



# Comparative Multi-Segment with Short-Segment Intramedullary Spinal Cord Tumors



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## Introduction

Intramedullary primary spinal cord tumors are rare, accounting for 4-10% of all central nervous system tumor [1-3]. Multi-segment involvement where the intramedullary tumor length occupying 3 or more vertebral body levels is considered as multi-segment intramedullary spinal cord tumor (MSICT) [4], and has a much lower incidence (about 1 MSICT for every 10 spinal tumors) [5,6]. Intramedullary primary spinal cord tumors occupying one and two vertebral body levels is considered as seldom segments tumors. Similar to several studies on intramedullary primary spinal cord tumors [1-5], there are also several studies on multi-segments intramedullary primary spinal cord tumors [6-8].

Ardeshiri [9] considered that patients with more than three involved segments showed a significantly higher risk for postoperative neurological deterioration compared to patients with seldom segments lesions. However, there was no difference of the resection rate based on the amount of the involved spinal segments. Up to now, no study focused on the comparative analysis of the difference in perioperative neurological function and long-term outcomes of patients with different involved intramedullary primary tumor spinal segments.

The most frequent histological types of intramedullary tumors are glial tumors (80%), astrocytomas, and ependymomas [10,11]. Multi-segment involvement where the intramedullary tumor length occupying 3 or more vertebral body levels is considered as multi-segment intramedullary primary spinal cord tumor (MSICT)[4], and has a much lower incidence (about 1 MSICT for every 10 spinal tumors) [5,6]. On the other hand, the intramedullary primary spinal cord tumors occupying one and two vertebral body levels is considered as seldom segments tumors. Similar to several studies on intramedullary primary spinal cord tumors [1-5], there were also several studies on multi-segments intramedullary primary spinal cord tumors [4-7].

Raco A [12] reviewed 202 patients with intramedullary primary spinal cord tumors and found that the average duration of symptoms before diagnosis was 3 years. Kutluk T [13] found the median interval between symptom onset and diagnosis of pediatric patients with intramedullary primary spinal cord tumors was 180

days (range: 10~1080 days). Moreover this interval did not differ with histopathological tumor type, but was longer in the case of low-grade tumors (6 months) than in the case of high-grade tumors (1.5 months,  $p=0.027$ ). Chang UK [14] found the period between initial symptom presentation and surgery was longer with a mean of 31.9 months for adult patients with ependymoma.

Gavin QD [15] performed their study on patients with ependymoma. He revealed that the longer symptom duration prior to treatment was associated with poorer functional outcome ( $P=0.006$ ). Multivariate analysis revealed that a shorter duration of symptoms prior to surgery predicted good post-operative ambulatory status but no other predictive factors were identified. Which kind of factors could affect the neurological function of the patients between seldom and multiple segments groups with intramedullary spinal cord primary tumors?

Ardeshiri A [9] considered that patients with more than three involved segments showed a significantly higher risk for postoperative neurological deterioration compared to patients with seldom segments lesions. However, there was no difference of the resection rate based on the amount of the involved spinal segments.

Ardeshiri A [9] concluded the same opinion that patients with more than three involved segments showed a significantly higher risk for postoperative neurological deterioration compared to patients with circumscribed lesions. However, we found that the difference of long-term neurological function ( $p=0.12$ ) between seldom and multiple segments group was not statistically significant. The neurological function of the patients with multiple segments intramedullary primary tumors was remarkable improved after physical therapy during long-term follow-up. Bansal S [11] followed-up 146 patients with spinal intramedullary tumors and found that the patient's outcome at final follow-up was correlated with age, sex, preoperative functional status, tumor size, location, pathology, extent of surgical resection and the presence of syrinx.

Moquin RR [16] considered that long-term functional outcome was also related to the patient's preoperative status, tumor location,

presence of myelomalacia, and presence of arachnoid scarring. Little improvement was seen in patients with long-standing deficits before surgery. The greatest improvement and least risk were seen in patients with short duration of neurological deficits before surgery and those with ependymomas.

