Evaluation of Prognostic Factors and Outcomes Following Intradural Extramedullary Spinal Tumor Resection

Avaliação de Fatores Prognósticos e de Resultados Após Ressecção de Tumor Intrudural Extramedular

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ABSTRACT

Introduction: Intradural extramedullary spinal tumors are usually treated with surgical excision in order to achieve functional improvement and quality of life. Objective: The aim of this study was to identify prognostic factors and to evaluate the outcome of surgical treatment. Methods: Data from medical records of 49 patients who underwent surgery for intradural extramedullary spinal tumor in a single institution - Hospital da Restauração - were collected. The outcome of the patients was assessed through the McCormick Scale and EuroQol-5 dimensions (EQ-5D) in the preoperative period and last follow-up. Results: Significant improvement in the functional status after surgical treatment was observed. There was 93.3% of improvement and 6.7% of stability. A worse functional result was related to a longer symptoms duration (p = 0.074). Age, symptoms duration, tumor location, histopathological diagnosis, and McCormick preoperative had no significant association with the McCormick at final follow-up (p>0.05). Conclusion: Surgical treatment significantly improved the quality of life and neurological deficits of the vast majority of patients. Age, symptoms duration, tumor location, histopathological diagnosis and McCormick preoperative grade did not present prognostic correlation in this study.

Keywords: Spinal cord; tumors; Intradural; Extramedullary; Meningiomas

RESUMO

Introdução: Os tumores espinhais extramedulares intraduais geralmente são tratados com excisão cirúrgica para obter melhora funcional e qualidade de vida. Objetivo: Identificar fatores prognósticos e avaliar o resultado do tratamento cirúrgico. Métodos: Foram coletados dados de prontuários de 49 pacientes submetidos a cirurgia de tumor intrudural extramedular espinhal em uma única instituição, Hospital da Restauração. A evolução dos pacientes foi avaliada por meio das dimensões da Escala McCormick e EuroQol-5 (EQ-5D) no período pré-operatório e último acompanhamento. Resultados: Observou-se melhora significativa do estado funcional após o tratamento cirúrgico. Houve melhora de 93,3% e estabilidade de 6,7%. Um pior resultado funcional esteve relacionado a uma maior duração dos sintomas (p = 0,074). Idade, duração dos sintomas, localização do tumor, diagnóstico histopatológico e pré-operatório de McCormick não tiveram associação significativa com o McCormick no acompanhamento final (p> 0,05). Conclusão: O tratamento cirúrgico melhorou significativamente a qualidade de vida e os déficits neurológicos da grande maioria dos pacientes. Idade, duração dos sintomas, localização do tumor, diagnóstico histopatológico e grau pré-operatório de McCormick não apresentaram correlação prognóstica neste estudo.

Palavras-chave: Medula espinhal; Tumores; Intradural; Extramedular; Meningiomas
INTRODUCTION

Tumors of the nerve sheath and meningiomas are responsible for most extramedullary intradural spinal tumors. Although the majority of these tumors are histologically benign it can cause significant impairment on functional capacity and quality of life due to pain and myeloradicular symptoms due to compressive effects. Management of symptomatic patients frequently involves surgical resection in order to achieve functional improvement and quality of life. The aim of this study was to identify prognostic factors and to evaluate the outcome of surgical resection of intradural extramedullary tumors.

MATERIAL AND METHODS

This descriptive retrospective study was conducted using prospectively collected data from inpatient and outpatient medical records of 49 consecutive patients who had undergone surgical procedures for intradural extramedullary spinal tumor between January 2016 and July 2020 at the neurosurgical center of Hospital da Restauração in Brazil.

Data was of epidemiological, clinical, tumor, operative aspects, and outcomes were collected. Patients with incomplete data in their records and patients who did not complete the postoperative follow-up for at least 3 months were excluded.

Outcome evaluation

The outcome of the patients was assessed through the McCormick Scale and EuroQol-5 dimensions (EQ-5D) in the preoperative period and last follow-up, based on the records anamnesis and physical examination of hospital and outpatient records.

