

# Analysis of Characteristics and Surgical Outcome of Intradural Extramedullary Tumors – a Retrospective Cohort Study of 52 Patients

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## Abstract

**Introduction:** Although intradural extramedullary tumors (IET) are relatively well studied, research on the typical epidemiological, demographic, and clinical characteristics of these malignancies is scanty.

**Aim:** The aim of this study was to investigate retrospectively the epidemiology, demographics, clinical presentation, imaging data, type of surgery, and the outcome of treatment of IETs.

**Materials and methods:** We performed retrospective chart review of medical history, clinical presentation, paraclinical and imaging data, and operative protocols of operated patients with IETs from January 2011 to August 2020. Special attention was paid to the onset of symptoms, clinical presentation at admission, imaging data, localization, type of surgery, histology, and outcome of the disease. The degree of neurological deficit and disability of the patients at admission, discharge, and follow-up was assessed by the Modified McCormick Scale and the Modified Rankin Scale, respectively. The follow-up period varied from 1 to 105 months (mean 43 months).

**Results:** Fifty-two patients (mean age 58 years, range 14-78 years) with IETs were surgically treated for the study period. At admission to the clinic, 48 patients (92.3%) had vertebralgia, 34 (65.4%) had concurrent radicular pain, 42 (80.8%) had motor deficit, and 18 (34.6%) had sphincter disorders. Total tumor removal was achieved in 47 patients (90.4%). Favourable outcome was registered in 43 patients (82.7%). The degree of disability (mRS) at admission ( $p=0.0001$ ), the McCormick grade at admission ( $p=0.0001$ ), gender ( $p=0.042$ ), and age ( $p=0.047$ ) of patients were significantly correlated with the functional status assessed by McCormick scale at discharge.

**Conclusions:** Most of the IETs can be successfully removed via a standard posterior or posterolateral surgical access. Favourable outcome of treatment depends on early diagnosis and total tumor resection.

## Keywords

intradural extramedullary tumor, neurological deficit, surgery, outcome, spine

## INTRODUCTION

The incidence of primary spinal neoplasms is about 5 per 1 000 000 in women and 3 per 1 000 000 in men, with in-

tradural extramedullary tumors (IETs) accounting for two-thirds of them in adulthood and about 50% in childhood.<sup>[1]</sup>

The most common IETs are spinal meningiomas (SM), tumors originating from the sheaths of the spinal cord

nerve roots (TOSSCR), and myxopapillary ependymomas (ME). The frequency varies in different studies: 25%–50% for meningiomas, 15%–60% for schwannomas and neurofibromas, and 5%–10% for ME.<sup>[2–6]</sup> Other considerably less common IETs are lipomas, teratomas, dermoid cysts, arachnoid cysts, metastases, and some others.<sup>[7]</sup>

Although IETs are relatively well studied, there are comparatively few publications in literature with a sufficient number of patients to guarantee an adequate analysis of epidemiology, demographics, histological characteristics, localization, and surgical outcomes.<sup>[2]</sup>

## AIM

The aim of this study was to investigate retrospectively the epidemiology, demographics, clinical presentation, imaging data, type of surgery, and the outcome of the treatment of IETs.

## MATERIALS AND METHODS

A total of 291 patients with spinal tumors were treated surgically at our institution from January 2011 to August 2020. Of these, 238 (81.8%) cases were extradural tumors, 52 were intradural extramedullary tumors (17.9%), and one was intramedullary tumor (0.3%). Only intradural extramedullary tumors were included for analysis.

We performed a retrospective chart review of medical history, clinical presentation, paraclinical and imaging data, and operative protocols. Special attention was paid to the onset of symptoms, clinical presentation at admission, imaging diagnostics, localization, type of surgery, histology, and outcome of the disease. The degree of neurological deficit and disability of the patients before treatment, at discharge and follow-up was assessed using the modified McCormick Scale and the modified Rankin Scale, respectively. The follow-up period varied from 1 to 105 months (mean 43 months).