Xiao R [17] considered aggressive tumor resection was believed to be critical to prevent permanent neurological deficits. Since greater extent of resection or gross total resection had been associated with superior progression-free survival for subtypes like ependymomas and hemangioblastomas, maximal safe tumor resection remain the mainstays of optimal management. However, no such correlation between gross total resection and progression-free survival had been established for astrocytomas. They had observed a general trend towards superior outcomes and neurological improvements over a median follow-up period of 54 months.

With a mean follow up of 5.5 years (ranged 6 months to 12 years), majority of patients with ependymoma, low-grade gliomas or miscellaneous tumors had neurological and clinical status that has stabilized or improved. For patients with high-grade gliomas, their mean follow up was significantly shorter and despite adjuvant therapy postoperatively, majority of them worsened over a mean follow up of several months [18].

Lee [19] retrospectively reviewed 69 patients who underwent surgical treatment for intramedullary primary spinal cord tumors, they found the following outcome for high-grade tumor, 42.8% of good outcome, 28.6% of fair outcome and 28.6% of poor outcome. On the other hand, for patients with low-grade tumor, 79% of patients showed good outcome, 12.9% showed fair outcome and 8.1% had poor outcome. Fakhreddine [20], retrospectively reviewed charts from a series of 83 patients with histologically confirmed spinal astrocytoma and found that WHO grade among infiltrative tumors was a significant prognostic indicator for overall survival and progression-free survival in both univariate and multivariate analyses.

Unsurprisingly, the extent of tumor resection was dependent on tumor types. Ependymomas, vascular tumors and schwannomas usually achieved gross total resection, while it was difficult to obtain gross total resection for gliomas. Our findings of lower resection rate for high-grade spinal gliomas compared to low-grade glioma were in keeping with the previous studies [4,7,18]. According to Kim [21], they reported that 39% of low-grade spinal cord gliomas obtained a gross total resection, while the rate was seen in only 20% of high-grade gliomas. In addition, Huddart et al. [22], reported distant metastases occurred in 50~60% of patients with high-grade spinal cord glioma. On the other hand, for patients with well-delineated intramedullary spinal tumor, the boundaries between tumor and normal spinal cord tissue were distinct and separable. Therefore, total or subtotal resection was obtained more readily, and has been reported in up to 95% of intramedullary ependymomas [5,4,14,15].

Furthermore, Yang et al. [23] found no difference of the resection rate on the amount of the involved spinal segments. In

contrast to others, Ardeshiri et al. [9] observed a different rate for complete resection based on the localization of the intramedullary lesion. Compared to other localizations, our data showed a significantly higher rate for complete resection for cervically located astrocytomas. Whereas the tumor localization was shown to correlate with rate of tumor resection, the extension of the involved spinal segment did not influence the resectability.

Xiao R [17] considered that the only established factor affecting prognosis was tumor grade. Older age at surgery was the only significant variable that predicted decreased probability of progress-free survival. Older age at surgery also trended towards predicting lack of neurological improvement and decreased overall survival.

Bansal S et al. [11] also concluded that the patient's outcome at final follow-up was correlated with age, sex, preoperative functional status, tumor size, location, pathology, extent of surgical resection and the presence of syrinx. We found that most dead patients had malignant glioma (50%, 4/8) and diffuse astrocytoma (25%, 2/8). Most survival patients had ependymoma (45%, 50/110), teratoma (18%, 20/110) and vascular tumor (13%, 14/110). Most malignant glioma (38%, 5/13) and diffuse astrocytoma (23%, 3/13) was inclined to recurrent and regrowth. On the other hand, most ependymoma (46%, 48/105), teratoma (17%, 18/105) and vascular tumor (13%, 14/105) were locally controlled. Most patients died from recurrence and regrowth of glioma (75%, 6/8). Most survival patients received locally controlled of glioma (94%, 103/110).

