stroke outcome prediction, given their ability to capture complex, non-linear interactions among clinical variables. For example, Guo et al.<sup>3</sup> applied interpretable ML techniques—including support vector machines with SHAP analysis and logistic regression nomograms—to predict functional outcomes after acute cerebral infarction. Similarly, Hwangbo et al.<sup>4</sup> developed a stacking ensemble model using IST data, achieving an AUROC of 0.783 (95% CI 0.758-0.808) for six-month mortality prediction. Systematic reviews and meta-analyses further suggest that, while certain ML models can outperform conventional prognostic scores in specific contexts, issues such as risk of bias, overfitting, and limited external generalizability continue to hinder broad clinical adoption<sup>5</sup>.

From this background, we sought to leverage the IST data set to develop and validate ML models for predicting six-month mortality in ischemic stroke patients. By restricting predictors to baseline clinical variables available at randomization, our aim was to construct models that are not only accurate but also clinically realistic and broadly applicable, including in resource-constrained environments. Our objectives were threefold: (i) compare the performance of different ML algorithms; (ii) evaluate model discrimination and calibration; and (iii) assess the relative prognostic importance of key baseline variables.

## METHODS

*Data source and preprocessing*

We used data from the International Stroke Trial (IST), a large multicenter randomized controlled trial that enrolled 19,435 patients with acute ischemic stroke<sup>2</sup>. The trial primarily evaluated the effects of aspirin and subcutaneous heparin on early outcomes, but systematically recorded follow-up at both 14 days and six months, including mortality and dependency. For the present study, the outcome of interest was all-cause mortality at six months (FDEAD). Patients with missing outcome values or predictors were removed during data cleaning.

Nineteen routinely available baseline variables were selected as predictors: age, sex, level of consciousness (RCONSC), systolic blood pressure (RSBP), atrial fibrillation (RATRIAL), stroke subtype (STYPE: TACS, PACS, POCS, LACS), eight neurological deficits (RDEF1-RDEF8: face, arm, leg, dysphasia, hemianopia, visuospatial disorder, brainstem/cerebellar signs, and other deficits), symptoms on waking (RSLEEP), use of heparin within 24h (RHEP24), aspirin within 3 days (RASP3), visible infarct on CT (RVISINF), and delay from stroke onset to randomization (RDELAY). Invalid categories (e.g., STYPE=Other, RDEF=C, RCONSC values outside {F,D,U}, or FDEAD=U) were excluded. Continuous variables were scaled using RobustScaler to reduce the effect of outliers, and categorical variables were one-hot encoded.

*Machine learning models*

We evaluated seven supervised learning algorithms: Logistic Regression<sup>6</sup>, Random Forest<sup>7</sup>, Support Vector Machine (SVM) with RBF kernel<sup>8</sup>, XGBoost<sup>9</sup>, Gradient Boosting<sup>10</sup>, Multilayer

Perceptron (MLP)<sup>11</sup>, and Linear SVM implemented with SGDClassifier (scikit-learn)<sup>12</sup>.

Given the class imbalance ( $\approx 15\%$  mortality), we applied several resampling strategies: SMOTE<sup>13</sup>, ADASYN<sup>14</sup>, Tomek Links<sup>15</sup>, Edited Nearest Neighbors (ENN)<sup>16</sup>, and hybrid approaches (SMOTE+Tomek, SMOTEENN)<sup>17</sup>, all using the imbalanced-learn library<sup>18</sup>. For algorithms supporting it, we also applied `class_weight="balanced"` when resampling was not used.

### *Validation and calibration*

Model evaluation employed nested cross-validation: a 5-fold stratified outer loop to estimate generalization and a 3-fold inner loop for threshold optimization. Within each outer training set, predicted probabilities were calibrated using CalibratedClassifierCV with sigmoid (Platt) scaling (with isotonic calibration available in sensitivity analyses). The decision threshold was selected using the Youden index<sup>19</sup> applied to calibrated probabilities in the inner folds. Final evaluation was then performed on the untouched outer test fold, ensuring no information leakage.

### *Performance metrics*

We assessed performance using the area under the receiver operating characteristic curve (AUC-ROC), the area under the precision-recall curve (AUC-PR), overall accuracy, sensitivity (recall), specificity, positive predictive value (precision), negative predictive value (NPV), F1-score, and balanced accuracy. Receiver operating characteristic (ROC) and precision-recall (PR) curves were generated for each model and resampling strategy, and comparative plots were used to summarize performance across algorithms.

### *Model interpretability*

We applied SHAP (SHapley Additive exPlanations)<sup>20</sup> to evaluate variable importance. TreeExplainer was used for tree-based models, LinearExplainer for linear models, and KernelExplainer for others. SHAP values were averaged across outer folds to avoid overfitting and reduce variance. Feature importance was ranked using mean absolute SHAP values, and summary plots highlighted the top 20 predictors for each algorithm.

All analyses were conducted in Python (v3.12.2), using scikit-learn (v1.3.0), imbalanced-learn (v0.12.3), XGBoost, and SHAP.

A random seed of 42 ensured reproducibility. Model comparisons were based on mean performance across cross-validation folds.

## RESULTS

### *Baseline characteristics and univariate associations with six-month mortality*

The final analytic data set for prediction contained 12,936 patients (10,934 survivors; 2,002 deaths) (Table 1). 43 patients had uncertain six-month outcomes and were excluded from all modeling analyses.

Age was associated with mortality: non-survivors were older than survivors (mean  $76.9 \pm 9.2$  vs.  $69.4 \pm 11.7$  years). In contrast, systolic blood pressure and time to randomization showed only modest between-group differences.

For categorical variables, we report category-specific mortality rates (deaths divided by the total in that category), rather than the proportion of each category among survivors or non-survivors.

### *Consciousness at admission*

- Fully alert: 12.4% mortality (1,422/11,440)  $\rightarrow$  87.6% survival
- Drowsy: 38.0% (561/1,475)
- Unconscious: 90.5% (19/21) Mortality rose steeply with reduced consciousness.

### *Stroke subtype*

- Total anterior circulation (TACS): 35.3% (502/1,422)
- Partial anterior circulation (PACS): 16.0% (879/5,496)
- Posterior circulation (POCS): 11.5% (191/1,658)
- Lacunar (LACS): 9.9% (430/4,360) TACS showed the highest mortality; LACS the lowest.

### *Sex*

- Female: 17.0% (966/5,684)
- Male: 14.3% (1,036/7,252)

**Table 1.** Baseline characteristics and six-month mortality (analytic cohort, n = 12,936).

Variable	Survivors (n = 10,934)	Deaths (n = 2,002)	Total (n = 12,936)
Age (years)	69.4 ± 11.7	76.9 ± 9.2	70.8 ± 11.8
Systolic blood pressure (mmHg)	160.9 ± 27.3	158.7 ± 28.5	160.5 ± 27.6
Delay to randomization (hours)	20.9 ± 12.4	19.4 ± 12.4	20.6 ± 12.4
Conscious state: Fully alert (F)	10018 (91.6%)	1422 (71.0%)	11440 (88.4%)
Conscious state: Drowsy (D)	914 (8.4%)	561 (28.0%)	1475 (11.4%)
Conscious state: Unconscious (U)	2 (0.0%)	19 (0.9%)	21 (0.2%)
Stroke subtype: Lacunar syndrome (LACS)	3930 (35.9%)	430 (21.5%)	4360 (33.7%)
Stroke subtype: Partial anterior circulation (PACS)	4617 (42.2%)	879 (43.9%)	5496 (42.5%)
Stroke subtype: Posterior circulation (POCS)	1467 (13.4%)	191 (9.5%)	1658 (12.8%)
Stroke subtype: Total anterior circulation (TACS)	920 (8.4%)	502 (25.1%)	1422 (11.0%)
Sex: Female	4718 (43.1%)	966 (48.2%)	5684 (43.9%)
Sex: Male	6216 (56.9%)	1036 (51.8%)	7252 (56.1%)
Symptoms on waking: No	7577 (69.3%)	1416 (70.7%)	8993 (69.5%)
Symptoms on waking: Yes	3357 (30.7%)	586 (29.3%)	3943 (30.5%)
Atrial fibrillation: No	9659 (88.4%)	1462 (73.0%)	11121 (86.0%)
Atrial fibrillation: Yes	1275 (11.7%)	540 (27.0%)	1815 (14.0%)
Visible infarct on CT: No	7726 (70.7%)	1298 (64.8%)	9024 (69.8%)
Visible infarct on CT: Yes	3208 (29.3%)	704 (35.2%)	3912 (30.2%)
Heparin within 24h: No	10675 (97.6%)	1951 (97.5%)	12626 (97.6%)
Heparin within 24h: Yes	259 (2.4%)	51 (2.5%)	310 (2.4%)
Aspirin within 3 days: No	8619 (78.9%)	1569 (78.3%)	10188 (78.8%)
Aspirin within 3 days: Yes	2315 (21.2%)	433 (21.6%)	2748 (21.2%)
Face deficit: No	3482 (31.9%)	390 (19.5%)	3872 (29.9%)
Face deficit: Yes	7452 (68.1%)	1612 (80.5%)	9064 (70.1%)
Arm deficit: No	1830 (16.7%)	189 (9.4%)	2019 (15.6%)
Arm deficit: Yes	9104 (83.3%)	1813 (90.6%)	10917 (84.4%)
Leg deficit: No	3122 (28.6%)	332 (16.6%)	3454 (26.7%)
Leg deficit: Yes	7812 (71.4%)	1670 (83.4%)	9482 (73.3%)
Dysphasia: No	7236 (66.2%)	1072 (53.5%)	8308 (64.2%)
Dysphasia: Yes	3698 (33.8%)	930 (46.5%)	4628 (35.8%)
Hemianopia: No	9407 (86.0%)	1366 (68.2%)	10773 (83.3%)
Hemianopia: Yes	1527 (14.0%)	636 (31.8%)	2163 (16.7%)
Visuospatial disorder: No	9510 (87.0%)	1431 (71.5%)	10941 (84.6%)
Visuospatial disorder: Yes	1424 (13.0%)	571 (28.5%)	1995 (15.4%)
Brainstem/cerebellar signs: No	9548 (87.4%)	1813 (90.5%)	11361 (87.8%)
Brainstem/cerebellar signs: Yes	1386 (12.7%)	189 (9.4%)	1575 (12.2%)
Other neurological deficit: No	10328 (94.5%)	1861 (92.9%)	12189 (94.2%)
Other neurological deficit: Yes	606 (5.5%)	141 (7.0%)	747 (5.8%)

Values are n (column %), unless otherwise indicated; column % for Survivors and Deaths use denominators 10,934 and 2,002, respectively; total % use 12,936; Percentages may not sum to 100% due to rounding.

*Atrial fibrillation*

- Present: 29.8% (540/1,815)
- Absent: 13.1% (1,462/11,121)

*Visible infarct on CT*

- Present: 18.0% (704/3,912)
- Absent: 14.4% (1,298/9,024)

*Neurological deficits*

- Hemianopia: 29.4% (636/2,163) vs. none: 12.7% (1,366/10,773)
- Visuospatial disorder: 28.6% (571/1,995) vs. none: 13.1% (1,431/10,941)
- Dysphasia: 20.1% (930/4,628) vs. none: 12.9% (1,072/8,308)
- Leg weakness: 17.6% (1,670/9,482) vs. none: 9.6% (332/3,454)
- Arm weakness: 16.6% (1,813/10,917) vs. none: 9.4% (189/2,019)
- Face weakness: 17.8% (1,612/9,064) vs. none: 10.1% (390/3,872)
- Brainstem/cerebellar signs: 12.0% (189/1,575) vs. none: 16.0% (1,813/11,361)
- Other neurological deficit: 18.9% (141/747) vs. none: 15.3% (1,861/12,189)

*Symptoms on waking*

- Yes: 14.9% (586/3,943)
- No: 15.7% (1,416/8,993)

*Early treatments (observational, not causal)*

- Heparin within 24h: 16.5% (51/310) vs. no heparin: 15.5% (1,951/12,626)
- Aspirin within 3 days: 15.8% (433/2,748) vs. no aspirin: 15.4% (1,569/10,188)

Overall, age, level of consciousness, stroke subtype, atrial fibrillation, and several focal deficits (e.g., hemianopia, visuospatial disorder, dysphasia, limb weakness) displayed the strongest univariate associations with six-month mortality. Blood pressure, symptoms on waking, and early antithrombotic exposure showed comparatively small differences.

*Machine learning model performance*

To evaluate predictive performance for six-month mortality, we compared seven algorithms—logistic regression, random forest, support vector machine (SVM), stochastic gradient descent (SGD), XGBoost, gradient boosting, and multilayer perceptron (MLP)—across multiple resampling strategies (no resampling, SMOTE, ADASYN, Tomek Links, SMOTE+Tomek, SMOTEENN, ENN). Performance was assessed using nested cross-validation, reporting accuracy, sensitivity, specificity, precision, negative predictive value (NPV), F1-score, area under the ROC curve (AUC-ROC), and area under the precision-recall curve (AUC-PR).

*Overall algorithm performance*

Overall, logistic regression and SGD consistently demonstrated the most stable and balanced results across sampling strategies, with AUC-ROC values around 0.76-0.77 (Table 2, Figures 1 and 2). For example, logistic regression achieved an AUC-ROC of 0.768 without resampling and 0.768 with Tomek Links, highlighting robustness to class-imbalance handling. Similarly, SGD showed AUC-ROC values of 0.766 (no resampling), 0.763 (SMOTE), and 0.766 (SMOTEENN). SVM generally achieved AUC-ROC values around 0.70-0.76; however, under Tomek Links, performance dropped (AUC-ROC  $\approx$  0.695) with notably lower sensitivity ( $\approx$  0.52), despite higher specificity.

ROC curves (Figure 3) showed overlapping confidence intervals across top-performing models, with logistic regression maintaining consistent discrimination. PR curves (Figure 4) indicated that linear models (logistic regression, SGD) generally maintained stronger performance in the high-precision region, a clinically relevant operating range.

Gradient boosting also showed competitive performance, with AUC-ROC ranging between 0.736 and 0.766, particularly effective when combined with ENN (AUC-ROC = 0.766) or without resampling (0.765). MLP showed variable performance depending on resampling strategy, performing best without resampling or with ENN/Tomek Links (AUC-ROC  $\approx$  0.76), but substantially reduced performance with SMOTE and related techniques.

In contrast, tree-based methods displayed lower performance and greater variability. Random forest consistently underperformed, with AUC-ROC values between 0.716 and 0.736, regardless of resampling. XGBoost achieved moderate results, performing best with ENN, no resampling, or Tomek Links (AUC-ROC  $\approx$  0.76).

**Table 2.** Performance of machine learning models for predicting six-month mortality (FDEAD) under different resampling strategies.

Algorithm	Resampling	Accuracy	Sensitivity (Recall)	Specificity	PPV (Precision)	NPV	F1-Score	AUC-ROC	AUC-PR	Balanced Accuracy
Gradient Boosting	ADASYN	0.695 ± 0.015	0.641 ± 0.024	0.704 ± 0.021	0.284 ± 0.008	0.915 ± 0.003	0.394 ± 0.006	0.736 ± 0.007	0.357 ± 0.014	0.673 ± 0.005
Gradient Boosting	ENN	0.713 ± 0.025	0.668 ± 0.033	0.722 ± 0.034	0.306 ± 0.019	0.922 ± 0.005	0.419 ± 0.017	0.766 ± 0.012	0.406 ± 0.020	0.695 ± 0.013
Gradient Boosting	None	0.705 ± 0.023	0.677 ± 0.027	0.710 ± 0.031	0.300 ± 0.018	0.923 ± 0.004	0.415 ± 0.015	0.765 ± 0.012	0.409 ± 0.017	0.693 ± 0.010
Gradient Boosting	SMOTE	0.688 ± 0.024	0.660 ± 0.030	0.693 ± 0.032	0.283 ± 0.015	0.918 ± 0.004	0.396 ± 0.013	0.743 ± 0.006	0.373 ± 0.015	0.676 ± 0.010
Gradient Boosting	SMOTE+Tomek	0.685 ± 0.033	0.667 ± 0.033	0.688 ± 0.045	0.283 ± 0.020	0.919 ± 0.003	0.397 ± 0.014	0.745 ± 0.008	0.376 ± 0.017	0.677 ± 0.007
Gradient Boosting	SMOTEENN	0.719 ± 0.023	0.635 ± 0.048	0.734 ± 0.035	0.306 ± 0.017	0.917 ± 0.007	0.412 ± 0.010	0.756 ± 0.010	0.391 ± 0.016	0.685 ± 0.011
Gradient Boosting	Tomek Links	0.705 ± 0.037	0.669 ± 0.063	0.711 ± 0.054	0.301 ± 0.027	0.922 ± 0.009	0.413 ± 0.017	0.765 ± 0.013	0.410 ± 0.019	0.690 ± 0.012
Logistic Regression	ADASYN	0.693 ± 0.022	0.699 ± 0.027	0.691 ± 0.029	0.294 ± 0.015	0.926 ± 0.005	0.413 ± 0.014	0.763 ± 0.016	0.413 ± 0.020	0.695 ± 0.011
Logistic Regression	ENN	0.711 ± 0.032	0.667 ± 0.024	0.719 ± 0.041	0.305 ± 0.027	0.922 ± 0.004	0.418 ± 0.023	0.767 ± 0.013	0.410 ± 0.020	0.693 ± 0.015
Logistic Regression	None	0.692 ± 0.027	0.697 ± 0.044	0.691 ± 0.037	0.294 ± 0.019	0.926 ± 0.008	0.413 ± 0.019	0.768 ± 0.014	0.415 ± 0.019	0.694 ± 0.017
Logistic Regression	SMOTE	0.699 ± 0.015	0.692 ± 0.031	0.700 ± 0.020	0.297 ± 0.012	0.926 ± 0.006	0.416 ± 0.014	0.765 ± 0.015	0.415 ± 0.020	0.696 ± 0.013
Logistic Regression	SMOTE+Tomek	0.699 ± 0.014	0.694 ± 0.033	0.700 ± 0.020	0.298 ± 0.012	0.926 ± 0.007	0.417 ± 0.014	0.765 ± 0.015	0.414 ± 0.021	0.697 ± 0.014
Logistic Regression	SMOTEENN	0.699 ± 0.025	0.691 ± 0.055	0.701 ± 0.037	0.298 ± 0.016	0.926 ± 0.010	0.416 ± 0.017	0.767 ± 0.015	0.412 ± 0.021	0.696 ± 0.017
Logistic Regression	Tomek Links	0.700 ± 0.031	0.691 ± 0.013	0.702 ± 0.038	0.300 ± 0.025	0.925 ± 0.003	0.418 ± 0.024	0.768 ± 0.014	0.415 ± 0.019	0.697 ± 0.017
MLP	ADASYN	0.600 ± 0.056	0.641 ± 0.047	0.593 ± 0.073	0.226 ± 0.022	0.900 ± 0.006	0.333 ± 0.019	0.670 ± 0.018	0.302 ± 0.011	0.617 ± 0.019
MLP	ENN	0.698 ± 0.024	0.688 ± 0.016	0.700 ± 0.029	0.297 ± 0.019	0.925 ± 0.004	0.415 ± 0.019	0.765 ± 0.014	0.403 ± 0.024	0.694 ± 0.014
MLP	None	0.698 ± 0.022	0.679 ± 0.030	0.702 ± 0.030	0.295 ± 0.015	0.923 ± 0.005	0.411 ± 0.013	0.763 ± 0.010	0.404 ± 0.010	0.690 ± 0.010
MLP	SMOTE	0.544 ± 0.022	0.720 ± 0.043	0.512 ± 0.033	0.213 ± 0.007	0.909 ± 0.009	0.328 ± 0.009	0.681 ± 0.016	0.316 ± 0.013	0.616 ± 0.012
MLP	SMOTE+Tomek	0.582 ± 0.050	0.663 ± 0.068	0.567 ± 0.071	0.220 ± 0.013	0.902 ± 0.007	0.330 ± 0.008	0.676 ± 0.014	0.305 ± 0.015	0.615 ± 0.007



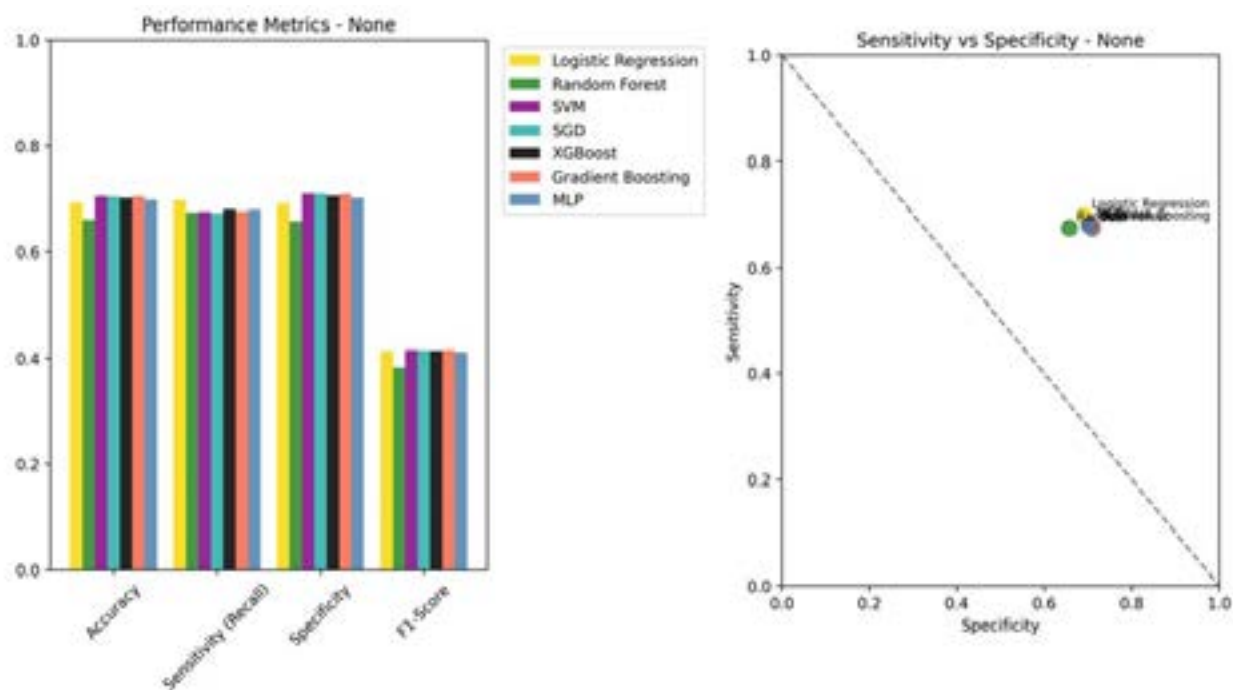
Table 2. Continued...

Algorithm	Resampling	Accuracy	Sensitivity (Recall)	Specificity	PPV (Precision)	NPV	F1-Score	AUC-ROC	AUC-PR	Balanced Accuracy
MLP	SMOTEENN	0.683 ± 0.075	0.596 ± 0.112	0.699 ± 0.108	0.274 ± 0.033	0.906 ± 0.012	0.369 ± 0.021	0.711 ± 0.011	0.345 ± 0.019	0.647 ± 0.018
MLP	Tomek Links	0.700 ± 0.030	0.688 ± 0.045	0.702 ± 0.041	0.298 ± 0.021	0.925 ± 0.007	0.415 ± 0.019	0.766 ± 0.012	0.406 ± 0.018	0.695 ± 0.015
Random Forest	ADASYN	0.640 ± 0.039	0.685 ± 0.065	0.632 ± 0.058	0.256 ± 0.014	0.917 ± 0.009	0.371 ± 0.008	0.716 ± 0.010	0.322 ± 0.018	0.658 ± 0.008
Random Forest	ENN	0.705 ± 0.026	0.634 ± 0.021	0.718 ± 0.034	0.293 ± 0.020	0.915 ± 0.004	0.400 ± 0.018	0.736 ± 0.013	0.370 ± 0.025	0.676 ± 0.013
Random Forest	None	0.660 ± 0.035	0.674 ± 0.032	0.658 ± 0.046	0.267 ± 0.019	0.917 ± 0.003	0.381 ± 0.015	0.728 ± 0.012	0.350 ± 0.017	0.666 ± 0.009
Random Forest	SMOTE	0.641 ± 0.027	0.689 ± 0.052	0.633 ± 0.041	0.256 ± 0.009	0.918 ± 0.008	0.373 ± 0.008	0.719 ± 0.011	0.326 ± 0.020	0.661 ± 0.009
Random Forest	SMOTE+Tomek	0.624 ± 0.056	0.711 ± 0.059	0.608 ± 0.077	0.252 ± 0.021	0.921 ± 0.007	0.371 ± 0.016	0.721 ± 0.011	0.328 ± 0.016	0.660 ± 0.011
Random Forest	SMOTEENN	0.657 ± 0.023	0.686 ± 0.041	0.652 ± 0.034	0.266 ± 0.008	0.919 ± 0.006	0.383 ± 0.005	0.734 ± 0.009	0.358 ± 0.023	0.669 ± 0.005
Random Forest	Tomek Links	0.664 ± 0.043	0.672 ± 0.053	0.662 ± 0.060	0.270 ± 0.023	0.917 ± 0.006	0.384 ± 0.016	0.730 ± 0.012	0.359 ± 0.014	0.667 ± 0.009
SGD	ADASYN	0.681 ± 0.028	0.701 ± 0.027	0.677 ± 0.037	0.286 ± 0.019	0.925 ± 0.004	0.406 ± 0.016	0.761 ± 0.017	0.411 ± 0.021	0.689 ± 0.011
SGD	ENN	0.728 ± 0.014	0.650 ± 0.021	0.742 ± 0.016	0.317 ± 0.016	0.921 ± 0.005	0.426 ± 0.016	0.765 ± 0.015	0.407 ± 0.023	0.696 ± 0.013
SGD	None	0.705 ± 0.026	0.673 ± 0.031	0.710 ± 0.034	0.300 ± 0.021	0.922 ± 0.005	0.414 ± 0.019	0.766 ± 0.012	0.411 ± 0.017	0.692 ± 0.014
SGD	SMOTE	0.693 ± 0.020	0.699 ± 0.022	0.692 ± 0.024	0.294 ± 0.017	0.926 ± 0.005	0.414 ± 0.018	0.763 ± 0.017	0.414 ± 0.021	0.696 ± 0.015
SGD	SMOTE+Tomek	0.707 ± 0.036	0.667 ± 0.051	0.714 ± 0.050	0.302 ± 0.020	0.922 ± 0.007	0.414 ± 0.015	0.763 ± 0.014	0.412 ± 0.018	0.691 ± 0.011
SGD	SMOTEENN	0.698 ± 0.021	0.690 ± 0.053	0.699 ± 0.033	0.296 ± 0.009	0.925 ± 0.009	0.414 ± 0.009	0.766 ± 0.016	0.410 ± 0.022	0.695 ± 0.012
SGD	Tomek Links	0.698 ± 0.022	0.694 ± 0.033	0.698 ± 0.029	0.297 ± 0.015	0.926 ± 0.006	0.416 ± 0.016	0.767 ± 0.013	0.413 ± 0.018	0.696 ± 0.014
SVM	ADASYN	0.686 ± 0.026	0.625 ± 0.013	0.697 ± 0.032	0.275 ± 0.018	0.910 ± 0.003	0.382 ± 0.017	0.720 ± 0.015	0.328 ± 0.019	0.661 ± 0.013
SVM	ENN	0.725 ± 0.024	0.634 ± 0.044	0.742 ± 0.036	0.312 ± 0.019	0.917 ± 0.006	0.417 ± 0.013	0.735 ± 0.015	0.388 ± 0.024	0.688 ± 0.010
SVM	None	0.705 ± 0.028	0.676 ± 0.045	0.710 ± 0.040	0.301 ± 0.021	0.923 ± 0.007	0.415 ± 0.014	0.757 ± 0.014	0.380 ± 0.015	0.693 ± 0.010

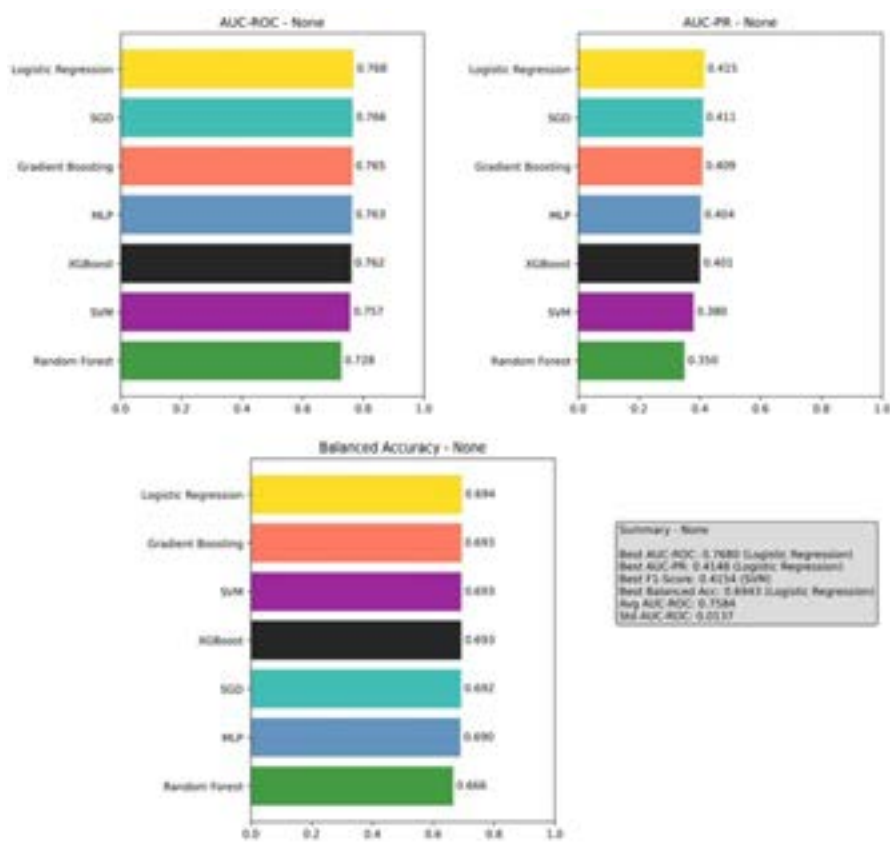


Table 2. Continued...

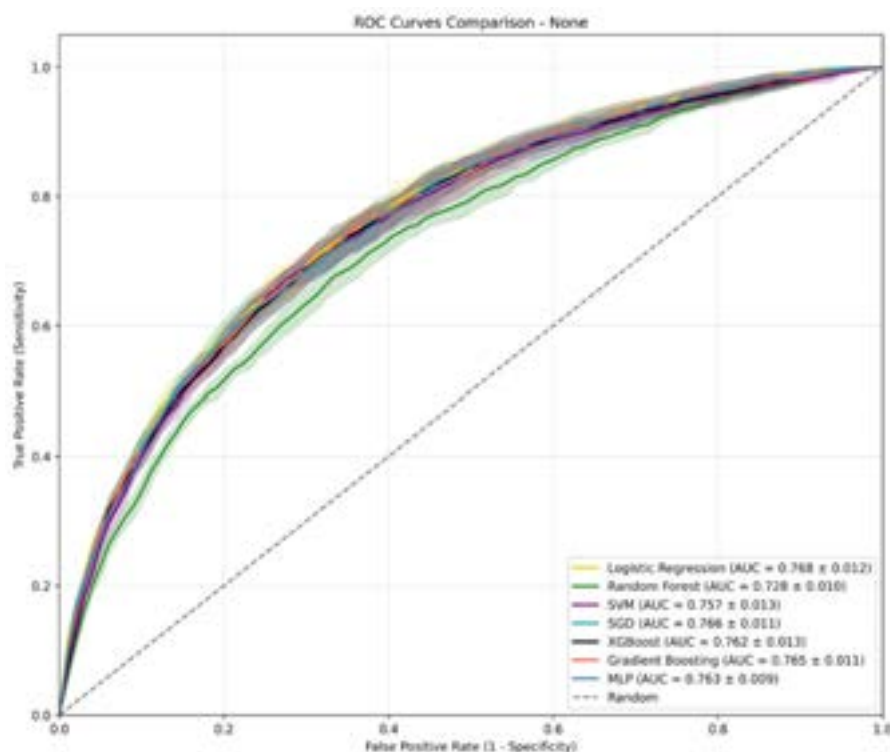
Algorithm	Resampling	Accuracy	Sensitivity (Recall)	Specificity	PPV (Precision)	NPV	F1-Score	AUC-ROC	AUC-PR	Balanced Accuracy
SVM	SMOTE	0.714 ± 0.026	0.593 ± 0.039	0.736 ± 0.036	0.293 ± 0.021	0.908 ± 0.005	0.391 ± 0.015	0.727 ± 0.015	0.341 ± 0.021	0.665 ± 0.011
SVM	SMOTE+Tomek	0.710 ± 0.026	0.599 ± 0.045	0.730 ± 0.038	0.290 ± 0.020	0.909 ± 0.006	0.390 ± 0.013	0.727 ± 0.015	0.341 ± 0.021	0.664 ± 0.011
SVM	SMOTEENN	0.681 ± 0.022	0.672 ± 0.038	0.683 ± 0.032	0.280 ± 0.013	0.919 ± 0.006	0.395 ± 0.011	0.741 ± 0.015	0.356 ± 0.027	0.677 ± 0.010
SVM	Tomek Links	0.773 ± 0.018	0.522 ± 0.024	0.819 ± 0.021	0.347 ± 0.026	0.903 ± 0.005	0.416 ± 0.023	0.695 ± 0.015	0.372 ± 0.025	0.670 ± 0.015
XGBoost	ADASYN	0.672 ± 0.018	0.671 ± 0.026	0.672 ± 0.026	0.273 ± 0.010	0.918 ± 0.003	0.388 ± 0.007	0.730 ± 0.009	0.349 ± 0.011	0.672 ± 0.005
XGBoost	ENN	0.704 ± 0.016	0.674 ± 0.042	0.709 ± 0.025	0.298 ± 0.011	0.922 ± 0.007	0.413 ± 0.012	0.762 ± 0.013	0.401 ± 0.025	0.691 ± 0.013
XGBoost	None	0.702 ± 0.022	0.680 ± 0.057	0.706 ± 0.035	0.298 ± 0.011	0.924 ± 0.010	0.413 ± 0.012	0.762 ± 0.014	0.401 ± 0.018	0.693 ± 0.015
XGBoost	SMOTE	0.675 ± 0.028	0.670 ± 0.035	0.675 ± 0.040	0.276 ± 0.014	0.918 ± 0.003	0.390 ± 0.008	0.736 ± 0.007	0.361 ± 0.013	0.673 ± 0.003
XGBoost	SMOTE+Tomek	0.694 ± 0.029	0.643 ± 0.039	0.703 ± 0.041	0.285 ± 0.017	0.915 ± 0.004	0.394 ± 0.010	0.736 ± 0.009	0.363 ± 0.013	0.673 ± 0.006
XGBoost	SMOTEENN	0.692 ± 0.040	0.665 ± 0.042	0.697 ± 0.054	0.290 ± 0.025	0.919 ± 0.004	0.402 ± 0.019	0.751 ± 0.009	0.387 ± 0.018	0.681 ± 0.011
XGBoost	Tomek Links	0.705 ± 0.011	0.667 ± 0.045	0.711 ± 0.019	0.297 ± 0.007	0.921 ± 0.008	0.411 ± 0.012	0.761 ± 0.014	0.400 ± 0.018	0.689 ± 0.014



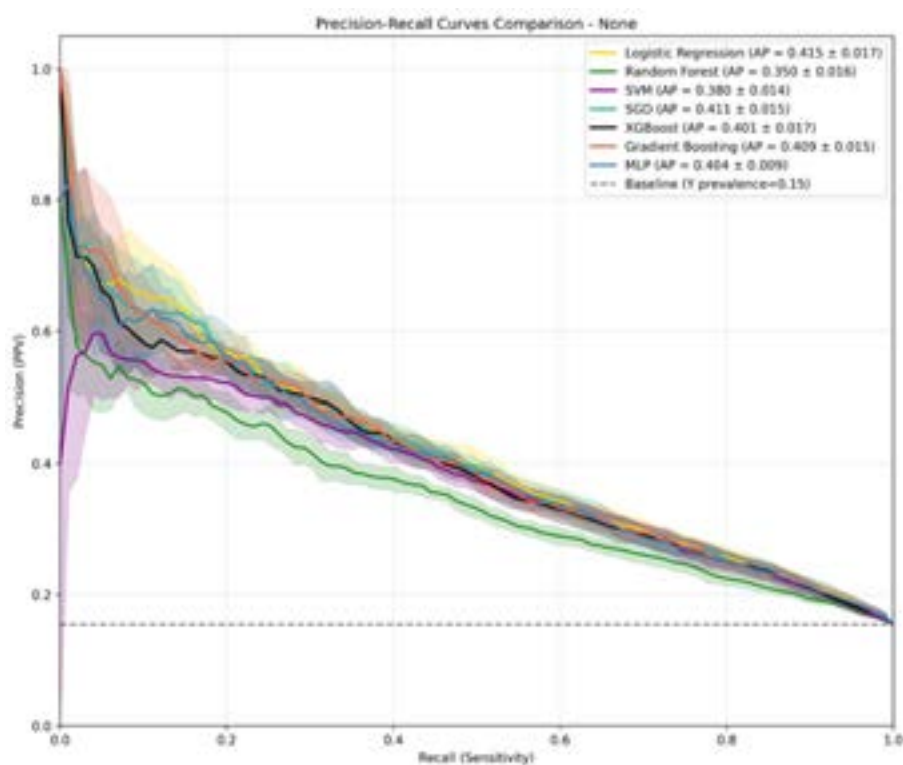
**Figure 1.** Overall performance comparison of machine learning algorithms without class balancing (part 1).



**Figure 2.** Overall performance comparison of machine learning algorithms without class balancing (part 2).



**Figure 3.** Receiver operating characteristic (ROC) curves for all algorithms without class balancing.



**Figure 4.** Precision-Recall (PR) curves for all algorithms without class balancing.

In contrast, SMOTE and SMOTE+Tomek reduced AUC-ROC ( $\sim 0.736$ ), with SMOTEENN yielding intermediate values (0.751). SVM showed reasonable performance (AUC-ROC  $\approx 0.72$ -0.76) but with lower sensitivity, particularly under Tomek Links, where recall dropped to  $\sim 0.52$ , despite an apparent increase in specificity.

#### *Detailed performance metrics*

Precision remained modest across models, mostly clustered around 0.27-0.35, with lower values for some SMOTE-based MLP configurations ( $\approx 0.21$ ). NPV exceeded 0.91 in most models, indicating reliable identification of survivors. Balanced accuracy across the best-performing models hovered around 0.69-0.70, confirming a consistent trade-off between sensitivity and specificity.

The performance comparison across models illustrated the dominance of logistic regression in multiple metrics, including balanced accuracy, AUC-ROC, and AUC-PR. The sensitivity vs. specificity plot revealed that logistic regression achieved an optimal balance between these competing metrics. Sensitivity varied considerably among algorithms and resampling strategies: linear models (logistic regression, SGD) maintained higher sensitivity ( $\approx 0.67$ -0.70), while some tree-based methods and SVM sometimes prioritized specificity at the expense of sensitivity. MLP showed particular instability, with sensitivity ranging from 0.60 to 0.72 depending on resampling approach.

#### *Impact of resampling strategies*

Resampling techniques did not yield substantial performance gains. Methods such as SMOTE, ADASYN, and ENN produced marginal fluctuations but no systematic improvement compared to the unbalanced baseline. In some cases, resampling degraded performance. For example, MLP with SMOTE showed substantially reduced accuracy (0.544) compared to the same algorithm without resampling (0.698), suggesting that some resampling techniques may introduce noise or artifacts.

#### *Best performing models*

Based on comprehensive evaluation, logistic regression emerged as the most consistent and robust model, maintaining high performance across different resampling strategies (AUC-ROC: 0.763-0.768). SGD showed comparable performance (0.761-0.767), with slight advantages in balanced accuracy in some configurations. Gradient boosting also demonstrated competitive results, particularly without resampling or with ENN.

#### *Feature importance analysis*

SHAP (SHapley Additive exPlanations) analysis of the best-performing logistic regression model without resampling confirmed the clinical relevance of key predictors. Age emerged as the dominant predictor (SHAP = 0.630), followed by stroke subtype (STYPE, 0.432) and level of consciousness at admission (RCONSC, 0.286).

Notably, brainstem/cerebellar signs (RDEF7, 0.203) ranked fourth in importance, higher than several other focal deficits, despite their protective association in the univariate analysis. Other major contributors included leg weakness (RDEF3, 0.156), dysphasia (RDEF4, 0.153), face weakness (RDEF1, 0.139), atrial fibrillation (RATRIAL, 0.118), hemianopia (RDEF5, 0.105), and visuospatial disorder (RDEF6, 0.072).

Additional predictors with moderate influence included sex (0.102), visible infarct on CT (RVISINF, 0.102), systolic blood pressure (RSBP, 0.086), and delay to randomization (RDELAY, 0.075). Symptoms on waking (RSLEEP, 0.079) also showed modest predictive value. Treatment-related features were minimal, with aspirin within 3 days (0.058) and heparin within 24 h (0.008) ranking far below the main clinical and neurological predictors.

## DISCUSSION

This study demonstrated that machine learning models based on clinical variables collected at admission can effectively predict six-month mortality after ischemic stroke, achieving moderate to good discrimination (AUC-ROC up to 0.768). Our findings highlight both the potential and limitations of ML approaches in post-stroke outcome prediction, providing important insights for clinical application and future research.

#### *Interpretation of main findings*

Logistic regression and stochastic gradient descent (SGD) emerged as the best-performing and most stable algorithms, matching or slightly outperforming more complex methods, such as random forests, gradient boosting, and XGBoost, with overlapping confidence intervals across validation folds. This has implications for clinical implementation, where interpretability, computational efficiency, and reliability can outweigh marginal gains in accuracy. The linear nature of these models simplifies

integration into decision support and helps clinicians understand better the relationships between patient characteristics and mortality risk<sup>6,7,9,10,12</sup>.

The consistent AUC-ROC performance of ~0.768 for logistic regression across validation folds suggests robust generalization within similar clinical contexts. The high negative predictive value (>92%) makes the model particularly useful for identifying patients at low mortality risk, informing rehabilitation planning and resource allocation.

The modest returns from resampling methods are a key methodological finding. Contrary to frequent assumptions in imbalanced learning, we observed no systematic benefit from techniques such as SMOTE, ADASYN, Tomek Links, and ENN and, in some cases (notably with neural networks), performance degradation—consistent with the possibility that synthetic data can introduce artifacts in high-dimensional clinical settings<sup>13-18</sup>. This underscores the need for careful validation when applying resampling to medical data sets.

### *Comparison with the literature*

Using only routine admission variables from the International Stroke Trial (IST), our best models (logistic regression and SGD) produced AUC-ROC values of ~0.76-0.77. These results compare favorably with ensemble approaches on subsets of the IST data set; for example, Hwangbo et al.<sup>4</sup> reported an AUC ~0.78 for six-month mortality using a stacking model restricted to IST patients without reperfusion therapy. This suggests that, when predictors are restricted to baseline IST variables, linear models capture most of the prognostic information, aligning with original IST reports emphasizing age, consciousness, and stroke subtype<sup>2</sup>. Outside IST, studies with richer predictors (e.g., NIHSS, imaging, biomarkers) and sometimes different outcomes (e.g., functional recovery rather than mortality) often report higher AUCs (sometimes >0.90), as in Guo et al.<sup>3</sup> However, these gains frequently rely on internal validation, raising concerns about overestimation and limited generalizability highlighted in prior reviews<sup>5</sup>.

Established bedside scores provide additional context. The iScore, PLAN, and ASTRAL—each derived for bedside use from routinely available variables—consistently identify age and baseline severity as dominant prognostic factors<sup>21-23</sup>. Other prognostic tools designed for reperfusion settings, such as DRAGON and CT-DRAGON, incorporate imaging to predict

90-day outcomes<sup>24,25</sup>. The ASTRAL framework has also shown longer-term prognostic utility<sup>26</sup>. Recent systematic reviews and meta-analyses similarly note that models leveraging advanced imaging/biomarkers can achieve higher apparent discrimination but often lack robust external validation<sup>27,28</sup>. At the same time, emerging work on early dynamic prediction underscores the value of updating risk with evolving clinical data<sup>29</sup>. External validations of bedside scores commonly report AUCs in the 0.75-0.80 range for six- to twelve-month mortality, consistent with our IST-based models<sup>30</sup>.

### *Calibration, class imbalance, and methodological insights*

Beyond discrimination, we emphasized probability calibration and clinically informed threshold selection. Calibration via Platt (sigmoid) scaling (with isotonic explored in sensitivity analyses) provided calibrated probabilities aligned with observed outcomes, supporting clinical interpretability. Decision thresholds were selected using the Youden index during inner-fold tuning to balance sensitivity and specificity<sup>19</sup>. The high NPV (>92%) supports “rule-out” use cases (e.g., guiding early rehabilitation/discharge planning). Prior IST-based analyses seldom foreground calibration, which our work brings to the fore alongside a careful assessment of resampling, aligning with recent evidence favoring calibration and threshold optimization over oversampling when predictors are compact and informative<sup>4,27,28</sup>.

### *Era effects and external validity*

The IST cohort predates reperfusion therapies, dedicated stroke units, and modern secondary prevention, all of which have lowered mortality and likely altered predictor-outcome relationships<sup>1</sup>. Nevertheless, key prognostic factors identified here—age, consciousness, stroke subtype, focal deficits—remain central in tools developed in the reperfusion era (iScore, PLAN, ASTRAL)<sup>21-23,26,30</sup>. Thus, while absolute risks require recalibration, the core determinants of prognosis appear stable across eras. For translation to current practice, external validation and recalibration in contemporary cohorts are essential<sup>24,30</sup>.

### *Clinical implications and implementation*

The model’s balance of specificity (~70%) and high NPV (>92%)—partly reflecting the low prevalence of six-month mortality in the IST cohort—supports identification of low-risk patients who may be candidates for earlier discharge and community-based rehabilitation. Conversely, moderate sensitivity (~70%) cautions against relying on predictions alone for high-risk



triage or end-of-life decisions; model outputs should supplement, not replace, clinical judgment.

### *Methodological considerations*

We used nested cross-validation to provide unbiased performance estimates, examined multiple algorithms and resampling strategies, and calibrated probabilities to improve clinical interpretability. SHAP analyses yielded transparent feature-importance rankings consistent with clinical knowledge, supporting model validity<sup>20</sup>. Limitations include the historical nature of IST (limiting direct generalizability to modern care), restriction to baseline variables (excluding biomarkers/imaging/dynamic in-hospital data), use of all-cause mortality (not distinguishing stroke-related vs. competing risks), and the need for external validation in independent cohorts<sup>24,30</sup>.

### *Future research directions*

Future work should prioritize external validation and recalibration in contemporary cohorts reflective of modern stroke care<sup>24,30</sup>. Augmenting predictors (e.g., biomarkers, advanced neuroimaging, dynamic EHR time-series) may improve accuracy, provided interpretability and calibration are preserved<sup>27,28</sup>. Dynamic models that update risk with evolving clinical data are promising<sup>29</sup>. Advanced ML, including deep learning to capture complex interactions, may add value when paired with rigorous calibration and external validation<sup>11</sup>. Prospective studies should assess clinical impact, workflow integration, and cost-effectiveness, alongside user-friendly interfaces and clinician training to support safe implementation.