## Statistical analysis

In the statistical analysis of the data, we used descriptive statistics to describe the studied measured values. Continuous variables were tested for normality with the Kolmogorov-Smirnov and Shapiro-Wilk tests. To compare continuous variables with normal distribution, we used the Student's *t*-test and the analysis of variance (ANOVA). Continuous variables without normal distribution were compared using the Kruskal-Wallis test and the Mann-Whitney U-test. The relationship between categorical variables was analysed using the  $\chi^2$ -test and Fisher's test. According to the normality of the continuous variables, the correlations were analysed using the Pearson correlation coefficient or the Spearman coefficient. A logistic regression was performed to explain the relationship between the variables. For the significance level

of the null hypothesis, we used  $p < 0.05$  at a 95% confidence interval. The analysis was performed using SPSS v. 23.0.

## RESULTS

Fifty-two patients with histologically proven IETs were identified and included in the study. From the studied IETs, the meningiomas were 30 (57.7%), schwannomas – 11 (21.5%), and neurofibromas – 3 (5.8%). Furthermore, myxopapillary ependymomas, lipomas, and metastases were observed in 2 cases each (3.8%) and dermoid and arachnoid cysts in one patient each (1.8%). Thirty-eight of the patients were females (73.1%) and 14 were males (26.9%). The mean age of patients was 57 years (range 14–78 years). The mean age of the female patients in the series was 61.4 years (37–78), and that of the males – 45.5 years. The distributions of the patients by gender and age in the different IETs are presented in **Tables 1, 2**.

At admission to the clinic, 48 patients (92.3%) had vertebralgia, 34 (65.4%) had concurrent radicular pain, 42 (80.8%) had motor deficit, and 18 (34.6%) had sphincter disorders. The type and degree of preoperative neurological deficit are presented in **Tables 3, 4**.

From the patients with paraparesis, 20 (76.9%) had meningiomas, 5 (19.2%) had schwannomas, and 1 (3.7%) had intradural metastasis. Three patients had paraplegia, 10 had sphincter disorders. The patients with quadriplegia and monoparesis had meningiomas. Cauda equina syndrome was found in one patient with ME, in one with lipoma, and in one with intradural metastases, as well as in those with arachnoid and dermoid cysts.

The localization of the different types of IETs is presented in **Table 5**.

The duration of symptoms before diagnosis of IETs in our series varied from 1 to 36 months (mean 9 months). In patients with meningiomas this period was identical, while in those with schwannomas and neurofibromas it was slightly longer but the difference was not statistically significant. In the rest of the patients, the period varied from 2 to 12 months (mean 5 months).

Magnetic resonance imaging (MRI) was the diagnostic tool of choice in the diagnosis of IETs. MRI was used in all patients from our series. The typical MRI features of spinal meningiomas, schwannomas and neurofibromas and ME are presented in **Figs 1, 2, 3**.

One-level laminectomy was performed in 5 patients (9.6%) and in the remaining 44 patients (84.7%) – on more than one level. We performed laminectomy on more than 2 levels in 4 patients (7.7%) who harboured larger tumors that extended over 2 or more segments. In dumbbell type schwannomas, we lateralized the surgical access via arthropediculotomy. In these cases, we also performed posterior pedicle screw fixation in order to avoid anticipated spinal instability.

Total removal was achieved in 47 patients (90.4%). In 2 patients (6.7%) with meningiomas, as well as in 3 patients

**Table 1.** Gender distribution of different IETs

Type of tumor	Number (%)	Men (%)	Women (%)
Meningiomas	30 (57.7)	2 (6.7)	28 (93.3)
Schwannomas and neurofibromas	14 (26.9)	5 (35.7)	9 (64.3)
Myxopapillary ependymoma	2 (3.8)	1 (50)	1 (50)
Lipomas	2 (3.8)	2 (100)	0 (0)
Metastases	2 (3.8)	2 (100)	0 (0)
Arachnoid cyst	1 (2)	1 (100)	0 (0)
Dermoid cyst	1 (2)	1 (100)	0 (0)
Total	52 (100)	14 (26.9)	38 (73.1)