For intradural spinal tumor, McCormick Scale is considered the standard outcome measure. It assesses global functional impairment based on neurological function and walking ability and it ranges from intact neurologic status to paraplegia or quadriplegia.

EQ-5D is useful for assessing the quality of life from the patient’s perspective. The EQ-5D contains five dimensions of a patient’s health state: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics (version 25.0, IBM).

Data were input descriptively using absolute and percentage frequencies for categorical variables and measures: mean, standard deviation (mean ± SD), and median for numeric variables. The Kruskal-Wallis test was used to evaluate the difference in relation to the numerical variables between categories. The Friedman test was used in the comparison between evaluations. Pearson’s chi-square test or Fisher’s exact test was used in the study of the association between two categorical variables when the condition for using the chi-square test was not verified. A posterior comparison test was used in case of significant difference by the Kruskal or Friedman tests. The choice of the Kruskal-Wallis and Friedman tests was due to the type of ordinal scale or the absence of normality in the numerical variables. The verification of normality was performed using the Shapiro-Wilk test. The margin of error used in the decision of the statistical tests was 5%.

RESULTS

The series of 49 patients with diagnosis of intradural extramedullary tumor comprised 16 males (32.7%) and 33 females (67.3%) with a mean age of 44.8 years (range 8 to 78 years).

Regarding to the symptoms, most of the patients had a symptom duration less than 12 months (63.3%). The most common symptoms were sensitive deficit (87.8%), weakness (83.7%), gait disturbances (79.6%), and pain (77.6%) (Table 1).
The most frequent tumor pathology was schwannoma \((n = 22, 44.9\%)\), followed by meningioma \((n = 17, 34.7\%)\) and neurofibroma \((n = 2, 4.1\%)\). The most common locations were in the thoracic \((46.9\%)\), cervical \((20.4\%)\), and lumbar regions \((18.4\%)\) (Table 2).

Thirty-one patients \((63.3\%)\) underwent a laminectomy followed by posterior instrumented fusion \((18.4\%)\) and laminoplasty \((18.4\%)\). Forty-six patients \((93.9\%)\) had complete tumor resection, 2 \((4.1\%)\) had subtotal resection (neurofibroma and schwannoma), and 1 \((2.0\%)\) had only biopsy performed (lipoma) (Table 2).

### Table 1. Evaluation of epidemiological and clinical data \((n=49)\)

| Variable                             | n  | %    |
|--------------------------------------|----|------|
| **Age range**                        |    |      |
| 6 - 19                               | 4  | 8.2  |
| 20 - 39                              | 14 | 28.6 |
| 40 - 59                              | 20 | 40.8 |
| 60 - 78                              | 11 | 22.4 |
| **Gender**                           |    |      |
| Male                                 | 16 | 32.7 |
| Female                               | 33 | 67.3 |
| **Time of Symptoms (months)**        |    |      |
| < 6                                  | 15 | 30.6 |
| 6 - 12                               | 16 | 32.7 |
| > 12 - 24                            | 10 | 20.4 |
| > 24                                 | 8  | 16.3 |
| **Disease symptoms** \(^{(1)}\)     |    |      |
| Sensitive deficit                    | 43 | 87.8 |
| Weakness                             | 41 | 83.7 |
| Gait disorders                       | 39 | 79.6 |
| Pain                                 | 38 | 77.6 |
| Paresthesia                          | 29 | 59.2 |
| Sphincter dysfunction                | 23 | 46.9 |
| Radicular pain                       | 22 | 44.9 |
| Headache                             | 2  | 4.1  |
| Scoliosis                            | 1  | 2.0  |

\(^{(1)}\) Considering that one patient had more than one symptom, the percentage values were obtained from the total number of 49 patients analyzed since all of them had at least one symptom of the disease.
Excluding the four patients who died, most patients were followed-up for at least one year (N = 33, 73.3%) and only 12 patients (26.7%) had a follow-up between 3 and 12 months.