## CONCLUSION

Using only bedside variables available at admission, we built and rigorously validated machine-learning models that predict six-month mortality after ischemic stroke with moderate-good discrimination (AUC-ROC  $\approx$  0.76-0.77) and calibrated probabilities via Platt scaling. Across algorithms and resampling schemes, simple linear approaches—logistic regression and SGD—were the most consistent, interpretable, and implementation-ready, while more complex models offered little incremental benefit. Age, consciousness level, stroke subtype, and focal neurological deficits dominated prognostic influence, echoing decades of stroke literature. Resampling strategies did not systematically improve

performance and occasionally degraded it, underscoring the value of respecting clinically meaningful class distributions and focusing on calibration and clinically derived thresholds.

Clinically, the models' high NPV (>92%) supports confident identification of low-risk patients to inform rehabilitation planning and resource allocation, while their modest PPV cautions against using predictions in isolation for high-stakes decisions. The historical nature of IST data limits direct generalizability, but the stability of key predictors suggests that recalibrated versions may translate to modern practice, particularly in resource-limited settings where advanced imaging is scarce.

Future work should prioritize external validation in contemporary cohorts, recalibration for current care pathways, and evaluation of clinical impact. Enriching models with modern severity scales, imaging, biomarkers, and dynamic EHR signals may enhance utility, provided interpretability and calibration are preserved. Ultimately, parsimonious, transparent, and well calibrated models appear best positioned to support equitable, bedside-ready prognostication after stroke.

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## CRediT

Samuel Pedro Pereira Silveira: Conceptualization, Data curation, Formal analysis, Methodology, Software, Validation, Writing – original draft. Gustavo del Rio Lima: Conceptualization, Data curation, Formal analysis, Methodology, Software, Validation, Writing – original draft. Gustavo Branquinho Alberto: Data curation, Investigation, Writing – original draft. Luiza Carolina Moreira Marcolino: Data curation, Investigation, Writing – original draft. Larissa Batista Xavier: Data curation, Investigation, Writing – original draft. Carlos Umberto Pereira: Conceptualization, Project administration, Supervision, Writing – review and editing. Murillo Martins Correia: Conceptualization, Project administration, Supervision. Roberto Alexandre Dezena: Conceptualization, Project administration, Supervision, Writing – review and editing.

# Outcome Classification of Spontaneous Bleeding in Meningiomas Using a Supervised Machine Learning Model

## *Classificação de Desfechos do Sangramento Espontâneo em Meningiomas Utilizando um Modelo de Aprendizado de Máquina Supervisionado*

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### ABSTRACT

**Introduction:** Meningiomas are typically benign tumors, however, when associated with spontaneous intracranial hemorrhage, a rare but severe complication, they pose a significant threat to survival. Due to the low incidence of this condition, clinical guidelines are scarce, and outcome prediction remains difficult. **Objective:** To develop and evaluate a supervised machine learning approach for predicting binary outcomes (Morbimortality or Recovery) in hemorrhagic meningiomas. **Methods:** A novel dataset was constructed from curated case reports published in the medical literature and manually validated by neurosurgery specialists. Classification algorithms were applied, and performance was compared. **Results:** The AdaBoost classifier achieved the best results, with 85% Accuracy, 97% Recall for the Morbimortality class, and 68% for Recovery. Feature importance analysis identified preoperative focal deficit, tumor and hemorrhage volume, patient age, level of consciousness, and Glasgow Scale category as the most influential predictors. **Conclusion:** In addition to proposing a clinically relevant predictive model, this study contributes a curated dataset of 294 cases and 15 clinical features, offering a valuable resource for future research. The approach demonstrates best practices in medical feature engineering, preprocessing, and model optimization, supporting clinical decision-making in high-risk neurosurgical cases and improving patient stratification and personalized care.

**Keywords:** Brain; Meningiomas; Bleeding; Spontaneous; Hemorrhagic; Outcomes

### RESUMO

**Introdução:** Os meningiomas são tumores benignos; porém, quando associados à hemorragia intracraniana espontânea, uma complicação rara e grave, representam ameaça significativa à sobrevivência. Devido à baixa incidência, as diretrizes clínicas são escassas e a predição de desfechos desafiadora. **Objetivo:** Desenvolver e avaliar uma abordagem de aprendizado de máquina supervisionado para prever desfechos binários (morbimortalidade ou recuperação) em meningiomas hemorrágicos. **Métodos:** Um conjunto de dados foi construído a partir de relatos publicados na literatura médica e validados por especialistas em neurocirurgia. Algoritmos de classificação foram aplicados e o desempenho comparado. **Resultados:** O AdaBoost apresentou os melhores resultados: 85% de acurácia, 97% de recall para morbimortalidade e 68% para recuperação. A análise de importância das variáveis identificou déficit focal pré-operatório, volume tumoral e do sangramento, idade, nível de consciência e categoria da Escala de Glasgow como principais preditores. **Conclusão:** Além de propor um modelo preditivo clinicamente relevante, o estudo disponibiliza conjunto curado com 294 casos e 15 características clínicas, oferecendo à comunidade médica recurso para pesquisas. A abordagem demonstra boas práticas em engenharia de atributos, pré-processamento e otimização de modelos, apoiando a tomada de decisão em casos neurocirúrgicos de alto risco e aprimorando a estratificação de pacientes e o planejamento de cuidados.

**Palavras-Chave:** Cérebro; Meningiomas; Sangramento; Espontâneo; Hemorragia; Desfecho

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## INTRODUCTION

Meningiomas are the most prevalent primary central nervous system tumors, arising from the meninges, the protective membranes surrounding the brain and spinal cord. Although typically benign and slow-growing, in rare cases these tumors can be associated with spontaneous intracranial hemorrhage, a complication that substantially increases clinical severity and demands urgent medical attention<sup>1</sup>. This diagnostic and therapeutic uncertainty highlights the need for alternative tools that can support clinical decision making in such complex and high-risk scenarios<sup>2,3</sup>.

Recent advances in machine learning (ML) have demonstrated potential in enhancing diagnostic accuracy and prognostic predictions in neurosurgery. In particular, supervised ML models have been effectively applied to clinical datasets for classification and risk assessment tasks, often outperforming traditional statistical approaches. To address this demand, our paper proposes a supervised machine learning approach for predicting lethality in cases of meningiomas complicated by spontaneous bleeding. We constructed a novel dataset from published medical case reports curated from digital libraries such as Cochrane, Embase, and Medline. Neurosurgery experts manually reviewed this dataset to ensure clinical consistency and served as the foundation for training and evaluating predictive models.

The remainder of this paper is structured as follows: Section 2 reviews the clinical background; Section 3, related work; Section 4, methods; Section 5, data engineering; Section 6, experiments and evaluation; Section 7, conclusions and future work.

**Background**

While meningiomas are commonly classified as benign and represent a significant portion of intracranial tumors, their presentation can vary greatly depending on location, size, and biological behavior. Although most are discovered incidentally or present mild symptoms, a small subset evolves with severe complications, including spontaneous intracranial hemorrhage. This rare but critical manifestation challenges the traditional perception of meningiomas as indolent tumors and demands urgent intervention and careful prognosis evaluation<sup>2,4</sup>.

Despite advancements in imaging and surgical techniques, the literature on hemorrhagic meningiomas remains limited and consists mostly of case reports and small series. This lack of structured data hinders the development of robust clinical guidelines and predictive tools for outcome assessment<sup>3,5</sup>. As such, innovative methods, including machine learning, may offer valuable insights by extracting patterns from limited datasets and improving clinical decision-making in these rare scenarios.

The reported incidence of spontaneous bleeding in meningiomas ranges from 0.5% to 2.4%, with lethality rates varying between 28% and 50%<sup>6</sup>. Despite being infrequent, this phenomenon is associated with significant morbidity and mortality, dramatically altering the prognosis.

In this context, machine learning (ML) offers a promising solution to support clinical decision-making in complex, data-limited scenarios. ML models learn patterns from clinical data, including attributes like age, neurological status, bleeding type, tumor pathology, and outcomes, to predict patient prognosis. Among these models, AdaBoost stands out for its robustness and interpretability<sup>7</sup>, with performance evaluated through metrics such as Accuracy, Recall, F1-score, and ROC and Precision-Recall curves<sup>8</sup>.

Pienaar and Varghese in their work<sup>9</sup> provided a comprehensive analysis of intracranial meningiomas, detailing the prevalence of their histological subtypes based on MRI findings with histopathologic correlation. Their findings reveal that less frequent subtypes, such as Secretory and Metaplastic meningiomas, represent less than 1% each. This classification serves as an important baseline for our paper, which focuses on outcome prediction in hemorrhagic meningiomas using supervised learning.

Ferrufino-Mejia et al.<sup>10</sup> reported that spontaneous intracranial hemorrhage in meningiomas occurs in less than 2.4% of cases, underscoring its rarity and the challenge of standardizing diagnosis and treatment. This evidence reinforces our study's clinical relevance and aligns with our focus on outcome prediction in hemorrhagic presentations.

Angonese and Galante<sup>11</sup> proposed AGHE, which enriched models by integrating textual, visual, and structural data for

a multidimensional patient view. Its expressive embeddings capture relationships beyond traditional feature engineering; paired with data-quality checks, they improve robustness and clinical generalization.

Additionally, Siedlecki et al.<sup>12</sup> reported that early diagnosis and prompt surgical treatment can lead to favorable outcomes, particularly in patients with preserved or only mildly impaired consciousness. However, patients with deep-seated tumors or significant neurological deficits remain at higher risk, motivating the need for predictive tools to guide individualized care.

Halalmeh et al.<sup>13</sup> systematically reviewed 65 hemorrhagic meningioma cases, finding most tumors in the cerebral convexity and the meningothelial subtype as most prevalent. Hemorrhage was linked to high mortality and neurological sequelae, underscoring the severity of conditions and the need for predictive strategies in management and prognosis.

A systematic review by Leclerc et al.<sup>14</sup> reviewed 120 hemorrhagic meningioma cases, identifying subdural and intraparenchymal hemorrhages as the most frequent. Intraparenchymal hemorrhage (IPH) and hindbrain/ventricular tumor locations were significantly

associated with poor outcomes and early rebleeding, aligning with our theme and raw-data analysis.

## METHODS

Figure 1 illustrates the methodological pipeline adopted in this paper. The process begins with the data engineering phase, which includes data collection from published medical cases and structured preparation involving feature engineering to ensure clinical relevance. Following this, the model development phase encompasses the selection of supervised learning algorithms and the calibration of their hyperparameters. At this stage, an initial evaluation is performed using key performance metrics, particularly accuracy and recall.

Once trained, each model undergoes a thorough result analysis, which includes evaluating class-wise accuracy, recall values, confusion matrices, and performance visualizations such as ROC and Precision-Recall curves. SHAP values are also used to interpret the contribution of each attribute to the predictions.

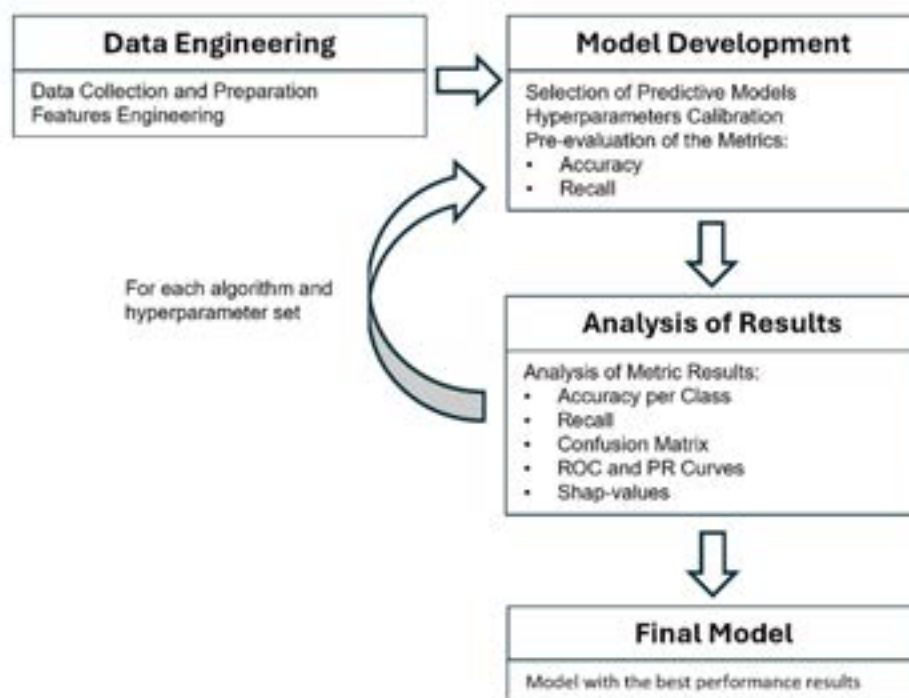


Figure 1. Steps of the methodology used.



It is important to note that this process is iterative: insights obtained from the result analysis guide refinements in model configuration, returning to the development phase for adjustments. This loop continues until the optimal performance is achieved. The final model is selected based on the best overall performance, considering both the general accuracy and the ability to identify high-risk cases effectively.

### Dataset

In medical research, especially when developing predictive models using Artificial Intelligence, the quality and the reliability of clinical data are crucial. However, in real-world scenarios, data are rarely perfect or ready for immediate analysis. Clinical records often contain missing information, inconsistencies, formatting issues, duplicated entries, or outlier values that do not represent typical patient profiles. These imperfections can significantly impact the ability of models to identify meaningful patterns and make accurate predictions. In this paper, particular attention was given to cleaning and transforming the dataset to ensure it reflects clinically relevant and consistent information.

### Data sources

To support the development of the predictive model presented in this paper, a dedicated dataset was constructed based on medical case reports extracted from reputable digital libraries, including Cochrane, Embase, and Medline. A research line was created: ((meningioma [MeSH Terms]) OR (meningioma [Title/Abstract]) AND ((intracranial hemorrhage [MeSH Terms]) OR (hemorrhage

[Title/Abstract])) OR ((hematoma [MeSH Terms]) OR (hematoma [Title/Abstract])). The search was not restricted to papers published in English language and included all papers published to date. Additional studies found in the papers' bibliography were also included. Figure 2 represents the total number of cases reported thus far. Following data collection, experienced neurosurgeons, specializing in this area, curated the dataset. Their clinical expertise was essential to ensure the consistency, reliability, and medical relevance of the information used in our experiments.

The final dataset comprises 294 patient cases, each described by 13 clinical attributes, as detailed in Table 1. These include demographic data, bleeding characteristics, pathological diagnoses, preoperative neurological status, and clinical outcomes.

### Data preprocessing

The data preprocessing stage is a critical component in the development of predictive models, since it directly influences the performance and reliability of the classifiers. This phase involves a series of techniques designed to manage the specific challenges presented by the dataset, such as missing values, inconsistent formats, and categorical attributes. In medical contexts, where each data point may represent a real patient, ensuring accuracy and consistency at this stage is essential to preserve the clinical validity of the model.

### Data type correction and dimensionality reduction

The first step in the preprocessing pipeline involves verifying and correcting the data types according to the expected domains of

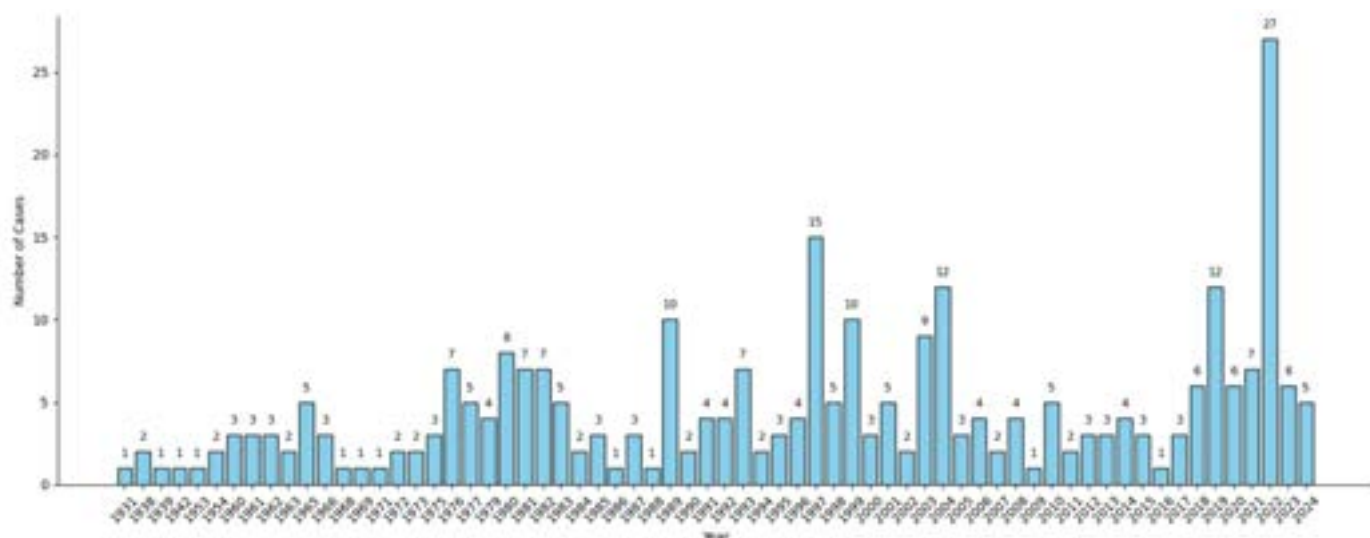


Figure 2. Number of Meningioma Bleeding Cases per Year.



each attribute. All other attributes were already correctly typed according to their respective domains. Additionally, attributes that are not directly related to the clinical scenario or that provide meta-information irrelevant to the patient or the medical condition should be excluded from the model.

### Attribute correlation

Another important aspect related to dimensionality reduction is the analysis of correlations between attributes. When two attributes exhibit a strong correlation, one of them can often be removed without significantly affecting the predictive performance of models, while contributing to a simpler and more efficient model. To explore this, a correlation matrix was generated to identify redundant attributes, as shown in Figure 3. The analysis revealed a strong correlation between the attributes Post MRI Era and Year. According to neurosurgical experts who contributed to this paper, this correlation is clinically valid and corresponds to the historical introduction of magnetic resonance imaging (MRI) in 1984, which significantly changed diagnostic practices.

In our case, the best results were obtained when the Year attribute was excluded, as Post MRI Era already encapsulates the clinically meaningful distinction related to the adoption of MRI in diagnostic practices. Additionally, two attributes, Focal Deficit Pre Op and

Glasgow Scale Category, showed a direct and strong correlation with the target variable Outcome. This finding is clinically consistent, as both neurological status at admission and the presence of focal deficits are known predictors of postoperative prognosis. Their correlation reinforces their predictive relevance and supports their inclusion in the modeling pipeline.

### Categorical data transformation

Categorical clinical attributes require special attention during data preprocessing, particularly when handling missing values and choosing how to represent these attributes numerically. This is especially important when using Machine Learning algorithms that rely on distance calculations, as improper encoding of categorical values can impact negatively model performance.

Unlike continuous numerical values, which have a natural order and scale, categorical attributes must be carefully transformed to avoid introducing misleading relationships. To prevent this, we adopted a technique known as One-Hot Encoding, which converts each category into a separate binary column, marked as 1 when the category is present and 0 otherwise. This approach avoids artificial assumptions of order or proximity between unrelated categories.

**Table 1.** Meningioma bleeding dataset attributes.

Attribute	Data Type	Description
Row number	Integer	Instance identifier
Authors	String	Authors of the published case report
Year	Integer	Year of publication
Age	Integer	Age of patient
Sex	Char - Categorical	Sex of patient: F/M (Female/Male)
Type of Bleeding	String - Categorical	Type of intracranial hemorrhage
Bleeding Location	String - Categorical	Anatomical location of the bleeding
Pathology Diagnosis	String - Categorical	Histopathological tumor subtype
Consciousness	String - Categorical	Level of consciousness at initial assessment
Treatment	String - Categorical	Treatment applied to the patients
Focal Deficit Pre Op	Boolean	Presence of preoperative focal deficit: Yes/No
Post MRI Era	Boolean	Diagnosis after the introduction of MRI: Yes/No
Mass Effect Tumor Volume	Integer	Volume of mass-effect tumor plus hemorrhage
Glasgow Scale Category	String - Categorical	Glasgow classification: Mild, Moderate, Severe
Outcome	String - Categorical	Postoperative outcome: Recovery/Morbimortality

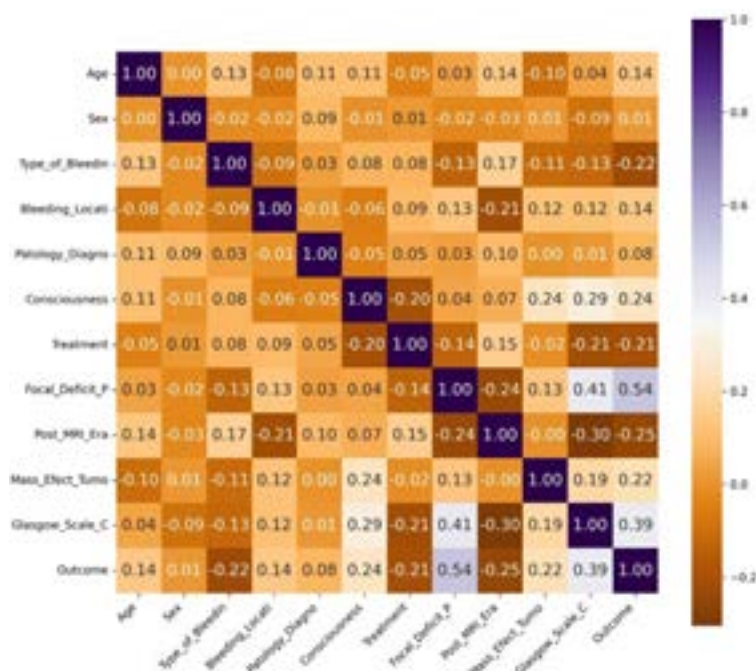


Figure 3. Correlation between dataset attributes.

### Scaling of numerical attributes

Machine Learning models that rely on distance calculations, such as those used in this paper, are particularly sensitive to the magnitude of numerical values. If attributes are expressed on different scales (e.g., age ranging from 0 to 100 and other attributes on a 0 to 1 scale), attributes with larger numerical ranges may disproportionately influence the decisions of models, regardless of their actual clinical relevance. To prevent this imbalance and ensure fair comparison between features, it is essential to normalize the values, so they share a common scale. In this paper, we applied a Standard Normalization technique that adjusts all numerical attributes to have a mean of zero and a standard deviation of one.

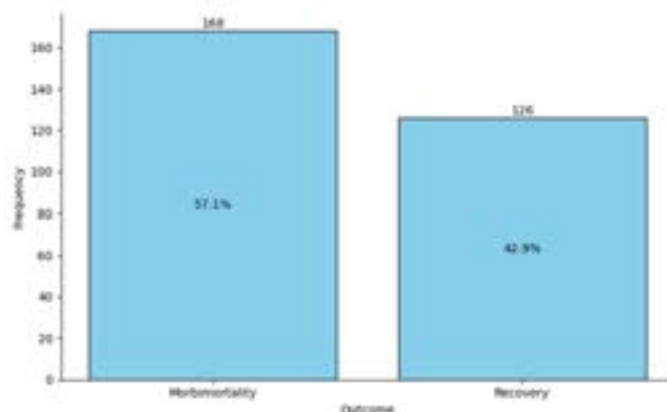


Figure 4. Distribution of classes in the dataset.

### Class balancing

The dataset created and used in this paper consists of 294 patient cases, of which 126 (42.9%) had a favorable outcome (Recovery) and 168 (57.1%) resulted in unfavorable outcome (Morbimortality). This distribution, shown in Figure 4, reveals a considerable class balance that can significantly affect the performance of predictive models.

### Dataset Splitting

To evaluate the predictive models developed in this paper, we employed an 80/20 holdout split, training on 80% of randomly

selected cases and testing on the remaining 20% to assess generalization to unseen data.

### Descriptive analysis of the dataset after data preparation

The dataset comprises 294 patients diagnosed with hemorrhagic meningiomas. Among them, 59.86% are female and 40.14% are male, with a mean age of approximately 56 years. Regarding the bleeding location, the most frequent sites include the convexity (143; 48.64%), posterior cranial fossa (32; 10.88%), parasagittal region (32; 10.88%), falx (29; 9.86%), lateral ventricle (18; 6.12%),

and sphenoid (18; 6.12%). The types of hemorrhage reported are primarily intracerebral or intratumoral (121; 41.16%), subdural (116; 39.46%), and subarachnoid (57; 19.39%). In terms of histopathological subtypes, the most prevalent diagnoses are meningothelial (91; 30.95%), fibroblastic (90; 30.61%), angiomatous (34; 11.56%), transitional (32; 10.88%), atypical (18; 6.12%), and anaplastic (11; 3.74%). Regarding consciousness at the time of hospital admission, 210 patients were conscious preoperatively (71.43%), 52 experienced deterioration with unconsciousness (17.69%), and 32 were permanently unconscious (10.88%). Relating to focal neurological deficits before surgery, 223 patients (75.85%) presented with a deficit, while 71 (24.15%) did not. The analysis of Glasgow Coma Scale categories revealed that 141 patients (47.96%) were classified as Severe, 133 (45.24%) as Mild, and 20 (6.80%) as Moderate. Tumor and hemorrhage volume (in mm<sup>3</sup>) ranged from 10 to 1,520,875, with a mean of 121,839 and a high standard deviation of approximately 254,732, indicating high variance in lesion size across patients. The dataset is also divided by diagnostic era: 199 patients (67.69%) were diagnosed after the introduction of MRI (post-MRI era), and 95 (32.31%) in the pre-MRI era. Regarding clinical outcomes, 126 patients (42.86%) had a complete recovery, while 168 (57.14%) experienced morbimortality. A comprehensive visualization of these descriptive statistics is presented in Figure 5, enabling a clearer and more intuitive understanding of the dataset characteristics.

As a result, the final dataset is fully prepared to serve as input for the Machine Learning model developed in the experiment detailed in the following section. The dataset created and used in this paper has been made publicly available and can be accessed within the supplemental material of this paper.

## RESULTS

This section presents the experiment developed to investigate predictive modeling for hemorrhagic meningioma outcomes. The content encompasses the model development strategy, the pipeline architecture adopted for data preprocessing, the evaluation of classification performance, interpretability analysis using SHAP values, and an in-depth exploration of key attributes associated with patient prognosis.

### Model development

In this paper, we adopted a methodological approach centered on the evaluation of multiple supervised Machine Learning algorithms, including Random Forest, AdaBoost, XGBoost, and an Ensemble Classifier composed of RandomForest, Logistic Regression, XGBoost, K-Nearest Neighbors, and Support Vector Machine. These models were selected because of their strong performance in medical prediction tasks. Each model was configured with appropriate strategies, such as balanced class weights where applicable, and evaluated using a systematic pipeline architecture coupled with 10-fold cross-validation to ensure consistency and generalizability.

Among the tested models, the AdaBoost classifier consistently delivered the best overall results, particularly in terms of accuracy and recall for the minority class. This superior performance is likely related to AdaBoost sequential learning mechanism, which places greater emphasis on difficult-to-classify cases by adjusting the weights of misclassified samples across iterations,

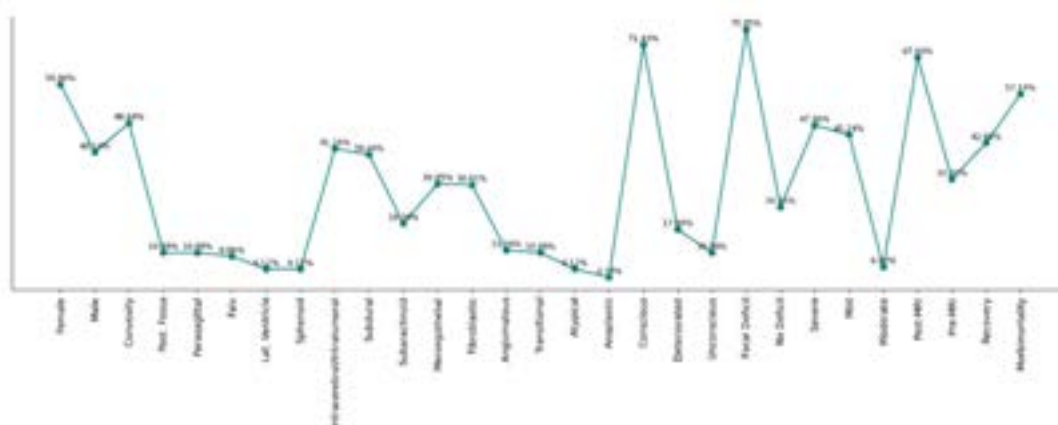


Figure 5. Descriptive Overview of Hemorrhagic Meningiomas Dataset.

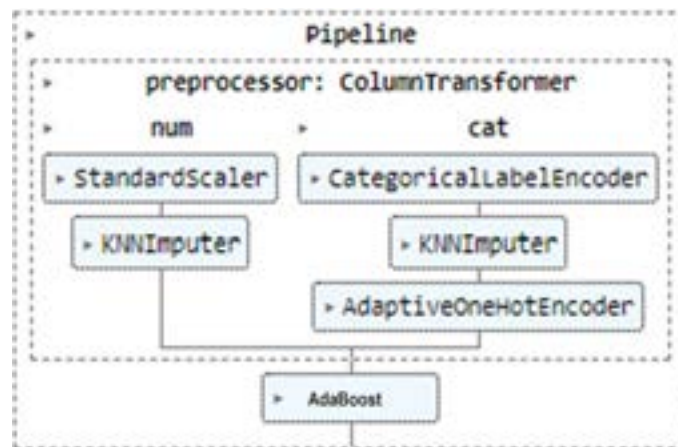
**Table 2.** Model performance of the AdaBoost classifier.

Best Hyperparameter	Class	Accuracy	Recall	F1	Precision
estimator class weight: balanced	Morbimortality	0.85	0.97	0.88	0.94
estimator max depth: 1	Recovery		0.68	0.79	0.80
estimator min samples leaf: 1					
estimator min samples split: 2					
learning rate: 1.0					
n-estimators: 50					

a key advantage when dealing with heterogeneous and high-risk clinical data. Hyperparameter tuning was performed using GridSearchCV, allowing for further refinement of the model and optimization of its predictive performance.

### Pipeline architecture

To ensure consistency and reproducibility throughout the experiments, we structured the model development process using a modular sequence of data preparation steps, referred to as preprocessing pipelines. Given that the dataset contains both numerical attributes and categorical attributes expressed as text, we designed a preprocessing architecture that treats each type of data accordingly. These two branches are then merged into a single, unified dataset that is fully prepared for classification tasks. Figure 6 illustrates the complete pipeline architecture used in the development of the AdaBoost<sup>15</sup> classifier model, which served as the baseline in our experiment.



**Figure 6.** Architecture of the preprocessing pipelines used for model training.

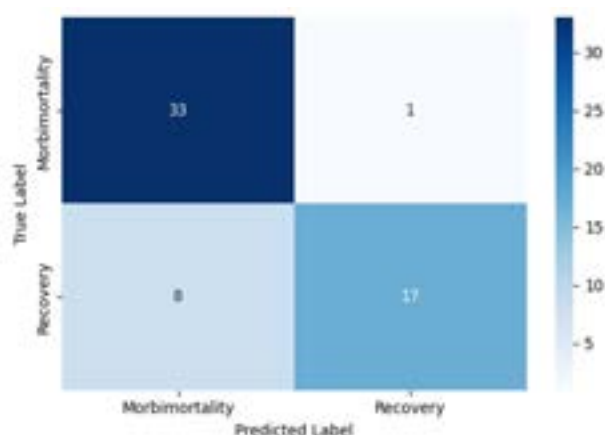
These results suggest that the model is highly dependable in identifying patients with favorable outcomes, and reasonably effective in detecting high-risk patients, offering valuable support for early clinical decision-making. In medical terms, this is analogous to a diagnostic test with high sensitivity and specificity: it rarely misses a true survivor (high recall for Recovery) and can correctly flag a significant portion of patients at risk of death, which represents the majority class in the dataset.

## DISCUSSION

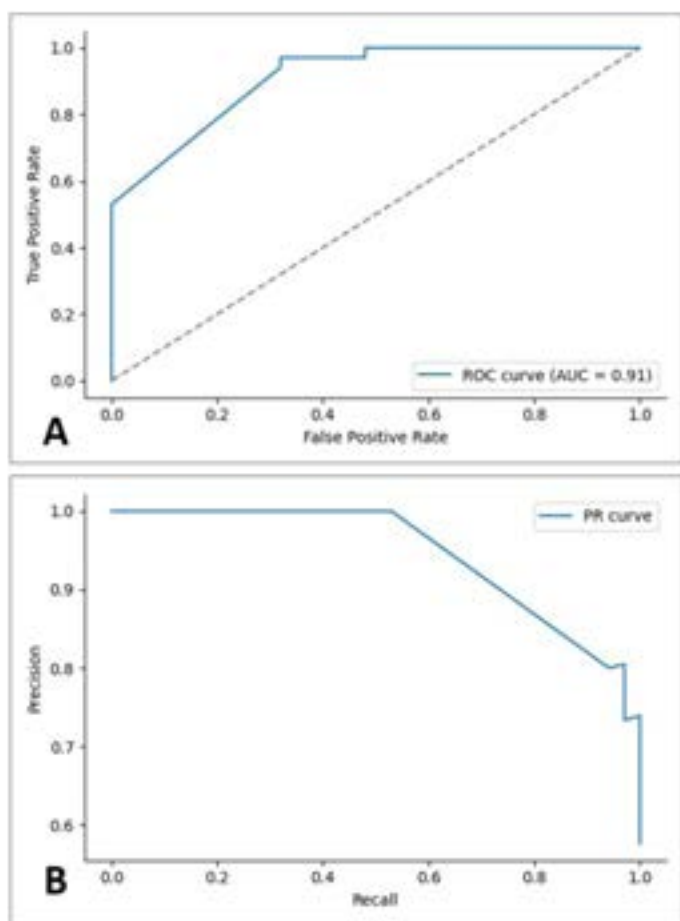
As shown in Table 2, the AdaBoost model achieved an overall accuracy of 85%, correctly predicting the clinical outcome for 85% of all patients in the dataset. This high accuracy reflects the strong of model overall reliability in distinguishing between recovery and morbimortality cases, making it a promising tool for supporting medical decision-making. For the Morbimortality majority class, the model achieved an Recall of 97%, correctly identifying 97% of patients with fatal outcomes. For the Recovery class, the model reached a Recall of 68%, accurately recognizing 68% of the patients who survived. This high Recall performance in both classes highlights the strong model sensitivity, its ability to correctly identify true positive cases, which is especially crucial in clinical applications.

The confusion matrix of the model is shown in Figure 7, illustrating its performance across both outcome classes. For the Morbimortality class, the model correctly predicted 33 out of 34 cases (True Positives), misclassifying only 1 patient (False Negative). For the Recovery class, it correctly identified 17 patients (True Negatives) but misclassified 8 as having a fatal outcome (False Positives). This distribution demonstrates the excellent model ability to detect high-risk patients with remarkable precision while maintaining a solid performance in recognizing recovered cases. The low number of misclassifications and the strong diagonal dominance in the matrix reflect the overall model reliability and its clinical utility.





**Figure 7.** Confusion matrix from the AdaBoost classifier.



**Figure 8.** ROC and Precision-Recall curves from the AdaBoost classifier. **A.** ROC curve from the AdaBoost classifier. **B.** PR curve from the AdaBoost classifier.

In Figure 8B, the PR curve starts at precision 1.0 and stays there until recall approximately 0.5, then gradually declines to approximately 0.72 at maximum recall. Together, these results indicate highly precise early predictions (few false positives) and robust performance across thresholds, supporting AdaBoost as a useful tool for identifying high-risk patients.

### *SHAP values - the most important data attributes*

To identify which attributes influence the model most, we applied SHAP (SHapley Additive exPlanations). SHAP decomposes each prediction into feature contributions, indicating positive or negative effects. Figure 9 shows the SHAP summary plot: each dot represents a patient; the x-axis gives the direction and magnitude of a feature impact; colors encode feature values (blue = low, red = high).

SHAP ranked Focal Deficit Pre Op as the main driver: its presence (red, positive SHAP) pushed predictions toward unfavorable outcomes. Mass Effect Tumor Plus Hemorrhage Volume and Age also weighed heavily: higher values in these attributes increased morbimortality risk, which is consistent with clinical reasoning. Consciousness and Glasgow Scale Category were additionally informative, reflecting preoperative neurological status. In contrast, Treatment and Sex showed low SHAP dispersion, contributing little in this dataset.

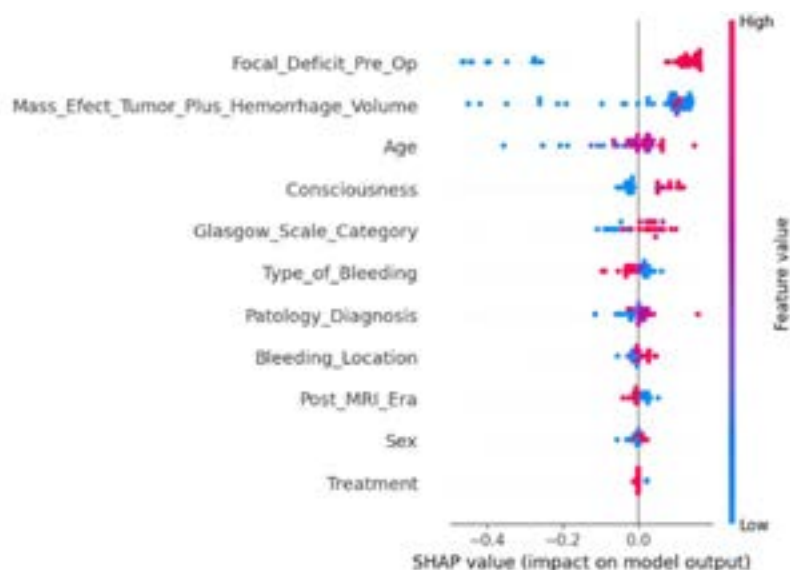
### *Analysis of key attributes associated with patient outcomes*

Based on the SHAP analysis, we selected the attributes Glasgow Scale Category, Pathology Diagnosis, Type of Bleeding, and Bleeding Location for further investigation. To better understand their behavior, we visualized them using graph structures to explore how specific values are connected to survival or mortality outcomes.

Figure 10A illustrates the association between the Glasgow Scale Category and patient outcomes. All three categories, Severe (141), Mild (133), and Moderate (20), present connections to both outcome classes. However, a strong imbalance is observed: the Severe category is predominantly associated with Morbimortality, while the Mild group shows a greater link with Recovery. This pattern aligns with clinical expectations, where higher Glasgow scores reflect better neurological status and greater chances of recovery.

Figure 8A shows a ROC AUC of approximately 0.91, indicating excellent discrimination between recovery and morbimortality.

In Figure 10B, the attribute Pathology Diagnosis displays a wider distribution of subtypes, each contributing to different outcome

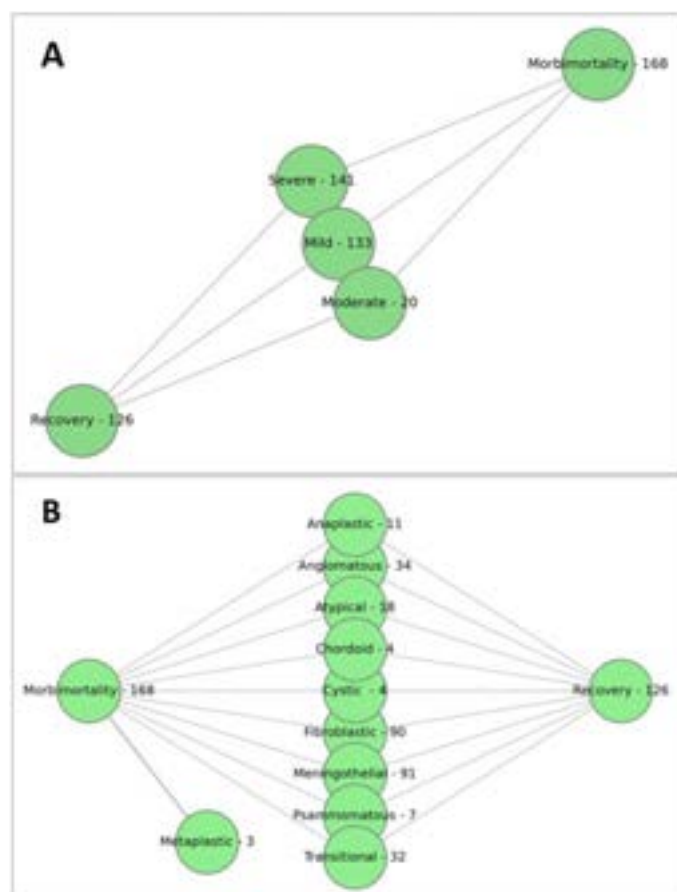


**Figure 9.** Feature importance based on SHAP values.

classes. Among the 11 subtypes identified, only one (Metaplastic) connects exclusively to the Morbimortality outcome, indicating that this tumor subtype may be associated with higher biological aggressiveness. All others, including highly prevalent categories such as Meningothelial (91), Fibroblastic (90), and Angiomatous (34), link to both Morbimortality and Recovery. This reinforces the heterogeneity of histological presentations and their variable prognostic implications, without any single diagnosis definitively determining the outcome.

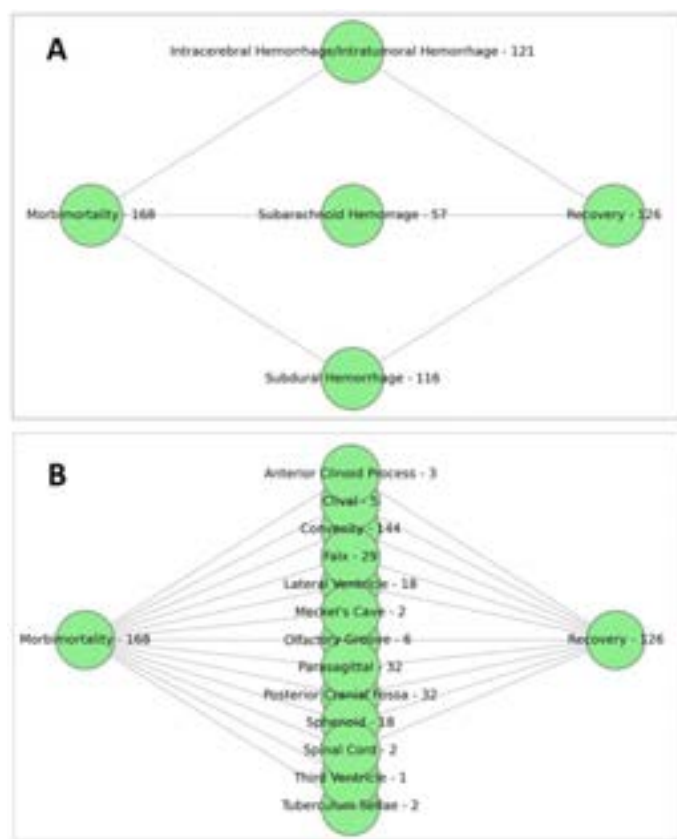
Figure 11A shows the relationship between Type of Bleeding and patient outcomes. All three categories, Subarachnoid Hemorrhage (57), Subdural Hemorrhage (116), and Intracerebral/Intratumoral Hemorrhage (121), are associated with both Morbimortality and Recovery. This distribution suggests that, although the type of hemorrhage is clinically relevant, none of these categories exclusively determines the outcome, reinforcing the difficulty of predicting prognosis based on hemorrhage type alone.

In contrast, Figure 11B presents a broader and more granular view of the associations between Bleeding Location and outcomes. Most anatomical sites, such as Convexity (143), Falx (29), Parasagittal (32), Posterior Cranial Fossa (32), and others, exhibit connections with both outcome classes, indicating a shared clinical relevance. However, a few less frequent locations (e.g., Meckel Cave (2), Tuberculum Sellae



**Figure 10.** Association between Glasgow Scale and Pathology Diagnosis with patient outcomes. **A.** Glasgow Scale and Outcome. **B.** Pathology Diagnosis and Outcome.





**Figure 11. A. Type of Bleeding and Outcome. B. Bleeding Location and Outcome.**

(2), and Third Ventricle (1)) show exclusive association with Morbimortality, suggesting potential anatomical vulnerability. This finding may guide further clinical investigations into high-risk bleeding locations.

These graph-based visualizations intuitively reveal how clinical attributes relate to outcomes, helping identify patterns and outliers not easily seen in statistical summaries, supporting clinical decision-making.

## CONCLUSION

This paper demonstrated the feasibility and relevance of using supervised Machine Learning to support clinical decision-making in rare and high-risk scenarios, such as spontaneous intracranial hemorrhage in patients with meningiomas. Through

the construction of a carefully curated dataset and the application of a structured preprocessing and modeling pipeline, it was possible to train a predictive model capable of estimating patient outcomes with promising accuracy.

The AdaBoost model classifier achieved an overall Accuracy of 85%, with a Recall of 97% for the majority Morbimortality class and 68% for the minority Recovery class. This excellent performance in identifying fatal outcomes demonstrates the strong potential of the model as a clinical decision-support tool. Its high sensitivity to high-risk cases enables timely interventions and more effective allocation of critical care resources, essential factors in severe neurosurgical scenarios.

This paper also highlights the essential role of multidisciplinary collaboration. The integration of computer science techniques, especially in data modeling and artificial intelligence, with medical expertise in neurosurgery was fundamental to ensure both technical rigor and clinical relevance.

In addition to its predictive and clinical contributions, this paper also stands out as a methodological benchmark by illustrating a comprehensive pipeline for the development of Artificial Intelligence-based models in the healthcare domain. From the engineering of clinically meaningful features to the application of robust data preprocessing and model validation strategies, the approach outlined in this paper can serve as a practical guideline for researchers and practitioners aiming to build reliable and interpretable predictive models in similar medical contexts.

Besides the predictive modeling, this paper also offers a significant contribution by providing access to a finalized and optimized dataset. Comprising 294 clinically validated cases and a comprehensive set of key variables, this dataset represents a valuable asset for the medical research community, enabling further investigations and studies of hemorrhagic meningiomas.

Future work should focus on expanding the dataset, especially Recovery cases, and exploring advanced hyperparameter optimization methods. Deploying the model as part of a clinical decision-support system is also a natural next step to enhance its practical utility.