**Table 2.** Age distribution of patients with different IETs

Type of tumor	<40 years (%)	40-60 years (%)	>60 years (%)
Meningiomas	1 (3.3)	13 (43.3)	16 (53.4)
Schwannomas and neurofibromas	1 (7.1)	7 (50)	6 (42.9)
Myxopapillary ependymoma	0 (0)	1 (50)	1 (50)
Lipomas	2 (100)	0 (0)	0 (0)
Metastases	0 (0)	2 (100)	0 (0)
Arachnoid cyst	1 (100)	0 (0)	0 (0)
Dermoid cyst	1 (100)	0 (0)	0 (0)
Total	6 (11.6)	23 (44.2)	23 (44.2)

**Table 3.** Neurological deficit at admission to the clinic

Neurologic symptoms	n (%)
Lower paraparesis	26 (50)
Lower paraplegia	4 (7.7)
Quadriparesis	4 (7.7)
Lower monoparesis	1 (1.9)
Cauda equina syndrome	5 (9.7)
Root paresis	2 (3.8)
No motor deficit	10 (19.2)
Sphincter disorder	18 (34.6)

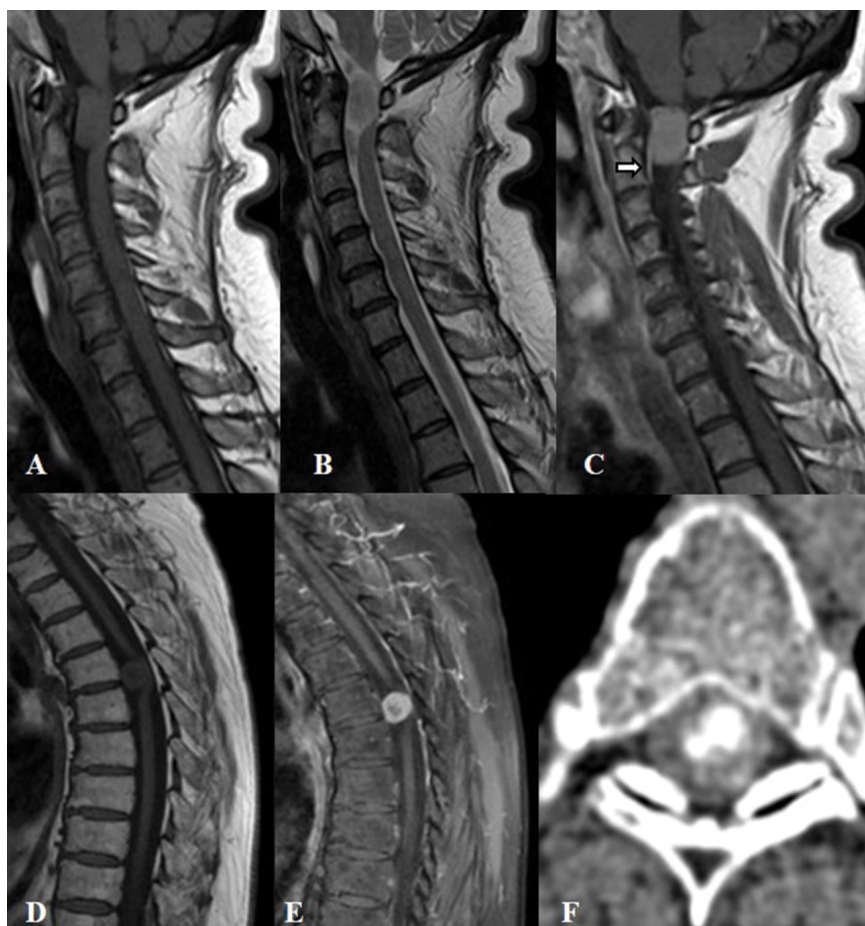
**Table 4.** Degree of neurological deficit and disability at admission