Moquin RR et al. [16] also concluded that the preoperative neurological status was an important predictor of outcome. Radical excision of low-grade astrocytomas was associated with minimal morbidity and excellent prognosis, when carried out before there was significant disability. Unlike ependymomas and benign astrocytoma, malignant astrocytomas are characterized by rapid and relentless clinical deterioration with a strong propensity to disseminate throughout the spinal axis and into the brain. There is a clear correlation between the grade of astrocytoma and survival, most patients with anaplastic astrocytomas and glioblastomas do not survive more than a year after diagnosis.

Abdullah et al. [24] concluded that there was a trend towards an increased probability of progress-free survival in intramedullary primary spinal cord tumors when gross total resection was achieved. The resection of these tumors was likely to halt, but not reverse, neurological deterioration. Behmanesh [25] considered that the overall survival of patients with intramedullary spinal cord glioblastoma is approximately 10~12 months. The prognosis for high-grade glioblastoma is extremely poor, and virtually all patients die as a consequence of progressive disease. For instance, in a series of 17 patients, Jallo et al. [26] found that prolonged survival was associated with more aggressive surgery for the 12 patients who had gross total resection with a 5-year survival rate of 82%. Furthermore, Yang et al. [18] established in a larger cohort of 62 patients that gross total resection was significantly more attainable in low-grade astrocytomas (41.1%) compared to high-grade tumors (16.7%).

Fakhreddine et al. [20] retrospectively reviewed charts from a series of 83 patients with histologically confirmed spinal astrocytoma, and found that WHO grade among infiltrative tumors was a significant prognostic indicator for overall survival and progress-free survival in both univariate and multivariate analyses. In our previous study, for patients with high-grade gliomas, their mean follow up was significantly shorter, and despite adjuvant therapy postoperatively, majority of them worsened over a mean follow up of several months. Similar to our study, Abd-El-Barr et al. [27] found that in contrast to ependymoma and pilocytic astrocytoma, infiltrative spinal cord astrocytoma (Grades 2-4) were more difficult to remove surgically and pose a higher risk of neurological injury with more aggressive surgery. When suspecting an infiltrating spinal cord astrocytoma, biopsy with maximal resection if possible should be performed with intraoperative neuromonitoring.

For low-grade astrocytomas, Venes [28,29] considered no significant difference in recurrence rates between patients who underwent gross total resection compared to subtotal resection of astrocytoma. Schebesch et al. [30] indicated that the risk of recurrence was higher for older patients with a higher grade of malignancy, astrocytic histology, and for patients who only received a tumor biopsy. Multivariate analysis revealed astrocytic histology, a higher grade of malignancy, and a high Ki-67 labeling index to be independent factors predictive for tumor recurrence. As expected, the recurrence rate was significantly influenced by the histological subtype of the tumor. Astrocytomas tended to recur significantly more often than all other spinal cord tumors of their series.

Klekamp et al. [31] Reported a series of 76 astrocytomas over 32 years with a 43% 10-year recurrence rate for all astrocytomas, and a 78% recurrence rate form malignant astrocytomas after 5 years. Five-year rates of local control (83%) and overall survival (83%) were also fairly high over follow-up. For low-grade astrocytomas, Sandler [32] reported no significant difference in recurrence rates between patients who underwent gross total resection compared to subtotal resection of astrocytoma.

In summary, vascular tumors, cyst, benign and malignant glioma as well as diffuse astrocytoma most commonly involved seldom vertebral segments, and ependymoma, teratoma, lipoma as well as neurinoma most commonly involved multiple vertebral segments. Perioperative neurological function of the patients with seldom segments glioma was better than the patients with multiple segments glioma, especially limbs strength. The neurological function of the patients with multiple segments intramedullary glioma was remarkable improved after physical therapy.

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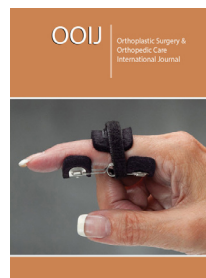
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