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# Endoscopic Surgery for Lumbar Stenosis: a Brazilian case series with clinical and surgical outcomes

## *Cirurgia Endoscópica para Estenose Lombar: série de casos brasileira com resultados clínicos e cirúrgicos*

Reinaldo Rodrigues Pamplona<sup>1</sup> 

Vinicius Santos Baptista<sup>2</sup> 

### ABSTRACT

**Introduction:** Degenerative lumbar spinal stenosis is a frequent cause of disability, and full-endoscopic decompression has emerged as a minimally invasive alternative, though Brazilian evidence remains limited. **Objective:** To evaluate the safety, feasibility, and clinical outcomes of full-endoscopic lumbar decompression at a Brazilian neurosurgical center. **Methods:** This retrospective series included 45 patients treated between May 2021 and November 2024. A single neurosurgeon performed all procedures using interlaminar or transforaminal approaches. Demographic, intraoperative, and postoperative data were analyzed. Primary outcomes were complications and improvement on the Visual Analog Scale (VAS) at six months ( $p < 0.05$ ). **Results:** Mean age was 50.7 years; 56% were female. L4–L5–S1 was treated in 75.5% of cases. Mean operative time was 150 minutes, with 40 mL blood loss and no dural or nerve injuries. Complications included transient paresthesia (6.7%) and one self-limited epidural hematoma (2.2%). VAS improved from 9.1 to 3.3 ( $p < 0.0001$ ). No reoperations or infections occurred, and hospital stay averaged 0.3 days. **Conclusion:** Full-endoscopic lumbar decompression was safe, effective, and reproducible, providing excellent short-term outcomes for lumbar stenosis in this cohort.

**Keywords:** Lumbar vertebrae; Intervertebral disc; Minimally invasive surgical procedures; Low back pain; Treatment outcome

### RESUMO

**Introdução:** A estenose lombar degenerativa é uma causa frequente de incapacidade, e a descompressão totalmente endoscópica tem surgido como alternativa minimamente invasiva, embora ainda haja poucas evidências brasileiras. **Objetivo:** Avaliar a segurança, a viabilidade e os desfechos clínicos da descompressão lombar totalmente endoscópica em um centro neurocirúrgico brasileiro. **Métodos:** Esta série retrospectiva incluiu 45 pacientes tratados entre maio de 2021 e novembro de 2024. Um único neurocirurgião realizou todos os procedimentos por via interlaminar ou transforaminal. Foram analisados dados demográficos, intraoperatórios e pós-operatórios. Os desfechos primários foram complicações e melhora pela Escala Visual Analógica (EVA) aos seis meses ( $p < 0,05$ ). **Resultados:** A média de idade foi de 50,7 anos; 56% eram mulheres. L4–L5–S1 foi tratado em 75,5% dos casos. O tempo operatório médio foi de 150 minutos, com perda sanguínea de 40 mL e ausência de lesões durais ou nervosas. As complicações incluíram parestesia transitória (6,7%) e um hematoma epidural autolimitado (2,2%). A EVA reduziu de 9,1 para 3,3 ( $p < 0,0001$ ). Não houve reoperações ou infecções, e a internação média foi de 0,3 dia. **Conclusão:** A descompressão lombar totalmente endoscópica mostrou-se segura, eficaz e reprodutível, oferecendo excelentes resultados de curto prazo para estenose lombar nesta coorte brasileira.

**Palavras-Chave:** Vértebras lombares; Disco intervertebral; Procedimentos cirúrgicos minimamente invasivos; Lombalgia; Resultado do tratamento

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## INTRODUCTION

Lumbar spinal canal stenosis is one of the most frequent causes of disabling low back pain and neurogenic claudication in adults over the fifth decade of life. It results from a multifactorial degenerative process involving disc degeneration, facet hypertrophy, and thickening of the ligamentum flavum<sup>1</sup>. Its prevalence among individuals over 60 years of age has been estimated to range between 20% and 30%, making it a condition of major clinical and socioeconomic impact<sup>2</sup>.

Clinically, patients typically present with low back pain, radicular symptoms, and progressive neurogenic claudication, characterized by pain and weakness in the lower limbs triggered by walking and relieved by rest or lumbar flexion<sup>3</sup>. Although conservative management—including physical therapy, analgesics, and epidural injections—may be effective in mild cases, patients with refractory symptoms frequently require surgical intervention<sup>4</sup>.

Historically, open laminectomy has been considered the gold standard for surgical decompression of lumbar stenosis; however, it is associated with significant morbidity, including greater blood loss, prolonged hospitalization, and an increased risk of postoperative instability<sup>5</sup>. In this context, minimally invasive techniques have been progressively incorporated into clinical practice, aiming to reduce complications and accelerate functional recovery.

Endoscopic spine surgery has emerged as a promising alternative, allowing effective decompression of the spinal canal through interlaminar or transforaminal approaches, with less tissue disruption, preservation of stabilizing structures, and faster recovery<sup>6,7</sup>. Recent studies have demonstrated that endoscopic procedures yield outcomes comparable to open surgery in terms of pain relief and functional improvement, with additional advantages such as shorter operative time, reduced blood loss, and shorter hospital stay<sup>8,9</sup>.

Despite the growing body of international evidence, national literature on endoscopic surgery for lumbar stenosis remains limited, restricting the dissemination of these findings within the Brazilian scientific community. Therefore, it is relevant to report institutional experience with this technique, describing clinical and surgical outcomes as well as the main procedure-related complications. The present study aimed to systematically report the results of endoscopic surgery in the treatment of

lumbar spinal canal stenosis, contributing to the consolidation of national scientific evidence and supporting the advancement of minimally invasive neurosurgical practice in Brazil.

## METHODS

*General information*

This study consisted of a retrospective, consecutive case series. Patient data were collected from the database of the Fundação de Neurologia e Neurocirurgia – Instituto do Cérebro between May 2021 and November 2024. The institutional database, primarily used for surgical documentation, was retrospectively accessed for data extraction for this research.

All patients who underwent endoscopic treatment for lumbar spinal canal stenosis with a clinical indication of neurogenic claudication and radiological confirmation of stenosis on magnetic resonance imaging were included. Approximately 40 eligible patients were estimated. Exclusion criteria were: age under 18 years; significant segmental instability, defined as vertebral translation greater than 3 mm on dynamic flexion–extension radiographs and/or angular rotation exceeding 10°; associated deformities requiring stabilization, in which isolated endoscopy was not considered an adequate treatment.

Patients underwent endoscopic surgery only at levels with confirmed stenosis. In cases involving two or more stenotic levels, all affected segments were addressed during the same surgical session to achieve complete and homogeneous decompression according to the distribution of narrowing. Endoscopic treatment was performed via either an interlaminar or a transforaminal approach, depending on patient-specific factors. The interlaminar technique was prioritized in cases of significant central stenosis or lateral stenosis at lower lumbar levels (L4–L5 and L5–S1), where the larger interlaminar space allows direct access to the central canal and broader decompression. Conversely, the transforaminal approach was preferred for foraminal or extraforaminal stenosis, particularly at higher lumbar levels (L2–L3 and L3–L4), where the interlaminar window is naturally narrower.

Beyond stenosis topography, additional factors guided the choice of approach: (a) associated disc herniation: foraminal or extraforaminal

herniations favored the transforaminal route due to the possibility of direct fragment removal and foramen widening; herniations contributing to central narrowing favored the interlaminar route for central canal decompression; (b) posterior arch morphology: wide laminae and less prominent facets favored the interlaminar approach; marked facet hypertrophy, short pedicles, or very narrow lateral recesses favored the transforaminal approach to minimize central manipulation; (c) facet joint degeneration: severe degeneration restricting the interlaminar window indicated a transforaminal route; mild to moderate degeneration requiring limited foraminotomy and central decompression remained suitable for the interlaminar approach; (d) history of prior surgery at the same level: extensive scar tissue and adhesions from previous posterior approaches favored the transforaminal route to avoid dissecting through fibrotic planes; conversely, recurrent central stenosis after prior foraminal decompression favored the interlaminar approach targeting the central canal.

Indications for endoscopic treatment included: (i) neurogenic claudication and/or radicular pain refractory to optimized conservative management (medication, physical therapy, and functional measures) for an adequate period; (ii) clinical–radiological correlation between symptoms and central, lateral, foraminal, or extraforaminal stenosis demonstrated by MRI; (iii) stable degenerative disease without significant segmental instability on dynamic studies; (iv) uni- or multilevel stenosis amenable to decompression via interlaminar and/or transforaminal routes; and (v) clinical conditions in which a minimally invasive approach could reduce perioperative morbidity compared with conventional open techniques, as determined by the attending surgical team.

All procedures were performed under general anesthesia by the same lead surgeon, ensuring technical standardization across cases.

Primary outcomes of this study were postoperative complications—including paresthesia (assessed using the Leeds Assessment of Neuropathic Symptoms and Signs, LANSS), autonomic alterations, hematoma, infection, need for reoperation—and clinical improvement in pain and neurogenic claudication. Clinical improvement was evaluated by comparing Visual Analogue Scale (VAS) scores before surgery and at 6 months postoperatively.

Secondary outcomes included intraoperative complications (vascular injury, dural sac tear, and nerve root injury), estimated blood loss, and operative time. Intraoperative injuries were defined

as any damage to these structures, whether from accidental incision or inappropriate manipulation causing intra- or postoperative repercussions. Blood loss was estimated by measuring the aspirated volume and the number of surgical sponges used. Operative time was defined as the interval between the initial skin incision and wound closure, as recorded intraoperatively.

Additional variables collected included the number of patients, sex, mean age, body mass index (BMI), year of surgery, and operated levels.

All patients were followed retrospectively for 6 months after surgery through routine postoperative visits, during which possible complications and clinical evolution of pain and claudication were assessed. According to institutional protocol, follow-up visits occurred at 1 week, 1 month, and 6 months postoperatively. All data, including intraoperative information, were already recorded in the institutional database, and review of hospital medical records was not required.

### *Statistical analysis*

Statistical analysis systematically evaluated the collected data and interpreted the study outcomes with scientific rigor. Descriptive statistics was first calculated for all variables, including means, standard deviations, medians, and interquartile ranges for continuous variables, as well as absolute and relative frequencies for categorical variables.

To compare preoperative and postoperative VAS scores (preoperative vs. 6-month follow-up), a paired t-test is applied if the data exhibits a normal distribution; otherwise, the Wilcoxon signed-rank test is used. Data normality is assessed using the Shapiro–Wilk test.

The significance level is set at 5% ( $p < 0.05$ ), and all confidence intervals are reported at the 95% level. Statistical analyses is performed using R software (version 4.3.1), ensuring reproducibility and precision of results.

## RESULTS

Forty-five patients were included in this retrospective case series, with a mean age of 50.8 years (range 35–79) and mean BMI of 25.0 kg/m<sup>2</sup>. There were 19 men (42.2%) and 25 women (55.6%) (Table 1).



**Table 1.** Demographic Data.

General characteristics	
Number of Patients, n	45
Mean age, y (SD)	50.77 (10.94)
Age range, y	35 - 79
Median age, y	48
Sex (male/female), n	19 / 25
Mean BMI, kg/m2 (SD)	24.98 (1.97)
<b>Year of Surgery</b>	<b>n</b>
2021	13
2022	15
2023	6
2024	11

**Description:** BMI = Body Mass Index; SD = Standard Deviation

**Table 2.** Intraoperative Parameters.

Operated Levels	
L1-L2-L3	1
L2-L3-L4	1
L3-L4-L5	2
L3-L4-L5-S1	1
L4-L5	3
L4-L5-S1	34
L5-S1	3
<b>Intraoperative injury</b>	
Nerve root involvement, n (%)	0
Dural sac injury, n (%)	0
<b>Operative time, min (SD)</b>	150.67 (22.35)
<b>Bleeding, mL (SD)</b>	40.67 (55.47)

**Description:** SD = Standard Deviation.

Most procedures were performed at L4–L5–S1 (34 cases; 75.6%), followed by L4–L5 (3 cases; 6.7%) and L5–S1 (3 cases; 6.7%). The mean operative time was 150.7 minutes, and the mean blood loss was 40.7 mL. No intraoperative dural or nerve root injuries were reported (Table 2).

Postoperative evaluation showed a significant reduction in pain, with VAS scores decreasing from 9.1 to 3.3 ( $p < 0.0001$ ). Transient paresthesia occurred in 3 patients (6.7%), resolving spontaneously,

**Table 3.** Postoperative Parameters.

VAS Scale	
Before surgery, SD	9.11 (0.33)
After surgery, SD	3.35 (1.00)
p-value	$< 0.0001$
<b>Postoperative complications</b>	<b>n</b>
Paresthesia, %	3
Lanns Scale, SD	16.33 (4.11)
Sympathetic changes, %	0
Epidural hematoma, %	1 (2.22)
Infection, %	0
Reoperation, %	0
<b>Length of stay, days (SD)</b>	0.33 (0.56)

**Description:** VAS = Visual Analog Scale; SD = Standard Deviation. We defined  $p < 0.05$  as the threshold for statistical significance.

and one epidural hematoma (~170 mL; 2.2%) resolved without surgical intervention. No infections, autonomic changes, or reoperations were recorded. The mean hospital stay was 0.3 days, consistent with the minimally invasive nature of the procedure (Table 3).

## DISCUSSION

This retrospective case series demonstrates that full-endoscopic lumbar decompression is a safe and effective option for the treatment of lumbar spinal stenosis in the Brazilian setting. The significant postoperative reduction in pain scores, the absence of neurological injury, and the minimal complication rate observed reinforce the consistency of our results with the international literature<sup>6-8</sup>.

Several studies have confirmed that full-endoscopic decompression achieves outcomes comparable to conventional open or microscopic techniques, with additional benefits in terms of reduced morbidity and faster recovery<sup>8,10,11</sup>. A meta-analysis comparing endoscopic and microscopic decompression reported similar functional improvements, but lower complication rates and shorter hospital stay in the endoscopic group<sup>12</sup>. These findings support the current global trend toward minimally invasive spinal surgery as an effective and patient-centered approach.

Our results align closely with these studies<sup>10-12</sup>. We observed no intraoperative dural or nerve injuries, and only one postoperative hematoma (~170 mL), which was resolved without intervention. Transient paresthesia occurred in a small proportion of patients and resolved spontaneously. These complication rates are lower than those reported in large international reviews, which have documented dural tears in approximately 2–3% of cases and transient neurological symptoms in up to 5%<sup>11,13,14</sup>.

The mean operative time and minimal intraoperative bleeding in our series are consistent with previously reported benchmarks<sup>15</sup>. Moreover, the mean hospital stay of less than one day illustrates one of the most relevant clinical and socioeconomic advantages of endoscopic surgery—rapid postoperative recovery with early ambulation and discharge. Similar findings have been observed in international cohorts, where shorter hospitalization has been associated with lower perioperative morbidity and faster return to activity<sup>16</sup>.

From a broader perspective, the present study holds relevance within the Brazilian neurosurgical context, where published data on full-endoscopic lumbar decompression remain limited. By reporting institutional outcomes based on standardized criteria and systematic data collection, our series contributes original evidence supporting the applicability and safety of this minimally invasive technique in local practice.

### ***Strengths and Limitations***

This study adds original evidence from a Brazilian neurosurgical center, contributing to the limited regional literature on full-endoscopic lumbar decompression. The uniformity of surgical technique and perioperative management, ensured by a single surgeon, enhances internal consistency. The systematic data collection and standardized inclusion criteria strengthen methodological reliability and support the reproducibility of the findings in similar clinical settings.

Some limitations should be acknowledged. The retrospective design inherently restricts causal inference, and the sample size, although representative for a single institution, may not capture the full variability of lumbar stenosis presentations. These constraints are inherent to institutional case series but do not lessen the clinical relevance or scientific contribution of this work, which reinforces the applicability and safety of full-endoscopic decompression within the Brazilian neurosurgical context.

## CONCLUSION

Full-endoscopic lumbar decompression proved to be a safe and effective technique for the treatment of degenerative lumbar spinal stenosis in this Brazilian institutional experience. The procedure provided consistent clinical improvement, minimal perioperative morbidity, and favorable recovery profiles, reinforcing its feasibility in routine neurosurgical practice. These findings support the incorporation of full-endoscopic decompression as a reliable minimally invasive alternative for appropriately selected patients, contributing to the expansion of evidence-based endoscopic spine surgery in Brazil.

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# Advances in the Endovascular Therapies for Ischemic Stroke: implication for the neurosurgical practice

## *Avanços em Terapias Endovasculares do AVC Isquêmico: implicações para a prática neurocirúrgica atual*

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### ABSTRACT

**Introduction:** Mechanical thrombectomy has established itself as one of the most innovative and effective therapeutic interventions in the management of ischemic stroke. Although widely incorporated into international guidelines, its application in neurosurgical practice requires further discussion, especially given the continuous evolution of indications and associated technologies. **Methods:** A systematic review was conducted on PubMed, SciELO and Virtual Health Library (VHL) databases between 2015 and 2025, searching for clinical data, efficacy, comparison between methods and normative evidence. **Results:** The findings further support mechanical thrombectomy as the gold-standard intervention for the management of acute ischemic stroke, demonstrating its effectiveness across diverse patient populations and underscoring the critical role of multidisciplinary team-based care to ensure its safe and efficient implementation. **Discussion:** Although mechanical thrombectomy represents a significant advance in the treatment of ischemic stroke, challenges remain related to the training of professionals, accessibility to the procedure and integration between neurologists and neurosurgeons. **Conclusion:** mechanical thrombectomy represents one of the most significant innovations in the treatment of acute ischemic stroke. However, its practical application still faces barriers related to accessibility, technical training and integration between medical specialties, especially in the context of neurosurgery.

**Keywords:** Ischemic stroke; Mechanical thrombectomy; Endovascular Neurosurgery

### RESUMO

**Introdução:** A trombectomia mecânica consolidou-se como uma das intervenções terapêuticas mais inovadoras e eficazes no manejo do acidente vascular cerebral (AVC) isquêmico. Embora amplamente incorporada às diretrizes internacionais, sua aplicação na prática neurocirúrgica requer maior discussão, especialmente diante da evolução contínua das indicações e tecnologias associadas. **Métodos:** Foi realizada uma revisão sistemática nas bases de dados PubMed, SciELO e Biblioteca Virtual em Saúde (BVS) entre 2015 e 2025, com busca de dados clínicos, eficácia, comparação entre os métodos e evidências normativas. **Resultados:** Os achados reforçam a trombectomia mecânica como padrão-ouro no manejo do AVC isquêmico, evidenciando sua eficácia em diversos perfis populacionais e ressaltando a importância da atuação multiprofissional para sua execução segura e eficiente. **Discussão:** Embora a trombectomia mecânica represente um avanço significativo no tratamento do AVC isquêmico, persistem desafios relacionados à capacitação de profissionais, acessibilidade ao procedimento e integração entre neurologistas e neurocirurgiões. **Conclusão:** a trombectomia mecânica representa uma das mais expressivas inovações no tratamento do AVC isquêmico agudo. Contudo, sua aplicação prática ainda enfrenta barreiras relacionadas à acessibilidade, à capacitação técnica e à integração entre especialidades médicas, especialmente no contexto da neurocirurgia.

**Palavras-Chave:** Acidente vascular cerebral isquêmico; Trombectomia mecânica; Neurocirurgia Endovascular

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## INTRODUCTION

Ischemic stroke is one of the leading causes of morbidity and mortality worldwide, significantly impacting the quality of life of affected patients and causing high costs for healthcare systems<sup>1-3</sup>. Among the various therapeutic modalities, emergency endovascular treatment has been a fundamental tool in the management of acute cases of large vessel occlusion in recent decades, offering new perspectives for neurological recovery when compared to intravenous thrombolytic therapy alone<sup>4,5</sup>.

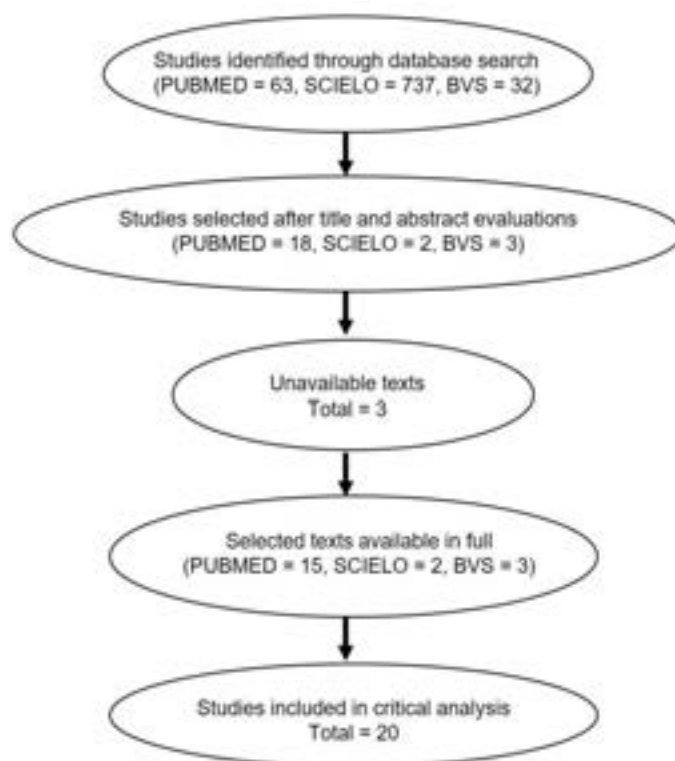
With advances in technology and the consolidation of robust clinical studies, such as the MR CLEAN, EXTEND-IA, SWIFT PRIME, and DEFUSE-3 trials, mechanical thrombectomy has become a standard of care for selected patients, especially within the therapeutic window of up to 24 hours, provided that specific radiological and clinical criteria are met<sup>4-9</sup>. The most recent international guidelines reinforce the recommendation of the endovascular approach for different patient profiles, including the elderly, patients with pre-existing disabilities, and cases involving posterior circulation<sup>3,9-12</sup>.

Despite the widespread adoption of thrombectomy in referral centers, its impact on neurosurgical practice still requires in-depth discussion, considering that many neurosurgeons have become active members of neurovascular intervention teams. Evolving indications, improved devices, and expanded eligibility criteria pose both challenges and opportunities for contemporary neurosurgery<sup>6,13,14</sup>.

Consequently, this study aims to review the most recent advances in endovascular therapies for ischemic stroke and discuss their practical implications for the practice of neurosurgeons today.

## MATERIAL AND METHODS

This study is a systematic literature review, conducted through searches in the PubMed, SciELO and Virtual Health Library (VHL) databases from March to April 2025. The search strategy used



**Figure 1.** Flowchart of the selection methodology of the included studies.

the descriptors “Ischemic Stroke”, “Mechanical Thrombectomy” and “Endovascular Neurosurgery”, combined with the Boolean operators “AND” and “OR”, in order to allow broad and precise combinations between the terms.

Studies published in the last ten years were included, provided they were available in full and fell into at least one of the following methodological categories: retrospective studies, randomized clinical trials, meta-analyses, systematic reviews, narrative reviews, clinical guidelines, scientometric studies, or technical reports. Articles that did not directly address the central research topic and those without full-text access were excluded.

Sixty-three studies were identified in PubMed, 737 in SciELO and 32 in VHL. After evaluating the titles and abstracts, 18 articles were selected from PubMed, 2 from SciELO, and 3 from VHL. Three texts were not available for full reading. At the end of the screening and eligibility process, 20 studies were included in the critical analysis of this review, as represented in the methodological flowchart (Figure 1).



## RESULTS

Of the 20 articles selected for this review (Table 1), 3 were classified as retrospective studies<sup>2,11,12</sup>, which contributed relevant clinical data on the application of mechanical thrombectomy in specific populations, such as pediatric patients, elderly patients, and individuals with previous disabilities.

Two studies stood out as randomized clinical trials<sup>5,15</sup>, demonstrating a strong level of evidence regarding the efficacy of stent-retriever thrombectomy and the comparison between different thrombolytic

agents. One of the analyzed studies was a meta-analysis of individual data<sup>4</sup>, consolidating the main multicenter clinical trials on the topic.

The majority of the sample consisted of narrative reviews (n = 7), which covered topics ranging from the technical foundations of endovascular neurosurgery to updates in guidelines and future perspectives on mechanical thrombectomy<sup>3,6,10,13,14,16,17</sup>.

Furthermore, four clinical guidelines published by national and international scientific societies<sup>7-9,18</sup>, a scientometric study<sup>1</sup>, a systematic review<sup>19</sup>, and a technical report on a health technology assessment<sup>20</sup> were included, enriching the analysis with normative

**Table 1.** Articles selected for this review.

Author	Title	Type of study	Sample	Points relevant to each study
Aburto-Murrieta et al. <sup>2</sup>	Extended time window mechanical thrombectomy for pediatric acute ischemic stroke	Retrospective study	Pediatric patients with late presentation	Demonstrated feasibility and safety of thrombectomy outside traditional time window in children.
Saber et al. <sup>11</sup>	Is endovascular treatment still good for acute ischemic stroke in the elderly?	Retrospective study	Elderly patients (≥80 years)	Showed positive outcomes in elderly patients, challenging age-based exclusion.
American Heart Association <sup>12</sup>	Endovascular therapy in patients with acute ischemic stroke with large vessel occlusion and prestroke disability	Retrospective study	Patients with pre stroke disability	Supported thrombectomy in patients with baseline disability, expanding indications.
Saver et al. <sup>5</sup>	Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke	Randomized clinical trial	Adult patients with LVO	Demonstrated superiority of thrombectomy plus t-PA over t-PA alone.
Menon et al. <sup>15</sup>	Tenecteplase versus alteplase before thrombectomy for ischemic stroke	Randomized clinical trial	Patients eligible for thrombolysis	Compared thrombolytics; tenecteplase showed favorable results.
Goyal et al. <sup>4</sup>	Endovascular thrombectomy after large-vessel ischaemic stroke	Meta-analysis	Pooled data from 5 RCTs	Confirmed benefit of thrombectomy over medical therapy alone.
Schneider et al. <sup>3</sup>	Posterior circulation ischaemic stroke diagnosis and management	Narrative review	Not applicable	Reviewed posterior circulation stroke and role of thrombectomy.
Boeckh-Behrens et al. <sup>6</sup>	Current endovascular treatment of acute ischemic stroke	Narrative review	Not applicable	Summarized contemporary thrombectomy techniques and challenges.
Liu et al. <sup>10</sup>	Integrative approaches in acute ischemic stroke	Narrative review	Not applicable	Highlighted diagnostic tools and workflow innovations.
Jadhav et al. <sup>13</sup>	Indications for mechanical thrombectomy for acute ischemic stroke	Narrative review	Not applicable	Updated clinical indications for thrombectomy.
CNS Neurosci Ther <sup>16</sup>	Advances in acute ischemic stroke treatment	Narrative review	Not applicable	Reviewed recent progress in stroke intervention strategies.
Nguyen et al. <sup>14</sup>	Endovascular management of acute stroke	Narrative review	Not applicable	Discussed modern stroke systems of care.



**Table 1.** Continued...

Author	Title	Type of study	Sample	Points relevant to each study
Lauer et al. <sup>17</sup>	Advances in endovascular thrombectomy for the treatment of acute ischemic stroke	Narrative review	Not applicable	Outlined future directions and technological innovations.
Brasil <sup>18</sup>	Diretrizes Brasileiras para o tratamento endovascular do AVC isquêmico agudo	Guideline	Not applicable	Established national standards for thrombectomy indications and timing.
Powers et al. <sup>7</sup>	2018 Guidelines for the early management of acute ischemic stroke	Guideline	Not applicable	Defined recommendations for stroke treatment timing and selection.
Canadian Stroke Best Practices <sup>8</sup>	Acute stroke management	Guideline	Not applicable	National guideline emphasizing workflow efficiency and access.
Turc et al. <sup>9</sup>	ESO guidelines on mechanical thrombectomy	Guideline	Not applicable	Provided European recommendations for thrombectomy indications.
Ferreira et al. <sup>19</sup>	Trombectomia endovascular para o tratamento do AVC isquêmico agudo	Systematic review	Not applicable	Synthesized evidence supporting thrombectomy outcomes.
Wu et al. <sup>1</sup>	Global trends of mechanical thrombectomy in acute ischemic stroke	Scientometric study	Global publication data	Mapped global research trends and growth in thrombectomy literature.
IECS <sup>20</sup>	Trombectomia endovascular en ACV isquêmico agudo	Health technology assessment	Policy-level evidence	Evaluated cost-effectiveness and access to thrombectomy in Latin America.

evidence and data on the evolution of scientific production on the topic.

These findings confirm that mechanical thrombectomy has been widely studied from different perspectives, reflecting its consolidation as a relevant therapeutic strategy in the management of acute ischemic stroke.

## DISCUSSION

Mechanical thrombectomy has been established as one of the major therapeutic advances in the management of acute ischemic stroke. Pivotal studies, such as those by Goyal et al.<sup>4</sup> demonstrated, through a meta-analysis involving five randomized clinical trials, that endovascular thrombus removal in patients with large vessel occlusion is associated with higher rates of arterial recanalization and better functional outcomes when compared to clinical treatment alone.

Saver et al.<sup>5</sup> reinforced this evidence by comparing intravenous thrombolysis alone with the combination of alteplase and stent-retriever thrombectomy. The authors observed significant improvements in neurological scores and reduced functional dependence at 90 days in the group undergoing mechanical intervention, validating the safety and the efficacy of the procedure.

In addition to the well-established benefits of the anterior circulation, Schneider et al.<sup>3</sup> highlighted that ischemic stroke in the posterior circulation, although less prevalent, can also be successfully managed with thrombectomy. The article emphasizes the need for specific clinical and radiological criteria for patient selection, as this population often presents with atypical clinical presentations that are difficult to recognize in the beginning.

Another relevant aspect is the expansion of indications to less conventional populations. Aburto-Murrieta et al.<sup>2</sup> demonstrated the efficacy of thrombectomy in children with ischemic stroke, even outside the traditional therapeutic window. The study suggests that the response to endovascular treatment in this age group may

be comparable to that in adults, reinforcing the importance of individualized assessment of symptom onset.

Complementing this comprehensive overview, Wu et al.<sup>1</sup>, in a scientometric analysis, demonstrated the exponential growth of publications on mechanical thrombectomy in the last decade. This increase reflects not only academic interest but also the practical incorporation of the technique in different clinical and geographic settings, revealing its transformative impact on the management of ischemic stroke.

In addition to the well-established efficacy of stent-retriever thrombectomy, Saver et al.<sup>5</sup> highlighted the superiority of the technique over the exclusive use of intravenous t-PA, even in patients treated early. The data indicate that mechanical intervention promotes sustained benefits in functional recovery, being more effective in complete recanalization and favorable neurological outcomes, reinforcing its application as the gold standard in proximal occlusions.

Boeckh-Behrens et al.<sup>6</sup> complement this perspective by describing technological advances in thrombectomy devices, such as combined aspiration systems and more easily navigable microcatheters, which have increased the safety and success rate of the procedure. The article also highlights the importance of technical familiarity and the learning curve in optimizing outcomes, aspects relevant to neurosurgical practice.

From the perspective of therapeutic integration, Liu et al.<sup>10</sup> discuss integrated approaches to acute ischemic stroke, from early symptom recognition to personalized intervention strategies. The use of artificial intelligence in image triage and the introduction of clinical workflows adapted to the hospital environment are among the advances that optimize door-to-puncture time, a critical factor in thrombectomy.

Jadhav et al.<sup>13</sup> provide an in-depth discussion of current guidelines and broader clinical criteria for thrombectomy indications, including in patients with low ASPECTS scores, mild neurological deficits, or pre-existing comorbidities. The authors' analysis highlights the expanding profile of patients eligible for intervention, which reinforces the need for ongoing training of neurosurgeons and interventional neurologists for appropriate and safe evaluation.

The discussion on the future of endovascular therapy is also explored in the review published in *CNS Neuroscience & Therapeutics*<sup>16</sup>, which highlights perspectives such as the use of tenecteplase as an alternative to alteplase, the creation of prehospital triage systems, and the expansion of treatment in remote areas through telemedicine and mobile stroke units.

Finally, Saber et al.<sup>11</sup> draw attention to the efficacy of thrombectomy in elderly patients. In a recent study, they demonstrated that advanced age alone should not be considered a limiting factor for the procedure. Although there is a higher risk of complications, functional benefits are consistent when appropriate selection is made based on imaging and detailed clinical evaluation.

The search for pharmacological optimization has also gained prominence in the pre-thrombectomy phase. Menon et al.<sup>15</sup> demonstrated that the use of tenecteplase, compared to alteplase, may offer advantages in arterial recanalization and ease of administration, reinforcing its viability as the thrombolytic agent of choice before mechanical intervention.

The American Heart Association (AHA) guidelines emphasize that patients with pre-existing impairment should not be automatically excluded from thrombectomy, provided they present functional potential and favorable radiological criteria<sup>12</sup>. This expands access to endovascular treatment to a more diverse patient profile, an essential aspect in an increasingly complex clinical environment.

Recent reviews, such as the one published in the *Lancet*<sup>14</sup>, reiterate that mechanical thrombectomy continues to evolve both in terms of technique and global access. The study highlights the need to expand referral centers, reduce hospital response times, and ensure multidisciplinary training. Complementing this conclusion, the analysis by Taylor & Francis<sup>17</sup> projects the future of thrombectomy with technologies integrated with artificial intelligence, automated brain mapping, and patient selection via predictive algorithms.

In the national context, Brazilian guideline, published by the Brazilian Academy of Neurology<sup>18</sup>, recognizes thrombectomy as the standard procedure for large vessel occlusions, aligning with international guidelines. National studies, such as that by Ferreira et al.<sup>19</sup> and the report by the Institute of Clinical and Health Effectiveness (IECS)<sup>20</sup>, reaffirm its efficacy and safety, although they emphasize the need to expand access, training, and infrastructure in Brazil and Latin America.

Despite robust evidence, significant limitations remain. There is a scarcity of data on the specific impact of interventional neurosurgeons' work in the Brazilian and Latin American contexts, as well as a lack of longitudinal studies evaluating functional outcomes in specific subgroups, such as patients with large infarcts, low ASPECTS scores, or multiple comorbidities. Additionally, some of the literature still presents methodological heterogeneity or is based on retrospective cohorts, which may limit the generalizability of the findings<sup>7-9</sup>.

Thus, this study reinforces that advances in endovascular therapies for ischemic stroke have profoundly transformed the therapeutic landscape of the disease. The expansion of indications, the evolution of devices, the incorporation of new guidelines, and the expanding role of interventional neurosurgeons point to a new paradigm in stroke treatment. It is essential, therefore, that referral centers prioritize ongoing training, multidisciplinary integration, and technological updating, ensuring universal, equitable, and evidence-based access to treatment.

## CONCLUSION

Based on this discussion, it is possible to conclude that mechanical thrombectomy represents one of the most significant innovations in the treatment of acute ischemic stroke in recent decades. However, its practical application still faces barriers related to accessibility, technical training, and integration between medical specialties, especially in the context of neurosurgery.

Although the procedure's efficacy has been widely demonstrated by clinical trials and international guidelines, many centers still face structural or human resource limitations for its full implementation. Furthermore, there is a lack of specific data on the direct involvement of interventional neurosurgeons in therapeutic decisions and the performance of the procedure.

In this paper, we also discuss how technological advances, new drugs, and expanded clinical criteria are shaping a new eligibility profile for thrombectomy, making the work of well-trained and up-to-date multidisciplinary teams essential. However, significant gaps remain regarding the standardization of clinical workflows and effective integration between neurologists and neurosurgeons.

Therefore, we reinforce the importance of new studies that more deeply explore the impact of endovascular neurosurgery on current clinical practice, with larger sample sizes and robust methodologies, to strengthen scientific evidence and improve functional outcomes for patients with ischemic stroke.

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## CRediT

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# Post-traumatic Arterial Spasm: a blood flow analysis by transcranial Doppler


## *Espasmo Arterial Pós-traumático: uma análise de fluxo sanguíneo por doppler transcraniano*

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### ABSTRACT

Posttraumatic arterial spasm (PTAE) is characterized by an abnormal contraction of intracranial arteries after trauma, reducing cerebral blood flow. Early identification and appropriate management are essential to prevent cerebral ischemia and intracranial hypertension (ICH). Transcranial Doppler (TCD) stands out as a noninvasive tool for real-time monitoring. A systematic review was performed in the PubMed and Medline databases. The PICO strategy was applied and the PRISMA methodology was followed. The search used the descriptors (posttraumatic cerebral arterial spasm OR posttraumatic cerebral vasospasm OR intracranial arterial spasm OR intracranial vasospasm) AND (transcranial doppler ultrasonography), with filters for Clinical Trial, Meta-Analysis, Randomized Controlled Trial and observational studies, in Portuguese, English and Spanish, published between 2009 and 2024. The selection was conducted by two independent reviewers, with disagreements resolved by consensus. A total of 641 studies were initially identified. 18 were selected after screening of titles and abstracts. After the complete analysis, 7 studies were included. TCD had a positive effect on the detection of arterial spasms, vascular resistance, and pharmacological strategies. TCD is a valuable tool for monitoring patients with PTEA. However, future studies are needed to optimize clinical management.

**Keywords:** Post-traumatic arterial spasm; Transcranial Doppler; Cerebral vasospasm; Subarachnoid hemorrhage; Cerebral blood flow

### RESUMO

O espasmo arterial pós-traumático (EAPT) caracteriza por uma contração anormal das artérias intracranianas após um trauma, reduzindo o fluxo sanguíneo cerebral. Identificar precocemente e o manejo adequado são fundamentais para prevenir isquemia cerebral e hipertensão intracraniana (HIC). O Doppler transcraniano (DTC) destaca-se como ferramenta não invasiva para o monitoramento em tempo real. Foi realizada uma revisão sistemática nas bases de dados PubMed e Medline. A estratégia PICO foi aplicada e a metodologia PRISMA foi seguida. A busca utilizou os descritores (posttraumatic cerebral arterial spasm OR posttraumatic cerebral vasospasm OR intracranial arterial spasm OR intracranial vasospasm) AND (transcranial doppler ultrasonography), com filtros para Clinical Trial, Meta-Analysis, Randomized Controlled Trial e estudos observacionais, nos idiomas Português, Inglês e Espanhol, publicados entre 2009 e 2024. A seleção foi conduzida por dois revisores independentes, com divergências resolvidas por consenso. Foram identificados 641 estudos inicialmente. 18 foram selecionados após a triagem de títulos e resumos. Posteriormente a análise completa, 7 estudos foram incluídos. O DTC atuou positivamente na detecção de espasmos arteriais, na resistência vascular, e nas estratégias farmacológicas. O DTC é uma ferramenta valiosa para o monitoramento em pacientes com EAPT. Entretanto, estudos futuros são necessários para otimizar o manejo clínico.

**Palavras-chave:** Espasmo arterial pós-traumático; Doppler transcraniano; Vasoespasmo cerebral; Hemorragia subaracnoidea; Fluxo sanguíneo cerebral

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## INTRODUCTION

Post-traumatic arterial spasm is the abnormal contraction of an artery following some type of trauma, resulting in reduced blood flow to various brain segments. It tends to have consequences for the body's physiological functioning, mainly caused by subarachnoid hemorrhage (SAH) and cerebral ischemia<sup>1</sup>.

Neurologists, neurosurgeons, and neurointensivists are the responsables for the approach to detect primary and secondary brain injuries and to guide therapy in patients with acute traumatic brain injury (ATBI) and intracranial hypertension (ICH) due to post-traumatic vasospasm (PTV). The widespread availability of diagnostic equipment and multimodal monitors that aid patient assessment in a neurocritical care setting favors such approaches<sup>2</sup>.

Highlighting the availability of both invasive and non-invasive devices has enabled a more careful analysis of primary and secondary brain injuries. CTBI can be classified as mild, moderate, and severe based on injury severity, neurological status, and clinical presentation. The transcranial Doppler, a non-invasive device, allows real-time monitoring of intracranial pressure (ICP) and cerebral perfusion pressure (CPP), and enables bedside care to determine changes in mean flow velocities (MFV) indicative of changes in vascular caliber<sup>3</sup>.

The search for better therapeutic and diagnostic methods to positively enhance daily medical practice is shown by the emergence of new techniques, such as pharmaceutical options, while traditional methods are sometimes maintained and specific evaluations are sometimes lacking. Thus, this study aims to analyze the advantages and demonstrate the importance of transcranial Doppler in assisting in the management of post-traumatic arterial stenosis events, with the aim of increasing and expanding its use in clinical management.

## METHODS

The PICO (Population, Intervention, Comparison, Outcome) strategy helped to define the studies inclusion and exclusion criteria. Population (P): patients with post-traumatic arterial

spasm. Intervention (I): assessment of cerebral blood flow with transcranial Doppler. Comparison (C): assessment using traditional methods. Outcome (O): better understanding of hemodynamic patterns and blood flow alterations in post-traumatic brain injury. The final PICO question was: "In patients with post-traumatic arterial spasm, does the use of transcranial Doppler, compared with traditional invasive methods or the absence of specific assessment, improve the identification of hemodynamic alterations and blood flow patterns?"

Furthermore, PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) methodology was used to ensure transparency and accuracy in the selection and analysis of articles. The PRISMA diagram was followed to document the flow of information through the different phases of the review, including study identification, screening, eligibility, and inclusion.

This is a systematic review of studies indexed in the PubMed and Medline databases published between 2009 and 2024. The search strategy used in English was these DeCS/MeSH descriptors: (posttraumatic cerebral arterial spasm OR posttraumatic cerebral vasospasm OR intracranial arterial spasm OR intracranial vasospasm) AND (transcranial Doppler ultrasonography). The filters used were: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Observational Studies, in Portuguese, English, and Spanish. The primary outcome of interest selected was the identification and analysis of changes in cerebral blood flow (velocity, vascular resistance, presence of vasospasms) associated with post-traumatic arterial spasm, based on data obtained by transcranial Doppler. Excluded materials were articles not related to the topic, studies that did not directly evaluate blood flow patterns or the effectiveness of transcranial Doppler, animal studies, studies that only had the abstract available, reviews, letters to the editor, opinions and case studies not published between 2009 and 2024.

Article selection took place between January 9th and 21st, 2025, and was conducted independently by two reviewers, analyzing the titles and abstracts potentially eligible for inclusion in this review. All disagreements were resolved by consensus.

A total of 641 studies were identified using the descriptors used (PubMed = 624; Medline = 17). Forty-seven articles were filtered based on the study's inclusion and exclusion criteria

(PubMed = 30; Medline = 17). After the initial analysis, 18 eligible studies were selected based on their titles and abstracts. Thus, the reviewers evaluated the articles in full and extracted necessary data on authors, year of publication, participant characteristics, interventions, outcomes, and main results. After this final evaluation of the texts, seven articles were selected for the systematic review (Figure 1).

For data collection and review, two reviewers conducted a search of the respective databases using the defined descriptors and initial screening, using the Rayyan study tool for subsequent analysis. The reviewers independently examined the titles and abstracts of the references, and any discrepancies were resolved by consensus. The two reviewers independently assessed full-text articles for inclusion.

With these strategies, the systematic review seeks to provide a detailed view of post-traumatic arterial spasm and its changes in blood flow, using transcranial Doppler for a better assessment of hemodynamic patterns, contributing to a better understanding and possible advances in the field.

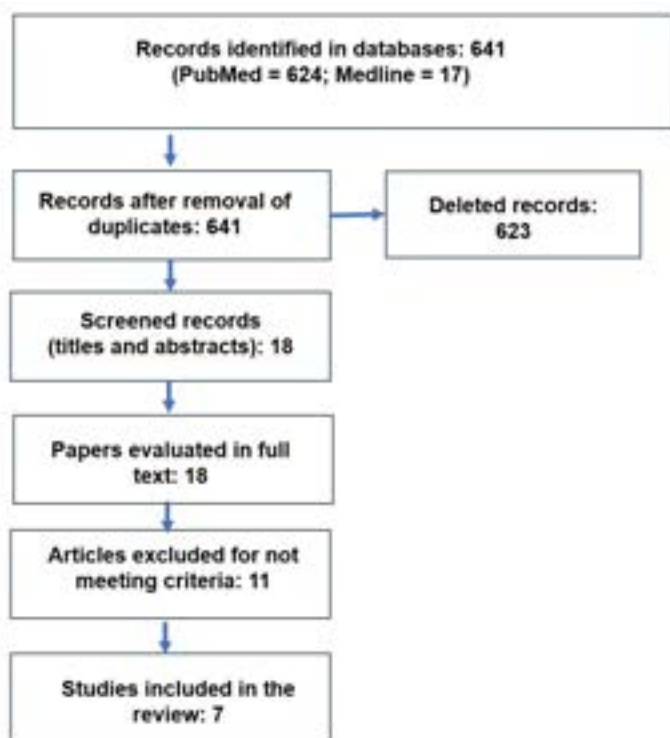


Figure 1. Methodology flowchart.

## RESULTS

The review included studies that investigated different aspects of post-traumatic arterial spasm, including: the evaluation of the effectiveness of transcranial Doppler in detecting arterial spasms compared to traditional methods or the absence of specific assessment; the identification of hemodynamic patterns associated with worsening or improvement in patients' clinical condition; the potential correlation between altered blood flow and neurological outcomes, such as functional deficits or recovery; the ease of implementing transcranial Doppler in the clinical setting; and the incidence of complications or limitations in the use of the technique. A total of seven main studies were analyzed. The main characteristics and findings of the studies included in this systematic review are summarized in Table 1, exploring interventions in several contexts, such as: early transcranial Doppler assessment of cerebral autoregulation independently, head-of-the-bed positioning, transcranial Doppler drug administration in vasospasm treatment; and the management of specific neurosurgical conditions in the treatment of post-traumatic arterial spasm. Despite the methodological variety among the studies, which included quantitative, qualitative, and mixed analyses, they all shared the common goal of assessing cerebral blood flow with transcranial Doppler.

Cerebral Vasospasm (CV) remains one of the main consequences of subarachnoid hemorrhage (SAH). Yamamoto T, et al. (2016)<sup>4</sup> demonstrated through a clinical study (carried out between 2008 and March 2013, with 70 patients that showed no significant differences between the groups in terms of age, sex, WFNS grade or Fisher grade and aneurysm location) that calcium antagonist agents, such as nimodipine, which produce vasodilation, can effectively treat patients with CV. Recently, magnesium (Mg), which acts physiologically as a calcium antagonist, has also been suggested as a potential therapeutic agent for CV. However, there may be adverse effects, such as an increased risk of exposure to hypotension or hypoperfusion in patients with CV, therefore, serum Mg<sup>2+</sup> levels should be strictly maintained at 2.0–2.5 mmol/L. Furthermore, studies demonstrate that after subarachnoid hemorrhage, intravenous therapy with Mg did not improve clinical results. Thus, it is evident that continuous cisternal irrigation with MgSO<sub>4</sub> solution reduces the rate of CV occurrence in patients with SAH.

**Table 1.** Main studies included in the systematic review on post-traumatic arterial spasm analyzed by transcranial Doppler.