Clinical presentation	n (%)
Modified McCormick Scale	
Grade I	1 (1.9)
Grade II	11 (21.2)
Grade III	20 (38.4)
Grade IV	16 (30.8)
Grade V	4 (7.7)
Modified Rankin Scale	
Grade 1	5 (9.6)
Grade 2	18 (34.6)
Grade 3	11 (21.2)
Grade 4	14 (26.9)
Grade 5	4 (7.7)

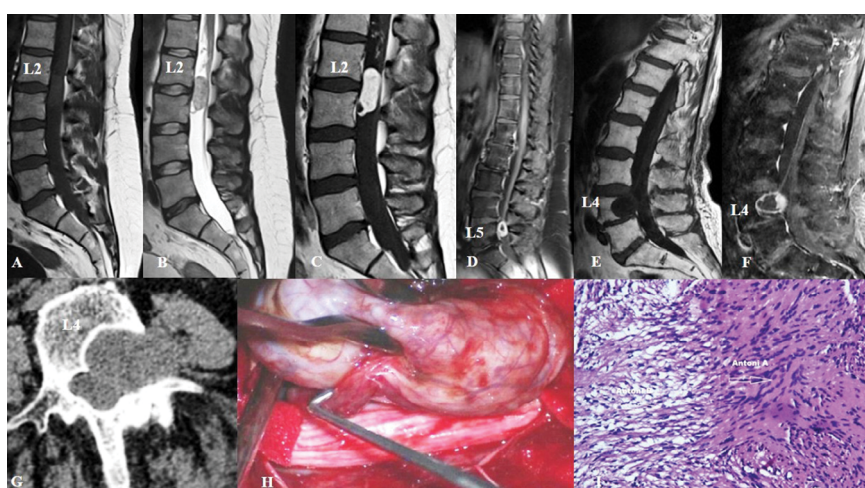
**Table 5.** Localization of the different types of IETs.

Localization	Cervical	Cervicothoracic	Thoracic	Thoracolumbar	Lumbar	Lumbosacral	Sacral
Meningiomas	5	2	20	2	1	0	0
Schwannomas and neurofibromas	1	0	5	1	6	1	0
Myxopapillary ependymoma	0	0	0	1	0	1	0
Lipomas	0	0	0	0	2	0	0
Metastases	0	0	1	0	0	0	0
Arachnoid cyst	0	0	0	0	0	0	1
Dermoid cyst	0	0	0	0	0	1	0
Total	6	2	26	4	9	3	1

\*One patient had leptomeningeal metastases in the cervical, thoracic, lumbar, and sacral regions.

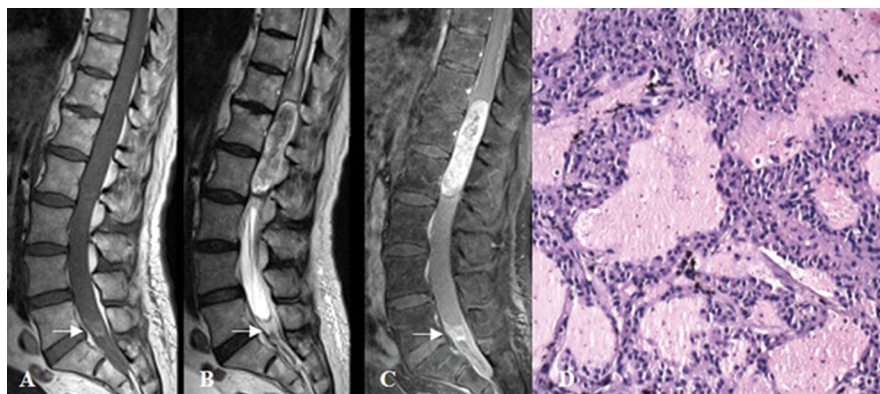


**Figure 1.** A-C) T1, T2 and enhanced T1 MRI demonstrates antero-laterally located meningioma at the level of C1-C2 with typical “dural tail” sign after gadolinium administration (arrow); D and E) T1 MRI before and after gadolinium administration demonstrates meningioma at the level of T3. On T1 MRI, the tumor is isointense with a hypointense center. The contrast media is accumulated at the periphery of the lesion, but not in the center, due to the presence of calcification; F) Axial CT of the same patient showing the presence of calcification.