According to the McCormick scale (Table 3), the percentage of patients in grade I was null at the preoperative period and 73.3% (n = 33) at the final follow-up (p<0.001). The percentage of patients evaluated in grade IV was 67.3% (n = 33) at the preoperative period and only 4.4% (n = 2) at the final follow-up (p<0.001) (Table 3). In our sample, the evolution was 93.3% improvement and 6.7% stability. There was no worsening in functional status.

**EQ-5D**
The mean preoperative EQ-5D value was 0.19. The mean EQ-5D value at the final follow-up was also significantly higher than the preoperative value (0.75, p<0.001) (Table 4).

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**Table 2. Tumor and surgical characteristics (n=49)**

| Variable                  | n   | %  |
|---------------------------|-----|----|
| **Histopathological diagnosis** |     |    |
| Schwannoma                | 22  | 44.9 |
| Meningioma                | 17  | 34.7 |
| Neurofibroma              | 2   | 4.1 |
| Myxopapillary ependymoma  | 1   | 2.0 |
| Lipoma                    | 1   | 2.0 |
| Dermoid cyst              | 1   | 2.0 |
| Epidermoid cyst           | 1   | 2.0 |
| Hemangioblastoma          | 1   | 2.0 |
| Melanoma                  | 1   | 2.0 |
| Undifferentiated malignancy | 1  | 2.0 |
| **Tumor location**        |     |    |
| Thoracic                  | 23  | 46.9 |
| Cervical                  | 10  | 20.4 |
| Lumbar                    | 9   | 18.4 |
| Thoracolumbar             | 4   | 8.2 |
| Cervicothoracic           | 2   | 4.1 |
| Sacral                    | 1   | 2.0 |
| **Surgical resection**    |     |    |
| Total                     | 46  | 93.9 |
| Subtotal                  | 2   | 4.1 |
| Biopsy                    | 1   | 2.0 |
| **Type of surgery**       |     |    |
| Laminectomy               | 31  | 63.3 |
| Arthrodesis               | 9   | 18.4 |
| Laminoplasty              | 9   | 18.4 |

(1) Considering that one patient had more than one symptom, the percentage values were obtained from the total number of 49 patients analyzed since all of them had at least one symptom of the disease.
Table 3. McCormick grade distribution by assessment

| Evaluation          | Grade I | Grade II | Grade III | Grade IV | P value |
|---------------------|---------|----------|-----------|----------|---------|
|                     | n %     | n %      | n %       | n %      |         |
| Preoperative [A]    | - -     | 10 20.4  | 6 12.2    | 33 67.3  | p<0.001*|
| Final follow-up [B] | 33 73.3 | 4 8.9    | 6 13.3    | 2 4.4    |         |

(*) Significant difference at the level of 5.0%
(1) Friedman test between the evaluation days comparing to that test
Note: If the letters in parentheses are distinct, there are significant differences between the corresponding days.

Table 4. Statistics of the variables EQ-5D by evaluation time

| Evaluation   | Preoperative | Final follow-up | P value |
|--------------|--------------|-----------------|---------|
|              | Average ± SD (Mean) | Average ± SD (Mean) |         |
| EQ-5D        | 0.19 ± 0.25 (0.04) [A] | 0.75 ± 0.27 (0.75) [C] | p<0.001*|

(*) Significant difference at the level of 5.0%
(1) Friedman test between the evaluation days comparing to that test
Note: If the letters in parentheses are distinct, there are significant differences between the corresponding days.

Complications
Postoperative complications were observed in 16 patients (32.6%). The most frequent postoperative complications were liquoric fistula (N=6, 12.2%), wound infection (N=5, 10.2%), urinary tract infection (N=4, 8.2%), and deep vein thrombosis (N=3, 6.1%). Five patients (10.2%) required reoperation due to liquoric fistula and wound infection. The mortality rate at follow-up was 8.2% with four deaths resulting from complications related to malignant tumor progression, acute myocardial infarction, massive pulmonary thromboembolism and upper digestive hemorrhagic complication (Table 5).