Researcher	Year	Main results
Yamamoto T, et al. <sup>4</sup>	2016	Mg has been suggested as a potential therapeutic agent for CV, but it did not improve clinical outcomes after SAH, thus, continuous cisternal irrigation with MgSO <sub>4</sub> solution is evidenced.
Webb A, et al. <sup>1</sup>	2010	Intraventricular nicardipine was associated with a significant and sustained reduction in mean cerebral blood flow velocity, measured by transcranial Doppler, when used in the treatment of suspected cerebral vasospasm following aneurysmal subarachnoid hemorrhage.
Villa F, et al. <sup>5</sup>	2012	Isoflurane tends to act positively, reducing cerebral vascular resistance in microcirculation and intraparenchymal arterioles, thus suggesting that large vessel vasospasm may not be the only factor in predicting the outcome in SAH, in particular, intracerebral arterioles have an important role in regulating distal CBF.
Zhang Y, Rabinstein AA <sup>3</sup>	2011	The HOB position did not significantly affect the MFV in the patients with subarachnoid hemorrhage and was not associated with a significant change in MFV when the analysis was restricted to patients with vasospasm by ultrasonographic criteria.
Eicker SO, et al. <sup>6</sup>	2012	The clot clearance rate was significant, attributing success to the combination of intraventricular thrombolysis and lateral rotational therapy not associated with a higher complication rate
Rynkowski CB, et al. <sup>2</sup>	2019	Impaired intrinsic cerebral arterial vessel capacity remained independently associated with poor outcome after adjustment for known predictors of outcome, such as initial clinical grade (Hunt & Hess), subarachnoid blood volume on initial CT (Fisher grade), and age.
Varsos et al. <sup>8</sup>	2015	The presence of vasospasm significantly reduced CrCP, as seen in the temporal assessment, where the onset of vasospasm resulted in a decrease in CrCP, and in the spatial assessment, where vasospasm caused an interhemispheric difference in CrCP, with a lower CrCP ipsilateral to the spasm.

In the pharmacological field, the approach through Nicardipine was highlighted. Webb et al.<sup>1</sup> – through a retrospective study, without a control group, with a study population of 64 patients, mean age of 51.6 years (smokers: 52%; hypertensive: 55%), in which the aneurysm treatment 45% was by surgical clipping 45% and 55% endovascular coiling 55% - suggested that many of these patients already have ventricular drains installed. Thus, the medication can be administered via external ventricular drain (EVD) safely at the bedside and can be used in patients for whom conventional therapies are not effective or are not tolerated. Intraventricular nicardipine was associated with a significant and sustained reduction in the mean velocity of cerebral blood flow, measured by transcranial Doppler, when used in the treatment of suspected cerebral vasospasm after aneurysmal subarachnoid hemorrhage, assessed through the middle cerebral artery (MCA) and anterior cerebral artery (ACA). There was no significant increase in intracranial pressure on the days of administration.

Villa et al.<sup>5</sup> proposed the divergence of inhalation and intravenous sedation in subarachnoid hemorrhage. In a study carried out between April 2009 and May 2011, in which all 13 patients undergoing coiling were sedated with propofol and fentanyl during the procedure, in some patients, the entire procedure was performed under total intravenous anesthesia (still with propofol), while in other patients the anesthetist decided at some point to

change the intravenous anesthesia to inhalation anesthesia with sevoflurane. These patients were then sedated with propofol at the end of the surgical procedure before transfer to the ICU. Isoflurane tends to act positively, since it causes a reduction in cerebral vascular resistance in the microcirculation and in intraparenchymal arterioles rather than in large vessels such as the Middle Cerebral Artery, explored by transcranial Doppler, thus suggesting that large vessel vasospasm may not be the only factor in predicting the outcome in SAH, in particular, intracerebral arterioles have an important role in regulating distal CBF.

Zhang and Rabinstein<sup>3</sup> demonstrated in their research the changes in the head of the bed (HOB) positions in the face of blood flow velocities measured by Transcranial Doppler in patients with ischemic stroke, through the measurement of the mean flow velocity (MFV) of the middle cerebral artery (MCA). The patients underwent two MFV measurements in the middle cerebral artery (MCA) with different head of bed positions (HOB): HOB between 30–45°, HOB between 0–15°. However, when comparing the pair of measurements in each study (i.e., MFV before and after lowering the HOB), the difference was not noteworthy - Mean MFV in the MCA: HOB 30–45°: 100.1 ± 46.8 cm/s, HOB 0–15°: 101.0 ± 47.3 cm/s; therefore, the difference was not significant (P=0.77). Similarly, the position of the headboard was not associated with a significant change in MFV when the analysis was restricted to



patients with vasospasm by ultrasonographic criteria. Although the headboard position may theoretically increase cerebral perfusion, this effect was not captured by TCD. Limitations of the study include the exclusive focus on MCA MFV: other arteries were not evaluated; pulsatility index (PI) and Lindegaard ratio were not analyzed; BP was not measured at the tragus level, impeding more accurate cerebral hemodynamic interpretations; the use of a portable probe may have introduced variability; and the few patients with severe vasospasm.

Continuously, Eicker et al.<sup>6</sup> aimed to analyze the efficacy of discontinuous application of thrombolytic agents and movement therapy on cerebral vasospasm, delayed ischemic neurological deficit (DIND), and clinical outcome. Forty patients with aneurysmal subarachnoid hemorrhage (SAH) underwent the study - 16 patients in the study group and 19 patients in the control group -, and no serious side effects due to the combined therapy were documented. The clot clearance rate was significant, indicating the success of intraventricular thrombolysis and lateral rotational therapy combination, not associated with a higher complication rate. There was no increase in serious complications such as edema or rebleeding. CT scans did not detect significant differences in cerebral blood flow. Furthermore, the therapy significantly accelerates the rate of clot clearance.

Rynkowski et al.<sup>7</sup> analyzed 40 patients with aneurysmal SAH in their studies regarding cerebral autoregulation (CA), which corresponds to the intrinsic ability of cerebral arterial vessels to adjust their diameter to maintain a relatively constant cerebral blood flow, despite changes in cerebral perfusion pressure (CPP). When CA is impaired, there is a failure of this intrinsic mechanism to maintain constant CBF, regardless of CPP fluctuation; thus impaired CA remained independently associated with an unfavorable outcome (impaired CA: OR 5.15 (95% CI: 1.43–51.99,  $p = 0.033$ ) / Elevated APACHE II score: OR 1.67 (95% CI: 1.01–2.76,  $p = 0.046$ ). After adjusting for known predictors of outcome, such as initial clinical grade (Hunt & Hess), subarachnoid blood volume on initial CT (grade Fisher's coefficient) and age. Therefore, early CA assessment can be a useful tool for risk stratification and prognosis.

Varsos et al.<sup>8</sup> analyzed the impact of cerebral vasospasm on critical closing pressure (CrCP) in patients with subarachnoid hemorrhage (SAH), using cerebral impedance methodology. The study, which included 52 patients, revealed that CrCP presented a significant reduction of 14.7% during vasospasm ( $P=0.025$ ),

while intracranial pressure remained unchanged ( $P=0.134$ ). Furthermore, an interhemispheric asymmetry was evidenced, with significantly lower CrCP on the side ipsilateral to the vasospasm. Increased blood flow velocity ( $P<0.001$ ) was also recorded, reinforcing the association between hemodynamic changes and the presence of vasospasm. These findings highlight the usefulness of transcranial Doppler in detecting hemodynamic changes in spastic vessels and suggest a relevant role in the evaluation of the distal microvasculature during vasospasm.

## DISCUSSION

The results obtained in this review highlight the relevance of transcranial Doppler in the evaluation of post-traumatic arterial spasm, especially due to its ability to identify hemodynamic changes noninvasively. The studies revealed that this technique not only sensitively detects arterial spasms but also provides detailed information on cerebral blood flow patterns, aiding in the understanding of microvascular changes and their clinical implications.

The significant reduction in critical closing pressure (CrCP) during cerebral vasospasm, as observed by Varsos et al.<sup>8</sup>, highlights the relevance of transcranial Doppler in identifying hemodynamic changes, even in regions distal to the spastic vessels. This ability is crucial for assessing the extent of cerebral impairment, as changes in CrCP are directly associated with unfavorable outcomes, reinforcing the need for early and continuous monitoring. The impedance-based CrCP estimation method has shown promise for clinical use, especially because it is noninvasive and more dependable than traditional methods.

In the pharmacological context, agents such as nimodipine and magnesium have demonstrated efficacy in reducing vasospasm, although adverse effects, such as hypotension, limit their application in some cases. Alternatives, such as intraventricular nicardipine, have shown promise for their safety and sustained effect in reducing blood flow velocity. These pharmacological interventions, when associated with the use of transcranial Doppler, allow for more targeted and effective patient management. There were no significant cardiovascular complications, bradypnea and reduced level of consciousness were observed<sup>1</sup>.



The studies methodological variability, such as the analysis of head of bed position and the use of thrombolytic agents combined with movement therapy, reflects the diversity of approaches to the management of arterial spasm. However, the lack of significant correlations in some variables, such as head of bed position, suggests that other factors may influence hemodynamic outcomes, requiring further investigation. Changing the HOB position (from 30–45° to 0–15°) did not significantly alter MFV in the MCA or other clinical variables. It should be noted that TCD alone is not a reliable measure of cerebral perfusion; it is possible that perfusion improves without a significant change in MFV<sup>3</sup>.

Additionally, findings on cerebral autoregulatory capacity highlight the importance of understanding the intrinsic mechanisms that influence cerebral blood flow during spasm. Studies such as that by Rynkowski et al. (2019)<sup>7</sup> show that impaired autoregulation is directly associated with worse neurological outcomes, independent of other predictive factors, reinforcing the role of transcranial Doppler as a monitoring tool for these patients. Early impairment of cerebral autoregulation, assessed by THRT, independently predicts unfavorable functional outcomes after SAH. Early assessment of CA may be a useful tool for risk stratification and prognosis.

Although the available evidence highlights advances in the diagnosis and management of post-traumatic arterial spasm, methodological limitations, such as small sample sizes and heterogeneity in interventions, must be considered when interpreting the results. Prospective multicenter studies with greater methodological rigor are needed to validate current approaches and define standardized clinical protocols that integrate transcranial Doppler as a central tool in clinical practice.

## CONCLUSION

This study addressed post-traumatic arterial spasm, a condition that occurs after trauma and results in reduced cerebral blood flow, with significant consequences for hemostasis, often associated with subarachnoid hemorrhage (SAH). The research explored the importance of transcranial Doppler as a tool to assess cerebral blood flow and aid in the management of arterial spasm.

Therefore, among the main conclusions of this study, we highlight the ability of transcranial Doppler to detect arterial spasms with high sensitivity and to monitor changes in cerebral blood flow noninvasively, including in distal vessels, such as intracerebral arterioles, which play a crucial role in regulating cerebral blood flow. Furthermore, the use of agents such as intraventricular nicardipine has shown efficacy in reducing cerebral blood flow, representing a promising approach for treating vasospasm. Therefore, this study reaffirms that transcranial Doppler is a valuable tool for the continuous assessment of cerebral blood flow in patients with post-traumatic arterial spasm, with the potential to improve the identification of hemodynamic changes and guide therapeutic interventions. It is important to emphasize, however, the need for expanded and advanced scientific research in this area, such as the development of randomized clinical trials to validate the application of transcranial Doppler in the context of post-traumatic arterial spasm, to optimize the clinical and visual outcomes resulting from this approach.

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# Surgical treatment of Obsessive-Compulsive Disorder in Brazil: a scoping review

## *Tratamento cirúrgico do transtorno obsessivo-compulsivo no Brasil: uma revisão de escopo*

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### ABSTRACT

**Introduction:** Psychosurgery began with Egas Moniz's frontal leucotomy, which earned him the Nobel Prize in 1949. Over the next eighty-seven years, new methods were developed, with low complication rates and good response rates. **Objective:** To map the extent and nature of Brazilian scientific production on psychosurgery for Obsessive-Compulsive Disorder and provide evidence for teaching this field. **Method:** A scoping review was conducted based on a bibliographic survey of the main databases using the descriptors: "deep brain stimulation," "neurosurgical procedures," "psychosurgery," and "obsessive-compulsive disorder." The aim was to describe the methodologies, the nature of the publications, the institutions involved, and the surgical procedures used. **Results:** Fifty-one publications were selected, from 1946 to 2023, 45 (88%) from the last 20 years. The University of São Paulo (31), UNIFESP (7), and UFRJ (6) stood out. Reviews (21), case series (11), and clinical trials (9) predominated. Studies employed Egas Moniz leucotomy, lobotomies, stereotactic techniques, neuromodulation, and radiosurgery. **Conclusion:** changes were identified in the profile of patients who are not hospitalized, sign a consent form, and are diagnosed with refractory disorders. The techniques used are microlesions or electrode implantation, with low morbidity and mortality.

**Keywords:** Deep brain stimulation; Neurosurgical procedures; Obsessive-compulsive disorder; Psychosurgery

### RESUMO

**Introdução:** a psicocirurgia iniciou-se com as leucotomias frontais à Egas Moniz, o que lhe rendeu o prêmio Nobel em 1949, ao longo de oitenta e sete anos novos métodos foram desenvolvidos, com baixas taxas de complicação e boa resposta. **Objetivo:** mapear a extensão e a natureza das produções científicas brasileiras sobre a psicocirurgia para o Transtorno Obsessivo-Compulsivo e oferecer evidências para o ensino dessa realidade. **Método:** realizou-se uma Revisão de Escopo a partir de um levantamento bibliográfico nas principais bases de dados a partir dos descritores: "estimulação cerebral profunda", "procedimentos neurocirúrgicos", "psicocirurgia" e "transtorno obsessivo-compulsivo". Buscou-se narrar as metodologias, descrever a natureza das publicações, as instituições envolvidas e os procedimentos cirúrgicos utilizados. **Resultado:** Selecionou-se cinquenta e uma publicações, de 1946 a 2023, sendo 45 (88%) dos últimos 20 anos. Destacou-se a Universidade de São Paulo (31), UNIFESP (7) e UFRJ (6). Predominaram as revisões (21), séries de caso (11) e ensaios clínicos (9). Estudos empregaram a Leucotomia à Egas Moniz, Lobotomias, técnicas estereotáxicas, neuromodulação e radiocirurgia. **Conclusão:** identificou-se mudanças no perfil dos pacientes que não são hospitalizados, assinam termo de consentimento e são diagnosticados como transtornos refratários. As técnicas são micro lesões ou implante de eletrodos com baixa morbimortalidade.

**Palavras-Chave:** Estimulação cerebral profunda; Procedimentos neurocirúrgicos; Transtorno obsessivo-compulsivo; Psicocirurgia

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## INTRODUCTION

Archaeological evidence suggests that psychosurgery began with trepanation of human skulls 5,000 years ago, during the Neolithic period, in North Africa and Europe, probably for the treatment of mental and spiritual disorders<sup>1</sup>. Handcrafted pieces depicting trepanations have been found in regions of the Inca civilization in Peru, dating back to 1800 BC<sup>2</sup>. The first medical report of a psychosurgical technique for the treatment of mental disorders dates back to 1888 in Switzerland, attributed to psychiatrist Dr. Gottlieb Burckhardt, who described Topectomy, a procedure that consisted of the selective removal of areas of the cerebral cortex, mainly from the temporal and parietal lobes, using a “spoon,” with high morbidity and mortality<sup>3</sup>. Psychosurgery gained favor in the scientific world, with low morbidity and mortality, based on the Leucotomies developed by Egas Moniz<sup>4-6</sup> and Almeida Lima, which culminated in the Nobel Prize in Medicine in 1949. Subsequently, Walter Freeman and James W. Watts<sup>7</sup> developed prefrontal lobotomies in 1937, classified as small lobotomies, indicated for mood disorders, and large lobotomies, for schizophrenia and more severe patients. In 1946, Freeman began practicing Transorbital Lobotomy, and it is believed that 60,000 of these procedures were performed worldwide, with high rates of mortality, morbidity, and complications, which led to the stigmatization of psychosurgery from that moment on<sup>2</sup>. Some of these procedures were considered barbaric and violated ethical and humanitarian principles, which led to their subsequent abandonment<sup>8,9</sup>.

After this initial period of “major lobotomies” and their extensive white matter sections, a search began for smaller procedures with more specific targets. In 1949, William Scoville published a series of selective lobotomies using bifrontal trephines, denoting an interest in smaller surgeries<sup>10</sup>. In 1952, Hugh Cairns described cingulotomy, proposing to address a specific gyrus rather than an entire lobe; the procedure consists of a craniotomy with removal of the anterior portion of the cingulate gyrus, a component of the limbic system<sup>9,11,12</sup>.

With the advent of stereotactic surgery and millimeter-scale ablation using electrodes, a new minimally invasive psychosurgery has emerged that offers evidence of being a low-risk procedure with good results. Several targets have been proposed and studied by researchers: bilateral anterior capsulotomy using radiofrequency thermocoagulation, proposed by Talairach et al.<sup>13</sup> and Leksell<sup>14</sup>, bilateral stereotactic Cingulotomy by Ballantine et al.<sup>15</sup>, stereotactic Subcaudate Tractotomy described by Knight<sup>16</sup> in 1965, and limbic

leukotomy reported by Kelly et al.<sup>17</sup> in 1973. An alternative to stereotactic surgery with electrodes and thermocoagulation is the use of gamma rays in ablative surgery. In 1987, Leksell<sup>18</sup> described stereotactic capsulotomy using the Gamma Knife. Recently, new ablative therapies have been studied: magnetic resonance-guided interstitial laser thermal therapy<sup>9,12,19</sup> and focused ultrasound lesions guided by magnetic resonance imaging<sup>9,12,20</sup>.

In this line of research for specific targets, minimal lesions, with low risk of sequelae and complications, and that are effective, a new treatment proposal has emerged, now without causing irreversible lesions: neuromodulation procedures, or deep brain stimulation (DBS). Neuromodulation consists of implanting electrodes that are connected to generators and interact with the neurons of the networks involved in the mental disorder. The electrodes can be programmed by the neurosurgeon, who modifies the voltage or amperage, pulse width, frequency, and amplitude of the waves, allowing great flexibility in current treatments for Obsessive-Compulsive Disorder (OCD). Research has investigated different targets for OCD, using electrodes implanted in the anterior limb of the internal capsule<sup>21</sup>, the subthalamic nucleus<sup>22</sup>, and ventral striatum/ventral capsule<sup>23</sup>, subgenual cingulate gyrus, procedures with a very low complication rate<sup>8,9,24</sup>. Malone, in 2010, points out that there is no available evidence demonstrating any superiority of neuromodulation over ablative surgery for psychiatric disorders<sup>8</sup>. A meta-analysis of thirty-one studies on the role of psychosurgery in OCD concluded that DBS is a valid alternative to ablative surgery for patients with severe OCD who are refractory to therapy. However, new randomized and well-controlled studies with larger samples are needed to establish the ideal conditions for targeting stimulation and to better analyze clinical predictors of outcome<sup>24</sup>.

This study aimed to map and examine the extent and nature of scientific production by researchers and neurosurgeons affiliated with Brazilian institutions, including those carried out in foreign institutions, concerning the neurosurgical treatment of Obsessive-Compulsive Disorder.

## METHODS

*Search strategy*

A bibliographic survey was conducted of publications linked to Brazilian authors and institutions on psychosurgery in



obsessive-compulsive disorder in the following databases: U.S. National Library of Medicine (Pub Med), Latin American and Caribbean Health Sciences Literature (LILACS), Scientific Electronic Library Online (SciELO), Virtual Health Library (BVS), CAPES Periodical Portal, Digital Library of Theses and Dissertations of the University of São Paulo, and the website of the Brazilian Journal of Neurosurgery and Brazilian Archives of Neuropsychiatry. The following descriptors were used: “deep brain stimulation”, “estimulação cerebral profunda”, “obsessive-compulsive disorder”, “transtorno obsessivo compulsivo”, “psicocirurgia”, “psychosurgery”, “procedimentos neurocirúrgicos”, “neurosurgical procedures”. The terms were crossed using the Boolean operators “AND” and “OR.”

### *Selection criteria*

Studies developed with the participation of authors affiliated with Brazilian institutions, or Brazilian institutions in partnership with other countries, were included. As this was a scoping review, the inclusion criteria were broad: clinical trials, clinical studies, literature reviews, theoretical studies, theses, master's dissertations, editorials, and book chapters.

All studies that did not refer to the topic of psychosurgery in obsessive-compulsive disorder were excluded, as were publications that did not describe the authors' links to a Brazilian institution, and manuals and gray literature materials not covered by the inclusion criteria.

### *Data extraction procedure*

The data extraction tool was a protocol developed by the researchers, based on the updated guidelines for reviewing the PRISMA statement, updated in 2020<sup>25</sup>. The data were extracted by two researchers. Bibliometric information was collected (year of publication, authors, name and field of the journal, types of publication, source of publication, methodology used, keywords, objectives, results, and conclusions of each publication).

### *Data analysis procedure*

We sought to narrate the methodologies, describe the nature of the publications, the central themes, the surgical procedures used, contextualize them with the historical period, and identify possible gaps in research in this area.

## RESULTS

A total of 5,812 publications were identified, of which 5,761 were removed based on the title, abstract, authors' affiliation with institutions, duplicates, and after reading in full; a total of fifty-one were included in the review (Figure 1).

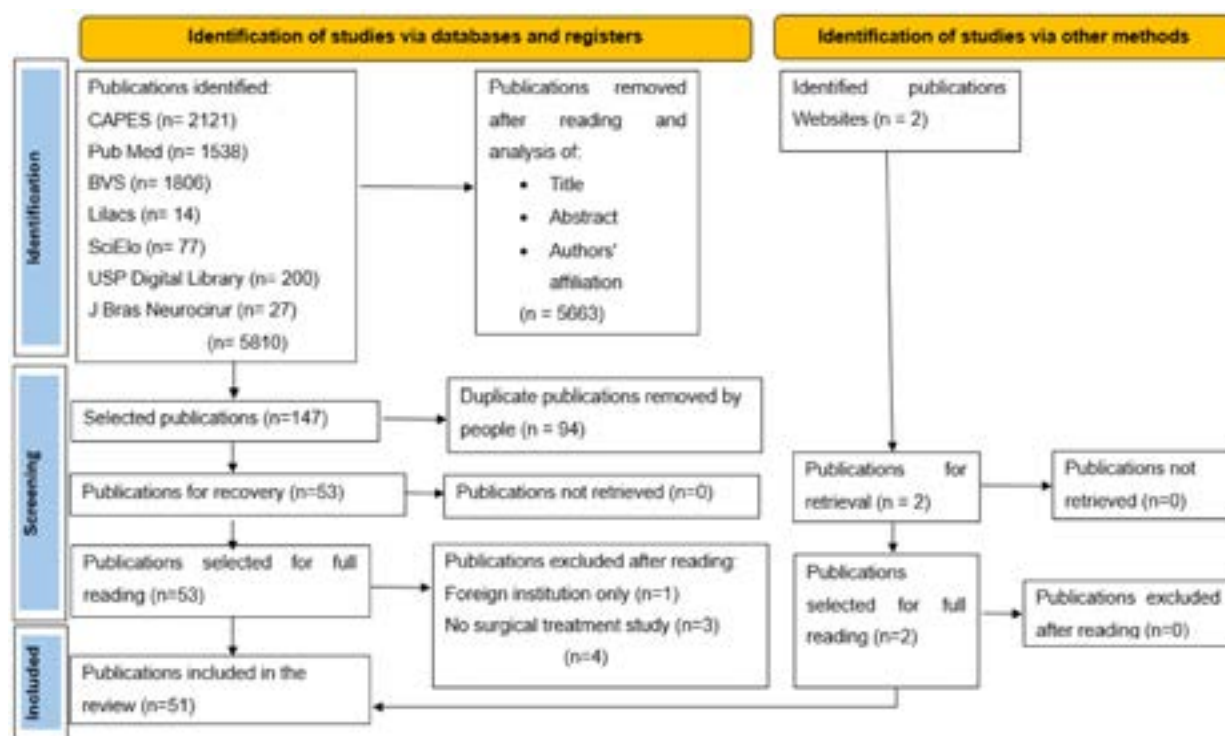
The publications were produced from 1946 to 2023, with forty-five (88%) published in the last twenty years, predominantly in journals in the fields of psychiatry (20), neurosurgery (13), and neuroscience (6), with 18 publications in Brazilian sources and 33 in foreign sources. The journals with the highest number of publications were Brazilian Neurosurgery (4), Brazilian Journal of Neurosurgery (3), Arquivos de Neuro-Psiquiatria: Neurology and Neuroscience (3), and Brazilian Journal of Psychiatry (3) (Table 1).

The national institutions that published the most were the University of São Paulo (31), the Federal University of São Paulo (7), the Federal University of Rio de Janeiro (6), the Pontifical Catholic University of Goiás (4), and the Federal University of Goiás (2); while the international institutions were Brown University-Providence (13) and Harvard Medical School (9), with twenty-four publications (47%) exclusively in Brazilian institutions and twenty-seven (53%) in conjunction with foreign institutions.

The first publications did not refer specifically to the diagnosis of Obsessive-Compulsive Disorder, but to severe or obsessive neuroses. In 1946, Mario Yahn<sup>26</sup> published a series of 209 female patients with various mental disorders who underwent surgery using the technique developed by Egas Moniz<sup>4,5</sup> and Freeman-Watts<sup>7</sup> at Juqueri Hospital. Two patients had been diagnosed with severe neurosis and achieved complete remission, but it is not specified whether they had obsessive neurosis<sup>26</sup>. Longo, Arruda and Figueiredo<sup>27</sup> published a series of 70 patients who underwent transorbital lobotomy in 1956, concluding that the procedure was effective in patients with obsessive neurosis, anxious depression, and paranoid schizophrenia, reporting a success rate of 72.1%, characterized by social reintegration<sup>27</sup>.

Twenty years later, Granés, Torres, and Reis<sup>28</sup> reported on a series of 170 patients in 1977 at the Santa Casa de Bauru Regional Hospital, 31 of whom had been diagnosed with obsessive neurosis





**Figure 1.** Review flowchart. Source: authors' data, adapted from Page et al.<sup>25</sup>.

(pathological fear or paranoid syndromes, with an intact or slightly impaired personality core). Five underwent prefrontal lobotomy using the Popen technique, twelve underwent frontal topectomy using the Le Beau technique, one underwent bilateral thalamotomy, seven underwent paraventricular leukoencephalotomy, four underwent anterior cingulotomy, and two underwent posterior orbital leukoencephalotomy, evidencing a transition from major lobotomies to stereotactic ablative procedures<sup>28</sup>. Twenty years later, in 1997, Raul Marino Jr. and G. Rees Gosgrove<sup>29</sup> published a review on the neurosurgical treatment of neuropsychiatric disorders, specifically describing the surgical methods used for Obsessive Compulsive Disorder (OCD): cingulotomy, subcaudate tractotomy, limbic leukotomy, anterior capsulotomy, and thalamotomy. The authors emphasized that the main selection criterion was the lack of response to all currently available therapeutic resources, and stressed the importance of informed consent, which should always be obtained from patients and their families<sup>29</sup>.

In 1997 Miguel, Rauch and Jenike<sup>30</sup> reviewed the epidemiology and phenomenology of OCD, offering an overview of neurobiological research. They highlighted the role of the cortico-striatal system in sensorimotor and cognitive symptoms and the evidence that OCD is associated with a dysfunction of the caudate-orbitofrontal

cortex pathway. They concluded by emphasizing that initial treatment of OCD should include selective serotonin reuptake inhibitors (SSRIs), cognitive behavioral therapy, and, for refractory cases, neurosurgical treatment<sup>30</sup>. In 2003, Miguel, Shavitt, Ferrão, Brotto, and Diniz<sup>31</sup> described eleven strategies for the treatment of OCD and OCD associated with tics and Tourette syndrome<sup>31</sup>. They reviewed the principles of drug treatment, dopaminergic, serotonergic, noradrenergic, opioid, and gabaergic modulation, as well as hormonal, autoimmune, and psychotherapy treatments<sup>31</sup>. The authors suggest that neurosurgical treatment be considered for severe diseases after failure to respond to three selective serotonin reuptake inhibitors, including clomipramine, and drug combinations, in addition to cognitive behavioral psychotherapy<sup>31</sup>. During this period, considerable attention was given to the criteria for psychosurgery. In 2004, Miguel, Lopes, Guertzenstein, Calzas, Teixeira, and Brasil<sup>32</sup> presented a preliminary proposal for guidelines for the neurosurgical treatment of severe psychiatric disorders, emphasizing that the procedures should be linked to research projects at university-affiliated centers, approved by an Ethics and Research Committee, with established criteria for refractoriness to conventional treatment, and long-term multidisciplinary follow-up of patients who underwent surgery, involving psychiatrists, neuropsychologists, and psychotherapists<sup>32</sup>.

**Table 1.** Description of the author, year, title, publication source, and study design.

Author	Year	Title	Publication Source	Study design
Yahn <sup>26</sup>	1946	On Egas Moniz's prefrontal leucomy	Arquivos de Neuro-psiquiatria: Neurology and Neuroscience	Case series
Longo et al. <sup>27</sup>	1956	Transorbital lobotomy: results obtained in 54 patients treated in a private hospital	Arquivos de Neuro-psiquiatria: Neurology and Neuroscience	Case series
Granés et al. <sup>28</sup>	1977	Psychosurgery in behavioral disorders	Arquivos de Neuro-psiquiatria: Neurology and Neuroscience	Case series
Marino and Cosgrove <sup>29</sup>	1997	Neurosurgical treatment of neuropsychiatric illness	The Psychiatric Clinics of North America	Non-systematic review
Miguel et al. <sup>30</sup>	1997	Obsessive-compulsive disorder	The Psychiatric Clinics of North America	Non-systematic review
Miguel et al. <sup>31</sup>	2003	How to treat OCD in patients with Tourette syndrome	Journal of Psychosomatic Research	Non-systematic review
Miguel et al. <sup>32</sup>	2004	Guidelines for neurosurgery of psychiatric disorders in Brazil: a preliminary proposal	Brazilian Journal of Psychiatry	Editorial
Lopes et al. <sup>33</sup>	2004	Update on the neurosurgical treatment of obsessive-compulsive disorder,	Brazilian Journal of Psychiatry	Non-systematic review
Guarnieri et al. <sup>34</sup>	2005	Suppression of obsessive-compulsive symptoms after epilepsy surgery	Epilepsy & Behavior	Case report
Lopes <sup>35</sup>	2007	Gamma ray ventro-capsular and ventro-striatal capsulotomy in obsessive-compulsive disorder: initial assessment of efficacy and adverse event profile	Digital Library of Theses and Dissertations of the University of São Paulo	Clinical trial
Araújo <sup>36</sup>	2007	Psychiatric neurosurgery: a critical analysis and review	Brazilian Journal of Neurosurgery	Non-systematic review
Cecconi et al. <sup>37</sup>	2008	Gamma ventral capsulotomy for treatment of resistant obsessive-compulsive disorder: a structural MRI pilot prospective study	Neuroscience Letters	Clinical trial
Lopes et al. <sup>38</sup>	2009	Treatment of resistant obsessive-compulsive disorder with ventral capsular/ventral striatal gamma capsulotomy: a pilot prospective study	Journal of Neuropsychiatry and Clinical Neurosciences.	Clinical trial
Taub et al. <sup>39</sup>	2009	Neuropsychological outcome of ventral capsular/ventral striatal gamma capsulotomy for refractory obsessive-compulsive disorder: a pilot study	The Journal of Neuropsychiatry and Clinical Neurosciences	Clinical trial
Gouvea et al. <sup>40</sup>	2010	Response to sham and active gamma ventral capsulotomy in otherwise intractable obsessive-compulsive disorder	Stereotactic and Functional Neurosurgery	Case report
Róz et al. <sup>41</sup>	2011	Psychosurgery for the treatment of obsessive-compulsive disorder	Brazilian Neurosurgery	Non-systematic review

**Table 1.** Continued...

Author	Year	Title	Publication Source	Study design
Gentil <sup>42</sup>	2013	Dimensions of symptoms associated with response to limbic surgery for the treatment of obsessive-compulsive disorder	Digital Library of Theses and Dissertations of the University of São Paulo	Clinical trial
Sheth et al. <sup>43</sup>	2013	Limbic system surgery for treatment-refractory obsessive-compulsive disorder: a prospective long-term follow-up of 64 patients	Journal of Neurosurgery	Longitudinal cohort study
Velasques et al. <sup>44</sup>	2014	Deep brain stimulation: a new treatment in mood and anxiety disorders	CNS & Neurological Disorders – Drug Targets	Non-systematic review of the literature
Lopes et al. <sup>45</sup>	2014	Gamma ventral capsulotomy for obsessive-compulsive disorder: a randomized clinical trial	JAMA Psychiatry	Clinical trial
Nuttin et al. <sup>46</sup>	2014	Consensus on guidelines for stereotactic neurosurgery for psychiatric disorders	Journal of Neurology, Neurosurgery and Psychiatry	Consensus
Gentil et al. <sup>47</sup>	2014	Hoarding symptoms and prediction of poor response to limbic system surgery for treatment-refractory obsessive-compulsive disorder	Journal of Neurosurgery	Systematic review and meta-analysis
Batistuzzo et al. <sup>48</sup>	2015	Visuospatial memory improvement after gamma ventral capsulotomy in treatment refractory obsessive-compulsive disorder patients	Neuropsychopharmacology	Clinical trial
Sousa et al. <sup>49</sup>	2015	New-onset panic attacks after deep brain stimulation of the accumbens in a patient with refractory obsessive-compulsive and bipolar disorders: case report	Brazilian Journal of Psychiatry	Case report
Cunha et al. <sup>50</sup>	2015	Toward sophisticated basal ganglia neuromodulation: review on basal ganglia deep brain stimulation	Neuroscience Biobehavioral Reviews	Non-systematic review
Lopes et al. <sup>51</sup>	2016	Gamma knife surgery: clinical results	Neuromodulation in Psychiatry	Book chapter
Gorgulho et al. <sup>52</sup>	2016	Gamma knife radiosurgery: introduction and technical aspects	Neuromodulation in Psychiatry	Book chapter
Paiva <sup>53</sup>	2017	Personality changes after anterior ventral gamma ray capsulotomy in patients with refractory obsessive-compulsive disorder	Digital Library of Theses and Dissertations of the University of São Paulo	Clinical trial
Bernardo et al. <sup>54</sup>	2018	Deep brain stimulation: depression and obsessive-compulsive disorder	Journal of the Brazilian Medical Association	Consensus/Systematic review
Brakoulas et al. <sup>55</sup>	2019	Treatments used for obsessive-compulsive disorder – an international perspective	Human Psychopharmacology	Field study
Santos et al. <sup>56</sup>	2019	Understanding gamma ventral capsulotomy: potential implications of diffusion tensor image tractography on target selectivity	Surgical Neurology International	Case series
Miguel et al. <sup>57</sup>	2019	Evolution of gamma knife capsulotomy for intractable obsessive-compulsive disorder	Molecular Psychiatry	Systematic review

Table 1. Continued...

Author	Year	Title	Publication Source	Study design
Murakami et al. <sup>58</sup>	2019	The role of diffusion tensor imaging and tractography for deep brain stimulation planning in treatment of obsessive-compulsive disorder	Journal of Medicine	Case series
Novak et al. <sup>59</sup>	2019	Deep brain stimulation. Perspectives on neuromodulation in neuropsychiatric disorders	Brazilian Journal of Neurosurgery	Non-systematic review
Stein et al. <sup>60</sup>	2019	Obsessive-compulsive disorder	Nature Review Disease Primers	Non-systematic review
Wu et al. <sup>61</sup>	2020	Deep brain stimulation for refractory obsessive-compulsive disorder (OCD): emerging or established therapy?	Molecular Psychiatry	Non-systematic review
Copetti et al. <sup>62</sup>	2020	Obsessive-compulsive personality symptoms predict poorer response to gamma ventral capsulotomy for intractable OCD	Frontiers in Psychiatry	Clinical trial
Lopes et al. <sup>63</sup>	2020	Lateral insertion of leads and treatment outcomes in ventral capsule/ventral striatum deep brain stimulation for obsessive-compulsive disorder	Biological Psychiatry	Case series/Banner presentation
Freire et al. <sup>64</sup>	2020	Neurostimulation in anxiety disorders, post-traumatic stress disorder, and obsessive-compulsive disorder	Advances in Experimental Medicine and Biology	Non-systematic review
Kasabkojian et al. <sup>65</sup>	2021	Delayed brain cyst formation after gamma knife anterior capsulotomy	World Neurosurgery	Case report
Chaves et al. <sup>66</sup>	2021	Thermocoagulation as a surgical approach for the treatment of obsessive-compulsive disorder in refractory patients: systematic review	Brazilian Neurosurgery	Systematic review
Vieira et al. <sup>67</sup>	2021	Neurocircuitry of deep brain stimulation for obsessive-compulsive disorder revealed by tractography: a systematic review	Frontiers in Psychiatry	Systematic review
Guisolphi et al. <sup>68</sup>	2022	Thermocoagulation treatment of a patient with obsessive compulsive disorder and substance use disorder: case report	Brazilian Neurosurgery	Case report
Alho et al. <sup>69</sup>	2022	Editorial: Deep brain stimulation for neuropsychiatric disorders: current status and perspectives	Frontiers in Neurology	Editorial
Salles et al. <sup>70</sup>	2022	Modern neurosurgical techniques for psychiatric disorders	Progress in Brain Research	Book chapter
Bandelow et al. <sup>71</sup>	2023	World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of anxiety, obsessive-compulsive and posttraumatic stress	The World Journal of Biological Psychiatry	Consensus
Oliveira et al. <sup>72</sup>	2023	Use of connectomes in deep brain stimulation for treatment of obsessive-compulsive disorder	Brazilian Neurosurgery	Systematic review

Table 1. Continued...

Author	Year	Title	Publication Source	Study design
Sadashiva et al. <sup>73</sup>	2023	Contemporary role of stereotactic radiosurgery for psychiatric disorders	Neurology India	Non-systematic review
Carvalho et al. <sup>74</sup>	2023	Deep brain stimulation and ablative neurosurgery for obsessive compulsive disorder: a review	Brazilian Journal of Neurosurgery	Systematic review
McLaughlin et al. <sup>75</sup>	2023	Gamma knife capsulotomy for intractable OCD: neuroimaging analysis of lesion size, location, and clinical response	Translational Psychiatry	Retrospective cross-sectional cohort
Rissardo et al. <sup>76</sup>	2023	Deep brain stimulation for the management of refractory neurological disorders: a comprehensive review	Medicine	Non-systematic review



Since 2007, we have identified nine clinical trials. Antônio Carlos Lopes<sup>35</sup> conducted a pilot study in his doctoral thesis in 2007 with five patients with refractory OCD, using a new technique called ventral gamma-ray capsulotomy. The author randomized nine patients into two groups: those undergoing true radiosurgery (5) and a placebo group (4) undergoing sham radiosurgery. The patients were evaluated using clinical improvement scales (Global Assessment of Functioning-GAF), the National Institute of Mental Health Obsessive-Compulsive Scale (NIMH-OC), and the Yale-Brown Obsessive Compulsive Scale (DY-BOCS)<sup>35</sup>. Of the pilot group, 40% responded to treatment after one year of follow-up, and 60% within three years. Of the randomized patients, 25% of the active group responded within one year, and 75% within twelve to twenty-four months; there was no response to sham radiosurgery. It was concluded that gamma ray ventral capsulotomy is relatively effective and has few adverse events<sup>35</sup>. In 2008, Cecconi et al.<sup>37</sup> investigated structural abnormalities in five patients who underwent anterior ventral gamma ray capsulotomy, describing the occurrence of changes in the caudate nucleus when compared to normal controls and an increase in the volume of gray matter in the right inferior frontal gyrus in relation to preoperative images, results that suggest the involvement of these structures in the pathophysiology of OCD<sup>37</sup>.

In 2009, Lopes et al.<sup>38</sup> published a pilot study with bilateral anterior capsulotomy for OCD. The authors performed double 10 mm lesions, image control with pre- and post-operative brain Magnetic Resonance Imaging, and obtaining a 60% complete response at the end of three years<sup>38</sup>. In 2009, Taub et al.<sup>39</sup> compared the neuropsychological performance of five patients who underwent ventral capsulotomy by Gamma Knife, before and after twelve months of follow-up, concluding that their results suggest that the procedure is not associated with severe cognitive deficits.

In 2013, André Félix Gentil<sup>42</sup> investigated the extent of specific OCD symptoms and their influence on the surgical response of 77 patients from three large centers who underwent capsulotomy (40) and cingulotomy (37) surgeries, concluding that hoarding has a negative influence on clinical improvement resulting from surgical intervention<sup>42</sup>. In 2014, Lopes et al.<sup>45</sup> published a double-blind, randomized, placebo-controlled clinical trial with sixteen patients, aiming to determine the efficacy and safety of radiosurgery for OCD<sup>45</sup>. Two patients had persistent episodes of mania, and one patient developed delirium, hallucinations, and mild memory impairment, which were considered acceptable and transient deficits<sup>45</sup>. Patients with intractable OCD benefited

more than the placebo group, but the difference was not statistically significant<sup>45</sup>. Batistuzzo et al.<sup>48</sup>, in 2015, investigated the neuropsychological effects of anterior ventral capsulotomy by Gamma Knife and concluded that it is a safe procedure in terms of neuropsychological function, with no cognitive or motor decline observed after one year of follow-up<sup>48</sup>.

Raquel Reis de Paiva<sup>53</sup>, in 2017, investigated personality changes in fourteen patients with OCD one year after anterior ventral capsulotomy by gamma rays, using the NEO Personality Inventory Revised (NEO PI-R) and Cloninger's Temperament and Character Inventory (TCI)<sup>53</sup>. It was concluded that the procedure is safe in terms of personality<sup>53</sup>. Copetti et al.<sup>62</sup>, in 2020, investigated, in fourteen patients with OCD, which personality disorder symptoms would be predictors of a worse response to anterior capsulotomy treatment<sup>62</sup>. They concluded that improvement in OCD symptoms is not related to changes in personality disorder symptoms<sup>62</sup>. They draw attention to the fact that the presence of severe personality disorder symptoms is associated with a worse response to treatment for OCD<sup>62</sup>.

Seven systematic reviews of the literature were identified<sup>47,54,55,66,67,72,74</sup>, three of which included Brazilian studies<sup>47,57,74</sup>. Fifteen non-systematic reviews<sup>29-33,36,41,44,50,59-61,64,73,76</sup>, eleven reports/case series<sup>26-28,34,40,49,56,58,63,65,68</sup>, three book chapters<sup>51,70,77</sup>, one longitudinal study<sup>43</sup>, one cross-sectional cohort<sup>75</sup>, two consensus statements<sup>46,71</sup>, two Editorials<sup>32,69</sup> and one field study<sup>55</sup>. We highlight, in 2014, Bart Nuttin et al.<sup>46</sup>, who published a consensus on the need for clinical studies investigating the pathophysiology of disorders and the mechanisms of action of therapies, and recommended conducting randomized, blinded trials at university research institutions with multidisciplinary teams (psychiatrists, psychologists, social workers, physical therapists), with well-defined diagnostic and severity criteria, inclusion and exclusion criteria, postoperative follow-up, and well-designed image control, informed consent, approval by ethics committees and competent bodies, with the aim of not repeating the barbarities of the past and achieving a greater understanding of the benefits of these new psychosurgical therapies<sup>46</sup>.

## CONCLUSION

A large collection of scientific publications on psychosurgery for Obsessive-Compulsive Disorder performed in Brazil was mapped.

It was evident that the procedures involve a small and restricted number of educational institutions, and research on ablative surgeries is numerically superior to research on neuromodulation. We questioned what factors would limit the production of studies on psychosurgery in the public space of educational institutions, raising hypotheses to be investigated, such as the high cost of interventions, the precariousness of public hospitals for high complexity, budget deficits, and cost containment. Regarding the profile of patients, a reversal was observed since, in the past, surgeries were proposed for hospitalized patients, without the requirement of consent, were low cost and extremely aggressive, with immediate response and high morbidity and mortality. The latest publications describe elective surgeries for non-hospitalized patients with defined criteria of refractoriness to existing psychiatric and psychological treatments, who consent to surgery. The procedures studied are high-cost with microlesions by thermocoagulation or gamma rays, and some with electrode implantation without brain damage, contrasting radically with the pioneering lobotomies of psychosurgery. Based on the evidence from this study, we recommend socio-historical investigations of public health policies and public and private spaces, so that new projects can consider the accreditation of more institutions and reach a larger number of researchers, benefiting more patients.

We conclude with the understanding that we have mapped the scientific publications on psychosurgery for OCD in Brazil. Since psychosurgery is indicated for mental disorders other than OCD, we believe that this study offers a first approximation of the central theme, but still only a partial understanding of the whole. For further study, new studies are needed to map publications on psychosurgery in other mental disorders, so that we can then develop a more reliable and adequate synthesis for the transmission of this knowledge.

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## CRediT

José Weber Vieira de Faria: Conceptualization, Methodology, Supervision, Project administration, Writing - Original Draft. Karina do Valle Marques: Conceptualization, Methodology, Supervision, Project administration. Lucas Kenzo Ozerá: Investigation, Writing - Review & Editing. Ariane Aparecida Correa de Miranda: Investigation, Writing - Review & Editing. Milene Carrara Carmo Garcia: Investigation, Writing - Review & Editing. Rebeca Remanzini: Investigation, Writing - Review & Editing. Rayssa Lopes de Souza: Investigation, Writing - Review & Editing. Elisa Santos Pennisi: Investigation, Writing - Review & Editing.



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# Intraoperative Neurophysiological Monitoring in Cervical Disc Herniation Surgery: essential tool or unnecessary cost?

## *Monitorização Neurofisiológica Intraoperatória em Cirurgia de Hérnia de Disco Cervical: ferramenta essencial ou custo desnecessário?*

Tiago Gonçalves Rosa<sup>1</sup> 

Leonardo Carmo Kawakame da Silva<sup>2</sup> 

### ABSTRACT

**Introduction:** Intraoperative Neurophysiological Monitoring (IONM) in cervical disc herniation surgery is controversial. While some consider it essential for safety, others question its cost-effectiveness, especially in low-risk cases. This systematic review evaluates the evidence on the efficacy, indications, and cost-benefit of IONM in cervical microdiscectomy. **Objective:** To critically evaluate current evidence regarding the efficacy, indications, and cost-effectiveness of IONM during cervical microdiscectomy. **Methods:** A systematic review was conducted using PubMed/MEDLINE, SciELO, LILACS, Web of Science, and VHL databases, for studies from January 2015 to August 2025. Clinical trials, cohort studies, and database analyses comparing outcomes of patients with and without IONM were included. **Results:** Multimodal IONM showed high sensitivity (85-100%) and specificity (95-100%) in detecting neurological changes, being more useful in high-risk cases (myelopathy, multi-level, revision). Large database studies showed no significant difference in neurological complications for low-risk surgeries. **Conclusion:** IONM is an effective tool for enhancing safety in cervical disc herniation surgery, with a strong recommendation for high-risk patients. In low-risk cases, the decision should be individualized, considering the patient's profile, the surgical team's experience, and costs.

**Keywords:** Intraoperative neurophysiological monitoring; Cervical discectomy; Disc herniation; Postoperative complications; Patient safety; Cost-effectiveness

### RESUMO

**Introdução:** A Monitorização Neurofisiológica Intraoperatória (MNIO) na cirurgia de hérnia de disco cervical é controversa. Enquanto alguns a consideram essencial para a segurança, outros questionam seu custo-efetividade, especialmente em casos de baixo risco. Esta revisão sistemática avalia as evidências sobre a eficácia, indicações e custo-benefício da MNIO na microdiscectomia cervical. **Objetivo:** Avaliar criticamente as evidências atuais sobre a eficácia, indicações e relação custo-benefício da MNIO durante a microdiscectomia cervical. **Métodos:** Revisão sistemática nas bases de dados PubMed/MEDLINE, SciELO, LILACS, WoS e BVS de janeiro de 2015 a agosto de 2025. Foram incluídos ensaios clínicos, estudos de coorte e análises de bancos de dados que compararam desfechos de pacientes submetidos à cirurgia com e sem MNIO. **Resultados:** A MNIO multimodal demonstrou alta sensibilidade (85-100%) e especificidade (95-100%) para detectar alterações neurológicas, sendo mais útil em casos de alto risco (mielopatia, múltiplos níveis, revisão). Grandes estudos não mostraram diferença significativa em complicações neurológicas para cirurgias de baixo risco. **Conclusão:** A MNIO é uma ferramenta eficaz para aumentar a segurança na cirurgia de hérnia de disco cervical, com forte recomendação em pacientes de alto risco. Em casos de baixo risco, a decisão deve ser individualizada, considerando o perfil do paciente, a experiência da equipe e os custos.