**Figure 2.** A-C) T1, T2 MRI and enhanced T1 MRI of schwannoma at the level of L2–L3 demonstrating hypointense signal on T1, moderately hyperintense signal on T2, and after contrast - pronounced non-homogeneous accumulation; D) T1 MRI with contrast accumulated at the periphery of the lesion; E and F) T1 MRI before and after enhancement which demonstrates neurofibroma at the level of L4 – non-homogeneous signal amplification of solid components with central cystic region; G) Axial CT of an dumbbell-type neurofibroma at the level of L4 shows enlargement of the left neuroforamen by the tumor and its propagation to the psoas major muscle; H) Intraoperative image; I) Histological specimen consistent with schwannoma; Hematoxylin-Eosin staining, magnification  $\times 100$ .





**Figure 3.** MRI of myxopapillary ependymoma (Grade II) at the level of T12-L2, with drop metastasis (arrows) visualized at the level of L5–S1. **A)** T1 MRI shows an isointense lesion; **B)** T2 MRI - the lesion is heterointense and extends downward to conus medullaris; **C)** Enhanced T1 MRI demonstrates heterogeneous accumulation of the contrast media; **D)** Histological specimen consistent with myxopapillary ependymoma; Hematoxylin-Eosin staining, magnification  $\times 100$ .

with lipomas and dermoid cysts, the resection was subtotal (**Table 6**). Adjuvant therapy (chemotherapy and radiation therapy) was performed in the patient with ME because of the presence of a drop metastasis.

The hospital stay of patients with IETs varied from 9 to 30 days (mean 17 days). The neurological status of the patients at the time of discharge and at follow-up was reassessed with the modified McCormick Scale in order to compare them with the values at admission. The follow-up period varied from 1 to 105 months, averaging 43 months. All patients were followed-up, except one who was not reachable. Out of the 29 patients surgically treated for spinal meningiomas, 3 patients died at 3, 24, and 36 postoperative months, respectively. Only one of the fatalities with

subtotally removed craniospinal meningioma, could be directly associated with perioperative spinal cord compromise. The other two patients had intradural extramedullary metastases in which the lethal outcome occurred within 3 to 6 months after surgery.

In the early postoperative period, all patients demonstrated neurological improvement. At admission to the clinic, patients with mild neurological deficit (grades I and II) were 12 (23.1%) and their number increased to 26 (50%) after surgery. At follow-up, their number further increased to 32 (61.5%). Before treatment, the patients with severe neurological deficits (grades IV and V) were 20 (38.5%), after treatment their number decreased to 10 (19.3%), and at follow-up to 3 (5.7%) (**Table 7**).

**Table 6.** Degree of tumor resection of the different IETs

Type of tumor	Total removal (%)	Subtotal removal (%)
Meningiomas	28 (93.3)	2 (6.7)
Schwannomas and neurofibromas	14 (100)	-
Myxopapillary ependymoma	2 (100)	-
Intradural metastases	2 (100)	-
Lipomas	-	2 (100)
Arachnoid cyst	1 (100)	-
Dermoid cyst	-	1 (100)
Total	47 (90.4)	5 (9.6)

**Table 7.** Degree of neurological deficit in patients with IETs at admission, discharge and follow-up

McCormick at admission	n (%)	McCormick at discharge	n (%)	McCormick at follow-up*	n (%)
Grade I	0 (0)	Grade I	4 (7.7)	Grade I	20 (38.4)
Grade II	12 (23.1)	Grade II	22 (42.3)	Grade II	12 (23.1)
Grade III	20 (38.4)	Grade II	16 (30.8)	Grade III	11 (21.2)
Grade IV	16 (30.8)	Grade IV	9 (17.3)	Grade IV	3 (5.7)
				Grade V	0 (0)
Grade V	4 (7.7)	Grade V	1 (1.9)	Abroad	1 (1.9)
				Died	5 (9.7)

## DISCUSSION

IETs represent 55%–65% of all primary spinal tumors which is similar to our findings (65%).<sup>[8–11]</sup> On the other hand, Traul et al. found that IETs represent as high as 70% of all intradural tumors.<sup>[12]</sup>

The female-to-male ratio in IETs varies between published series from 1.2:1 to 1:2.4.<sup>[13,14]</sup> In our series, the female-to-male ratio was 2.7:1.