Table 5. Evaluation of complication features (n=49)

| Variable                              | n  | %  |
|---------------------------------------|----|----|
| Postoperative complications [1]       |    |    |
| None                                  | 33 | 67.3|
| Cerebrospinal fluid fistula           | 6  | 12.2|
| Surgical wound infection              | 5  | 10.2|
| Urinary infection                     | 4  | 8.2 |
| Deep vein thrombosis                  | 3  | 6.1 |
| Pulmonary Thromboembolism             | 1  | 2.0 |
| Meningitis                            | 1  | 2.0 |
| Acute myocardial infarction           | 1  | 2.0 |
| Reoperation                           | 5  | 10.2|
| Reason for reoperation                |    |    |
| Cerebrospinal fluid fistula           | 2  | 4.1 |
| Cerebrospinal fluid fistula + Surgical wound infection | 2 | 4.1 |
| Surgical wound infection              | 1  | 2.0 |
| Death                                 | 4  | 8.2 |

(1) Considering that a patient had more than one postoperative symptom, the total was recorded as the basis for calculating the percentages.
A greater proportion of McCormick I patients (75.8%) at final follow-up had less than 12 months of symptoms whereas most of McCormick III and IV patients (66.6% and 100% respectively) had more than 12 months of symptoms. There was no statistically significant association between those variables though there was a trend for correlation (p = 0.074). The others variable (age range, tumor location, histopathological diagnosis, and McCormick preoperative) also had no significant association with the McCormick at final follow-up (p>0.05) (Table 6).

Table 6. Evaluation of the McCormick variable at the final follow-up according to age range, symptoms duration, tumor location, histopathological diagnosis, and preoperative McCormick

| Variable                              | I       | II      | III     | IV      | Death    | Total group | P value |
|---------------------------------------|---------|---------|---------|---------|----------|-------------|---------|
| n | % | n | % | n | % | n | % | n | % | n | % |
| TOTAL | 33 | 100.0 | 4 | 100.0 | 6 | 100.0 | 2 | 100.0 | 4 | 100.0 | 49 | 100.0 |
| **Age range**                          |         |         |         |         |          |             |         |
| 0-19 | 4 | 12.1 | - | - | - | - | - | - | - | - | - | 4 | 8.2 |
| 20-39 | 10 | 30.3 | - | - | 1 | 16.7 | 2 | 100.0 | 1 | 25.0 | 14 | 28.6 |
| 40-59 | 14 | 42.4 | 1 | 25.0 | 3 | 50.0 | - | - | 2 | 50.0 | 20 | 40.8 |
| 60-78 | 5 | 15.2 | 3 | 75.0 | 2 | 33.3 | - | - | 1 | 25.0 | 11 | 22.4 |
| **Time of Symptoms (months)**          |         |         |         |         |          |             |         |
| < 6 | 10 | 30.3 | 2 | 50.0 | 2 | 33.3 | - | - | 1 | 25.0 | 15 | 30.6 |
| 6-12 | 15 | 45.5 | - | - | - | - | - | - | 1 | 25.0 | 16 | 32.7 |
| > 12-24 | 4 | 12.1 | 2 | 50.0 | 2 | 33.3 | 1 | 50.0 | 1 | 25.0 | 10 | 20.4 |
| > 24 | 4 | 12.1 | - | - | 2 | 33.3 | 1 | 50.0 | 1 | 25.0 | 8 | 16.3 |
| **Tumor location**                      |         |         |         |         |          |             |         |
| Thoracic | 16 | 48.5 | 4 | 100.0 | 1 | 16.7 | 1 | 50.0 | 1 | 25.0 | 23 | 46.9 |
| Cervical | 6 | 18.2 | - | - | 3 | 50.0 | - | - | 1 | 25.0 | 10 | 20.4 |
| Lumbar | 6 | 18.2 | - | - | 1 | 16.7 | - | - | 2 | 50.0 | 9 | 18.4 |
| Thorac-lumbar | 3 | 9.1 | - | - | 1 | 16.7 | - | - | - | - | 4 | 8.2 |
| Thorac-cervical | 1 | 3.0 | - | - | - | - | 1 | 50.0 | - | - | 2 | 4.1 |
| Sacral | 1 | 3.0 | - | - | - | - | - | - | - | - | 1 | 2.0 |
| **Histopathological diagnosis**         |         |         |         |         |          |             |         |
| Schwannoma | 16 | 48.5 | 2 | 50.0 | 5 | 83.3 | 1 | 50.0 | - | - | 24 | 49.0 |
| Meningioma | 12 | 36.4 | 2 | 50.0 | 1 | 16.7 | - | - | 2 | 50.0 | 17 | 34.7 |
| Miscellaneous | 5 | 15.2 | - | - | - | - | 1 | 50.0 | 2 | 50.0 | 8 | 16.3 |
| **Preoperative McCormick**              |         |         |         |         |          |             |         |
| II | 10 | 30.3 | - | - | - | - | - | - | - | - | 10 | 20.4 |
| III | 5 | 15.2 | - | - | 1 | 16.7 | - | - | - | - | 6 | 12.2 |
| IV | 18 | 54.5 | 4 | 100.0 | 5 | 83.3 | 2 | 100.0 | 4 | 100.0 | 33 | 67.3 |