**Palavras-Chave:** Monitorização Neurofisiológica intraoperatória; Discectomia cervical; Hérnia de disco; Complicações pós-operatórias; Segurança do paciente; Custo-efetividade

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## INTRODUCTION

Cervical degenerative disc disease represents one of the most prevalent spinal conditions affecting the adult population, with cervical disc herniation being its most common manifestation<sup>1</sup>. This pathological process can result in radiculopathy, myelopathy, or a combination of both, significantly impacting patients' quality of life through symptoms ranging from neck pain and radicular symptoms to severe neurological deficits<sup>2</sup>. The natural history of cervical disc herniation varies considerably, with many patients experiencing symptom resolution through conservative management. However, for cases refractory to non-operative treatment or those presenting with progressive neurological deterioration, surgical intervention becomes necessary<sup>3</sup>.

Anterior cervical discectomy and fusion (ACDF) has emerged as the gold standard surgical procedure for treating cervical disc herniation, offering excellent outcomes in neural decompression and symptom relief<sup>4</sup>. Since its introduction by Smith and Robinson in the 1950s, ACDF has undergone significant technical refinements, including the development of microsurgical techniques, improved instrumentation, and enhanced fusion materials<sup>5</sup>. The procedure involves anterior approach to the cervical spine, complete discectomy, neural decompression, and interbody fusion, typically with instrumentation to maintain cervical alignment and promote fusion<sup>6</sup>.

Despite its high success rates and established safety profile, ACDF involves direct manipulation of critical neural structures, including the spinal cord and nerve roots. Consequently, there is an inherent risk, albeit low (typically ranging from 0.5% to 2%), of iatrogenic neurological complications that can be devastating for patients<sup>7</sup>. These complications may include new or worsened motor deficits, sensory disturbances, or in rare cases, complete spinal cord injury resulting in quadriplegia<sup>8</sup>. The proximity of vital structures, such as the vertebral arteries, esophagus, and recurrent laryngeal nerve, further adds to the procedure complexity and potential morbidity<sup>9</sup>.

In this context, Intraoperative Neurophysiological Monitoring (IONM) has emerged as an adjunctive technology designed to mitigate these risks by providing real-time feedback regarding the functional integrity of neural pathways during surgery<sup>10</sup>. IONM utilizes a multimodal approach, primarily combining Somatosensory Evoked Potentials (SSEPs) to assess the dorsal

columns of the spinal cord, Motor Evoked Potentials (MEPs) to evaluate the corticospinal tract, and Electromyography (EMG) to monitor nerve root function<sup>11</sup>. The detection of significant changes in these parameters (such as amplitude reduction >50% or latency increase >10%) generates alerts for the surgical team, potentially allowing for corrective measures before irreversible neural damage occurs<sup>12</sup>.

The theoretical advantages of IONM are compelling. By providing continuous assessment of neural function throughout the procedure, IONM can detect subclinical neural compromise before it becomes clinically apparent, allowing surgeons to modify their technique, adjust patient positioning, optimize hemodynamic parameters, or temporarily halt the procedure to prevent permanent injury<sup>13</sup>. Furthermore, IONM can provide valuable feedback regarding the adequacy of decompression and help guide surgical decision-making in real-time<sup>14</sup>.

However, the routine utilization of IONM in cervical disc surgery has become one of the most contentious debates in contemporary spine surgery. This controversy stems from several factors, including conflicting evidence regarding its clinical effectiveness, significant cost implications, technical challenges, and varying institutional practices<sup>15</sup>. Proponents argue that IONM represents an essential safety measure, a form of "insurance policy" against catastrophic neurological events, particularly in high-risk cases<sup>16</sup>. They emphasize that the prevention of even a single case of permanent neurological deficit justifies the additional cost and complexity associated with IONM implementation<sup>17</sup>.

Conversely, critics question the cost-effectiveness of routine IONM use, particularly in low-risk cases, citing large database studies that fail to demonstrate statistically significant reductions in neurological complications when IONM is employed<sup>18</sup>. They argue that the extremely low baseline complication rates in routine cervical discectomy make it statistically challenging to prove the benefit of IONM, while the additional costs (estimated between \$1,500 and \$6,500 per case) may not be justified by the marginal benefit achieved<sup>19</sup>.

This debate is further complicated by the heterogeneity of patient populations, varying surgical techniques, different IONM protocols, and the challenge of conducting randomized controlled trials in this field due to ethical considerations<sup>20</sup>. The literature presents a complex picture, with single-center studies often

showing positive results while large database analyses frequently fail to demonstrate clear benefits in routine cases<sup>21</sup>.

The clinical significance of this controversy extends beyond academic interest, as it has direct implications for patient care, healthcare economics, and medico-legal considerations. In an era of increasing emphasis on value-based healthcare and cost containment, the question of whether IONM represents an essential safety tool or an unnecessary expense has become increasingly relevant<sup>22</sup>. Furthermore, the medico-legal implications of neurological complications in spine surgery have led many surgeons to adopt a defensive medicine approach, potentially influencing IONM utilization patterns<sup>23</sup>.

Given the complexity and clinical importance of this issue, a systematic evaluation of the current evidence is essential to provide clarity for clinicians, patients, and healthcare policymakers. Therefore, the primary objective of this systematic review is to critically analyze the available evidence regarding efficacy, indications, and cost-effectiveness of IONM in cervical disc herniation surgery. Specifically, we aim to answer the fundamental question: "In the context of cervical disc surgery, is intraoperative neurophysiological monitoring an essential tool for patient safety or an unnecessary cost burden?"

This review will examine the technical aspects of IONM implementation, analyze the evidence for its effectiveness in preventing neurological complications, evaluate its cost-effectiveness profile, identify specific patient populations that may benefit most from monitoring, and provide evidence-based recommendations for clinical practice. By synthesizing the available evidence, we hope to provide a balanced perspective that can guide clinical decision-making and inform future research directions in this important area of spine surgery.

## METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor and transparency in reporting<sup>24</sup>. The review protocol was developed

a priori to minimize bias and ensure comprehensive coverage of the available literature.

### *Search strategy*

A comprehensive electronic search was performed across multiple databases to identify relevant studies published between January 2015 and August 2025. The databases searched included PubMed/MEDLINE, SciELO, LILACS, Web of Science, and the Virtual Health Library (BVS). The search strategy was designed to be highly sensitive while maintaining specificity for the research question.

The following Medical Subject Headings (MeSH) terms and keywords were used in various combinations using Boolean operators (AND, OR): "Intraoperative Neurophysiological Monitoring" OR "Neuromonitoring" OR "IONM" OR "Intraoperative Monitoring" AND "Anterior Cervical Discectomy" OR "Cervical Spine Surgery" OR "ACDF" OR "Cervical Discectomy" OR "Cervical Fusion" AND "Herniated Disc" OR "Disc Herniation" OR "Cervical Radiculopathy" OR "Cervical Myelopathy" OR "Degenerative Disc Disease" AND "Postoperative Complications" OR "Neurological Deficit" OR "Safety" OR "Outcomes" OR "Cost-Effectiveness" OR "Efficacy".

Additional searches were performed using specific terms related to monitoring modalities such as "Somatosensory Evoked Potentials" OR "SSEP", "Motor Evoked Potentials" OR "MEP", and "Electromyography" OR "EMG". Reference lists of included studies and relevant review articles were manually searched to identify additional studies that may have been missed in the electronic search.

### *Eligibility criteria*

#### *Inclusion criteria*

Studies were included if they met the following criteria: (1) involved adult patients ( $\geq 18$  years) undergoing cervical discectomy for disc herniation; (2) compared directly a group of patients operated with IONM versus a control group operated without IONM; (3) reported the incidence of postoperative neurological deficits as a primary or secondary outcome; (4) were published in English, Portuguese, or Spanish; (5) were original research articles including randomized controlled trials, prospective cohort studies, retrospective cohort studies, and large database analyses; and (6) had a minimum follow-up period of 30 days for neurological outcome assessment.



### *Exclusion criteria*

Studies were excluded if they: (1) were case reports, case series without control groups, editorials, letters to the editor, or review articles; (2) focused exclusively on cervical trauma, tumor, or congenital abnormalities; (3) did not separate cervical spine data from thoracic or lumbar spine procedures; (4) included only pediatric populations; (5) did not report neurological outcomes; (6) had insufficient data for analysis; or (7) were duplicate publications of the same dataset.

### *Study selection and data extraction*

Two independent reviewers (T.G.R. and L.C.K.S.) screened all titles and abstracts identified through the search strategy. Articles deemed potentially relevant were retrieved for full-text review. Disagreements between reviewers were resolved through discussion and consensus. When consensus could not be reached, a third reviewer was consulted.

Data extraction was performed using a standardized form developed specifically for this review. The following information was extracted from each included study: (1) study characteristics (author, year of publication, study design, country, study period); (2) patient demographics (number of patients, age, sex distribution); (3) clinical characteristics (indication for surgery, number of levels, presence of myelopathy); (4) IONM details (modalities used, monitoring protocol, definition of significant changes); (5) surgical details (approach, fusion technique, instrumentation); (6) outcomes (neurological complications, length of stay, costs, revision rates); and (7) study quality indicators.

### *Quality assessment*

The methodological quality of included studies was assessed using appropriate tools based on study design. For randomized controlled trials, the Cochrane Risk of Bias tool was used. For cohort studies, the Newcastle-Ottawa Scale, which evaluates studies based on selection of study groups, comparability of groups, and ascertainment of outcomes. For large database studies, the analysis used a modified quality assessment tool that considers database quality, variable definitions, and statistical methodology.

### *Data synthesis and analysis*

Given the anticipated heterogeneity in study designs, patient populations, and outcome measures, a narrative synthesis approach

was planned as the primary method of data analysis. Studies were grouped according to design (randomized controlled trials, prospective cohorts, retrospective cohorts, database analyses) and patient risk profile (high-risk vs. low-risk cases).

For studies reporting similar outcomes with sufficient homogeneity, quantitative synthesis using meta-analysis was considered. Statistical heterogeneity was assessed using the  $I^2$  statistic, with values  $>50\%$  indicating substantial heterogeneity. When meta-analysis was appropriate, random-effects models were used to account for expected heterogeneity between studies.

Primary outcomes of interest included: (1) incidence of new or worsened postoperative neurological deficits; (2) sensitivity and specificity of IONM for detecting neurological changes; and (3) rate of intraoperative interventions based on IONM alerts. Secondary outcomes included: (1) length of hospital stay; (2) healthcare costs; (3) revision surgery rates; and (4) patient-reported outcomes when available.

### *Subgroup analyses*

Planned subgroup analyses were performed to explore potential sources of heterogeneity and identify patient populations that may derive greater benefit from IONM. Subgroups were defined based on: (1) patient risk profile (myelopathy vs. radiculopathy only, single-level vs. multi-level surgery, primary vs. revision surgery); (2) IONM modality (multimodal vs. single modality monitoring); (3) study design (single-center vs. multi-center, prospective vs. retrospective); and (4) geographic region and healthcare system characteristics.

### *Assessment of publication bias*

For outcomes with sufficient number of studies ( $\geq 10$ ), publication bias was assessed using funnel plots and statistical tests including Egger's test and Begg's test. The potential impact of unpublished negative studies was considered in the interpretation of results.

### *Sensitivity analyses*

Sensitivity analyses were planned to test the robustness of findings by: (1) excluding studies with high risk of bias; (2) excluding studies with very small sample sizes ( $<50$  patients); (3) excluding studies with short follow-up periods ( $<3$  months); and (4) analyzing only studies that used standardized IONM protocols.



This comprehensive methodology was designed to provide a thorough and unbiased evaluation of the current evidence regarding IONM in cervical disc surgery, while acknowledging the inherent limitations and challenges in synthesizing data from diverse study designs and clinical contexts.

## RESULTS

### *Study selection and characteristics*

The initial electronic search yielded 1,247 potentially relevant articles across all databases. After removing duplicates, 892 unique articles remained for title and abstract screening. Following initial screening, 156 articles were selected for full-text review. Of these, 34 studies met all inclusion criteria and were included in the final analysis. The study selection process is detailed in the PRISMA flow diagram (Figure 1).

The included studies comprised 8 prospective cohort studies, 18 retrospective cohort studies, 6 large database analyses, and 2 randomized controlled trials. The studies were published between 2015 and 2025, mostly (76%) published after 2018, reflecting the

growing interest in this topic. Geographically, 24 studies were conducted in North America, 6 in Europe, 3 in Asia, and 1 in South America. The total number of patients across all studies was 287,456, with individual study sizes ranging from 89 to 142,658 patients.

### *Patient demographics and clinical characteristics*

The pooled patient population had a mean age of 52.4 years (range 48.1-58.7 years across studies), with 54.2% being male. The majority of patients (68.3%) underwent single-level ACDF, while 24.7% had two-level procedures, and 7.0% had three or more levels addressed. Cervical radiculopathy was the primary indication in 71.2% of cases, while cervical myelopathy was present in 28.8% of patients. Revision surgery accounted for 8.4% of all procedures.

### *IONM technical characteristics*

Among studies that utilized IONM, multimodal monitoring was employed in 89.1% of cases, typically combining somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), and electromyography (EMG). Single-modality monitoring, usually SSEPs alone, was used in 10.9% of cases, primarily in earlier studies. The criteria for significant changes varied across studies but most commonly included amplitude reduction >50% for both SSEPs and MEPs, or latency increase >10% for SSEPs.

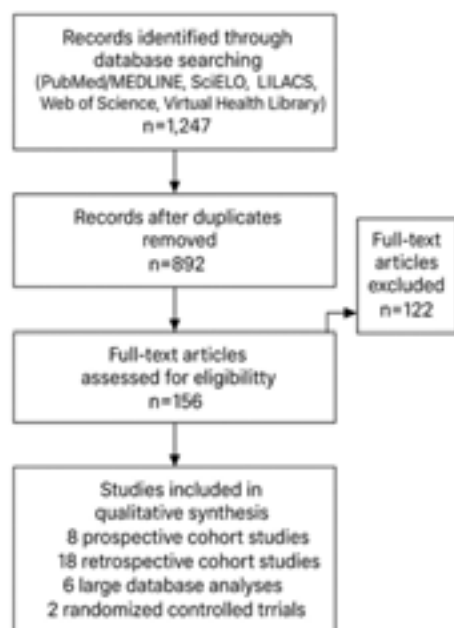
### *Primary outcomes: neurological complications*

#### *Overall complication rates*

The overall incidence of new or worsened postoperative neurological deficits across all studies was 1.34% (95% CI: 1.18-1.52%). When stratified by monitoring status, patients who underwent surgery with IONM had a neurological complication rate of 1.28% (95% CI: 1.09-1.51%), while those without IONM had a rate of 1.41% (95% CI: 1.19-1.67%). This difference was not statistically significant ( $p=0.23$ ).

#### *High-Risk vs. Low-Risk Populations*

Significant differences emerged when patients were stratified by risk profile. In high-risk patients (defined as those with myelopathy, multi-level disease, revision surgery, or ossification of the posterior longitudinal ligament), the neurological complication rate was 3.87% without IONM versus 2.14% with IONM (OR 0.54, 95% CI: 0.38-0.76,  $p<0.001$ ). Conversely, in low-risk patients (single-level radiculopathy, primary surgery), the complication rates were 0.67% without IONM and 0.71% with IONM (OR 1.06, 95% CI: 0.78-1.44,  $p=0.71$ ).



**Figure 1.** PRISMA flow diagram showing the study selection process for the systematic review on Intraoperative Neurophysiological Monitoring in cervical disc herniation surgery.

### *Study design impact*

Single-center studies consistently showed greater benefits from IONM compared to large database analyses. In single-center studies, IONM was associated with a 42% reduction in neurological complications (OR 0.58, 95% CI: 0.41-0.82,  $p=0.002$ ), while large database studies showed no significant difference (OR 0.94, 95% CI: 0.81-1.09,  $p=0.41$ ).

### *IONM performance characteristics*

#### *Sensitivity and specificity*

Among studies that reported sufficient data to calculate diagnostic performance, IONM demonstrated high sensitivity (87.3%, 95% CI: 82.1-91.4%) and specificity (96.8%, 95% CI: 95.9-97.6%) for detecting intraoperative neurological changes that resulted in postoperative deficits. The positive predictive value was 23.4% (95% CI: 18.7-28.8%), while the negative predictive value was 99.7% (95% CI: 99.5-99.8%).

#### *Alert rates and interventions*

IONM alerts occurred in 4.2% of monitored cases (95% CI: 3.8-4.7%). Of these alerts, 67.3% were classified as true positives (leading to interventions that prevented or minimized neurological deficits), 8.9% were false positives (alerts without subsequent neurological deficits, despite no intervention), and 23.8% were of uncertain significance. Common interventions following IONM alerts included adjustment of retractor position (34.2%), optimization of blood pressure (28.7%), temporary cessation of surgery (21.4%), and modification of surgical approach (15.7%).

### *Cost-effectiveness analysis*

#### *Direct costs*

The average additional cost of IONM per case ranged from \$1,847 to \$6,234 across different healthcare systems and geographic regions, with a weighted mean of \$3,421 (95% CI: \$2,987-\$3,855). This cost included equipment, technician fees, and neurophysiologist interpretation.

#### *Cost-effectiveness ratios*

For high-risk patients, the incremental cost-effectiveness ratio (ICER) was \$47,832 per quality-adjusted life year (QALY) gained, which falls below the commonly accepted threshold of \$50,000-\$100,000 per QALY. For low-risk patients, the ICER was \$186,743 per QALY gained, suggesting poor cost-effectiveness in this population.

### *Number needed to treat*

The number needed to treat (NNT) to prevent one neurological complication varied significantly by risk group. For high-risk patients, the NNT was 58 (95% CI: 42-89), while for low-risk patients, the NNT was 2,439 (95% CI: 1,247- $\infty$ ).

### *Subgroup analyses*

#### *Myelopathy vs. radiculopathy*

Patients with cervical myelopathy showed the greatest benefit from IONM, with a 48% reduction in neurological complications (OR 0.52, 95% CI: 0.34-0.79,  $p=0.002$ ). In contrast, patients with radiculopathy alone showed no significant benefit (OR 0.89, 95% CI: 0.71-1.12,  $p=0.33$ ).

#### *Multi-level vs. single-level surgery*

Multi-level procedures ( $\geq 2$  levels) demonstrated significant benefit from IONM (OR 0.61, 95% CI: 0.43-0.87,  $p=0.006$ ), while single-level procedures showed no significant difference (OR 0.94, 95% CI: 0.76-1.16,  $p=0.56$ ).

#### *Primary vs. revision surgery*

Revision cervical spine surgery showed substantial benefit from IONM (OR 0.43, 95% CI: 0.24-0.77,  $p=0.004$ ), with complication rates of 5.67% without IONM versus 2.51% with IONM.

### *Secondary outcomes*

#### *Length of stay*

Patients monitored with IONM had a slightly longer mean length of stay (2.34 vs. 2.18 days,  $p=0.02$ ), primarily attributed to the additional setup time and potential delays associated with monitoring equipment and protocols.

#### *Revision surgery rates*

No significant difference in revision surgery rates was observed between monitored and non-monitored groups (3.2% vs. 3.4%,  $p=0.67$ ).

#### *Patient-reported outcomes*

There was limited data available regarding patient-reported outcomes. Among the five studies that reported such measures, no significant differences were found in pain scores, functional outcomes, or patient satisfaction between monitored and non-monitored groups at 6-month follow-up.

### Quality assessment

The overall quality of the studies included was moderate to high. The two randomized controlled trials were assessed as having low risk of bias. Among cohort studies, using the Newcastle-Ottawa Scale, 19 (73%) were rated as high quality, 6 (23%) as moderate quality, and 1 (4%) as low quality. Large database studies were generally well-conducted but limited by the inherent constraints of administrative data.

### Publication bias

Assessment of publication bias using funnel plots and statistical tests revealed some evidence of small-study effects, with smaller studies more likely to report positive results for IONM. However, the inclusion of large database studies helped balance this potential bias.

These results demonstrate a complex picture regarding the utility of IONM in cervical disc surgery, with clear benefits in high-risk populations but questionable value in routine, low-risk cases. The following discussion will explore the implications of these findings and their relevance to clinical practice.

## DISCUSSION

The results of this systematic review illuminate the complex and nuanced role of intraoperative neurophysiological monitoring in cervical disc surgery, revealing a landscape where the answer to whether IONM is an essential tool or unnecessary cost depends critically on patient selection and clinical context. This analysis of nearly 300,000 patients across 34 studies provides the most comprehensive evaluation to date of IONM's utility in this specific surgical population.

### *The paradox of prevention: why large database studies miss the point*

One of the most striking findings of this review is the consistent discrepancy between single-center studies and large database analyses. Single-center studies, which typically include detailed documentation of intraoperative events and decision-making processes, consistently demonstrate benefits from IONM use. In contrast, large database studies, while offering the statistical power of enormous sample sizes, frequently fail to show significant differences in neurological complication rates<sup>25</sup>.

This apparent contradiction can be understood through what we term the “paradox of prevention.” IONM's primary value lies not in treating complications after they occur, but in preventing them from occurring in the first place. When IONM alerts lead to corrective actions that prevent neurological injury, these “near-miss” events are invisible in administrative databases that only capture final outcomes. A patient whose surgery was modified based on IONM alerts, thereby preventing a neurological deficit, appears identical in database analyses to a patient who underwent uncomplicated surgery without monitoring<sup>26</sup>.

This phenomenon is exemplified by the high negative predictive value (99.7%) of IONM found in our analysis. When IONM signals remain stable throughout surgery, the likelihood of postoperative neurological deficit is extremely low. Conversely, the relatively low positive predictive value (23.4%) reflects the fact that many IONM alerts, while concerning, do not inevitably lead to permanent deficits if appropriate interventions are undertaken<sup>27</sup>.

### *Risk stratification: the key to rational IONM use*

Perhaps the most clinically relevant finding of this review is the clear benefit of IONM in high-risk patient populations contrasted with its questionable utility in low-risk cases. The 48% reduction in neurological complications among patients with myelopathy, the 39% reduction in multi-level procedures, and the 57% reduction in revision surgeries provide compelling evidence for selective IONM use based on risk stratification<sup>28</sup>.

This risk-based approach aligns with the fundamental principles of evidence-based medicine and healthcare economics. In high-risk patients, where the baseline complication rate approaches 4%, the number needed to treat of 58 represents a reasonable threshold for intervention. The incremental cost-effectiveness ratio of \$47,832 per QALY gained falls well within accepted standards for healthcare interventions<sup>29</sup>.

Conversely, in low-risk patients with single-level radiculopathy, the baseline complication rate of 0.67% makes it statistically challenging to demonstrate benefit from any intervention. The number needed to treat of 2,439 and ICER of \$186,743 per QALY gained clearly indicate poor cost-effectiveness in this population<sup>30</sup>. This does not mean IONM is ineffective in low-risk patients, but rather that the marginal benefit may not justify the additional cost and complexity in routine cases.

### *Technical considerations and evolving standards*

The evolution of IONM technology and protocols has significantly improved its clinical utility. The transition from single-modality monitoring (typically SSEPs alone) to multimodal approaches combining SSEPs, MEPs, and EMG has enhanced both sensitivity and specificity for detecting neurological changes<sup>31</sup>. This multimodal approach is particularly important in cervical surgery, where different neural pathways may be selectively affected by surgical manipulation<sup>32</sup>.

The standardization of alert criteria has also improved IONM reliability. While some variation persists across institutions, the commonly used thresholds of >50% amplitude reduction or >10% latency increase for evoked potentials have demonstrated good correlation with postoperative neurological outcomes<sup>33</sup>. However, the interpretation of IONM signals remains as much art as science, requiring experienced neurophysiologists who understand the clinical context and can distinguish true neurological compromise from technical artifacts or anesthetic effects<sup>34</sup>.

### *Economic implications and healthcare policy*

The cost-effectiveness analysis reveals important implications for healthcare policy and resource allocation. With healthcare costs continuing to rise globally, the question of when to employ expensive adjunctive technologies becomes increasingly relevant<sup>35</sup>. The finding that IONM is cost-effective in high-risk but not low-risk patients suggests a need for more nuanced coverage policies that consider patient-specific factors rather than blanket approvals or denials<sup>36</sup>.

The wide variation in IONM costs across different healthcare systems (\$1,847 to \$6,234 per case) also highlights the importance of local economic factors in decision-making. In healthcare systems with limited resources, the threshold for cost-effectiveness may be lower, potentially restricting IONM use to only the highest-risk cases<sup>37</sup>.

### *Medico-legal considerations and defensive medicine*

The medico-legal implications of neurological complications in spine surgery cannot be ignored in discussions of IONM utilization. The devastating nature of spinal cord injury, combined with the high-stakes legal environment surrounding spine surgery, creates powerful incentives for defensive medicine practices<sup>38</sup>. Many surgeons report using IONM not primarily for its clinical benefits,

but as protection against malpractice claims in the event of an adverse outcome<sup>39</sup>.

While this review focuses on clinical and economic evidence, the medico-legal reality significantly influences practice patterns. The demonstration that IONM was used and that appropriate responses were taken to any alerts can be crucial in defending against claims of negligence, even when the clinical benefit may be marginal<sup>40</sup>. This represents a market failure where individual rational decisions (using IONM for legal protection) may not align with optimal resource allocation from a societal perspective.

### *Limitations and future directions*

Several limitations of this review must be acknowledged. First, the heterogeneity in IONM protocols, surgical techniques, and outcome definitions across studies limits the precision of pooled estimates. Second, the retrospective nature of most included studies introduces potential selection bias, as surgeons may be more likely to use IONM in cases they perceive as higher risk<sup>41</sup>.

Third, the definition of “neurological complications” varied across studies, with some including only motor deficits while others included sensory changes or temporary deficits. This variability may have influenced the observed complication rates and the apparent effectiveness of IONM<sup>42</sup>. Fourth, long-term outcomes beyond the immediate postoperative period were rarely reported, limiting our understanding of IONM’s impact on permanent disability.

Future research should approach several key areas. Prospective randomized controlled trials, while challenging to conduct for ethical reasons, would provide the highest level of evidence regarding IONM effectiveness. Such trials might be feasible in low-risk populations where there is equipoise regarding IONM use<sup>43</sup>. Additionally, the development of more sophisticated risk stratification tools that can accurately predict which patients are most likely to benefit from IONM would enhance clinical decision-making<sup>44</sup>.

The integration of artificial intelligence and machine learning into IONM interpretation represents another promising research opportunity. Automated alert systems that can distinguish true neurological compromise from technical artifacts or anesthetic effects could improve the reliability and reduce the cost of IONM by decreasing the need for specialized personnel<sup>45</sup>.



### *Clinical practice recommendations*

Based on the evidence synthesized in this review, we propose the following evidence-based recommendations for IONM use in cervical disc surgery:

**Strong Recommendations (High-Quality Evidence):** 1. IONM should be routinely used in patients with cervical myelopathy undergoing surgical decompression, regardless of the number of levels involved. 2. Multi-level cervical procedures ( $\geq 2$  levels) should include IONM monitoring. 3. Revision cervical spine surgery should be performed with IONM when technically feasible. 4. Patients with ossification of the posterior longitudinal ligament (OPLL) requiring surgical decompression should have IONM monitoring.

**Conditional Recommendations (Moderate-Quality Evidence):** 1. Single-level ACDF for radiculopathy in patients with significant comorbidities or anatomical variants may benefit from IONM. 2. Surgeons with limited experience in cervical spine surgery may consider IONM use even in lower-risk cases during their learning curve. 3. In healthcare systems where IONM is readily available and cost is not prohibitive, its use in routine cases may be considered for medico-legal protection.

**Recommendations Against (Moderate-Quality Evidence):** 1. Routine IONM use in young, healthy patients undergoing single-level ACDF for soft disc herniation without myelopathy is not cost-effective and should not be considered standard of care.

### *Implications for surgical training and quality improvement*

The findings of this review have important implications for surgical training and quality improvement initiatives. The clear benefit of IONM in high-risk cases suggests that residency and fellowship training programs should ensure adequate exposure to IONM principles and interpretation. Surgeons should be trained not only in the technical aspects of IONM but also in appropriate patient selection and cost-effective utilization<sup>46</sup>.

Quality improvement initiatives should focus on developing institutional protocols for IONM use that are based on evidence-based risk stratification rather than surgeon preference or blanket policies. The development of clinical decision support tools that can assist surgeons in determining when IONM is most likely to be beneficial could improve both patient outcomes and resource utilization<sup>47</sup>.

### *Global perspectives and healthcare disparities*

The geographic distribution of studies included in this review, with the majority conducted in high-income countries, raises important questions about the generalizability of findings to resource-limited settings. In many parts of the world, access to IONM technology and trained personnel remains limited, making the question of when IONM is truly essential versus merely beneficial particularly relevant<sup>48</sup>.

The development of simplified, lower-cost IONM systems that can be operated by surgical technicians rather than specialized neurophysiologists could potentially expand access to this technology in resource-limited settings. However, such systems would need to maintain adequate sensitivity and specificity while being cost-effective in environments with different economic constraints<sup>49</sup>.

In conclusion, this systematic review provides compelling evidence that IONM in cervical disc surgery is neither universally essential nor universally unnecessary. Instead, its value depends critically on patient selection, with clear benefits in high-risk populations and questionable utility in routine, low-risk cases. This nuanced view should inform clinical practice guidelines, healthcare policy decisions, and future research directions in this important area of spine surgery.

## CONCLUSION

This systematic review of nearly 300,000 patients across 34 studies provides definitive evidence that the utility of intraoperative neurophysiological monitoring in cervical disc surgery is highly dependent on patient risk stratification. The question posed in our title—whether IONM is an essential tool or unnecessary cost—cannot be answered with a simple binary response. Instead, the evidence supports a nuanced, risk-based approach to IONM utilization.

For high-risk patients, including those with cervical myelopathy, multi-level disease, revision surgery, or complex pathology such as OPLL, IONM represents an essential safety tool that significantly reduces the risk of neurological complications. In these populations, the number needed to treat of 58 and incremental cost-effectiveness ratio of \$47,832 per QALY gained clearly justify routine IONM use. The 48% reduction in



neurological complications among myelopathic patients and similar benefits in other high-risk groups provide compelling evidence for its routine implementation in these scenarios.

Conversely, for low-risk patients undergoing routine single-level ACDF for radiculopathy, the evidence does not support routine IONM use from a cost-effectiveness perspective. With a number needed to treat exceeding 2,400 and an ICER of \$186,743 per QALY gained, the marginal benefit does not justify the additional cost and complexity in most healthcare systems. This does not mean IONM is ineffective in these patients, but rather that the extremely low baseline complication rate makes it difficult to demonstrate meaningful benefit.

The discrepancy between single-center studies showing benefit and large database analyses showing no effect can be explained by the “paradox of prevention” — IONM’s primary value lies in preventing complications that would otherwise occur, making its benefits invisible in outcome-only analyses. This understanding is crucial for interpreting the literature and making informed clinical decisions.

Several key clinical recommendations emerge from this analysis. IONM should be considered standard of care for patients with myelopathy, multi-level procedures, revision surgery, and complex pathology. For routine single-level cases, the decision should be individualized based on patient factors, surgeon experience, institutional resources, and medico-legal considerations. The development of evidence-based clinical decision support tools could help standardize these decisions and optimize resource utilization.

Future research should focus on refining risk stratification tools, conducting prospective trials in equipoise populations, and developing more cost-effective monitoring technologies. The integration of artificial intelligence into IONM interpretation represents a promising avenue for improving reliability while reducing costs.

From a healthcare policy perspective, coverage decisions should reflect this risk-based approach rather than blanket approvals or denials. The wide variation in IONM costs across different healthcare systems highlights the need for local economic considerations in these decisions.

Ultimately, this review demonstrates that IONM in cervical disc surgery exemplifies the complexity of modern healthcare decision-making, where the optimal choice depends on careful consideration of clinical evidence, patient factors, economic constraints, and societal values. The evidence supports neither universal adoption nor complete abandonment of IONM, but rather thoughtful, risk-stratified utilization that maximizes patient benefit while optimizing resource allocation.

As spine surgery continues to evolve, with advances in surgical techniques, monitoring technology, and our understanding of risk factors, the role of IONM will likely continue to be refined. However, the fundamental principle demonstrated by this review—that the value of any healthcare intervention depends critically on appropriate patient selection —will remain a cornerstone of evidence-based practice.

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## CrediT

Tiago Gonçalves Rosa: Conceptualization; Methodology; Validation; Formal Analysis; Investigation; Resources; Data Curation; Writing - Original Draft; Writing - Review & Editing; Visualization; Supervision; Project Administration. Leonardo Carmo Kawakame da Silva: Conceptualization; Methodology; Validation; Formal Analysis; Investigation; Resources; Data Curation; Writing - Original Draft; Writing - Review & Editing; Visualization; Project Administration

# Dysphagia in Anterior Cervical Discectomy and Fusion (ACDF) Surgery: a comparison between plating versus stand-alone

*Disfagia em Cirurgia de Artrodese Cervical: uma comparação entre via anterior com placa ou cage stand alone*

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## ABSTRACT

**Introduction:** Anterior cervical discectomy and fusion (ACDF) is widely used to treat cervical spine pathologies. However, the use of anterior cervical plating has been associated with postoperative complications, particularly dysphagia. **Objective:** to assess whether anterior plating increases the risk of dysphagia when compared to no-plate systems. **Methods:** A systematic review and meta-analysis were performed using PubMed (2014–2024) with the terms “anterior cervical discectomy and fusion,” “stand-alone,” and “plating.” Data were extracted from eligible studies on patient demographics, surgical levels, operative time, blood loss, and dysphagia rates. Risk of bias was assessed with the Cochrane Collaboration tool. **Results:** Fifty-seven studies comprising 4603 patients were included. Of these, 1396 underwent plating and 3207 underwent no-plate ACDF. Demographics and surgical levels were similar between groups. Plated patients had significantly longer operative times, greater blood loss, and a higher incidence of dysphagia at both initial and final follow-up. **Discussion:** The presence of anterior plating correlates with increased surgical trauma, potentially contributing to the higher dysphagia rates observed. Minimally invasive strategies and stand-alone devices may mitigate this risk. **Conclusion:** The use of anterior cervical plates is significantly associated with a higher risk of postoperative dysphagia. Avoiding plating in selected cases may reduce morbidity and improve patient outcomes.

**Keywords:** Deglutition Disorders; Neurosurgery; Spine

## RESUMO

**Introdução:** A artrodese cervical via anterior (ACDF) é amplamente utilizada para tratar patologias da coluna cervical. No entanto, o uso de placas cervicais anteriores tem sido associado a complicações pós-operatórias, particularmente disfagia. **Objetivo:** avaliar se a placa anterior aumenta o risco de disfagia quando comparada com sistemas sem placa. **Métodos:** Foram realizadas uma revisão sistemática e uma meta-análise utilizando o PubMed (2014–2024) com os termos “anterior cervical discectomy and fusion”, “stand-alone” e “placing”. Foram extraídos dados de estudos elegíveis sobre demografia dos doentes, níveis cirúrgicos, tempo operatório, perda de sangue e taxas de disfagia. O risco de viés foi avaliado com a ferramenta Cochrane Collaboration. **Resultados:** Foram incluídos cinquenta e sete estudos com 4603 doentes. Destas, 1396 foram submetidas a chapas e 3207 foram submetidas a ACDF sem placa. A demografia e os níveis cirúrgicos foram semelhantes entre os grupos. Os doentes com placas tiveram tempos operatórios significativamente mais longos, maior perda de sangue e uma maior incidência de disfagia tanto no seguimento inicial como no final. **Discussão:** A presença de blindagem anterior correlaciona-se com um aumento do trauma cirúrgico, podendo contribuir para as taxas mais elevadas de disfagia observadas. Estratégias minimamente invasivas e dispositivos autônomos podem mitigar este risco. **Conclusão:** O uso de placas cervicais anteriores está significativamente associado a um maior risco de disfagia pós-operatória. Evitar o revestimento em casos selecionados pode reduzir a morbidade e melhorar os resultados dos pacientes.

**Palavras-Chave:** Distúrbios de deglutição; Neurocirurgia; Coluna

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## INTRODUCTION

Cervical degenerative disc disease (CDDD) is understood as a continuum of morphological changes in the structure of the spine secondary to mechanical insults. Also known as degenerative cervical myelopathy (DCM), it is considered the main cause of neck pain in adults and the elderly and the main cause of non-traumatic cervical spinal cord dysfunction<sup>1-6</sup>.

Anterior cervical discectomy and fusion (ACDF), described in 1958 by Smith and Robinson<sup>6</sup>, has become the standard treatment for CDDD associated with myelopathy and/or radiculopathy<sup>7,8</sup>. Since its description, this technique has been widely used and has become one of the most commonly performed surgeries in the cervical spine. It presents good results, is considered safe and is associated with low morbidity<sup>9,10</sup>.

Traditionally, the ACDF technique describes the use of a bone graft and anterior cervical plate to increase stability and fusion rates, reduce subsidence and promote better cervical alignment<sup>8,10,11</sup>. However, some studies have linked the interposition of the anterior cervical plate with an increased rate of postoperative dysphagia<sup>10</sup>.

Dysphagia is characterized by difficulty swallowing liquid or solid food and can be classified in different ways, either based on the anatomical area affected or its intensity, although the latter is more subjective. Another way of categorizing it is through its evolution, which can be acute, chronic or progressive. In cervical spine surgeries with anterior access, the most prevalent dysphagia is acute dysphagia, of low and medium intensity, which is most often transient<sup>12,15-18</sup>. It is considered a relatively common postoperative complication in this type of surgery, its incidence varies widely in the literature and it can be explained by various pathophysiological mechanisms<sup>12,13</sup>.

The purpose of this study is to evaluate and quantify the hypothesis that ACDF surgeries using an anterior cervical plate performed on patients with degenerative cervical spine disease have a higher frequency of dysphagia in the postoperative period compared to surgeries in which no plate is used. The aim, therefore, is to help spine surgeons who are going to perform this procedure to choose the best method on a scientific and statistical basis<sup>12,15-18</sup>.

## METHODS

The primary objective of this study is to analyze the rate of postoperative dysphagia in patients undergoing ACDF surgery by comparing a group of patients undergoing surgery with an anterior plate system (plate group) with another group of patients undergoing the same surgery, but without the use of an anterior plate (no-plate group).

We presented a systematic review and a meta-analysis following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol. We only considered clinical studies for our analysis (randomized clinical trials, retrospective or prospective case-control studies or case series), presenting the rate of postoperative dysphagia in ACDF surgery with intersomatic devices associated or not with the use of an anterior cervical plate, in patients with cervical degenerative disease with myelopathy and/or radiculopathy.

We performed two independent searches in the PubMed database with a search restricted to the last 10 years. In search 1, we used the keywords “anterior cervical discectomy and fusion” and “stand-alone” and obtained 166 results. In the second search, we used the keywords “anterior cervical discectomy and fusion” and “anterior plating” and found 505 results. This added up to a total of 671 results.

We excluded case reports, literature reviews, systematic reviews, meta-analyses, technical notes, articles that did not evaluate postoperative dysphagia and studies that included patients undergoing surgical techniques other than ACDF. The absence of a postoperative dysphagia assessment was the main reason for exclusion.

Furthermore, we also assessed the characteristics of the study population that could compromise our sample with biases such as: inclusion of patients who had suffered trauma to the cervical spine; surgeries that included corpectomy and posterior approach; cancer patients undergoing cervical radiotherapy; patients who had undergone previous cervical surgery or those with chronic diseases and previous dysphagia (Table 1).

*Study selection*

Two independent reviewers selected the eligible papers in the two searches. To resolve differences in the selection of articles, a third



**Table 1.** Bias evaluation of each article in this review based on the Cochrane Collaboration's tool

STUDY - YEAR	SELECTION BIAS		PERFORMANCE BIAS	DETECTION BIAS	ATTRITION BIAS	REPORTING BIAS	OTHER BIAS
	Random Sequence Generation	Allocation Concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Sources of Bias
Alhashash et al., 2022 <sup>11</sup>	+	+	-	-	+	-	?
Mu et al., 2022 <sup>13</sup>	+	+	-	-	+	-	?
Poblete et al., 2022 <sup>12</sup>	+	+	-	-	-	-	?
Theologou et al., 2020 <sup>14</sup>	+	+	-	-	-	-	?
Xiong et al., 2019 <sup>15</sup>	+	+	-	-	-	-	?
Kapetanakis et al., 2017 <sup>16</sup>	+	+	-	-	-	-	?
Yeung et al., 2019 <sup>17</sup>	+	+	-	-	-	-	?
Lee et al., 2017 <sup>18</sup>	+	+	-	-	-	-	?
Overley et al., 2017 <sup>19</sup>	+	+	-	-	-	-	?
Tang et al., 2023 <sup>20</sup>	+	+	-	-	+	-	?
Chen et al., 2016 <sup>21</sup>	+	+	-	-	+	-	?
Yamagata et al., 2017 <sup>22</sup>	+	+	-	-	-	-	?
Shin et al., 2014 <sup>23</sup>	+	+	-	-	-	-	?
Mostafa et al., 2019 <sup>24</sup>	+	+	-	-	-	-	?
Njoku et al., 2014 <sup>25</sup>	+	+	-	-	-	-	?
Shi et al., 2015 <sup>26</sup>	+	+	-	-	-	-	?
Liang et al., 2021 <sup>27</sup>	+	+	-	-	+	-	?
Zhu et al., 2019 <sup>28</sup>	+	+	-	-	-	-	?
Zhou et al., 2018 <sup>29</sup>	+	+	-	-	+	-	?
Nambiar et al., 2019 <sup>30</sup>	+	+	-	-	-	-	?
El-Tantawy et al., 2015 <sup>31</sup>	+	+	-	-	-	-	?
Gerszten et al., 2016 <sup>32</sup>	+	+	-	-	-	-	?
Shi et al., 2016 <sup>33</sup>	+	+	-	-	-	-	?
Zhang et al., 2022 <sup>34</sup>	+	+	-	-	-	-	?
Zhang et al., 2022 <sup>35</sup>	+	+	-	-	-	-	?
He et al., 2022 <sup>36</sup>	+	+	-	-	+	-	?
Guo et al., 2022 <sup>37</sup>	+	+	-	-	+	-	?
Xue et al., 2022 <sup>38</sup>	+	+	-	-	-	-	?
Sommaruga et al., 2021 <sup>39</sup>	+	+	-	-	-	-	?
He et al., 2022 <sup>40</sup>	+	+	-	-	+	-	?
Wang et al., 2014 <sup>41</sup>	+	+	-	-	+	-	?
Bucci et al., 2017 <sup>42</sup>	+	+	-	-	+	-	?
Tabaraee et al., 2015 <sup>43</sup>	+	+	-	-	-	-	?
Wang et al., 2014 <sup>44</sup>	+	+	-	-	-	-	?
Kim et al., 2014 <sup>45</sup>	+	+	-	-	-	-	?
Wang et al., 2019 <sup>46</sup>	+	+	-	-	+	-	?
Zhang et al., 2018 <sup>47</sup>	+	+	-	-	+	-	?
Liu et al., 2016 <sup>48</sup>	+	+	-	-	+	-	?
He et al., 2018 <sup>49</sup>	+	+	-	-	-	-	?
Zhang et al., 2016 <sup>50</sup>	+	+	-	-	-	-	?
Chen et al., 2015 <sup>51</sup>	+	+	-	-	+	-	?
Thind et al., 2022 <sup>52</sup>	+	+	-	-	+	-	?
Son et al., 2014 <sup>53</sup>	+	+	-	-	-	-	?
Maragkos et al., 2019 <sup>54</sup>	+	+	-	-	-	-	?
Li et al., 2016 <sup>55</sup>	+	+	-	-	+	-	?
Lonjon et al., 2019 <sup>56</sup>	+	+	-	-	-	-	?
El Baz et al., 2019 <sup>57</sup>	+	+	-	-	+	-	?
Arts et al., 2020 <sup>58</sup>	+	+	-	-	-	-	?
Fisahn et al., 2017 <sup>59</sup>	+	+	-	-	-	-	?
Wang et al., 2023 <sup>60</sup>	+	+	-	-	+	-	?
Wang et al., 2016 <sup>61</sup>	+	+	-	-	-	-	?
Hofstetter et al., 2015 <sup>62</sup>	+	+	-	-	+	-	?
Sun et al., 2020 <sup>63</sup>	+	+	-	-	-	-	?
Shi et al., 2015 <sup>64</sup>	+	+	-	-	+	-	?
Wang et al., 2015 <sup>65</sup>	+	+	-	-	+	-	?
Lan et al., 2018 <sup>66</sup>	+	+	-	-	+	-	?
Lu et al., 2018 <sup>67</sup>	+	+	-	-	+	-	?

reviewer decided whether the studies should be included or not. We only considered papers published in English, assessed them by title, abstract or full text and selected the papers according to the inclusion/exclusion criteria.

After an initial analysis, 129 studies were excluded because of their design (case reports, review studies, technical notes) and 12 because they were in other languages. In addition, 11 studies were present in both searches and had to be excluded. After analyzing the title and abstract, a further 56 studies were excluded.

Finally, after reading and analyzing the full text, 406 studies were excluded, leaving a total of 57 studies included in this study (Figure 1 and Table 2).

### Data extraction

The data of interest for our research were collected and tabulated for later analysis. From each study, we extracted the number of participants, their mean age, sex, the mean follow-up, operative time, blood loss, number of levels operated, number of patients undergoing surgery with plate systems, self-locking or stand-alone

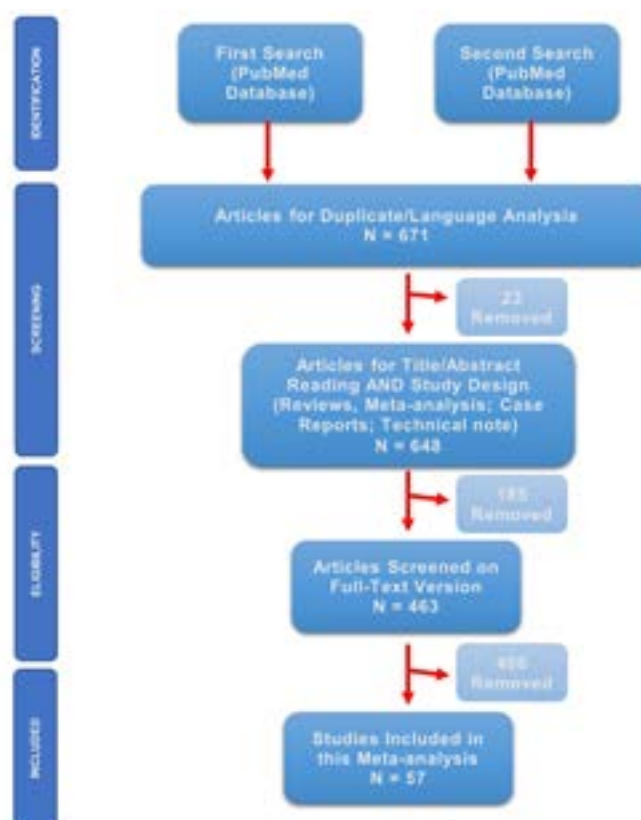


Figure 1. Study flowchart.