TOSSCR are considered to be the most common IETs ranging from 32.7% to 67%.<sup>[13,15]</sup> Others reported that the most common IETs were meningiomas, with a frequency of up to 70.6%.<sup>[16–18]</sup>

The mean age of patients with IETs ranges from 39.3 to 49.3 years, while in our study it was 58, with a mean age of 64.5 years in males and 48.5 years in females, respectively.<sup>[4,7,12,18,19]</sup> We found two peaks of the disease within the age groups 40–60 years and over 60 years. The mean age of our patients with meningiomas was 65 years and was identical to that reported in literature<sup>[17]</sup>, while the mean age of patients with schwannomas and neurofibromas was lower (mean 58 years).

The most common localization of IETs is in the thoracic, followed by the lumbar and cervical regions.<sup>[7,13,19–21]</sup> This was confirmed by our study, in which the localization IETs in the thoracic region was 50%. The second most common localization was the lumbar region (17.3%). The histological distribution in this location included 66.7% schwannomas and neurofibromas, 22.2% lipomas, and 11.1% meningiomas. Three of the lesions (neurofibroma, myxopapillary ependymoma, and dermoid cyst) (5.8%) were located in the lumbosacral region. Five meningiomas and one schwannoma were located in the cervical region (11.5%). Our statistical analysis did not establish a significant correlation between tumor localization and disease outcome ( $p=0.245$ ).

The majority of IETs are benign tumors with slow progression, so the period from the disease onset to diagnosis varies on average from 11 to 59 months.<sup>[7,19,22]</sup> The duration of symptoms until diagnosis in patients with IETs in our series ranged from 1 to 36 months (mean 9 months). Similar to Stawicki and Guarnaschelli, we also found that in patients with schwannomas the period is slightly longer than in those with SM.<sup>[19]</sup> In the remaining patients with other intradural extramedullary lesions, this period varied from 2 to 12 months (mean 5 months). Similarly to Westwick et al., we found that the duration of symptoms was significantly correlated with the preoperative degree of neurological deficit ( $p=0.041$ ) and disability ( $p=0.038$ ).<sup>[6]</sup>

Vertebralgia can be persistent for a long time and may be the only initial symptom of IETs.<sup>[17]</sup> Radicular pain is another common symptom, especially in patients with schwannomas and neurofibromas.<sup>[17]</sup> In 48 of our patients (92.3%), the disease debuted with back pain, and in 34 (65.4%) there was concomitant radiculopathy. Gradually, the growing tumor mass causes compression of the adjacent neural structures such as spinal cord or cauda equina which may lead to myelopathy, isolated muscle group paresis, or cauda equina

syndrome. Motor deficit was noted in 42 (80.8%) patients and sphincter disorders in 18 patients (34.6%).

Most studies reported favourable outcomes associated with total tumor resection, ranging from 75% to 94%, at the cost of minimal morbidity and mortality, regardless of histological type of the tumor.<sup>[2,22,23]</sup> In our study, we found that the degree of disability (mRS) at admission ( $p=0.0001$ ), the McCormick grade at admission ( $p=0.0001$ ), gender ( $p=0.042$ ) and age ( $p=0.047$ ) of the patients were significantly correlated with the functional status assessed by McCormick scale at discharge.

In our series, we achieved total resection in 90.4% of the cases and registered postoperative complications in 3 patients (5.8%) (hemorrhagic stroke, postoperative CSF leak).