(1) Fisher’s exact test.
A total of 49 patients with extramedullary intradural tumors surgically treated at Hospital da Restauração, a reference center for neurosurgery in the northeastern region of Brazil, was reviewed. Initial presentation with radicular pain (or not characteristic) and subjective sensitivity disorders often hinders early diagnosis of intradural tumors. In general, it takes a long time before a patient presents an evident neurological condition with loss of strength, difficulty in walking, loss of sensation and sphincter disorders. In the present study more than one third (36.7%) had symptoms for more than 12 months.

It was analyzed five variables aiming to identify prognostic factors that had influence on the McCormick score at final follow-up. Symptoms duration was the only variable that had a trend for impact on neurological outcome. A worse functional result (McCormick grade III+IV) was related to a longer symptoms duration (p = 0.074). Ahn et al. also found that longer preoperative duration of symptoms was related to worse surgical outcome1. The other variables (age, tumor location, histopathological diagnosis and preoperative McCormick score can’t be considered as prognostic factors in this study because had no significant association with the McCormick score at final follow-up (p>0.05). Prevedello et al. (2003) reported that age and histopathological diagnosis also hadn’t prognostic correlation whereas tumors in the thoracic region were associated with worse prognostic (p=0.014)9. It was observed an improvement in quality of life and functional status after surgical treatment. In our sample, the evolution was 93.3% of improvement and 6.7% of stability. There was no worsening in functional status. This is also consistent with the results of other studies that showed a good response and improved quality of life in patient follow-up4-10. Riad et al., for example, observed a sensory and / or motor improvement in 87% of the patients and 85% of those who presented gait changes at admission were able to walk autonomously at the end of the follow-up8. Gottfried et al. reviewed six large series that reported functional improvement in 53 to 95% of cases and neurological deterioration in 0 to 10%7.

In the present study, patients who did not complete the postoperative follow-up for at least 3 months were excluded. This cut-off value was chosen considering the analysis of Bellut et al. that reported the importance of monitoring the clinical outcome following of intradural spinal tumor resection for more than 3 months and the potential for clinical improvement over a longer postoperative period. According to Bellut et al., there was no statistically relevant difference between the scores on the McCormick Scale preoperatively and at the 3-month follow-up (p = 0.073) whereas comparisons between both scores versus 12-month follow-up showed a statistically significant improvement in each case (p < 0.004)2.

There are some limitations to this study. Our sample size was small compared with those of large, multicenter studies, and the follow-up time of approximately 27% of patients was less than 12 months. However, taking into account the rarity of these tumors and the limited literature addressing this topic in our country, we highlight the importance of our study by reporting the surgical treatment experiences of this tumor pathology at a neurosurgical reference center in the northeast of the country.

Surgical treatment significantly improved the quality of life and neurological deficits of the vast majority of patients. Age, symptoms duration, tumor location, histopathological diagnosis and McCormick preoperative score did not present prognostic correlation. Therefore, surgical intervention is recommended for intradural spinal tumors even for patients with prolonged or severe neurological symptoms.
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