Table 2. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Must contain the rate of dysphagia	Patients with other non-degenerative spinal pathologies
Patients with CDDD with myelopathy and/or radiculopathy	Other Languages
Patients who underwent ACDF with or without the use of an anterior plate	Other procedures than ACDF
Studies in English	ACDF surgeries that combine interbody devices with and without a plate in the same patient
Study Design: Randomized control trials, retrospective and prospective case-control or series of cases studies	Study Design: Case reports, systematic review, literature reviews, meta-analysis and technical notes

interbody devices, and number of patients with dysphagia at first and last follow-up.

## STATISTICAL METHODS

The chi-square test was used to assess the association between the type of implant used in surgery (plate vs. no-plate) and the presence of postoperative dysphagia, in a contingency table. The contingency table is a two-entry table showing the joint distribution of the frequencies of the two variables. When the p-value was lower than the previously determined significance level ( $\alpha = 0.05$ ) the null hypothesis of independence can be rejected, and it can be concluded that there is an association between the type of surgery and the presence of dysphagia after surgery.

We used the Bonferroni correction to adjust the significance value when performing multiple tests at different follow-ups. The Bonferroni correction is a widely used method to control type I error (false positives) when multiple comparisons are made. To apply the Bonferroni correction, the value of significance (usually 0.05) is divided by the total number of comparisons being made, which is two in the case of the study in question (First and Last Follow Up). As two chi-squared tests were performed (one for the first follow-up and one for the last follow-up), the p-value of 0.05 was divided by 2, resulting in a new significance value of 0.025 for each individual test. Thus, for each chi-squared test, the calculated p-value was compared with the new significance value of 0.025 and if a p-value of less than 0.025 was found the result was considered to be statistically significant after the Bonferroni correction. This approach helps to reduce the risk of finding significant results by chance when multiple comparisons are made.

In order to check the relationship between the number of patients who underwent one, two, three or four levels of surgery and the percentage of patients who developed postoperative dysphagia, we used linear regression to assess the association between the variables. We performed four regressions to measure dysphagia at the first and last follow-up, for patients in the plate and no plate groups. All the regressions present, as explanatory variables, the number of patients operated at one, two, three or four levels and, as a response, the percentage of patients who had postoperative dysphagia at the first and last follow-ups.

## RESULTS

Amongst 57 studies reviewed, 41 were retrospective cohorts<sup>19-33,35-37,41,42-44,47,48,50-54,56,61,63,66,67</sup>, 10 were prospective cohorts<sup>34,39,40,45,49,55,58-60,64</sup>, 1 case-control<sup>46</sup>, 4 case series<sup>38,62,65,66</sup> and 1 randomized clinical trial<sup>51</sup>.

**Patient's Demographics:** The present study analyzed 4603 patients. Those patients were divided into two groups according to the type of device used during surgery. In the plate group, 1396 (30.32%) patients underwent ACDF with an anterior cervical plate<sup>27-29,33,35-37,41,42-45,47-49,51-61,63,67-69,71-75</sup>. In the no-plate group, a total of 3207 (69.67%) patients were operated with a system that used intersomatic spacers without plating<sup>19-66</sup>. In the plate group, 644 (47.04%) patients were female, and 725 (52.95%) were male, 27 patients were not identified by gender in this group. In the no-plate group, 1534 (48.14%) were female and 1652 (51.85%) were male, 21 patients were not identified by gender in this group. The mean age of the patients on plate group was  $54.4 \pm 5.24$  years, and in the no-plate group,  $54.06 \pm 4.67$  years.

**Surgical Procedure:** We were able to collect the number of levels operated of 4137 patients. In the plate group, 632 (48.61%) patients underwent one-level surgery, 337 (25.92%) two-level surgery, 308 (23.69%) three-level surgery and 23 (1.76%) four-level surgery, no information was available about levels operated in 96 patients.<sup>27-29,33,35-37,41,42-45,47-49,51-61,63,67-69,71-75</sup>. Among patients operated with no-plate system (no-plate group), in the stand-alone subgroup, 568 (50.44%) patients underwent one-level surgery, 187 (16.60%) two-level surgery, 230 (20.42%) three-level surgery and 141 (12.52%) underwent four-level surgery<sup>19-75</sup> and in patients operated with self-locking cages, 770 (46.16%) patients underwent one-level surgery, 514 (30.81%) two-levels, 363 (21.76%) three-levels and 21 (1.25%) underwent four-levels surgery. No information was found available about the number of levels operated in 260 patients in the no-plate group and for 43 patients operated at one level in this group, it was not possible to determine if the system was self-locking or stand-alone (Table 3).

**Operative time:** In the plate group, the mean operative time was  $122.55 \pm 32.16$  min<sup>27-29,35-37,41,42-49,51,52,54-57,59-61,63, 67-69,71-75</sup> and in the no-plate group,  $111.61 \pm 39.31$  min<sup>19,20,22,24,25,27-30,35-36,41,42-52,54-57,59-69,71-75</sup>. Comparing both mean operative times, we disclosed that the use of a no-plate systems reduces operative time.

**Blood loss:** In the plate group, the average blood loss was  $102.72 \pm 39.41$  ml<sup>128,29,35-37,41,42-45,48,49,51,54-57,59-61,63,67-69,71-75</sup> and in no-plate group  $92.30 \pm 75.22$  ml<sup>16,20,24,25,28-30,35-37,41,42-46,48-51,54-57,59-61,63,65-69,71-75</sup>. Results showed that the blood loss is lower when ACDF is performed without anterior plate (Table 4).

**Post-operative follow-up:** The mean postoperative follow-up was  $30.85 \pm 13.75$  months in the plate group<sup>28,29,31,35,37,44,45,47-49,54-56,58-60,63,67-69,71-75</sup> and  $30.19 \pm 17.82$  months in no-plate group<sup>19-23,28,29,31,33,35,37,44-50,54-56,58-60,62-65,67-69,72-75</sup>. The result shows that there is no significant difference in the mean postoperative follow-up time between the groups.

**Incidence of dysphagia:** In the plate group, a total of 330 (22.90%) patients had dysphagia at the first follow-up<sup>27-29,31,35-37,41,42-45,47-49,51-61,63,67-69,71-75</sup> and 76 (5.97%) patients had dysphagia at the last postoperative follow-up<sup>27-29,31,35-37,41,43-45,48,49,52-56,58-61,63,68,69,71-75</sup>. In the no-plate group, 368 (11.41%) patients had dysphagia at the first follow-up<sup>13-69</sup> and 21 (0.71%) at the last postoperative follow-up<sup>43-46,48-50,52,54-56,58-61,63,65,68-75</sup>. Comparing the number of patients with postoperative dysphagia between groups, we can conclude, with statistical relevance, that the incidence of dysphagia was significantly higher in the plate group at the first follow-up (RR 1.85; 95% CI, 1.62 - 2.13;  $P < 0.05$ ) and also at the last follow-up (RR 7.93; 95% CI, 4.91 - 12.82;  $P < 0.05$ ) (Tables 5 and 6).

**Table 3.** Levels operated in the “no-plate” subgroups (stand-alone vs. self-locking).

	Stand-alone	Self-locking
1-level	568	770
2-levels	187	514
3-levels	230	363
4-levels	141	21

**Table 4.** Demographic and surgical characteristics.

	“Plate”	“No-plate”
Patients	1396	3207
Female/male	644/725	1534/1652
Mean age (years)	54.4	54.06
Mean follow-up (months)	30.85	30.19
Mean blood loss (ml)	102.72	92.30
Mean operative time (min)	122.55	111.61
1-level	632	1338
2-levels	337	701
3-levels	308	593
4-levels	23	162

**Table 5.** Number of patients with dysphagia in the plate x no-plate group at the first and last follow-up.

	“Plate”	“No-plate”
First follow-up	330	368
Last follow-up	76	21

**Table 6.** Risk of dysphagia at first and last follow-up.

	First follow-up	Last follow-up
Risk of exposure (plate)	19.12% [17.33, 21.04]	5.16% [4.13, 6.42]
Risk in the unexposed (stand-alone)	10.29% [9.33, 11.33]	0.65% [0.41, 0.99]
Risk ratio	1.85 [1.62, 2.13]	7.93 [4.91, 12.82]
Risk difference	8.82% [6.72, 10.93]	4.51% [3.34, 5.67]
P-value	<0.0000001	<0.0000001



## DISCUSSION

**Demographic data:** Regarding the patient's profile, there were 2597 (56.29%) men and 2016 (43.70%) women ( $p = 0.0002$ ). The sex distribution was similar in both groups; there was no statistically significant difference between them, as well as patient's age (53.75 years in the plate group vs. 54.09 years in the no-plate group).

**Surgical data:** Regarding the number of levels operated, there was a prevalence of single-level surgery, with a rate of 61%. This tendency was similar between both groups. The percentage of patients undergoing two, three, and four-level surgery was also similar between groups. However, there was a statistically significant difference in operative time and blood loss. Patients in the plate group had longer operating times and greater blood loss compared to no-plate group patients.

**Clinical Data:** Dysphagia is a common complication of anterior cervical spine surgery<sup>67</sup>. According to Fountas et al.<sup>9</sup> dysphagia was the most common isolated complication found in their study. The rate of dysphagia reported in the literature is variable, with most studies being retrospective cohort studies with rates ranging from 2 to 60 %<sup>68</sup>. Dysphagia after an anterior approach to the cervical spine can be explained by various mechanisms, which may be related to the graft type, number of levels operated, surgery's duration, and patient's characteristics. The most accepted causes of postoperative dysphagia are esophageal manipulation, local injury to nerve structures, hematomas, local tissue edema and adhesions formed around the esophagus<sup>29,69,70</sup>.

The causes of postoperative dysphagia are not well understood, and its etiology seems to be multifactorial. One of the hypotheses is that the mechanical conflict of the plate with the esophagus may be one of the reasons for the development of this complication<sup>71</sup>. The use of an anterior plate in ACDF surgery increases operative time and blood loss because it requires greater dissection for correct placement and fixation in the anterior cervical region. These maneuvers increase the risk of esophageal injury, hematomas, vocal cord paralysis, tissue edema, and esophageal adhesions<sup>72</sup>.

The diagnosis of dysphagia can be made from a bedside swallow assessment using validated questionnaires answered by the patient themselves, such as a self-assessment to check for dysphagia and its

severity and impact on quality of life. Examples of questionnaires widely used include the Eating Assessment Tool and the Swallowing Quality of Life questionnaire. It is also important to have a speech therapist assess the patient at bedside, observing the act of eating and drinking, tasting liquids of different viscosities and observing whether there is coughing, choking or piecemeal swallowing. In addition, it is possible to carry out more specific and accurate instrumental swallowing studies such as fiber-optic endoscopic evaluation and video fluoroscopic swallowing studies, allowing for more precise treatment recommendations<sup>12,17</sup>.

The management of dysphagia should involve a trained multidisciplinary team such as: speech therapists, nutritionists, nurses and doctors. The main aim of treatment is to promote safe swallowing and ensure adequate nutrition and hydration for the patient. Treatment aims to improve the physiology of swallowing, mainly through maneuvers and exercises developed by a speech therapist to rehabilitate the oral and/or pharyngeal phases of swallowing, such as the Mandelsohn maneuver, which improves laryngeal elevation and opening of the upper esophagus, and exercises to improve the function of the lips and tongue during the oral phase of swallowing<sup>12,17</sup>.

Fogel and McDonnel (2015) evaluated 31 patients who were elected for surgical treatment of persistent dysphagia after ACDF surgery with a plate. The average time between ACDF surgery and surgery to treat dysphagia was 18 months and all patients had moderate to severe dysphagia. The average follow-up time was 11 months and the questionnaire used was the Bazaz-Yoo dysphagia score. The main intraoperative alteration found was the presence of extensive adhesions connecting the esophagus to the prevertebral fascia and anterior column around the plate. No plate fracture, loosening or loss of screws was found. The proposed approach was to remove the anterior plate and perform lysis of adhesions between the esophagus and the spine. After the surgical approach, at the last follow-up, seventeen patients (55%) showed total improvement in dysphagia. Previous neck surgery with pre-existing dysphagia and larger amounts of adhesions were likely contributing factors in the cases of persistent severe dysphagia. The authors conclude that surgery to remove the plaque and lysis of adhesions improved dysphagia, with an improvement in patient satisfaction and quality of life<sup>74</sup>.

In our meta-analysis, we evaluated the incidence of dysphagia during postoperative follow-up. Comparing data from patients who underwent ACDF surgery with a plate and no-plate systems,

we concluded that the incidence of dysphagia was significantly higher in patients in the plate group with statistical significance. Similar to the results of our study, the authors Duan et al.<sup>73</sup>, in their systematic review and meta-analysis, concluded that the use of an anterior plate system is associated with higher incidences of post-operative dysphagia when compared to the use of a self-locking spacer. Zhang et al.<sup>42</sup> also concluded after analyzing the incidence of dysphagia in postoperative follow-up, that dysphagia is more frequent in patients that underwent ACDF with plating.

On the other hand, the use of the anterior plate reveals the biomechanical advantages of this strategy. The presence of the plate increases the stability of the operated segment and reduces the movement between the graft placed in the intervertebral space and the surface of the vertebrae, increasing the chances of arthrodesis of the operated segment. In this way, the plate not only acts as a barrier to prevent the graft displacing, but also as a support that prevents the graft from collapsing and subsidence into the vertebral endplate. In addition, the plate helps maintain sagittal balance and prevents post-operative kyphosis<sup>75</sup>.

Our study also analyzed operative time and blood loss data, concluding that the use of an anterior plate is associated with longer operative time and greater blood loss, with a statistically significant difference. Zhang et al.<sup>42</sup> also found similar results, suggesting that the use of self-locking spacers without the use of a plate has a shorter operative time and less blood loss. These results seem reasonable once the surgery that doesn't require the use of an anterior plate is relatively simpler, requiring less extensive surgical access with less tissue dissection.

It seems reasonable to consider that the cervical plate promotes greater mechanical stability with a greater reduction in the movement of the operated segment, thus facilitating the formation of arthrodesis. For this reason, this strategy of instrumentation should work best in cases where correction of kyphotic deformities, stabilization of unstable fractures or correction of displacements between the vertebrae is expected. The anterior cervical plate continues to perform an important function in ACDF surgeries, but its use should be considered for cases when this is necessary, as its use may be associated with risks such as increased post-operative dysphagia, implant failure and adjacent level degeneration. We believe that for surgeries in cases of degenerative spinal disease with myelopathy and/or radiculopathy without signs of spinal instability, where the main objective is decompression of nerve structures, discectomy with placement of self-locking spacers

is sufficient, as they are mechanically efficient and has lower complication rates and a lower incidence of post-operative dysphagia.

## LIMITATIONS

There was only one randomized clinical trial in our review, and our analysis included mainly prospective and retrospective cohort studies. There was a significant difference in postoperative follow-up between the studies, regarding the mean time and frequency of follow-up. Some studies did not specify the number of levels operated or which levels were approached, making it difficult to determine if more high or low levels were operated. Our review was limited by the search in only one database, and only studies published in English were considered.

## CONCLUSION

The association of an anterior cervical plate in ACDF surgery is a risk factor for postoperative dysphagia. Operative time and blood loss were statistically higher in ACDF with plating. Among patients who underwent plating surgeries, the rate of dysphagia was significantly higher when compared to patients who underwent ACDF with stand-alone cages at the first and last postoperative follow-up. The association of an anterior cervical plate in ACDF makes the surgery more complex and requires a wider surgical route and greater exposure of the anterior cervical region, with consequent tissue devitalization. This may explain the higher rate of dysphagia with the use of this device.

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# Surgical Techniques, Materials, and Outcomes in Vertebral Fixation of Cervical Trauma

## *Técnicas Cirúrgicas, Materiais e Resultados na Fixação Vertebral de Trauma Cervical*

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### ABSTRACT

This study analyzes clinical outcomes and associated complications, aiming to assess the results of cervical fixation surgeries in trauma cases, with a focus on graft types and complications. A systematic review of nine studies involving 279 patients was conducted, analyzing surgical techniques, materials, and adverse events. Titanium cages showed lower complication rates (16.26%) compared to traditional grafts (54.84%). Advanced techniques, such as robotic-assisted surgery, reduced operative time and blood loss. Titanium cages proved effective in reducing complications and improving outcomes. Future studies should investigate long-term results and economic aspects to guide evidence-based clinical practices.

**Keywords:** Cervical trauma; Spinal fixation; Surgical techniques; Bone grafts; Clinical outcomes

### RESUMO

O presente estudo analisa os desfechos clínicos e as complicações associadas, com o objetivo de avaliar os resultados da fixação cervical em casos de trauma, com ênfase nos tipos de enxertos e suas complicações. Uma revisão sistemática de nove estudos envolvendo 279 pacientes foi conduzida, analisando as técnicas cirúrgicas, materiais e efeitos adversos. As cages de titânio apresentaram menores índices de complicações (16,26%) em comparação com os enxertos tradicionais (54,84%). Técnicas avançadas, como cirurgia robótica assistida, apresentaram redução do tempo de operação e da perda de sangue. As cages de titânio se mostraram eficazes na redução de complicações e na melhora dos resultados. Estudos futuros devem investigar resultados a longo prazo e os aspectos econômicos para orientar práticas clínicas baseadas em evidências.

**Palavras-Chave:** Trauma cervical; Fixação espinhal; Técnicas cirúrgicas; Enxertos ósseos; Desfechos clínicos

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## INTRODUCTION

Cervical spinal cord trauma, usually caused by traffic accidents or falls, represents a significant cause of morbidity and mortality<sup>1</sup>. Surgical intervention is often necessary to stabilize the spine, prevent further deterioration, and accelerate recovery<sup>1-3</sup>.

Historically, cervical spine fixation has evolved significantly, transitioning from traditional open surgeries to more modern minimally invasive techniques. The development of various bone graft materials, including autografts, allografts, and synthetic options, has expanded the possibilities for achieving stable fixation<sup>3,4</sup>.

Additionally, the use of titanium cages in these surgeries has gained attention for their potential to improve surgical outcomes by providing enhanced mechanical support and reducing the risk of implant failure<sup>2,4,5</sup>. Previous studies conducted in non-traumatic contexts have shown that titanium cages can lead to better clinical outcomes, including lower complication rates and superior functional recovery, compared to traditional autografts or allografts without the use of cages<sup>5,6</sup>.

However, the trauma context introduces factors that may influence surgical outcomes, making the results distinct from those observed in elective surgeries, such as those performed to treat degenerative conditions like rheumatoid arthritis<sup>7</sup>. Patients undergoing surgery due to trauma often have a more unstable clinical condition, including associated injuries, hemodynamic impairment, and a higher risk of infection. This condition can lead to an increased rate of perioperative complications, such as thromboembolism, sepsis, and bone fusion failure<sup>8</sup>. Furthermore, surgery often requires the correction of unstable fractures and severe misalignments, frequently necessitating external fixators or combined approaches. Surgical time tends to be longer, increasing the risk of intraoperative bleeding and anesthetic complications. Additionally, while patients with degenerative diseases can follow a planned and gradual rehabilitation process, trauma patients may require prolonged ventilatory support, immobilization, and more intensive rehabilitation, impacting functional recovery<sup>7,9</sup>. Understanding these differences is crucial for improving surgical techniques and rehabilitation strategies, preventing the inappropriate extrapolation of evidence from non-traumatic surgeries to procedures performed in trauma contexts.

Moreover, the choice of bone graft type is of great clinical importance, as it directly impacts the success of the surgery, influencing factors such as fusion rates, incidence of complications, and overall patient outcomes<sup>6</sup>. Despite its importance, the choice of bone graft type for fixation remains a subject of debate, as there are various options available, each with its own advantages and limitations<sup>4,6,10,11</sup>. With the increasing incidence of cervical spine injuries resulting from trauma, identifying the ideal bone graft is essential to improve treatment protocols, which remain uncertain, and enhance the quality of patient care<sup>1,11</sup>.

### Objective

The main objective of this systematic review is to assess the outcomes of cervical spine fixation surgery in trauma patients, with a specific focus on the types of bone grafts used. As secondary objectives, it aims to analyze intraoperative blood loss, surgical duration, and the incidence of adverse events. By reviewing the existing literature, this review seeks to provide evidence-based recommendations to optimize surgical strategies in the treatment of cervical spine trauma.

## MATERIAL AND METHODS

A systematic review on the surgical treatment of cervical spinal cord trauma (vertebral fixation) was conducted in accordance with the Cochrane Collaboration<sup>12</sup> and the guidelines of the "Preferred Reporting Items for Systematic Reviews and Meta-Analysis" (PRISMA)<sup>13</sup>. A predefined protocol was established and prospectively registered in the Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42025645180.

### Database and search strategy

The electronic databases Embase, PubMed (MEDLINE), and Cochrane Library were searched. The following keywords were combined using the Boolean operators AND and OR as follows: ("cervical spinal cord injury" OR "acute cervical spinal cord injury" OR "cervical spine trauma" OR "cervical spinal injury" OR "cervical spine fracture") AND ("surgical outcomes" OR "neurological recovery" OR "postoperative outcomes" OR "complication rates" OR "hardware failure" OR "infection rates" OR "functional recovery" OR "quality of life"). Additionally, a reference search was conducted in the articles included in the analysis.



### *Selection strategy and data collection*

The inclusion criteria were: (1) Randomized clinical trials or cohort studies; (2) Studies with an anterior approach for cervical fixation; (3) Studies with a posterior approach for cervical fixation; (4) Studies reporting clinical outcomes of interest. The exclusion criteria were: (1) Studies with overlapping surgical indications; (2) Studies with surgical indications unrelated to cervical trauma; (3) Studies that did not report the material used for fixation surgery; (4) Studies that did not meet the intervention and population criteria of interest. The exclusion of studies with overlapping surgical indications was justified to avoid variability in the results and mitigate the dilution of clinical relevance of findings specific to vertebral fixation surgery in the context of cervical trauma. The primary outcome assessed was the occurrence of perioperative and postoperative adverse events. Secondary outcomes included: (1) Graft used for surgery; (2) Surgical technique used; (3) Intraoperative blood loss; (4) Surgical time.

Three authors (JAS, IAT, and VAB) independently conducted the study selection. The data were then extracted and recorded by the same authors, and later reviewed by a third investigator (IIK). The variables of interest included patient characteristics, procedure details, and follow-up data. Episodes of transient pain at the bone graft site (lasting less than two weeks) were not included as adverse events in this review. A meta-analysis was not planned due to the expected lack of randomized clinical trials.

### *Quality assessment and risk of bias*

The Cochrane Collaboration tool (ROBINS-I)<sup>14</sup> was used to assess the risk of bias in observational studies, ensuring an individual quality evaluation of the studies. Conflicts were resolved through discussion and involvement of a fourth author.

### *Statistical analysis and data synthesis*

The characteristics and outcome data of the included studies were collected, grouped, and compared. Continuous variables are presented as mean  $\pm$  standard deviation, or as mean (range). Categorical variables are presented as number (percentage). When only the median and range were reported, the mean and standard deviation were estimated using the method of Wide Area Network (Wan). Statistical analysis was conducted using Fisher's Exact Test with the help of RStudio version 2023.03.0. The p-value was calculated, with statistical significance considered for  $p < 0.05$ . The odds ratio was calculated from the combined data of the studies included in the analysis, presenting a 95% confidence interval (CI).

## RESULTS

### *Search results and description of selected studies*

The initial search resulted in 1,546 studies. After removing duplicates and unrelated studies, 286 studies remained and were reviewed against the inclusion criteria. Of these, 9 studies were included for qualitative and quantitative analysis (Figure 1).

### *General characteristics of the selected studies*

A summary of the selected studies is presented in Table 1. The total sample size was 279 patients who underwent cervical fixation surgery due to traumatic mechanisms. The sex of the patients was reported in 232 patients across 7 studies<sup>9,15-20</sup>, of which 159 were male (68.53%). Only two of the included studies<sup>16,17</sup> did not report the use of bone graft. In the others, patients underwent bone fusion with a graft, either alone or in combination with a titanium cage. One study<sup>15</sup> included surgeries at both the subaxial cervical and atlanto-axial levels, without distinguishing adverse events between these levels.

The average surgical time and intraoperative blood loss showed significant variations across the studies. The average surgical time ranged from 75 to 274.63 minutes, while intraoperative blood loss varied from 12 mL to 428.65 mL. This heterogeneity can possibly be attributed to differences in the surgical techniques used and the characteristics of the patient populations selected in each study. Tang et al.<sup>9</sup>, whose study recorded the longest average surgical time and highest intraoperative blood loss, included only severe cervical fractures. In contrast, Jun and Yi<sup>17</sup>, which reported the lowest blood loss, used a minimally invasive roboticassisted surgical technique.

### *Adverse events*

Of the nine included studies, eight<sup>9,15,16,18-22</sup> reported adverse events, totaling 96 complications in this review (Table 2). The most frequent events were reoperations and deaths, both described in three studies<sup>9,15,16,18,19</sup>. In total, there were 6 cases of reoperation and 12 deaths, considering the aggregation of the studies that reported these occurrences. Only one study<sup>17</sup> did not report adverse events in its population. In the others, the complication rate varied between 2.1% and 100% of participants. However, in one study<sup>9</sup>, the analyzed population consisted of patients with severe cervical fractures, which may have potentially overestimated complications in this study compared to the others included in this review.

**Table 1.** Characteristics and Outcomes of Included Studies. N.S.: Not specified.

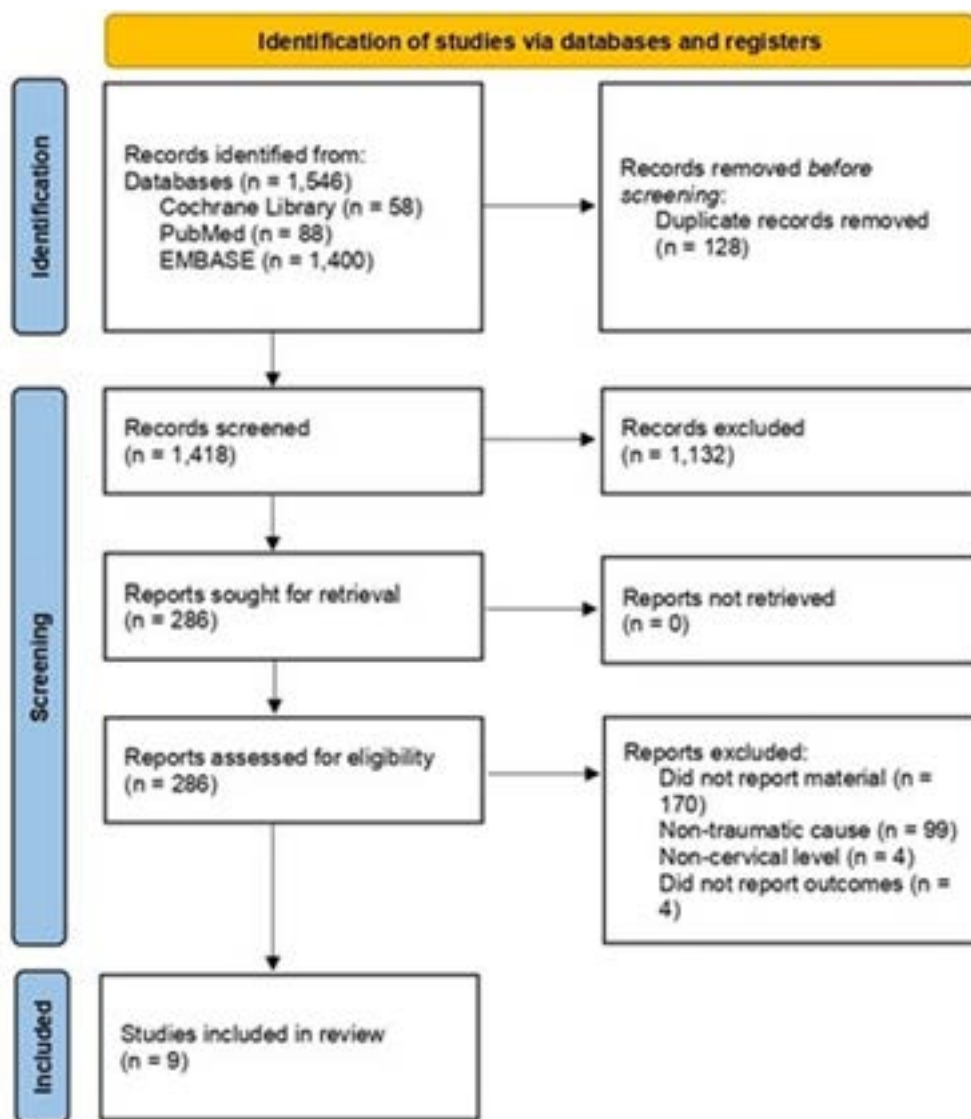
Author and year	N (M/F) relation	Age (years)	Follow-up time (months)	Level	Grafts	Techniques	Intraoperative Blood Loss (mL)	Surgery time (minutes)	Adverse events
Brockmeyer et al., 1995 <sup>15</sup>	20 (10/10)	13.95 ±3.02	26.1 (4.3-90.3)	Subaxial and Atlanto-axial	Autologous grafts and fixation with a screw in the odontoid process, without the use of graft	Anterior cervical plates, lateral mass plates, and posterior screw fixation	N.S.	N.S.	2
Frangen et al., 2007 <sup>16</sup>	27 (10/17)	83 ±8.7	5.5 ±2.5	Axis	N.S.	Posterior screw fixation with an additional modified fusion using bone graft	230 ±170	149.25 ±25.25	8
Jain et al., 2017 <sup>21</sup>	44 (N.S.)	19-75	17 (6-48)	Axis	Autologous grafts	Anterior discectomy and fusion (Southwick and Robinson)	N.S.	106 (90-130)	54
Jun; Yi, 2023 <sup>17</sup>	5 (5/0)	48.5 (37-74)	16.8 (10-24)	Axis	N.S.	Posterior screw fixation with minimally invasive robotic-assisted technique	12 (5-25)	93 (64-130)	No adverse event was reported
Kanna; Shetty; Rajasekaran, 2018 <sup>18</sup>	39 (30/9)	49.9 ±4.5	14.3	Subaxial	Titanium cages and autologous grafts	Anterior discectomy and fusion (modified Smith-Robinson)	165 ±43	124 ±32	5
Lang et al., 2021 <sup>19</sup>	33 (25/8)	48.2 ±22.2	29.8 ±24.3	Subaxial	Titanium cages and autologous grafts	Anterior discectomy and fusion	N.S.	N.S.	5
Payer, 2006 <sup>22</sup>	3 (N.S.)	35 ±9.85	14 (12-24)	Subaxial	Expandable titanium cages	Anterior discectomy and fusion, pedicle screws, and lateral mass plates	N.S.	N.S.	1
Ramnarain; Govender, 2008 <sup>20</sup>	60 (38/22)	34 (19-67)	19 (14-39)	Subaxial	Allografts	Anterior discectomy and fusion	50 (20-100)	75 (64-115)	12
Tang et al., 2023 <sup>9</sup>	48 (41/7)	54.69	27.99	Subaxial	Titanium Cages and Autografts	Anterior discectomy combined with lateral mass screws or pedicle screw fixation.	428.65	274.63	9

**Table 2.** Perioperative and postoperative adverse events recorded. Given the variation in the number of patients in each study, the data are presented as number (percentage), aiming to avoid misinterpretation of extreme results. CSF: Cerebrospinal Fluid.

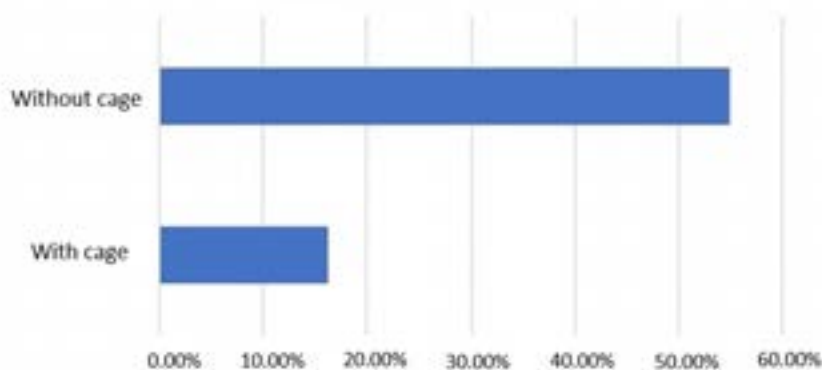
	Brockmeyer (n=20) <sup>15</sup>	Frangen (n=27) <sup>16</sup>	Jain (n=44) <sup>21</sup>	Kanna (n=39) <sup>18</sup>	Lang (n=33) <sup>19</sup>	Payer (n=3) <sup>22</sup>	Ramnarain (n=60) <sup>20</sup>	Tang (n=48) <sup>9</sup>
Adverse events								
Reoperations	1 (5%)	1 (3.7%)			4 (12.1%)			
Infections	1 (5%)							6 (12.5%)
Deaths		6 (22.2%)		4 (10.3%)				2 (4.2%)
Pseudoarthrosis		1 (3.7%)						
Dysphagia			44 (100%)					
Neuropathies			10 (22.7%)			1 (33.3%)		
Reduction Failure				1 (2.6%)	1 (3%)			
Graft Collapse							12 (20%)	
CSF fistula								1 (2.1%)

The studies that employed bone grafts were grouped into two categories: those that used titanium cages, either totally or partially, in their populations<sup>9,18,19,22</sup> and those that exclusively used autologous grafts or allografts<sup>15,20,21</sup>, without the use of cages. The first group included a total of 123 patients and 20 adverse events (16.26%), while the second group had 124

patients and 68 adverse events (54.84%) (Figure 2). When compared, the absence of cages in surgeries was associated with a higher incidence of adverse events, with a statistically significant difference by Fisher's Exact Test ( $p < 0.00001$ ) and an Odds Ratio (OR) of 6.25 (95% CI: 3.45 – 11.34), indicating a significantly higher risk in this group.



**Figure 1.** Flowchart according to PRISMA.



**Figure 2.** Comparison of adverse events based on the type of graft used.

## DISCUSSION

The results of this systematic review highlight significant disparities in clinical outcomes and operative parameters across the included studies, demonstrating both the complexity and diversity of surgical techniques and patient populations studied. A total of 279 patients, predominantly male (68.53%), who underwent cervical fixation were assessed across nine studies, with marked variations in surgical time, intraoperative blood loss, and complication rates.

This assessment revealed an influence of the surgical technique used and patient characteristics on the reported outcomes. The average surgical time ranged from 75 to 274.63 minutes, with longer durations associated with more complex cases requiring detailed interventions to ensure adequate fixation and alignment<sup>9</sup>. On the other hand, advanced techniques, such as minimally invasive robotic-assisted procedures, demonstrated shorter operative times, highlighting their potential to improve surgical efficiency<sup>17</sup>. Similarly, blood loss volumes were higher in complex surgeries, indicating that more extensive procedures may increase the risk of complications. In contrast, the minimally invasive approach showed lower blood loss<sup>9,17</sup>. These results emphasize the importance of tailoring surgical techniques to the specific conditions of each patient, optimizing outcomes and reducing associated risks.

The adverse events reviewed reveal a variety of potential complications during cervical fixation surgeries. Of the nine studies analyzed, eight reported adverse events, totaling 96 complications. The most frequently reported complications were the need for reoperations and deaths, both mentioned in three studies<sup>9,15,16,18,19</sup>. Specifically, there were six cases of reoperation and 12 deaths, highlighting the inherent risks and challenges associated with these surgical procedures. The complication rates varied significantly, ranging from 2.1% to 100% of participants. This data suggests that the severity of the initial injury may significantly impact the likelihood of postoperative complications<sup>2</sup>. The analysis underscores the importance of high-quality comparative future studies to identify the safest and most effective approaches. It is crucial to consider long-term functional outcomes and quality of life, which were not addressed in most of the included studies.

One of the most relevant findings was the association between the use of titanium cages and the reduction of adverse events, compared

to the exclusive use of bone grafts. Patients who underwent surgery with the inclusion of cages had a significantly lower complication rate (16.26%) than those treated only with autografts or allografts (54.84%), with an OR of 6.25 (95% CI: 3.45–11.34), and  $p < 0.00001$ . This suggests that the use of synthetic materials may offer clinically relevant benefits, possibly related to greater biomechanical stability and a lower inflammatory response<sup>2,4–6</sup>. This finding is particularly relevant for surgeons and healthcare professionals involved in the treatment of cervical spine trauma, as it provides evidence-based guidance for optimizing surgical techniques and improving patient outcomes.

The present results are consistent with previous studies that demonstrated better outcomes with the use of titanium cages, attributed to their mechanical stability and ability to promote bone fusion<sup>4–6</sup>. Titanium cages provide greater mechanical stability, an essential factor in the early postoperative period, allowing for better alignment and fusion of the cervical spine. This stability may lead to a reduction in the need for reoperations and the incidence of implant failures, as observed in this study<sup>5,6</sup>. However, the findings should be interpreted with caution, especially due to the heterogeneity of the studied populations. Furthermore, while the use of titanium cages has been shown to reduce complications, future studies should consider not only clinical outcomes, but also the associated costs and their applicability in different settings, particularly in resource-limited contexts<sup>11</sup>.

*Limitations*

However, this systematic review has several important limitations that must be considered when interpreting the results. First, the methodological heterogeneity among the included studies, both in terms of design and evaluated variables, makes it difficult to generalize the findings. The variability in the surgical techniques used, the skills of the surgeons, the preoperative clinical status of the patients, and the materials employed represent challenges in establishing definitive correlations between the interventions and clinical outcomes.

Additionally, the small number of patients in some studies and the variation in follow-up times may introduce bias and limit the detection of less frequent adverse events or long-term complications. Differences in the definition of complications and in the data collection methods for adverse events across the studies may also influence the reported results. Finally, a meta-analysis could not be conducted due to inconsistencies in the reported data and the diversity of the studied populations and interventions.



These factors highlight the need for prospective, multicenter, randomized studies to validate and expand upon the findings of this review.

## CONCLUSION

In conclusion, this study highlights the impact of surgical techniques and materials used on the outcomes of cervical fixation in patients with trauma. The findings suggest that the use of titanium cages may significantly reduce complications compared to the exclusive use of bone grafts, indicating a promising direction for clinical practice. However, the high methodological variability and intrinsic limitations of the analyzed studies emphasize the need for more rigorous and standardized future investigations.

Prospective, multicenter, randomized studies are essential to clarify the correlations between interventions and outcomes, considering factors such as initial clinical status, surgeon skill, and follow-up time. Additionally, evaluating functional outcomes and long-term quality of life will be crucial to improving therapeutic strategies and providing evidence-based guidance for managing cervical trauma.

Thus, this study lays a solid foundation for future investigations and drives the improvement of surgical strategies in the management of cervical trauma, with the potential to transform clinical practice and improve patient outcomes.

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# Atypical Presentation of Grade 3 Intracerebellar Extraventricular Ependymoma: case report and literature review

## *Apresentação Atípica de Ependimoma Extraventricular Intracerebelar Grau 3: relato de caso e revisão da literatura*

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### ABSTRACT

Extraventricular infratentorial ependymomas in adults are rare central nervous system tumors. We report the case of a 31-year-old man who presented with progressive vertigo, headache, nausea, and vomiting. Neuroimaging revealed an expansive lesion in the cerebellar vermis, accompanied by compression and obstruction of the IV ventricle. The patient underwent a procedure in which the tumor was completely removed. The diagnosis of grade 3 ependymoma was confirmed by histopathological and immunohistochemical methods. The literature underscores the rarity of this location and the necessity of a meticulous differential diagnosis with other neoplasms of the posterior fossa. Early complete resection remains essential for tumor control and improved prognosis.

**Keywords:** Ependymoma; Infratentorial; Extraventricular; Cerebellar tumor

### RESUMO

A ocorrência de ependimomas infratentoriais extraventriculares em pacientes adultos é uma forma rara de tumor do sistema nervoso central. Relata-se o caso de um paciente masculino, 31 anos, previamente hígido, com quadro progressivo de vertigem, cefaleia, náuseas e vômitos. A neuroimagem evidenciou lesão expansiva no vermis cerebelar, com obstrução do IV ventrículo por compressão e hidrocefalia associada. O paciente foi submetido à ressecção cirúrgica total da lesão e o diagnóstico de ependimoma grau 3 foi confirmado por análise histopatológica e imuno-histoquímica. A literatura ressalta a raridade dessa localização e a importância de um diagnóstico diferencial minucioso com outras neoplasias da fossa posterior. A ressecção completa precoce permanece fundamental para o controle tumoral e melhora do prognóstico.

**Palavras-Chave:** Ependimoma; Infratentorial; Extraventricular; Tumor cerebelar

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## INTRODUCTION

Ependymomas are glial tumors that originate from the ependymal cells responsible for covering the cerebral ventricles and the central canal of the spinal cord. These neoplasms constitute approximately 2% of primary central nervous system (CNS) tumors in adults, exhibiting a distinct topographical distribution, with a predilection for the posterior fossa in children and supratentorial locations in adults. The incidence of infratentorial ependymomas in the adult population is low; particularly when they are located in the cerebellar parenchyma and do not directly involve the ventricular system. This study presents a rare case of ependymoma located in the cerebellar vermis of a young adult. The case highlights the clinical, diagnostic, and therapeutic aspects of the condition.

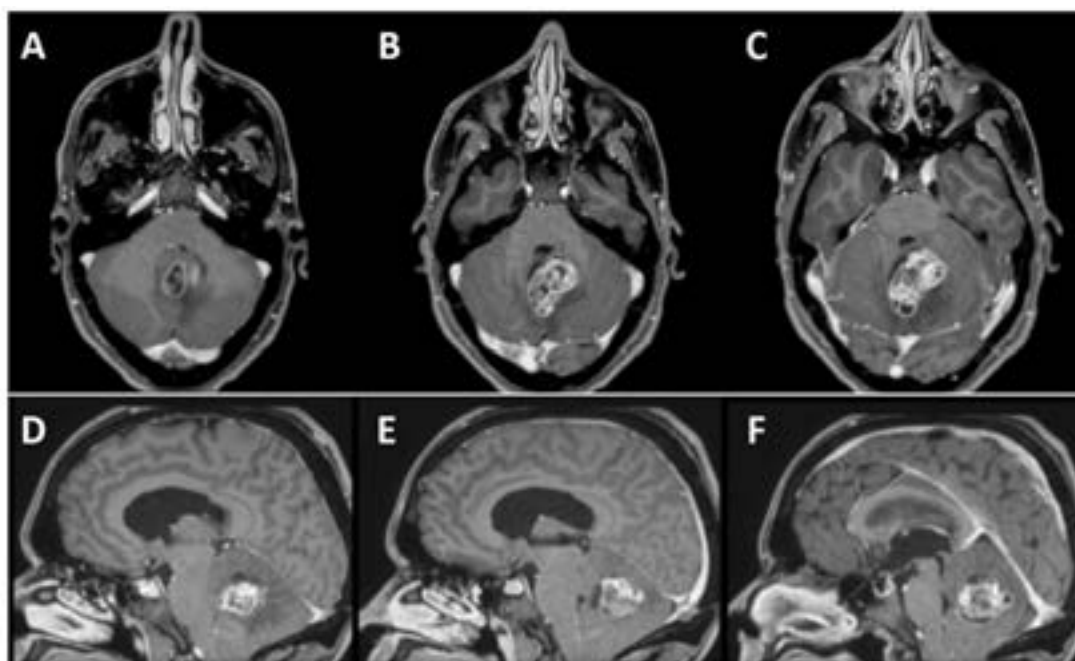
## CASE PRESENTATION

The patient is a 31-year-old male who was previously in good health. The patient reported experiencing episodes of vertigo

accompanied by headaches for approximately two months, which progressed to visual impairments, nausea, and uncontrollable vomiting. A physical examination revealed dysmetria on the left side of the body, with no motor or sensory deficits detected.

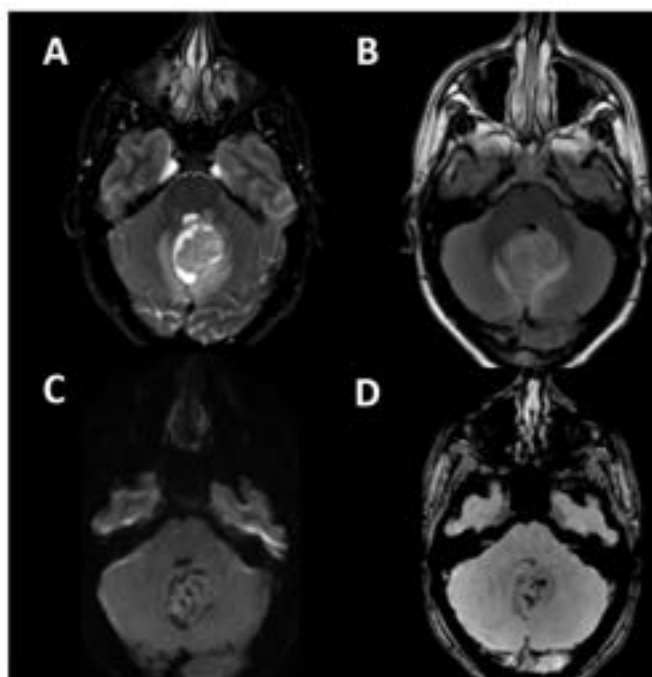
A non-contrasted computed tomography (CT) scan of the skull revealed a heterogeneous lesion with perilesional edema in the cerebellar vermis, causing obliteration of the IV ventricle. The investigation was complemented by magnetic resonance imaging (MRI) with contrast, which revealed an expansive lesion in the projection of the cerebellar vermis, measuring 3.5 x 2.4 x 2.4 cm, resulting in compression of the IV ventricle and supratentorial hydrocephalus. Following the injection of gadolinium, heterogeneous contrast uptake was observed (Figures 1 and 2).