In elderly patients with ME, the percentage of detected preoperative drop metastases varies between 36.4% and 50%, while 73% of them do not cause neurological progression or clinical symptoms, which is also observed in our case.<sup>[24,25]</sup> We fully agree that irradiation should be performed in cases of ME associated with drop metastases, therefore, patients should be closely monitored for occurrence of clinical symptoms or neurological progression caused by the disseminated lesions.<sup>[24]</sup>

Despite the benign nature of lipomas, their total removal is not always possible due to massive adhesions to the surrounding nerve structures and the high risk of significant neurological complications.<sup>[26]</sup> According to Arslan et al., the degree of lipoma removal does not affect the long-term postoperative results and total tumor removal is not mandatory to alleviate clinical symptoms, as long as optimal decompression of the surrounding nerve structures has been achieved.<sup>[26]</sup> Even after partial tumor removal, patients have significant improvement in neurological functions, and the condition remains stable at follow-up for a period of 8 months to 5 years, which is confirmed by our two cases.<sup>[27]</sup>

Significant improvement after surgical treatment of IETs was observed in 77%–90.6%, while deterioration of neurological status was seen in 1%–5% of the cases.<sup>[28–30]</sup> The preoperative neurological deficit improved in most patients within 2 months, and in all cases within 1 year postoperatively.<sup>[31]</sup> In this study, patients demonstrated statistically significant postoperative neurological improvement assessed by the McCormick scale that remained stable over time.

## CONCLUSIONS

IETs are usually benign and slow-growing tumors which remain asymptomatic for a long period of time. Vertebralgia and radicular pain are the initial and most common clinical symptoms. IETs are more common in people over the age of 40. Meningiomas, schwannomas, and neurofibromas were the most common IETs, predominantly observed in females. These tumors can be successfully removed via a standard posterior or posterolateral surgical access. Favourable outcome depends on early diagnosis and total removal of the lesion.

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# Анализ характеристик и хирургических результатов интрадуральных экстрamedулярных опухолей – ретроспективное когортное исследование 52 пациентов

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## Резюме

**Введение:** Хотя интрадуральные экстрamedулярные опухоли (ИЭО) относительно хорошо изучены, исследования типичных эпидемиологических, демографических и клинических характеристик этих злокачественных новообразований немногочисленны.

**Цель:** Целью данного исследования было ретроспективное изучение эпидемиологии, демографии, клинической картины, данных визуализации, типа операции и результатов лечения ИЭТ.

**Материалы и методы:** Проведён ретроспективный анализ анамнеза, клинической картины, параклинических и визуализационных данных, а также оперативных протоколов оперированных больных с ИЭТ с января 2011 г. по август 2020 г. Особое внимание уделялось дебюту симптомов, клинической картине при поступлении, данные визуализации, локализация, тип операции, гистология и исход заболевания. Степень неврологического дефицита и инвалидизации больных при поступлении, выписке и динамическом наблюдении оценивали по модифицированной шкале Макормака и модифицированной шкале Рэнкина соответственно. Срок наблюдения варьировал от 1 до 105 мес. (в среднем 43 мес.).

**Результаты:** 52 пациента (средний возраст 58 лет, диапазон от 14 до 78 лет) с ИЭТ подверглись хирургическому лечению за период исследования. При поступлении в клинику у 48 (92.3%) пациентов отмечалась вертебральная боль, у 34 (65.4%) – сочетанная корешковая боль, у 42 (80.8%) – двигательный дефицит, у 18 (34.6%) – сфинктерные нарушения. Тотальное удаление опухоли было достигнуто у 47 пациентов (90.4%). Благоприятный исход зарегистрирован у 43 больных (82.7%). Степень инвалидности (mRS) при поступлении ( $p=0.0001$ ), шкала McCormick при поступлении ( $p=0.0001$ ), пол ( $p=0.042$ ) и возраст ( $p=0.047$ ) пациентов достоверно коррелировали с оцениваемым функциональным статусом по шкале Макормака при выписке.

**Заключение:** Большинство ИЭТ могут быть успешно удалены с помощью стандартного заднего или заднебокового хирургического доступа. Благоприятный исход лечения зависит от ранней диагностики и тотального удаления опухоли.

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## Ключевые слова

интрадуральная экстрamedулярная опухоль, неврологический дефицит, операция, исход, позвоночник

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