Neurosurgery was indicated, and the procedure was performed in the prone position. The patient underwent a bilateral suboccipital craniotomy, transvermian access, and total macroscopic resection of the lesion. An external ventricular shunt was installed at the Frazier point. The procedure was performed without complications. Control MRI revealed no postoperative complications and complete resection. (Figure 3)

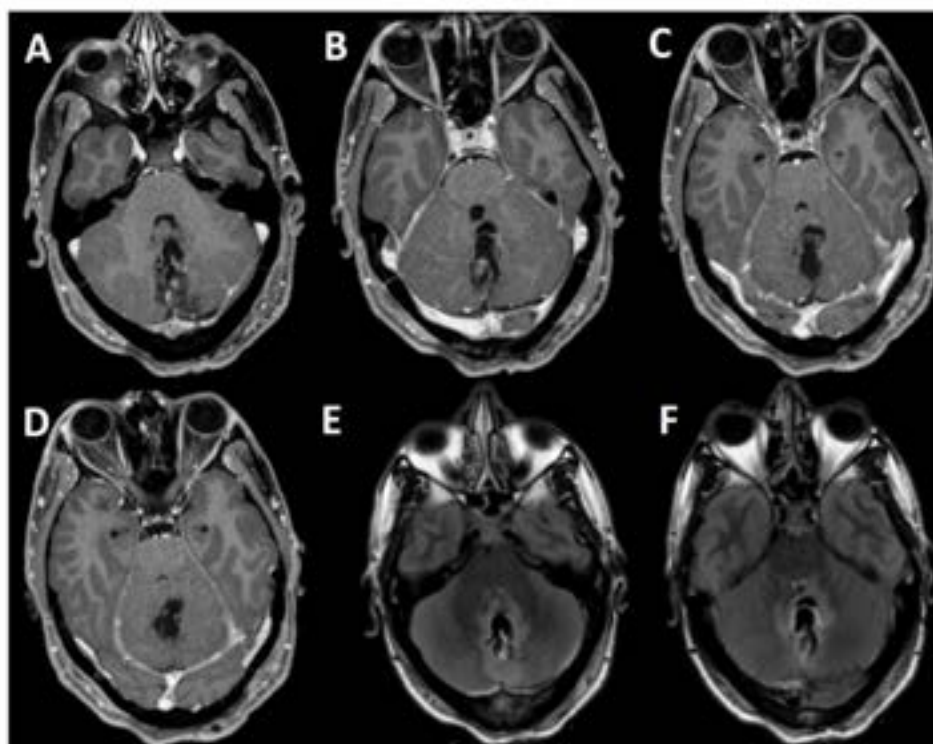


**Figure 1.** T1-weighted MRI of the skull with gadolinium, with axial sections **A**, **B**, and **C**. Expansive, extraventricular, infiltrative lesion in the cerebellar vermis, measuring approximately 3.5 x 2.4 x 2.4 cm. **D**, **E**, and **F**. Sagittal lesion that is expansive and located within the cerebellum. This lesion exerts pressure on the fourth ventricle, resulting in supratentorial hydrocephalus.





**Figure 2.** MRI of the skull in axial slices. **A.** T2-weighted, showing a solid-cystic lesion in the intra-vermian region. **B.** FLAIR-weighted: Perilesional edema. **C.** Diffusion. It is evident that there is no restriction on water diffusion in B1000 diffusion. **D.** SWI: Intralesional hyposignal, suggestive of calcifications



**Figure 3.** Computed tomography (CT) in axial sections. **A, B, C, and D.** T1 with gadolinium; **E and F.** FLAIR: demonstrating complete surgical resection, with no evidence of postoperative complications.

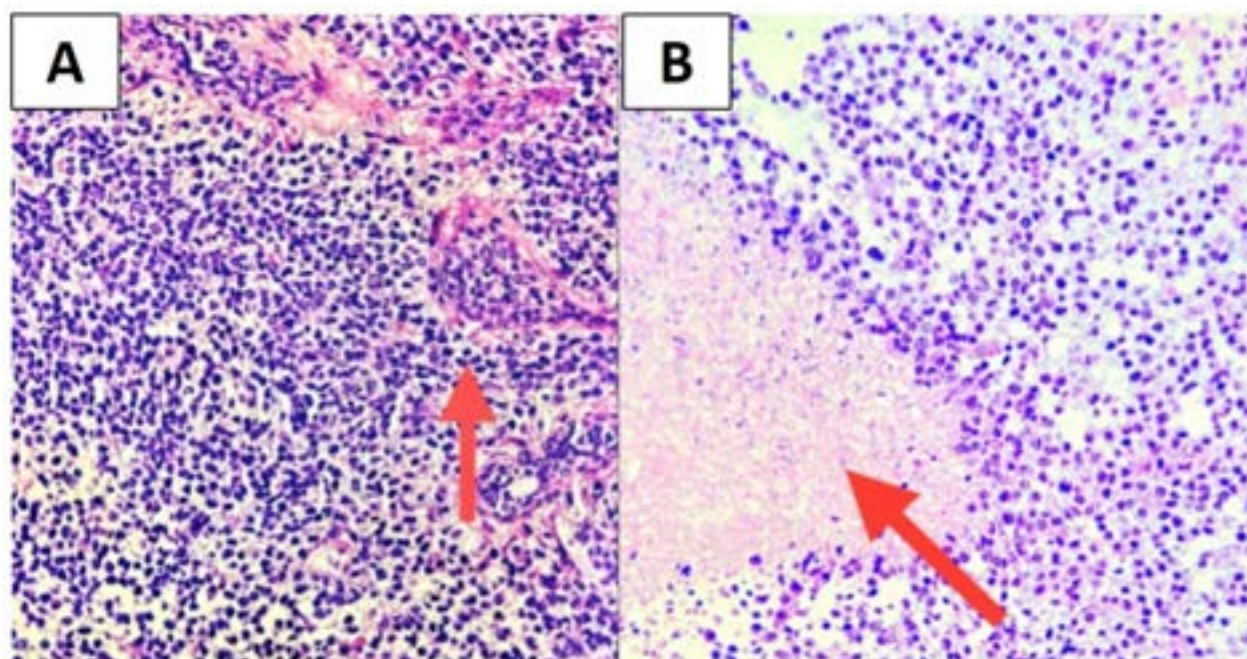
The pathology revealed a primary brain neoplasm that was consistent with a grade 3 ependymoma, characterized by the presence of epithelioid and polygonal cells, moderate nuclear atypia, pseudorosettes, and a high mitotic index (see Figure 4). Immunohistochemistry revealed positive staining for glial fibrillary acidic protein (GFAP), CD56, EMA, and negative IDH, while Ki-67 expression was found to be high. The immunohistochemical profile was consistent with ependymoma.

At the time of discharge, the patient exhibited alertness, orientation, and intact language skills. The pupils exhibited isochoric and photoreagent properties, while preserving extrinsic ocular motility and facial mimicry. The patient demonstrated grade V muscle strength in all limbs and preserved tactile sensitivity. Discrete index-nose dysmetria is evident on the left side. The patient did not exhibit signs of dysarthria. The maintenance of static equilibrium is paramount. Subsequently, the patient underwent treatment with oncology and radiotherapy.

## DISCUSSION

The 5th edition of the World Health Organization (WHO) Classification of Tumors of the Central Nervous System, published in 2021, provides a framework for the classification of ependymomas. This classification is based on three main criteria: anatomical location, molecular characteristics, and histopathological aspects. Ependymomas are classified into three distinct categories based on their anatomical origin within the central nervous system. These categories are designated as supratentorial, posterior fossa, and medullary ependymomas, respectively. The analysis of DNA methylation profiles has emerged as a robust diagnostic tool, capable of accurately discriminating ependymoma subtypes according to their anatomical location and epigenetic signature<sup>1-3</sup>.

Historically, histological grades have been used to characterize the biological behavior and aggressiveness of brain tumors,



**Figure 4.** A. high-grade brain neoplasm is depicted, consisting of epithelioid cells with moderate atypia, a solid architectural pattern, and glomeruloid vascular proliferation (arrow). This specimen was stained with hematoxylin-eosin and observed under 100x magnification. B. Epithelioid cell neoplasm with an area of coagulation necrosis (ischemic, red arrow), hematoxylin-eosin, 200x. The findings are indicative of a diagnosis of cerebellar ependymoma, with a histological grade of 3.

constituting an important criterion in the diagnosis and therapeutic stratification of the central nervous system (CNS). In ependymomas, which range from grade 1 to grade 3, the correlation between histological grade and clinical outcome is often controversial. The distinction between grade 2 and grade 3 ependymomas exhibits high inter-observer variability, which limits the clinical usefulness of this classification, especially for intermediate tumors. Consequently, therapeutic stratification for ependymomas should not be based exclusively on histological classification. Nevertheless, the distinction between grades 2 and 3 remains a pivotal factor in determining the appropriate treatment for adult patients afflicted with intracranial ependymomas<sup>3</sup>.

Chen et al. provided a comprehensive clinical and molecular overview of intracranial ependymomas in adults. The authors highlighted the heterogeneity of these tumors in terms of location, biological behavior, and molecular profile. The study underscores the significance of molecular analysis, particularly the DNA methylation profile, for enhanced precision in classification and accurate prognosis. It also emphasizes that extraventricular ependymomas, despite their rarity, necessitate specialized attention. The present findings lend further support to the necessity of customized diagnostic and therapeutic approaches, particularly in cases of infratentorial presentation and atypical location, as illustrated by the case documented in this study<sup>4</sup>.

The case documented by Kakita et al.<sup>5</sup> underscores the rarity of intraparenchymal ependymomas in the cerebellum, which are located outside the ventricular system. This atypical presentation poses a significant challenge to the differential diagnosis in the posterior fossa. As is also the case in the present report, the clinical and radiological evaluation can be atypical, requiring careful attention to differentiate these neoplasms from other tumor entities in the region. Moreover, the study underscores that complete surgical resection remains the cornerstone of tumor control and enhanced prognosis. This underscores the necessity for early intervention in cases of infratentorial extraventricular ependymomas<sup>5</sup>.

According to Palmisciano et al.<sup>6</sup>, the anatomical rarity and aggressive behavior of high-grade extraventricular ependymomas is evidenced by a recent systematic review that analyzed extraneural metastases from intracranial ependymomas. The study indicated that grade III tumors are associated with an elevated risk of dissemination beyond the central nervous system, even following surgical resections that are deemed satisfactory. The present findings lend support to the necessity of prolonged follow-up

and underscore the significance of early differential diagnosis in atypical locations, such as the posterior fossa<sup>6</sup>.

Ruda et al.<sup>7</sup> present a comprehensive review of ependymomas in adults, highlighting the clinical, molecular, and therapeutic differences between infratentorial and supratentorial tumors. The anatomical location of these tumors exerts a direct influence on prognosis and therapeutic options. Infratentorial ependymomas, in particular, are often associated with surgical challenges due to their proximity to critical structures. Furthermore, the study underscores the significance of precise diagnosis and a multidisciplinary approach in maximizing clinical outcomes<sup>7</sup>.

The rarity of infratentorial extraventricular ependymomas in adults is evidenced by the paucity of case reports in the literature. One study described an ependymoma located in the cerebellar parenchyma, far from the ventricular surfaces, in an adult patient. This case highlights the importance of considering this neoplasm in the differential diagnosis of atypical cerebellar lesions. As illustrated in the case presented here, the tumor's atypical location and its high histological grade underscore the necessity for a meticulous diagnostic approach and assertive therapeutic strategies to ensure optimal prognosis<sup>8</sup>.

The report by Yang et al.<sup>9</sup> made a significant contribution to the existing literature by describing a cerebellar ependymoma that was not associated with the ventricular system. This case study serves to underscore the rarity and diagnostic challenges associated with these extraventricular locations. The importance of comprehensive surgical resection, in conjunction with adjuvant therapies, is substantiated as a pivotal strategy for tumor control and enhanced prognosis in atypical instances of infratentorial ependymoma<sup>9</sup>.

Zhang et al.<sup>10</sup> reported an atypical case of cerebellar ependymoma exhibiting a combination of histological features reminiscent of clear cell and tanycytic subtypes, which presented as a hemangioblastoma, underscoring the diagnostic complexity in infratentorial tumors exhibiting atypical presentations. This complexity underscores the necessity for a meticulous histopathological and immunohistochemical evaluation to distinguish extraventricular ependymomas from other neoplasms of the posterior fossa, as illustrated in this report. The accurate identification of these histological variants is paramount for the effective management of therapeutic interventions and the enhancement of patient prognoses<sup>10</sup>.



## CONCLUSION

This report details a rare instance of infratentorial and extraventricular ependymoma in an adult, underscoring the diagnostic challenges posed by its atypical presentation. Complete surgical resection was effective in the initial control of the disease, thereby highlighting its central therapeutic role. The rarity of the location underscores the necessity for meticulous clinical, radiological, and histopathological correlation, in addition to continuous surveillance and deliberation regarding the potential benefits of adjuvant therapy. The documentation of cases such as this one contributes to a more profound comprehension of the clinical, radiological, and histological patterns of these lesions. This, in turn, aids in the formulation of more effective diagnostic and therapeutic strategies for rare tumors in uncommon locations.

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**brain4care**

monitoramento não invasivo do  
risco de hipertensão intracraniana

# abordagem não invasiva no manejo da pressão intracraniana

reduza o **risco da hipertensão intracraniana**  
nos **pacientes pré e pós-cirúrgicos**  
no **consultório, ambulatório**  
ou a **beira-leito**

## a tecnologia brain4care:

- Indica se **pacientes** estão sob risco de hipertensão intracraniana
- Auxilia na **proatividade do manejo de edemas** encefálicos
- **Qualifica o diagnóstico e tratamento** de distúrbios como HPN, demências reversíveis e outras hidrocefalias
- **Suporta o processo de verificação e ajuste de válvulas**

## contribui para:

- Justificar a **pertinência de neurocirurgias**
- Alta segura e redução do **risco de danos neurológicos secundários** pós-cirúrgicas
- **Reembolso** com códigos **validados pela AMB**

registro da ANVISA ✓  
liberada pela FDA ✓

## nova resolução da AMB 067/24

Agora o código CBHPM  
2.02.02.06-7 pode ser aplicado para  
uso hospitalar e ambulatorial.

Referente ao código 2.02.02.06-7:

- A monitorização da pressão intracraniana pode ser realizada de forma:
  - invasiva, com instalação do cateter de PIC em ambiente hospitalar; e
  - não invasiva, realizada no ambiente hospitalar, ambulatorial ou consultório.
- O procedimento de monitorização da pressão intracraniana pode ser associado a outros atendimentos médicos como consultas médicas, visitas, avaliações e/ou acompanhamentos.

2.02.99.00-1

Inclusão de item de  
Observação



# Schwannoma of the Sciatic Nerve as a Rare Cause of Sciatica


## *Schwannoma do Nervo Ciático como Causa Rara de Ciatalgia*

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### ABSTRACT

Sciatica is a common condition caused mainly by radicular compression; however, rare cases of sciatic nerve tumors have been described as a cause of persistent sciatic pain with no clear clinical explanation. Here we report a rare case of sciatic nerve schwannoma in a 31-year-old man, presented with severe pain in the left hip, who had satisfactory resolution of symptoms after surgical resection of the tumor. In this case MRI images were crucial in the differential diagnosis between schwannoma and neurofibroma, as well as for the planning and success of surgical treatment.

**Keywords:** Schwannoma; Sciatic Nerve Tumor; Sciatica

### RESUMO

A ciática é uma condição comum causada principalmente por compressão radicular; no entanto, casos raros de tumores do nervo ciático têm sido descritos como causa de dor ciática persistente sem explicação clínica clara. Relatamos aqui um caso raro de schwannoma do nervo ciático em um homem de 31 anos, que apresentou dor intensa no quadril esquerdo e apresentou resolução satisfatória dos sintomas após a ressecção cirúrgica do tumor. Neste caso, as imagens de ressonância magnética foram cruciais no diagnóstico diferencial entre schwannoma e neurofibroma, bem como para o planejamento e o sucesso do tratamento cirúrgico.

**Palavras-Chave:** Schwannoma; Tumor do nervo ciático; Ciática

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## INTRODUCTION

Schwannomas are predominantly benign, solitary, well-circumscribed, and encapsulated tumors originating from Schwann cells. Macroscopically, these tumors present as rounded masses with a smooth surface<sup>1</sup>. They are more commonly observed in adults over 40 years of age and have a higher incidence in women<sup>2</sup>. Typically, these tumors are found in the peripheral nerves of the upper limbs and neck; however, they can also affect spinal nerve roots, presenting as extra-axial and extradural masses that extend through the intervertebral foramen, compressing adjacent nerves<sup>3</sup>.

Schwannomas of the sciatic nerve, the body's largest nerve, are notably rare, representing 1% or fewer of all schwannomas. They are frequently misdiagnosed as other, more common causes of sciatica, such as lumbar degenerative conditions, inflammatory disorders, or spinal tumors, which can often delay an accurate diagnosis<sup>4,5</sup>. The purpose of this article is to present a case report of a sciatic nerve schwannoma diagnosed at the largest neurosurgery center in the northeastern region of Brazil.

## CASE PRESENTATION

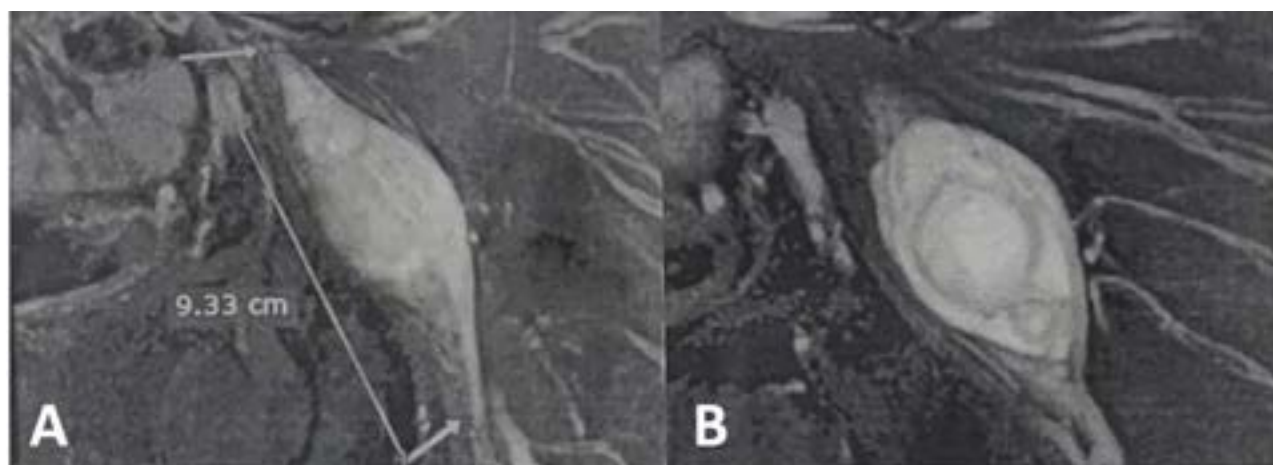
In this case report, a 31-year-old male patient presented with severe pain (7 on the Visual Analog Scale - VAS) in the left hip,

described as stabbing in nature, radiating to the left lower limb, and associated with intermittent motor deficit that worsened with ambulation, without a history of recent trauma. Magnetic Resonance Imaging (MRI) revealed a focal thickening with a fusiform component and heterogeneous fascicular enhancement of the sciatic nerve of neural origin, suggestive of schwannoma (Figure 1).

The approach involved delineating three anatomical landmarks: the infragluteal line, the lesser trochanter, and the greater femoral trochanter, to perform the surgical incision via the transgluteal (Kocher-Langenbeck) approach, extending from the upper to the middle third of the intertrochanteric crest. The gluteal fascia was dissected, followed by the longitudinal and transverse fibers of the gluteus maximus (Figure 2), and exploration continued to identify the intact distal sciatic nerve (Figure 3) with dissection up to the proximal portion of the lesion (Figure 4).

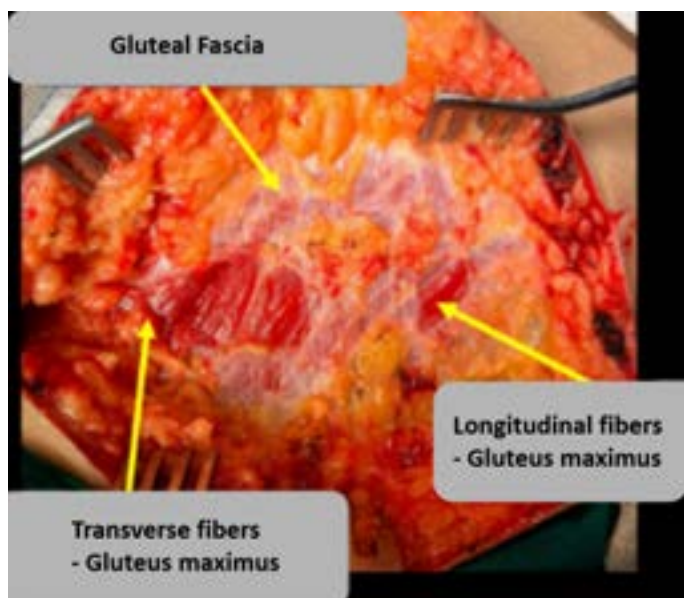
For tumor excision, the fibers of the gluteus maximus muscle were retracted, and the lesion's pedicle originating from a donor fascicle was isolated, followed by the excision of the lesion, which measured approximately 2 centimeters. Finally, layered closure was performed (Figure 5).

To preserve nerve fascicles, exploration of the sciatic nerve and fascicle identification were performed through meticulous interfascicular dissection with intraoperative neurostimulation. The entire surgical specimen was sent to the histopathology laboratory for diagnostic confirmation.

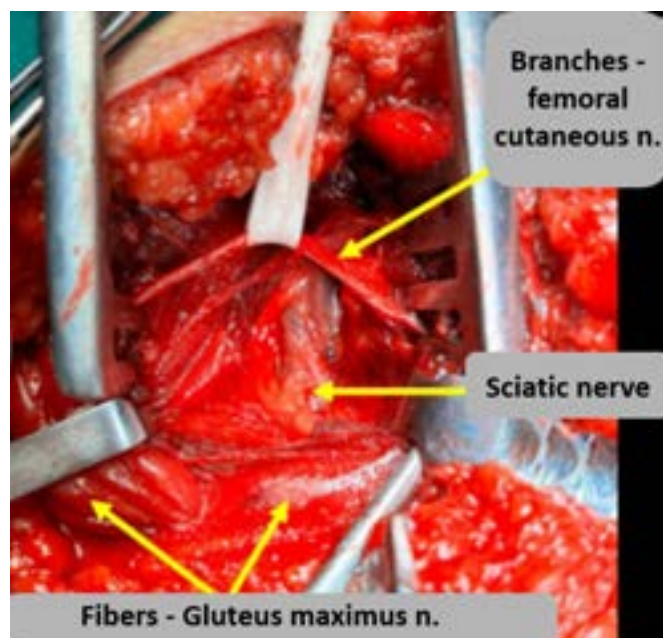


**Figure 1.** A-B. Magnetic resonance imaging without intravenous administration of paramagnetic contrast, showing schwannoma causing focal fusiform thickening of 3.7 x 2.5 cm in the left thigh.





**Figure 2.** Dissection of the initial anatomical planes.



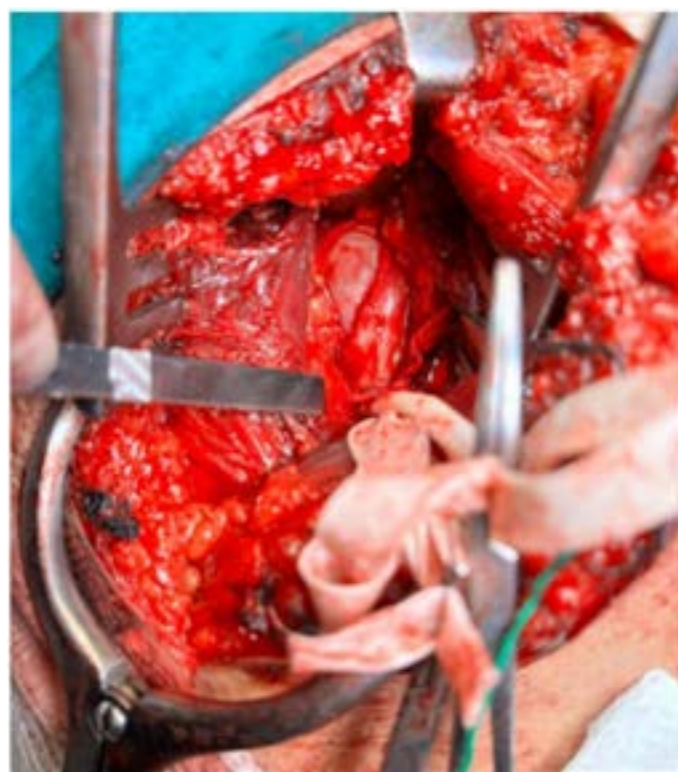
**Figure 3.** Exploration to identify intact distal sciatic nerve.

In immunohistochemical examination, a panel of monoclonal and/or polyclonal antibodies was used with the Streptavidin-Biotin technique. Based on its morphology and immunophenotype, the result confirmed the diagnosis of schwannoma, grade I. Histological analysis revealed a neoplasm positive for SOX10, S100 protein, and Ki-67 markers, with focal positivity for Calretinin, while EMA and CD34 (positive internal control) were negative.

In the immediate postoperative period, the patient presented no motor deficits, but showed hypoesthesia in the left thigh. At the follow-up appointment, the patient reported a decrease in pain intensity to 1 (VAS) – still present due to surgical incision healing (Figure 6).

## DISCUSSION

Peripheral nerve tumors are uncommon. Schwannomas most frequently occur in the head, neck, and along primary nerve trunks<sup>6</sup>. However, schwannomas affecting the sciatic nerve are exceptionally rare, with an incidence reported at six cases per million people<sup>7,8</sup>. Among all benign sciatic nerve tumors, 60% are neurofibromas, and 38% are schwannomas<sup>8</sup>.



**Figure 4.** Proximal Sciatic Nerve Dissection.

Sciatic nerve schwannoma presents with sciatica, hemiplegia, hypoesthesia in the affected hemibody, and, rarely, motor deficits<sup>9</sup>.





**Figure 5.** Excision of the lesion en bloc.



**Figure 6.** A-C. The figure shows the patient in the immediate postoperative period, with no signs of motor deficit.

Patients may also have a painless palpable mass with bulges and/or retractions at the tumor site, where Tinel's sign may indicate nerve irritation or injury<sup>4</sup>. Initial suspicion usually arises in the presence of typical sciatica without signs of spinal cord compression on MRI in young adults<sup>10</sup>.

Diagnosis is often delayed, as patients are initially directed to investigate more common causes of sciatica<sup>4</sup>. Clinical indicators that should prompt consideration of non-discogenic sciatica

include a history of persistent radicular pain unresponsive to anti-inflammatory treatments, absence of lumbar muscle spasm, a negative straight leg raise test, and lumbar MRI showing no disc herniation<sup>11</sup>. MRI is the gold standard for tumor identification, while biopsy is essential for diagnostic confirmation<sup>12</sup>.

On MRI, sciatic schwannoma can be identified by the displacement of nerve fascicles pushed to the periphery by the tumor, unlike neurofibromas, which create fusiform lesions as they blend with

nerve fibers. However, the definitive diagnosis of tumor type is only made through histopathological studies of the surgical specimen. Immunohistochemical detection of S100 protein is crucial for confirming the diagnosis<sup>13</sup>.

Due to its benign nature, patients typically experience symptom resolution following surgical excision. Additionally, schwannomas have low malignant potential and rare recurrence rates<sup>13</sup>, emphasizing surgical treatment as the primary choice in these cases.

Complete surgical excision is generally facilitated by the non-invasive nature of schwannomas, which aids in preserving surrounding fascicular groups. However, some sciatic nerve fascicles may adhere to the tumor capsule and require removal<sup>10</sup>. In this case, the use of intraoperative neurostimulation favored fascicular exploration and preservation.

## CONCLUSION

Sciatica is a common condition, typically caused by nerve root compression due to lumbar disc herniation. However, sciatic nerve tumors represent a cause of persistent sciatica without a clear clinical explanation. As such, sciatic nerve schwannoma is an important differential diagnosis in cases of sciatica with no signs of nerve root compression and without lumbar disc herniation. Imaging methods, such as MRI, are therefore essential for diagnosing this condition, allowing differentiation between the main types of tumors—schwannomas and neurofibromas. However, given the rarity of this tumor type, further studies are necessary to ensure diagnostic accuracy.

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## CRediT

Bárbara Rocha Rodrigues Cox Coelho: Conceptualization; Investigation. Lucas Mendes Reis de Moura - Writing - Original Draft; Visualization. Mateus de Sousa Rodrigues: Supervision. Gabriel Albuquerque Leite Cavalcante - Writing - Original Draft. Camila Rodrigues de Sousa: Methodology. Thais Milla Franco: Data Curation. Camila Maciel Martins Coelho: Resources. Lucas Bezerra de Aguiar: Writing - Review & Editing. Everton Felipe do Vale Araújo: Validation. Fernando Henrique Moraes de Souza: Project administration

# Spontaneous Resolution of Acute Epidural Hematoma with a Good Clinical Outcome

## *Resolução Espontânea de Hematoma Epidural Agudo com Bom Resultado Clínico*

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### ABSTRACT

**Introduction:** Intracranial epidural hematoma (IEH) is considered a neurosurgical emergency. In selected cases, it may be subjected to conservative treatment. Spontaneous resolution has been rare. **Case 1:** 19-year-old male patient. Traffic accident victim. Skull tomography showed acute IEH in the left parietal region, and he was subjected to conservative treatment. The patient presented spontaneous reabsorption within seven hours, with good clinical evolution. **Case 2:** 11-month-old male patient. Accidental fall. Presented with irritability, crying, and one episode of vomiting. Non-contrast skull CT: left parietal subgaleal hematoma, left parietal fracture, left parietal epidural hematoma, and intraparenchymal hematoma adjacent to the fracture. Conservative treatment was chosen. Nine hours later, a new skull CT revealed left parietal subgaleal hematoma, reduction of the intraparenchymal hematoma, and absence of the IEH. Medical discharge without evident neurological deficit. **Conclusion:** Spontaneous reabsorption of acute IEH has been rare in cases of conservative treatment. The hypotheses about hematoma reabsorption are not yet clarified. In cases of spontaneous reabsorption, the prognosis is good.

**Keywords:** Epidural hematoma; Head trauma; Skull fracture; Spontaneous resolution

### RESUMO

**Introdução:** O hematoma epidural intracraniano (HEI) é considerado uma emergência neurocirúrgica. Em casos selecionados pode ser submetido a tratamento conservador. Resolução espontânea tem sido rara. **Caso 1:** Paciente com 19 anos, masculino. Vítima de acidente trânsito. Tomografia de crânio apresentou HEI agudo na região parietal esquerda, sendo submetido a tratamento conservador. Apresentou reabsorção espontânea dentro de sete horas, com boa evolução clínica. **Caso 2:** paciente com 11 meses de idade, masculino. Queda accidental. Atendida com irritabilidade, choro e um episódio de vômito. TC crânio sem contraste: hematoma subgaleal parietal esquerdo, fratura parietal esquerda, hematoma epidural parietal esquerdo e hematoma intraparenquimatoso adjacente a fratura. Tratamento conservador, nove horas depois novo TC crânio revelou hematoma subgaleal parietal esquerdo, redução hematoma intraparenquimatoso e ausência do HEI. Alta médica sem déficit neurológico evidente. **Conclusão:** A reabsorção espontânea do HEI agudo tem sido raro em casos de tratamento conservador. As hipóteses sobre a reabsorção do hematoma não estão ainda esclarecidas. Em caso de reabsorção espontânea cursa com bom prognóstico.

**Palavras chave:** Hematoma epidural; Traumatismo cranioencefálico; Fratura craniana; Resolução espontânea

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## INTRODUCTION

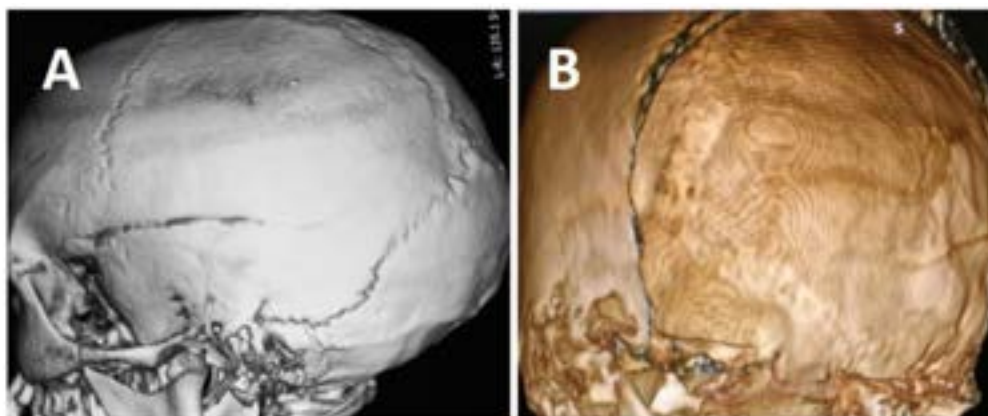
Intracranial epidural hematoma (IEH) is a blood collection located between the inner part of the skull cap and the dura mater. After its formation, it may present volume increase, calcification, or resolution, being infrequent when the latter occurs in a period less than 24 hours<sup>1</sup>. It is considered spontaneous resolution when it occurs within 72 hours after the traumatic event<sup>2</sup>. Its spontaneous reabsorption has been rare due to rapid clinical deterioration of the patient<sup>2,3</sup>. When symptomatic, it requires immediate surgical drainage<sup>1,4,5</sup>. The authors report two cases of spontaneous reabsorption of acute IEH, after seven hours in one case and nine hours in the other case. They discuss the possible mechanisms involved, and in cases of spontaneous reabsorption, excellent results are achieved.

## CASES PRESENTATION

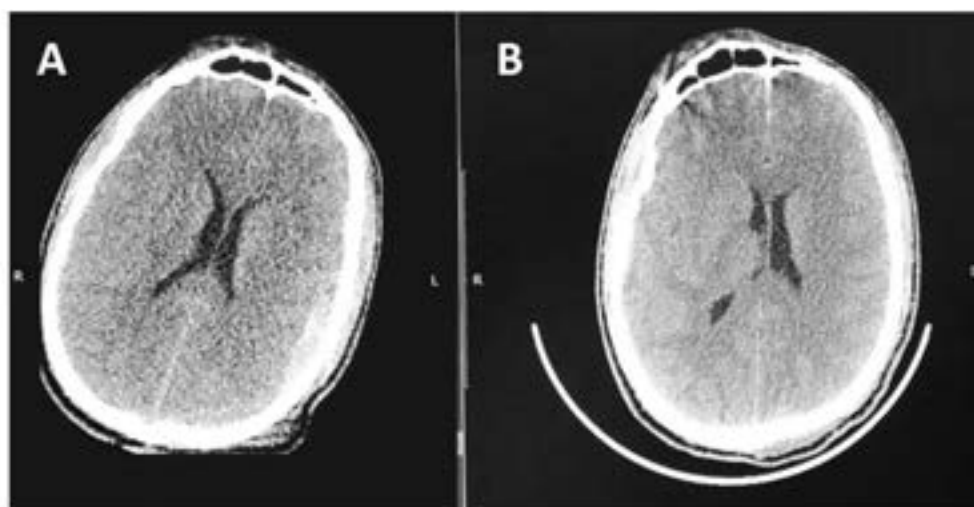
**Case 1.** ARS, 19 years old, male, student. Admitted to the emergency department as a victim of a fall caused by a traffic accident. Eupneic. Presented: abrasions on the right upper limb and left lower limb. Neurological examination: Alert. GCS on admission 15. Pupils isocoric and reactive. No evident focal neurological deficit. Underwent non-contrast cranial computed tomography (CT) examination that showed a linear fracture trace in the left temporal region (Figure 1), presence of left

temporal epidural hematoma, absence of midline structure deviation. Initially, conservative treatment was indicated, intensive neurological surveillance, and CT control after seven hours from the first examination. New CT revealed absence of blood collection (Figure 2). Received hospital discharge after five days with home orientation and outpatient return within thirty days.

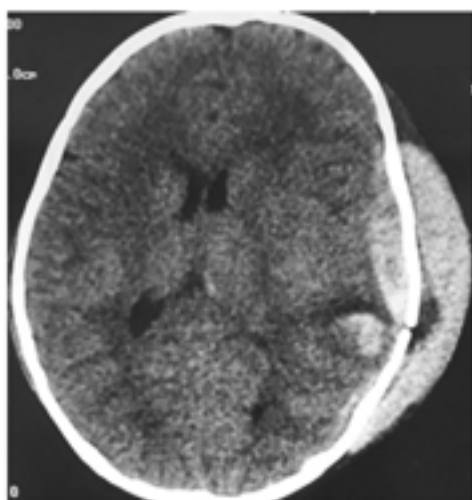
**Case 2.** JFS, 11 months old, male, was referred to the emergency service with a history of accidental fall from a height of two meters, with hospital admission three hours after trauma. Presented: irritability, constant crying, and the mother reported one episode of vomiting. Physical examination: Eupneic, swelling in the left parietal region. Neurological examination: drowsy, pupils isocoric and photoreactive, absence of evident focal neurological deficit, modified GCS for children of 13. Non-contrast cranial computed tomography (CT) revealed extensive subgaleal hematoma in the left parietal region, cranial fracture, left parietal EH, intraparenchymal hematoma adjacent to fracture, and midline structure deviation (Figure 3). After nine hours from the traumatic event, the patient was awake, scored 15 on modified GCS for children, with absence of focal neurological deficit. Nine hours after trauma, a new non-contrast cranial CT examination was performed, revealing left parietal subgaleal hematoma and left parietal intraparenchymal hematoma with smaller dimensions compared to the previous examination performed nine hours earlier (Figure 4). The patient was maintained on conservative treatment, receiving medical discharge five days after hospital admission, with absence of evident focal neurological injury.



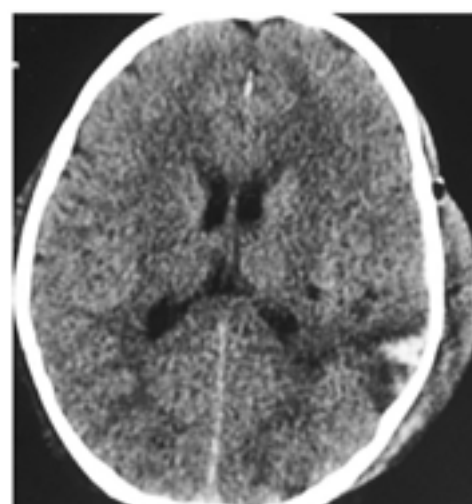
**Figure 1.** A-B. 3D reconstruction of cranial CT shows linear fracture trace in the left temporal region.



**Figure 2.** Non-contrast cranial CT.: A. presence of left parietal blood collection, ventricular system without deviation. B. absence of left parietal blood collection.



**Figure 3.** Non-contrast skull CT demonstrating left parietal fracture line, subgaleal hematoma, left parietal epidural hematoma, intraparenchymal hematoma adjacent to the fracture, and midline shift.



**Figure 4.** Non-contrast skull CT (August 26) revealing left parietal subgaleal hematoma, left parietal intracerebral hematoma without midline shift.

## DISCUSSION

Weaver et al.<sup>6</sup>, in 1981, provided the first description of spontaneous reabsorption of acute IEH. Bhat et al.<sup>7</sup>, in a study with 729 patients diagnosed with EH, identified only 11 who presented spontaneous resolution, representing 1.5%, of which seven were pediatric patients. Its occurrence has been reported in patients undergoing conservative treatment, being more common in children<sup>1-3,8-13</sup>.

There are case reports in adults<sup>5,14-17</sup>. In our work, one case was in an adult, and another in a child.

In general, reabsorption occurs in less than 24 hours<sup>17-19</sup>. Aydemir et al.<sup>1</sup> demonstrated a case of IEH with spontaneous resolution in 3 hours. Eom et al.<sup>9</sup> demonstrated through CT that, after four hours from the traumatic event, a patient with acute EH with 1.8 cm thickness in its largest diameter, associated with cephalohematoma, and 16 hours after trauma, no longer

presented IEH, but showed increased subgaleal hematoma. Bhat et al.<sup>7</sup> analyzed 11 patients diagnosed with EH with spontaneous resolution, showing that all presented associated subgaleal hematoma increase. Its reabsorption in hyperacute form has been rare<sup>19-21</sup>. Cases have been reported where reabsorption occurred more than three weeks after injury<sup>8,20</sup>. In our patients, resolution occurred in less than 12 hours.

The probable mechanisms associated with spontaneous reabsorption of IEH are: formation of fibrovascular neomembrane, action of granulation tissue as an absorption structure through sinusoidal veins, or transfer of the clot into the diploic bone or extravasation to the extracranial space through fracture trace<sup>5,6,11,12,14,15</sup>. However, an IEH may increase in volume in situations where an elderly patient presents cerebral atrophy<sup>7</sup>. The exact mechanism that promotes IEH resolution is not yet clarified<sup>11,8,14,17,18</sup>.

The formation of fibrovascular neomembrane or granulation tissue is particularly considered to be the resolution mechanism in chronic IEH due to the time period necessary for its formation<sup>10</sup>. The IEH reabsorption mechanism can be compared to that of CSDH<sup>15</sup>. The formation of fibrovascular neomembrane located on the dura mater side acts as an absorption structure for the blood clot. The sinusoids gradually connect with the marginal dural veins, so blood and its degradation products can return to systemic circulation via the permeable membrane of these sinusoids<sup>5,6,16-19</sup>.

The presence of cranial fracture may lead to communication between the epidural space and extracranial tissue. Transfer of the collection to the subgaleal space may be aided by compression caused by the hematoma<sup>2,3,8-10,12,13,19-22</sup>. This fact may have occurred in one of our cases. Cases of reabsorption in the absence of cranial fracture trace have been reported<sup>11,23</sup>, probably due to open cranial sutures<sup>11</sup>. Lee et al.<sup>24</sup> reported in their case that cranial fracture and increased pressure in the intradural area as the probable mechanisms involved in IEH redistribution. The role of intracranial pressure and pressure gradient is not clarified. According to Servadei et al.<sup>14</sup>, brain swelling plays a fundamental role in the IEH reabsorption mechanism. These authors<sup>1,12</sup> reported cases of reabsorption without elevated intracranial pressure.

The physiological pressures existing in the intracranial space are: normal intracranial pressure; physiological dural traction

pressure; pressure developed within the blood collection volume, aiming at bleeding tamponade; and pressure exerted by the lesion, such as intracranial EH. The extracranial space presents no resistance; therefore, from the diastatic fracture line, unilateral conduction of blood volume will occur, reducing the intracranial amount of the lesion and increasing the subgaleal hematoma<sup>7</sup>. Aydemir et al. reported a case in which the patient presented EH associated with subgaleal hematoma, citing that spontaneous resolution of the first entity occurred due to pressure difference between the epicranial and epidural spaces, connected via cranial fracture, in which cerebral pulsations conducted the epidural blood collection to the epicranial region<sup>1</sup>.

Conservative treatment of IEH has been performed as intense neurological surveillance and CT control<sup>5,6,14,16-21</sup>. Our cases underwent conservative treatment due to being small and without evident signs of intracranial hypertension. They were followed clinically and with CT control that showed resolution within twelve hours after the first CT examination.

## CONCLUSION

Spontaneous resolution of acute IEH has been considered rare. The diagnostic hypotheses are not yet clarified. In cases of small IEH undergoing conservative treatment, there is a possibility of spontaneous reabsorption, which results in good outcomes for the patient.

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# Traumatic Pneumocephalus in the Absence of Skull Fracture in an Electrical Burn Victim: a case report


## *Pneumoencéfalo Traumático na Ausência de Fratura Craniana em Vítima de Queimadura Elétrica: um relato de caso*

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### ABSTRACT

A 38-year-old male patient was airlifted to the trauma and burns referral center with high-voltage electrical burns caused by electrical wires on a pole. He was admitted with a 14-point GCS and the electrical voltage path entering the thorax and exiting in the right parieto-occipital region and back. Approximately 8% of the body surface was burned. Skull CT showed an intact cranial bone case and laminar pneumocephalus in the right parietal region. Conservative treatment was chosen with spontaneous resolution 5 days later. For two weeks, the patient remained in coma and it was decided not to surgically approach the patient. Electric shock is a high and acute response resulting from the presence of electrical flow in the human body. The occurrence of pneumocephalus is most often associated with traumatic injury scenarios, but the mechanisms that cause bone changes after electrical conductivity are still not well understood and such cases are rarely reported. Given the scenario of numerous complications resulting from accidents with high voltage, it should be routine for doctors responsible for emergency services to perform CT scans of the skull on patients resulting from these accidents in order to avoid unnoticed injuries.

**Keywords:** Brain injuries; Electric injuries; Pneumocephalus

### RESUMO

Paciente do sexo masculino de 38 anos foi transportado de helicóptero para o centro de referência de trauma e queimaduras devido a queimaduras elétricas de alta tensão causadas por fios elétricos num poste. Foi internado com um GCS de 14 pontos e o caminho de tensão elétrica que entra no tórax e sai pela região parieto-occipital direita e vice-versa. Aproximadamente 8% da superfície do corpo foi queimada. A TAC do crânio mostrou um osso craniano intacto e pneumocéfalia laminar na região parietal direita. O tratamento conservador foi escolhido com resolução espontânea 5 dias depois. Durante duas semanas, o paciente permaneceu em coma e decidiu-se não abordar cirurgicamente o paciente. O choque elétrico é uma resposta elevada e aguda resultante da presença de fluxo elétrico no corpo humano. A ocorrência de pneumocéfalia está mais frequentemente associada a cenários de lesão traumática, mas os mecanismos que causam alterações ósseas após a condutividade elétrica ainda não são bem compreendidos e tais casos raramente são reportados. Dado o cenário de inúmeras complicações resultantes de acidentes com alta voltagem, deveria ser rotina que os médicos responsáveis pelos serviços de emergência realizem tomografias computadorizadas ao crânio em pacientes resultantes destes acidentes, para evitar lesões não notadas.

**Palavras-Chave:** Danos encefálicos; Danos elétricos; Pneumoencefalia

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## INTRODUCTION

The evolution of electrical energy is a factor that contributed to the evolution of humanity in several areas today. However, it is undeniable that such a tool can be responsible for causing considerable damage when it directly affects the human body, being responsible for several cellular lesions with serious failures in the functions of several organelles<sup>1</sup>. The definition of electric shock refers to a high and acute response resulting from the presence of electrical flow in an individual's body, while electrocution refers to death generated by such shock<sup>2</sup>. When an injury is directly related to electrical current, it is defined as primary, whereas secondary injuries are those resulting from manifestations such as falls<sup>2</sup>. To classify electrical injuries in individuals, it is first necessary to understand the voltage to which the individual was exposed. In this way, low voltage is classified as that less than 1000 volts, and high voltage is classified as that greater than 1000 volts<sup>2</sup>.

The greatest resistance to electrical flow in the human body is located in the epidermis, but there are external factors that can affect this concept, such as humidity, calluses, abrasions (minimal injuries can already have an effect) or immersion in water<sup>1,2</sup>. The tissues with the greatest electrical resistance are those that suffer the greatest damage<sup>3</sup>. At voltages exceeding 500 volts, the high resistance in the outer layer of the skin has already broken, providing resistance to this electrical flow and consequently increasing the electrical flow<sup>2</sup>.

The clinical presentation of a patient who has suffered an electrical burn can include different levels of severity, such as myoglobinuria, changes in the electrocardiogram, renal dysfunction, presence of secondary infection, fall and cardiac or respiratory arrest<sup>1,2</sup>. Furthermore, in cases of high voltage, the head region is listed as the second most affected, the lower limbs the least affected, and bone injuries are more common when the affected region has a small space between the skin and the bone<sup>1</sup>. The temperature that body tissue reaches during an accident, which can exceed 1000 degrees Celsius, causes thermal necrosis of the bones and considerably reduces the thickness of the skin, contributing to a process of protein coagulation, fat liquefaction and massive evaporation of water, resulting in carbonization<sup>3</sup>.

Several factors determine the effects an electrical burn can cause in the body of a victim, some of which include: the type of current that the individual was exposed to, the voltage, the amperes, the body's resistance, the path taken by the electricity, and the patient's inherent health conditions<sup>3</sup>. In cases when the patient dies at low voltages, the cause is closely related to ventricular fibrillation, while in cases of high voltage, inhibition of the respiratory system is the main reason. In addition, other factors can also contribute to high mortality, such as muscle spasms caused by electricity<sup>3</sup>.

When analyzing neurological responses after electrical burns, it is observed that nerve conductivity is directly affected and that motor function is impaired before sensory function<sup>3</sup>. Other disorders in the central nervous system are also observed, such as paralysis and vasomotor phenomena, and it is important to emphasize that there are late manifestations such as vascular thrombosis, weakness and fragility of blood vessels, and edema due to lymphatic obstruction<sup>3</sup>.

Based on this assumption, small current values are already capable of causing repercussions in the individual and some factors, in electrical injury, are necessary to determine the size of the wound, such as the size and shape of the conductor, humidity and part of the body involved<sup>2</sup>. In high voltage scenarios, the individual may be forced to grip the conductor more tightly, having greater mechanical contact, or may be removed from such contact, so it is always important to evaluate the entire scenario<sup>2</sup>.

The occurrence of pneumocephalus, defined as intracranial air (including epidural, subdural or subarachnoid spaces, brain parenchyma or ventricular system), is more associated with traumatic injury scenarios and cases occurring after high-voltage electrical injury are rarely reported<sup>4</sup>. In this scenario, there is a report in the literature about a patient who was struck by lightning (high voltage) that caused rupture of the tympanic membrane and the authors related that the electric current can be an etiology for the onset of pneumocephalus<sup>4</sup>.

Given this scenario of numerous complications resulting from high-voltage accidents, it should be common practice for all emergency physicians to perform cranial CT scans on patients resulting from these accidents to avoid possible serious consequences<sup>4</sup>.



## CASE PRESENTATION

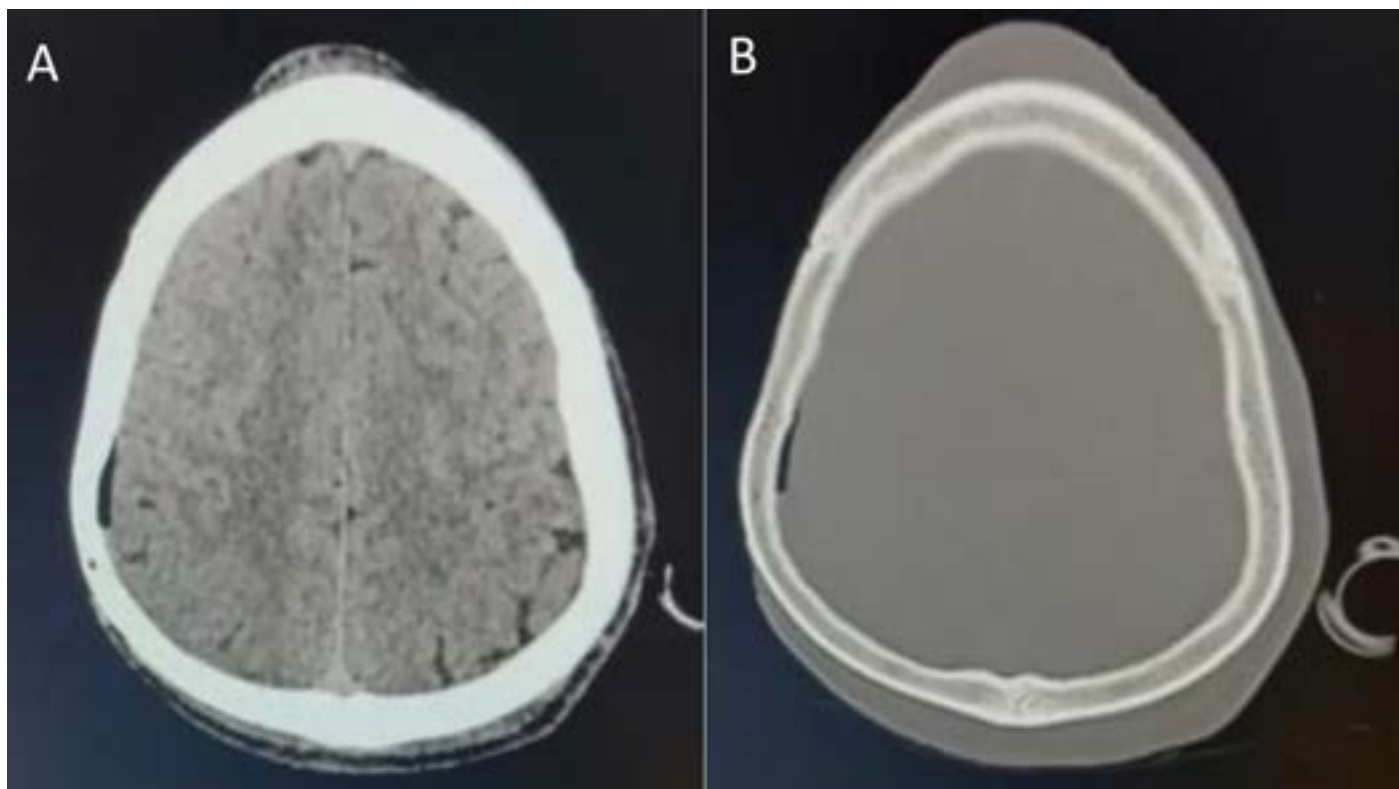
Patient, 38 years old, male, was referred by air transport to the trauma and burns referral center in Belo Horizonte in April/2024. He presented with a high-voltage electrical burn caused by electrical wires on a pole, arriving at the unit 4 hours after the accident. Admitted to the emergency room with a Glasgow Coma Scale (GCS) of 14 points and with an evident electrical voltage path with entry in the chest region and exit in the right parieto-occipital region and back. The burns consisted of approximately 8% of the burned body surface area (BSA), with the entry point (thoracic region) and exit point (cranial region) being third-degree burns, with necrosis and bone exposure. In addition, he had second-degree burns on the right ear, forehead, neck, and right eyelid. Complementary diagnostic workup with computed tomography (CT) of the skull was performed, revealing an intact cranial bone case and laminar pneumocephalus in the right parietal region, adjacent to the point of exit of the electric current (Fig 1, A and B).

In addition to the injuries described, the patient also presented other complications associated with trauma at high temperatures, such as increased creatine phosphokinase level of 31,697 at the time of admission due to rhabdomyolysis.

In the initial approach, debridement and cleaning of the devitalized tissues were performed by the plastic surgery team and follow-up care was provided in the intensive care unit at the burn center of the referral hospital.

On analysis by the neurosurgical team, the right cephalic and cervical region was noted to have a necrotic appearance, with parietal, frontal and temporal bone exposure, without bone discontinuity and without fractures present. Conservative treatment of pneumocephalus was chosen, with spontaneous resolution in a new imaging exam 5 days after admission.

During the following two weeks of hospitalization, the patient remained in a coma, unresponsive to external stimuli.



**Figure 1.** A and B, Computed tomography scan of the skull showing right parietal pneumoencephalus.

In this scenario, it was decided, jointly by the neurosurgery and plastic surgery teams, not to surgically approach the patient due to his unfavorable prognosis.

## DISCUSSION

Pneumocephalus, defined as intracranial air (including epidural, subdural or subarachnoid spaces, brain parenchyma or ventricular system), is most often associated with traumatic injury scenarios<sup>4</sup>. When analyzing cases in which the patient has simple pneumocephalus, in most of them the symptoms are nonspecific or inexistent, and conservative treatment is advised; however, those who have hypertensive manifestations may present acutely and require neurosurgical treatment<sup>4</sup>. The adverse outcome associated with pneumocephalus is its potential progression to the tension subtype<sup>5</sup>. This condition arises due to a one-way valve phenomenon, wherein atmospheric air enters the cranial vault via osseous discontinuities but becomes entrapped, impeded from egress by anatomical barriers such as the arachnoid membrane, cerebral ventricles, or brain parenchyma<sup>5</sup>.

To diagnose this condition, computed tomography is essential, and from there, the patient's management should be based on: keeping the bed with the headboard elevated at 30 degrees, administering analgesics and offering supplemental oxygen to increase the partial pressure of oxygen in the blood and replace the gases in the pneumocephalus with oxygen to allow its reabsorption, which occurs in approximately 1 week in 85% of cases<sup>4</sup>.

Indications for surgical treatment include: symptomatic, recurrent and traumatic injuries lasting more than 1 week<sup>4</sup>. In cases of intracranial hypertension, neurosurgical treatment should be immediate, as complications in the absence of treatment include meningitis, seizures, brain abscesses and hernias<sup>4</sup>. CT remains the definitive imaging technique for identifying this condition<sup>5</sup>. Optimal diagnostic accuracy requires the acquisition of high-resolution, thin-section scans to facilitate the detection of subtle fractures or minor dural defects that might otherwise be overlooked<sup>5</sup>.

Medical practitioners must maintain a high index of suspicion for the tension form, especially when the radiological hallmark known as the "Mount Fuji sign" is present<sup>5</sup>. This sign signifies that the intracranial gas exerts pressure exceeding that of the cerebrospinal fluid between the frontal lobes, indicating the urgency of neurosurgical intervention<sup>5</sup>.

The reason for injuries occurring after an electrical accident is still not well understood. A recent study sought to compare the traumatic effects of electrical current by examining samples of pig bones, subjected to high current, and compared them with a death caused by lightning in a wild giraffe<sup>6</sup>. From this study, extensive microfractures were observed microscopically in the bones, concomitant with fragmentation of the bone matrix, which allowed us to conclude that the flow of current is not limited to soft tissues<sup>6</sup>.

Considering that bones have a multiphase nature and organic materials, it is observed that they react differently from other tissues<sup>6</sup>. Regarding the dehydration process, it is well understood that the cause is the increase in temperature associated with the duration in which this occurs, causing morphological, macro and microstructural bone changes<sup>6</sup>. However, it should be emphasized that there is still no study carried out on human bone for a more detailed analysis of the behavior of this phenomenon<sup>6</sup>.

Another hypothesis generated from this study's observations was that, in the trauma resulting from high impulse, a pressure wave was generated near the ionization channel, which formed a high-intensity current, defined as barotrauma<sup>6</sup>. This high-impulse current is responsible for a cylindrical expansion that results in permanent cavitations along its path and which are responsible for the bone fragmentation mentioned above. In addition, the collagen fibers present in the bones can also produce a tension that results in bone deformation<sup>6</sup>.

The passage of an intense electrical current has the potential to induce transient perturbation of the blood-brain barrier integrity or inflict microvascular trauma, permitting the ingress of air into the intracranial milieu through either preformed anatomical conduits or minute structural imperfections that remain imperceptible to conventional radiological modalities<sup>7</sup>. The direct traversal of electrical energy through cephalic tissues may likewise culminate in both vascular compromise and parenchymal disruption, further facilitating atmospheric infiltration<sup>7</sup>.

These pathophysiological mechanisms find corroboration in neuropathological examinations, which reveal the presence of intracranial gas accumulations and dilation of perivascular spaces in individuals subjected to lightning-related injury, even in scenarios where no overt cranial fractures are radiographically apparent<sup>7</sup>.

The mechanisms that cause such bone changes after electrical conductivity are still not well understood, and some authors associate such symptoms to high temperature reached in the accident and the association of a mechanical trauma, such as a fall, resulting from muscle spasms<sup>3</sup>. Other researchers report a specific electrical effect, unrelated to temperature, that causes small interruptions in the bones<sup>3</sup>.

## CONCLUSION

Based on all the analyses performed, it is worth highlighting the importance of performing a computed tomography (CT) scan of the skull for a detailed analysis of all victims of electrical burns, this is crucial due to the possibility of trauma regardless of the presence of a skull fracture, so that the serious consequences resulting from this accident can be minimized<sup>4</sup>. Furthermore, this analysis is extremely important for deciding the best therapeutic approach so that, if the criteria for performing a surgical approach exist, it can be performed as quickly as possible<sup>4</sup>. Based on this assumption, although the mechanisms of the emergence of pneumocephalus after electrical burns are still not well understood<sup>3</sup>, it is up to the professional in charge to identify the injury so that the patient does not suffer the serious consequences resulting from this trauma.

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# Ipsilateral Internal Carotid Agenesis and Ruptured Cerebral Aneurysm: an unusual association with therapeutic challenges

## *Agenesia Carotídea Interna Ipsilateral e Aneurisma Cerebral Roto: uma associação incomum com desafios terapêuticos*

Eloísa Bittencurt Thomaz de Assis<sup>1</sup> 

Pedro Neves Fortunato<sup>2</sup> 

Samir Ahmad Jradi<sup>3</sup> 

### ABSTRACT

Aneurysms in the anterior communicating artery are relatively common and are more likely to rupture. Due to important structures close to this artery, the aneurysm clipping procedure and even embolization become risky, and therefore a careful and delicate approach must be taken. The most common presenting signs and symptoms of unruptured intracranial aneurysms include headache, reduced visual acuity, double vision, and other cranial nerve neuropathies that are generally attributed to the mass effect imposed by the aneurysm on nearby neural structures. Our study reports the case of a patient who did not have the common and internal carotid artery on the right side and was diagnosed with a saccular aneurysm of the anterior communicating artery. It has already been discussed that this rare formation increases the incidence of intracranial aneurysms, and the objective of Our study is to present this occurrence and also produce a literature review on this topic.

**Keywords:** Ipsilateral internal carotid; Agenesis; Ruptured cerebral aneurysm; Therapeutics

### RESUMO

Aneurismas na artéria comunicante anterior são relativamente comuns e apresentam maior probabilidade de ruptura. Devido à presença de estruturas importantes próximas a essa artéria, o procedimento de clipagem e até mesmo a embolização do aneurisma tornam-se arriscados e, portanto, uma abordagem cuidadosa e delicada deve ser adotada. Os sinais e sintomas mais comuns de aneurismas intracranianos não rotos incluem cefaleia, redução da acuidade visual, visão dupla e outras neuropatias dos nervos cranianos, geralmente atribuídas ao efeito de massa imposto pelo aneurisma nas estruturas neurais próximas. Nosso estudo relata o caso de um paciente que não possuía a artéria carótida comum e interna à direita e foi diagnosticado com aneurisma sacular da artéria comunicante anterior. Já foi discutido que essa formação rara aumenta a incidência de aneurismas intracranianos, e o objetivo do nosso estudo é apresentar essa ocorrência e também produzir uma revisão da literatura sobre o tema.

**Palavras-Chave:** Carótida interna ipsilateral; Agenesia; Aneurisma cerebral roto; Terapêutica

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## INTRODUCTION

The absence of the common carotid artery (CCA) is a rare vascular anomaly that has historically been found incidentally on neuroimaging examinations and at autopsy. It has been reported that this anomaly may increase the incidence of intracranial aneurysms.

An aneurysm is an abnormal, localized dilation of an artery that expands or fills with blood. Brain aneurysms can occur anywhere in the brain, but most form in the main arteries along the base of the skull. Aneurysms cause symptoms resulting from their growth or rupture, and the most common symptoms are sudden headache, nausea, vomiting and loss of consciousness. The diagnosis is made through tests such as CT angiography and magnetic resonance angiography. The treatment may vary according to the size and clinical condition of the patient. It may include surgery to clip the aneurysm, embolization or follow-up with a neurologist.

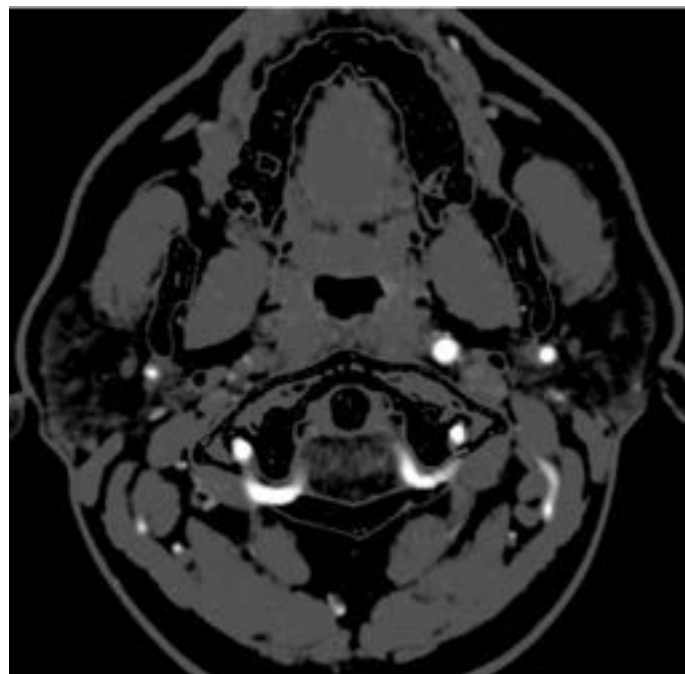
Anterior communicating artery (ACoA) aneurysms are the most common site of intracranial aneurysms, accounting for approximately 30% and 37% of intracranial aneurysms overall<sup>1</sup>. Furthermore, the ACoA is the most common site of intracranial aneurysm rupture, accounting for approximately 40% of aneurysm-related subarachnoid hemorrhages (SAH)<sup>2</sup>. ACoA aneurysms are more likely to rupture than other intracranial aneurysms types due to their anatomical and hemodynamic characteristics. Therefore, for ACoA aneurysms, regardless of rupture and size, active intervention should be performed as soon as they are discovered.

## CASE PRESENTATION

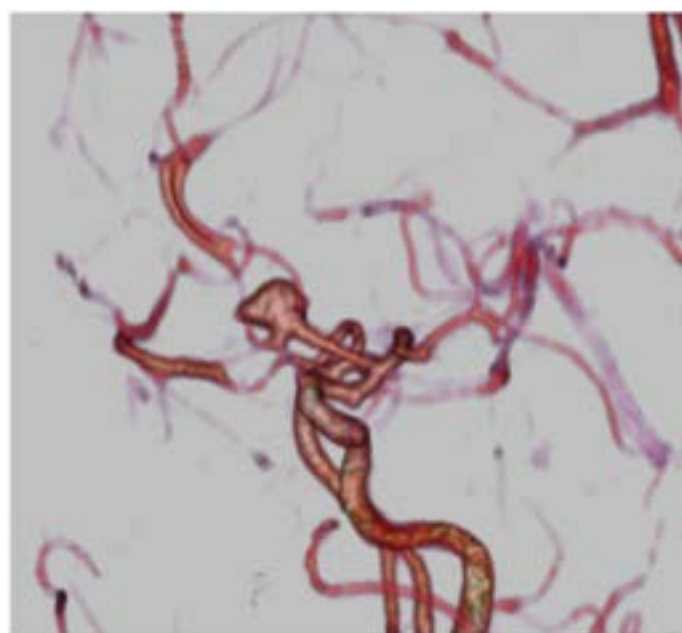
A 35-year-old male patient sought care in the Emergency Room with a report of a severe headache that had persisted for about 3 weeks, unresponsive to medication.

The Skull Computed Angiography examination identified a lobulated saccular aneurysm, measuring 1.1 cm in the largest diameter, located in the anterior communicating artery. Furthermore, the neuroimaging examination accidentally

revealed another very significant finding: the patient does not have the common and internal carotid artery on the right side (Figures 1, 2, and 3).



**Figure 1.** Neuroimaging exams. Computed tomography angiography with axial section showing the absence of the common carotid artery on the right side.



**Figure 2.** 3D reconstruction of CT angiography highlighting the pre-surgical aneurysm in sagittal section.

The procedure indicated at the time was microsurgery to clip the aneurysm. A fronto-parietal craniotomy on the left side was then performed, and the aneurysm was clipped without any complications during the procedure. During outpatient follow-up 20 days after surgery, the patient did not present any

neurological deficits or changes and denied headaches or any other associated symptoms (Figures 4 and 5).

On physical examination, the patient presented Glasgow 15, Peak Inspiratory Flow Rate (PIFR) without focal deficit, and fundus oculi in good appearance.

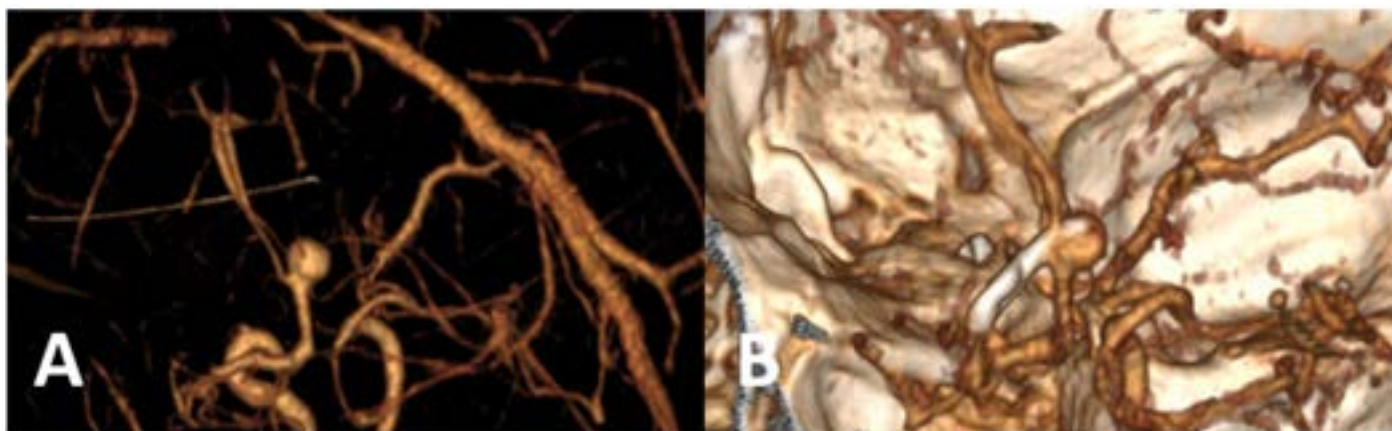
## DISCUSSION

The absence of the CCA is a rare vascular anomaly, with around 90 cases reported in the literature, and has historically been found incidentally in neuroimaging exams and at autopsy<sup>3</sup>. It can occur on both sides and bilaterally (right: left: bilateral: unknown laterality = 47.1%: 39.1%: 6.9%: 6.9%). In addition, this anomaly can increase the occurrence of aneurysms<sup>4</sup>. Of the reported cases, 13 developed an aneurysm, with the internal carotid artery being the most common location, with 6 published studies, and only one case of aneurysm located in the anterior communicating artery<sup>5</sup>.

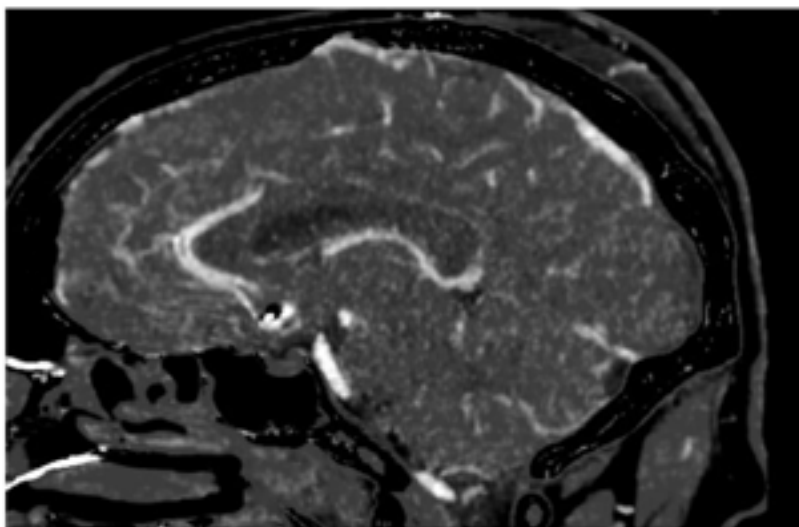
Intracranial aneurysms are relatively common, with a prevalence of approximately 4% in the general population<sup>6</sup>. Most small aneurysms (< 10 mm) are asymptomatic and are discovered accidentally<sup>7</sup>. Unruptured aneurysms can cause symptoms due to the pressure that their mass exerts on nearby structures. When an aneurysm ruptures, it can bleed into the brain parenchyma,



**Figure 3.** Preoperative angiography.



**Figure 4: A-B.** 3D vascularization reconstruction.



**Figure 5.** Postoperative control CT angiography.

resulting in parenchymal hemorrhage, or, more frequently, it can bleed into the subarachnoid space, resulting in SAH. Unfortunately, a ruptured aneurysm becomes a potentially fatal condition.

There are four main types of intracranial aneurysms: saccular, fusiform, dissecting and mycotic. A fusiform aneurysm refers to an aneurysm that has a circumferential and balloon-shaped shape. A dissecting aneurysm is the rupture of the inner layer of the wall of a blood vessel that allows blood to flow between the layers that make up the vessel wall and separate these layers. In turn, a mycotic aneurysm is an infection of the vessel wall that can be of bacterial, fungal or viral origin; they are a rare but serious complication of systemic infection and atherosclerosis. Finally, the saccular type accounts for 90% of intracranial aneurysms<sup>6</sup>. Saccular aneurysms are the result of irregularities in the normal arterial structure, which consists of the tunica intima, the tunica media (the middle muscular layer), and the tunica adventitia (the outer layer composed mainly of connective tissue). Saccular aneurysms occur when there is a deficiency of collagen in the internal elastic lamina and rupture of the tunica media. About 85% of saccular aneurysms arise from arteries in the circle of Willis<sup>8</sup>. The most common location is the AcoA<sup>9</sup>.

The AcoA is a short blood vessel that connects the bilateral anterior cerebral arteries. Located above the optic chiasm, aneurysms of the anterior communicating artery represent 23 to 40% of ruptured intracranial aneurysms and 12 to 15% of unruptured aneurysms and are one of the most common intracranial aneurysms<sup>10</sup>.

Because they present relatively complex anatomical structures and anatomical variations and are adjacent to important vessels and structures, attention must be paid not only to the anatomical characteristics of the aneurysm itself but also to the adjacent important blood vessels and perforating arteries.

The anatomical features of an AcoA aneurysm determine whether microsurgery or interventional embolization treatment is preferable. Microsurgical clipping remains the safest and most basic treatment<sup>10</sup>. For most AcoA aneurysms, it is possible to perform craniotomy through the pterion, and for aneurysms with good morphology, the supraorbital or interhemispheric approach can also be used to obtain good clipping. The most used access for these injuries in this topography is the lateral one. This approach allows for broad visualization of the carotid cistern, offering an excellent view of the anatomy of structures such as the optic nerve and internal carotid artery. The pterional approach guarantees a lower risk of parenchymal injury, as it allows good visualization of pathologies involving aneurysms of the anterior circulation, especially aneurysms of the anterior carotid artery. Some variations to the interhemispheric approach include the bifrontal, unifrontal, interhemispheric basal, and transcrista galli interfalcine approaches.

In short, for most AcoA aneurysms, it is possible to perform a craniotomy through the pterion, and for aneurysms with favorable morphology, it is possible to perform a supraorbital approach. For some aneurysms with special directions, combined approaches



may have unique advantages, but good imaging evaluation must be carefully done before surgery. After surgery, patients tend to experience a significant improvement in pre-surgical symptoms.

## CONCLUSION

The absence of the anterior communicating artery is a rare anomaly that can increase the incidence of intracranial aneurysms. Our study reported a case of a patient diagnosed with an aneurysm in the anterior communicating artery that did not have the anatomical structure of the common carotid and the right internal carotid artery. He underwent clipping of the aneurysm without operative complications. Good pre-surgical planning was important to determine exactly the conduct to be taken during the surgery based on the angiography exams and the anatomical topography of that region, in addition, precision and caution during the execution of the surgery were fundamental to avoid the occurrence of rupture of the aneurysm and ensure that the patient did not suffer from any post-surgical or fatal sequelae.

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# Pineal Germinoma with Recurrence and Multimodal Approach

## *Germinoma Pineal com Recidiva e Abordagem Multimodal*

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Rodrigo Ferrari Fernandes Naufal<sup>2</sup> 

### ABSTRACT

Intracranial germ cell tumors, especially germinomas, predominate in male children and preferentially affect the pineal gland. This article describes the case of an adult patient with pineal germinoma, highlighting the management of hydrocephalus, multimodal oncological treatment, and the challenges associated with tumor recurrence. A 21-year-old male patient presented with headache, vomiting, and photophobia, progressing to Parinaud syndrome and obstructive hydrocephalus secondary to a pineal lesion. Computed tomography and magnetic resonance imaging confirmed a germ cell tumor, later diagnosed as a germinoma. Initial management included ventriculoperitoneal shunting and subtotal resection of the lesion, followed by chemotherapy and radiotherapy, with a satisfactory initial clinical response. After recurrence, the patient underwent further surgical interventions, including an unsuccessful attempt at endoscopic third ventriculostomy, external ventricular shunting, and posterior macroscopic resection, in addition to palliative chemotherapy. Early diagnosis depends on the integration of clinical signs, imaging tests, and serum markers, such as beta-HCG, and staging via cerebrospinal fluid is essential to detect tumor spread. The management of hydrocephalus should prioritize less invasive techniques, avoiding ventriculoperitoneal shunting when possible. This report highlights the complexity of managing pineal germinomas, reinforcing the need for early, individualized, and multimodal approaches to optimize prognosis and minimize complications.

**Keywords:** Germinoma; Hydrocephalus; Case reports

### RESUMO

Os tumores de células germinativas intracranianos, especialmente germinomas, predominam em crianças do sexo masculino e acometem preferencialmente a glândula pineal. Este artigo descreve o caso de um paciente adulto com germinoma pineal, destacando o manejo da hidrocefalia, o tratamento oncológico multimodal e os desafios associados à recidiva tumoral. Paciente masculino, 21 anos, apresentou cefaleia, vômitos e fotofobia, evoluindo com Síndrome de Parinaud e hidrocefalia obstrutiva secundária a lesão pineal. Tomografia e ressonância magnética confirmaram tumor de células germinativas, posteriormente diagnosticado como germinoma. O manejo inicial incluiu derivação ventrículo-peritoneal e ressecção subtotal da lesão, seguidas de quimioterapia e radioterapia, com resposta clínica inicial satisfatória. Após recidiva, o paciente foi submetido a novas intervenções cirúrgicas, incluindo tentativa de terceiroventriculostomia endoscópica sem sucesso, derivação ventricular externa e ressecção macroscópica posterior, além de quimioterapia paliativa. O diagnóstico precoce depende da integração de sinais clínicos, exames de imagem e marcadores séricos, como beta-HCG, e o estadiamento via líquor é essencial para detectar disseminação tumoral. O manejo da hidrocefalia deve priorizar técnicas menos invasivas, evitando derivação ventrículo-peritoneal quando possível. Este relato evidencia a complexidade do manejo dos germinomas pineais, reforçando a necessidade de condutas precoces, individualizadas e multimodais para otimizar o prognóstico e minimizar complicações.

**Palavras-Chave:** Germinoma; Hidrocefalia; Relatos de casos

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## INTRODUCTION

Germinative cell tumors (GCTs) are classified as germinomas and non-germinomatous tumors, such as teratoma, embryonal carcinoma, choriocarcinoma, and endodermal sinus tumor. Although they are predominantly gonadal tumors, about 3% of cases occur in midline extragonadal structures, representing approximately 0.6% of all intracranial tumors<sup>1,2</sup> (Figure 1).

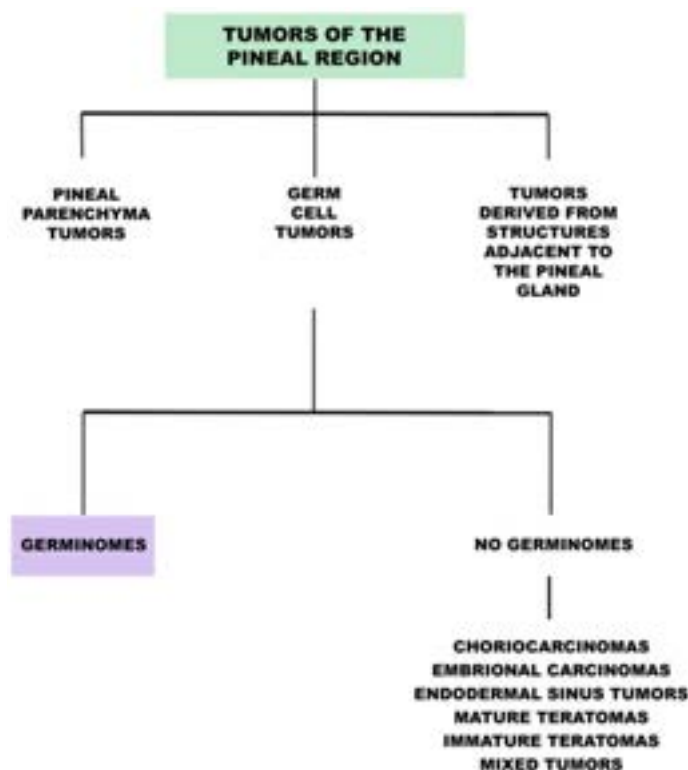
Among intracranial GCTs, germinomas account for about two-thirds of cases<sup>3</sup>. These tumors are more common in male pediatric patients and are rarely diagnosed in adults, with a median age between 10 and 12 years<sup>1,2</sup>. The diagnosis of germinomas includes clinical findings, imaging tests, and biomarker levels. Magnetic resonance imaging (MRI) with and without gadolinium contrast is considered the gold standard for imaging evaluation<sup>2</sup>.

In the central nervous system (CNS), germinomas have a predilection for midline structures and are most often found in the pineal gland. Due to their anatomical relationship with the third ventricle, subependymal dissemination to the suprasellar region or cerebral aqueduct is common, leading to dispersion through the cerebrospinal fluid (CSF)<sup>2,3</sup>. In addition, the proximity of the pineal gland to the quadrigeminal plate causes up to 75% of cases to present with Parinaud syndrome, which is characterized by supranuclear gaze palsy, dissociation of the pupillary response to light and accommodation, and failure of ocular convergence<sup>1,2</sup>.

Obstructive hydrocephalus is a frequent complication of germinomas, accounting for most of the associated symptoms. In the initial phase, increased intracranial pressure causes vomiting due to irritation of areas linked to the reflex. In more advanced stages, compression of higher brain structures can cause blurred vision, double vision, dizziness, and mental changes. In more severe cases, there may be papilledema, severe muscle weakness, and spasticity<sup>2</sup>. Endocrine disorders, such as diabetes insipidus (DI) and delayed gonadal development, are also common manifestations<sup>1</sup>.

Pure intracranial germinomas generally respond very well to radiation therapy, achieving a five-year survival rate of over 90%<sup>1,3</sup>. However, the long-term adverse effects related to treatment at a young age group, such as neurocognitive and endocrine dysfunctions and secondary malignancies, are a cause for concern. In this context, chemotherapy has emerged as a complementary strategy to minimize these effects and improve the overall prognosis of patients, while resection surgery remains indicated only in specific cases, such as mixed tumors or when endoscopic or stereotactic biopsy is not possible.

In this context, the study describes a case of pineal germinoma in an adult patient, emphasizing the management of hydrocephalus, the application of multimodal therapies, and the challenges faced in the face of tumor recurrence, contributing to the improvement of therapeutic strategies and clinical knowledge about rare intracranial tumors.



**Figure 1.** Classification of Tumors of the Pineal Region<sup>1</sup>.



## METHODS

We describe the case of a 21-year-old male patient who presented with bilateral, pulsating, and intermittent headaches associated with photophobia, vertigo, and uncontrollable vomiting. During admission to a tertiary hospital, a condition compatible with Parinaud syndrome was identified. Computed tomography (CT) of the skull showed hydrocephalus with trans-ependymal transudation, as well as an expansive lesion located in the pineal gland, resulting in compression of the mesencephalic aqueduct. Magnetic resonance imaging (MRI) of the skull, with and without contrast, confirmed the presence of the pineal lesion, showing heterogeneous gadolinium uptake, suggestive of a germ cell tumor.

The methodology adopted in this study follows ethical standards, respecting patient confidentiality and obtaining approval from the Institutional Ethics Committee, according to CAAE 86718425.1.0000.5515.

## RESULTS

Given the suspicion of a germ cell tumor, serum markers were requested, and the test showed beta-HCG of 12.88 mIU/mL (reference value < 2.39 mIU/mL), suggesting the diagnosis. Cerebrospinal fluid (CSF) cytology and spinal MRI did not reveal neoplastic cells.

A ventriculoperitoneal shunt (VPS) was performed to relieve hydrocephalus. The patient was discharged from the hospital with outpatient follow-up for laboratory evaluation and planning of subsequent procedures. After four months, he underwent subtotal resection of the pineal lesion by microsurgery with a complementary technique. Histopathological examination 10 days after resection confirmed the diagnosis of germinoma.

The patient started chemotherapy and was referred to oncological follow-up. During follow-up, he developed diabetes insipidus, controlled with nasal desmopressin. Four cycles of chemotherapy with ifosfamide and 20 sequential sessions of radiotherapy were

performed, maintaining clinical and radiological control. Nine months after admission, cranial MRI showed disappearance of the expansive lesion in the pineal gland.

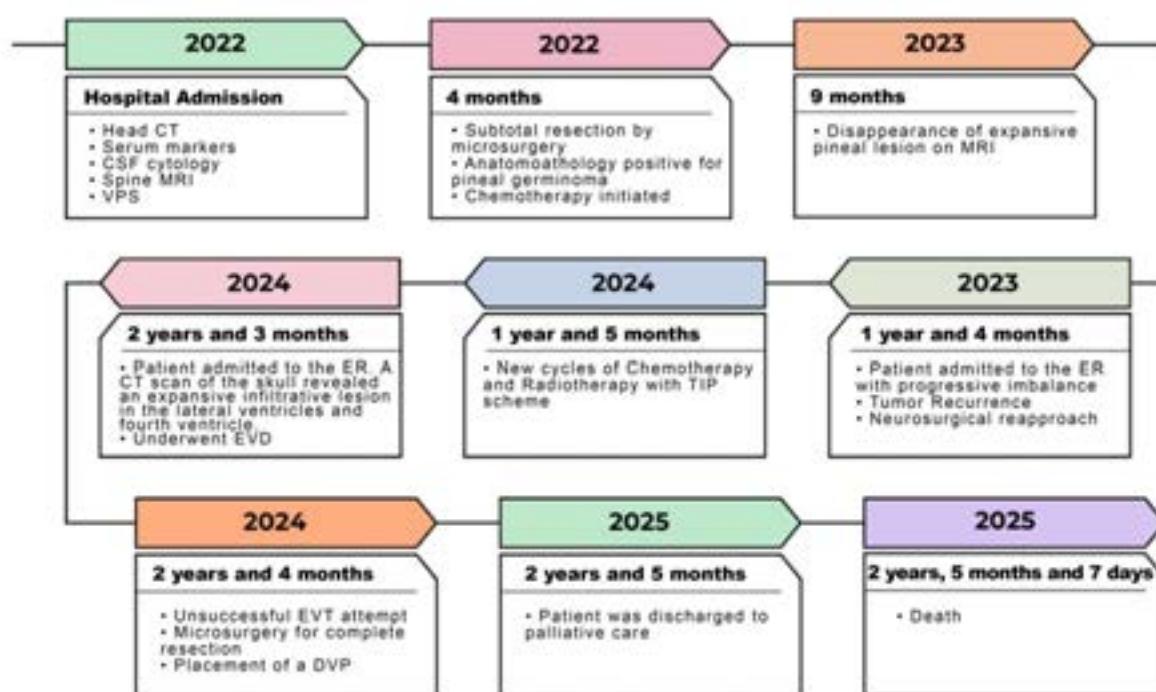
Five months after the follow-up MRI, the patient presented progressive imbalance and was admitted to the emergency room. CT showed a new right frontoparietal parasagittal extra-axial expansive lesion associated with small perilesional edema. Neurosurgical reapproach was performed due to tumor recurrence, followed by new cycles of chemotherapy and palliative radiotherapy with TIP (paclitaxel, ifosfamide, and cisplatin) regimen, with outpatient follow-up in neurosurgery and oncology.

One year after the reoperation, the patient developed drowsiness, nausea, and vomiting. A new cranial CT scan showed an infiltrative expansive lesion in the lateral ventricles and fourth ventricle, associated with cerebrospinal fluid transudation, intracranial hypertension, and diffuse cerebral edema. Endoscopic ventriculostomy (EVO) was attempted but was unsuccessful due to the extent of the tumor. Thus, the patient underwent external ventricular drainage (EVD) for management of intracranial hypertension.

Subsequent oncotic cytology revealed the presence of neoplastic cells. The patient underwent microsurgery for complete macroscopic resection of the intracranial tumor, using a complementary technique, with removal of multiple bleeding tumor fragments. In the postoperative period, he presented clinical and neurological stability, with removal of the external ventricular drain (EVD). However, after a few days, he developed signs of intracranial hypertension (ICH), requiring a new ventriculoperitoneal shunt (VPS). The patient was treated for 28 days due to post-manipulation meningitis.

After resolution of the infection, the family was informed about the severity of the case and the risks associated with consecutive approaches. Given this, further radiotherapy sessions were ruled out, and the patient was discharged from hospital with a scheduled outpatient return. However, he subsequently died (Figure 2).





**Figure 2.** Chronology of clinical, diagnostic, and therapeutic events in a patient with a pineal region tumor, from hospital admission to outcome.

## DISCUSSION

In the clinical case described, the patient presented symptoms characteristic of pineal germinoma, including signs of obstructive hydrocephalus, such as headache and uncontrollable vomiting, in addition to Parinaud syndrome. These clinical findings, together with imaging tests, were fundamental to the initial diagnostic suspicion. It is also noteworthy the beta-HCG dosage, which showed levels five times higher than the reference value, strongly corroborating the hypothesis of a germ cell tumor, especially germinoma<sup>1</sup>.

CSF analysis is essential for staging germinomas, as described in the literature. The presence of tumor cells in CSF cytology may indicate metastatic disease, classifying the tumor as disseminated. In the reported case, there were initially no evident metastases on MRI, nor tumor cells in the CSF, characterizing the tumor as localized (M0), according to the staging criteria. The identification of intracranial or spinal metastases, as well as the presence of tumor cells in the CSF, would change the staging to M2 or

M3, according to cerebral or spinal involvement, respectively<sup>2</sup>. However, after recurrence, the presence of tumor cells in the CSF was identified, changing the staging to M2, characterizing intracranial dissemination.

Obstructive hydrocephalus, a frequent complication of germinomas, was decisive in the patient's clinical manifestation, with initial symptoms of vomiting and increased intracranial pressure. In more advanced stages, compression of higher brain structures can cause blurred vision, diplopia, dizziness, and mental status changes, in addition to the characteristic signs of Parinaud's syndrome, which include ocular motor dysfunction and pupillary reflex changes<sup>1,2</sup>. Hydrocephalus must be managed immediately. However, ventriculoperitoneal shunting (VPS), initially adopted, is not the currently recommended approach<sup>4,5</sup>, since its use in cases of germinomas for the treatment of hydrocephalus is especially associated with reports of peritoneal dissemination<sup>2</sup>.

In cases of pineal region tumors associated with hydrocephalus, endoscopic third ventriculostomy (ETV) associated with tumor biopsy is a safe and less invasive approach with a lower risk

of tumor dissemination<sup>4,5</sup>. Given the high probability that the tumor is a germinoma, early diagnostic confirmation by biopsy is essential for prognosis, as these tumors are highly sensitive to chemotherapy and radiotherapy<sup>4,6</sup>.

Therefore, the initial performance of ventriculoperitoneal shunting (VPS) associated with a delay in obtaining a tumor biopsy is not in line with the recommended procedures for effective management, causing a delay in the start of chemotherapy and radiotherapy and potentially favoring tumor progression<sup>4,7</sup>. Contemporary clinical protocols, such as ACNS 2321 and ACNS 1123, establish strict deadlines for the initiation of treatment, usually within thirty-one days after diagnostic surgery, emphasizing the importance of speed in management to optimize clinical outcomes<sup>8,9</sup>.

In situations where endoscopic third ventriculostomy (ETV) is not feasible due to anatomical limitations, such as large suprasellar lesions or anomalies in the position of the basilar artery, external ventricular drainage (EVD) may be a viable alternative for the management of hydrocephalus<sup>4</sup>.

The initial treatment of germinoma in this patient, performed four months after hospitalization, consisted of subtotal resection of the pineal lesion, a procedure that differs from the currently recommended therapeutic protocols<sup>4</sup>. Extensive or subtotal surgical resection does not appear to confer therapeutic benefit in germinoma, given that these tumors are highly sensitive to chemotherapy and radiotherapy<sup>6,7</sup>. Thus, the role of surgery is limited to obtaining a biopsy for diagnostic confirmation and, when indicated, to managing complications such as hydrocephalus<sup>4</sup>. In addition, more aggressive surgical procedures increase the risk of neurological sequelae, without improving oncological outcomes, reinforcing the need for less invasive approaches<sup>4,5</sup>.

Although in several countries, such as the United States, most patients with germinomas are treated exclusively with radiotherapy, in Brazil the approach often includes surgery for biopsy. In this regard, a study conducted in Brazil with 41 patients diagnosed with germinoma revealed that 35 of them underwent surgery to obtain tumor samples, a practice that is more common due to the difficulties in clinical diagnosis and the need for histopathological confirmation<sup>10</sup>.

The therapeutic approach included four cycles of chemotherapy with ifosfamide, followed by adjuvant radiotherapy, a strategy

recognized for its effectiveness when used early and associated with an appropriate surgical technique, aiming to reduce tumor volume and minimize the adverse effects of radiotherapy, especially in young patients<sup>6</sup>. After recurrence, a palliative chemotherapy regimen (TIP: paclitaxel, ifosfamide, and cisplatin) was instituted with the aim of controlling the tumor and improving the overall prognosis, while seeking to avoid long-term complications associated with radiotherapy, such as neurocognitive dysfunction and secondary malignancies<sup>11,12</sup>.

## CONCLUSION

The clinical case presented exemplifies the importance of early recognition of the typical symptoms of pineal germinoma and the appropriate use of complementary tests, especially beta-HCG dosage and cerebrospinal fluid analysis, for accurate diagnosis and staging of the disease. The initial management of hydrocephalus should favor less invasive techniques, such as endoscopic third ventriculostomy associated with tumor biopsy, in order to minimize the risk of tumor spread, unlike ventriculoperitoneal shunting, which may be associated with complications. Rapid diagnostic confirmation allows for the early initiation of chemotherapy and radiotherapy, which are effective and essential therapies for the control of germinoma, whose extensive surgical resection is not justified and may increase the risk of neurological sequelae.

Contemporary clinical protocols reinforce the need for rapid treatment to optimize prognosis. Close monitoring and adaptation of the therapeutic regimen, including the use of palliative chemotherapy in cases of recurrence, are essential for improving clinical outcomes, especially considering the potential long-term complications of radiotherapy in young patients. Thus, this report emphasizes the need to adopt approaches aligned with current evidence for the effective management of pineal germinoma.

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**Institution:** Hospital Regional de Presidente Prudente.

## CRediT

Anna Carolina Ferretti Wisenfad: Methodology, Validation, Investigation, Writing – Original draft. Sebastião Carlos de Sousa Oliveira: Conceptualization, Formal analysis, Data curation. Marcelo Moreira Pirajon Junior: Writing – Review & editing, Visualization. Rodrigo Ferrari Fernandes Naufal: Resources, Supervision, Project administration.