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Spinal cord compression in relation to clinical symptoms in patients with spinal meningiomas

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ABSTRACT

Objective: Spinal meningiomas are common primary tumors of the spinal canal and the resulting spinal cord compression (SCC) is intrinsically related to symptoms and outcome, but literature concerning this association is limited. We aimed to present data on both degree of SCC and tumor occupancy percentage in relation to neurological symptoms and outcome.

Methods: Patients ≥ 18 years with a histological diagnosis of spinal canal meningioma treated between 2000 and 2017 were retrospectively evaluated for symptoms and neurological outcome in relation to SCC (i.e. compression of spinal cord at maximal tumor compression compared to maximum area above/below compression) and tumor occupancy percentage (percentage of dural sac area occupied by tumor at maximal tumor compression). Area segmentation of spinal cord, tumor and dural sac (as marker of spinal canal) was performed manually on magnetic resonance imaging (MRI) scans. The neurological deficit was assessed pre- and postoperatively according to the McCormick score. A logistic regression was made with a training set to identify the cut-off level for motor deficit.

Results: The cohort included 111 patients with a mean age of 62.5 years and 77.5% were female. The dominating symptoms preoperatively were sensory disturbance (91.0%), motor deficit (80.2%) and gait disturbance (67.6%). Postoperatively 53.2% of patients, also in some of those with severe deficit and high tumor occupancy, improved their neurological deficit and 43.2% were unchanged. Patients with intradural meningioma and assessable MRI scans were included to evaluate SCC (n = 83). The mean extent of SCC was 50.6%. Exploration of tumor occupancy percentage identified a cut-off at 65% tumor occupancy to best discriminate between patients with or without motor deficit.

Conclusion: Patients with an intradural tumor occupancy percentage of > 65% are more likely to have a preoperative symptom and deficit, validating previous findings. Therefore, we suggest that even in asymptomatic, otherwise fit, patients with tumor occupancy approaching 65% should be considered for surgery since there is a high risk of developing deficit with even minimal growth. Concerning recovery, patients with tumor both high tumor occupancy and significantly impaired function tended to improve their functional level postoperatively.

1. Introduction

Meningioma is a common spinal canal tumor comprising 25–30% of primary tumors affecting the spine, and approximately 8% of all meningiomas [1–4]. The presentation ranges from asymptomatic to severe para- and quadriparesis. Spinal meningiomas are more common in females, and most common in the thoracic spine, followed by cervical spinal canal [4,5]. Surgery is the main treatment modality of intraspinal meningiomas and a low rate of recurrence (1.3–6.4%) has been reported [6].

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The majority of patients with a neurological deficit prior to surgery improve postoperatively, although some patients will have a worsened neurological function after surgery [7–9]. Previous studies have as factors associated with worse functional outcome suggested anterior or anterolateral location, sphincter dysfunction at first examination, surgery on recurrence, large tumor size, meningioma classified as World Health Organization (WHO) grade 2, signal changes in the spinal cord on T2-weighted magnetic resonance imaging (MRI) sequences, and severe preoperative functional status [10–12]. Nevertheless, others have demonstrated that even patients with severe neurological deficit prior to surgical treatment can experience good neurological outcome [13–15].

In clinical practice, the degree of spinal cord compression (SCC) has a great impact on clinical decision making, but it has rarely been studied regarding its impact on surgical outcome. Davies et al. found that the degree of compression of the spinal cord, when examined with cross-sectional area measurements using MRI, had no obvious relationship to function prior to or after surgery [16]. In contrast to this finding, Yamaguchi et al. suggested a meningioma occupancy percentage of 64% or more of the spinal canal as a threshold to cause motor deficit [17], similar to Baro et al. who found that patients with larger spinal meningiomas with higher compression may have both lower function prior and after surgery [18].

SCC may also be associated with onset of the patient's symptoms. Due to increased availability of MRI scanners the incidence numbers of intraspinal meningiomas are rising and asymptomatic patients may pose a surgical dilemma of whether to operate [19]. A clear association between compression and symptom onset could help clinicians predict clinical course and when to offer surgery based upon presumed symptom onset and surgical outcome.

We aim to elucidate the relationship between the degree of SCC and presenting symptoms and outcome postoperatively. Additionally, we explored which tumor occupancy percentage in the spinal canal is most likely to give rise to motor deficit and if high tumor occupancy would indicate low chance of neurological recovery postoperatively.

2. Methods

2.1. Patient characteristics

Our department of neurosurgery covers a population of approximately 1.7 million inhabitants regarding surgical treatment of spinal meningiomas. Patients 18 years and older with histological diagnosis of meningioma WHO grade 1–3 after primary surgery of spinal meningioma between 2000 and 2017 were retrospectively identified and 111 patients were included. MR evaluation for SCC was performed on a subset of 83 patients with intradural growth – exclusion of 13 patients due to possible segmentation bias caused by possible intraforaminal growth and lack of assessable MRI scans in 17 patients.

2.2. Clinical and outcome variables

The following clinical variables were included: age at date of surgery, preoperative symptoms, preoperative neurologic status (according to the McCormick score [20]), Karnofsky performance score [21], neurological outcome, surgical technique, recurrence in need of surgery, tumor WHO grade, and complications according to the Clavien-Dindo classification system [22]. The McCormick score is mainly used to assess functional status before and after surgery. The score spans from grade I to V: I = intact neurology (neurologically intact or mild focal deficit not affecting function); II = mild motor deficit or sensory disturbance (maintains functional independence), III = moderate deficit and limitation of function (independent with external aid), IV = severe motor deficit or sensory disturbance (limit of function with dependent patient), and V = denotes paraplegia or quadriplegia (severe deficit requiring wheelchair) [20,23]. The McCormick score has previously been used with regards to neurological deficit after surgery and was selected as a marker of neurological outcome in this study [6,11,12,24,25]. The patients are routinely assessed at a follow-up visit approximately 3 months postoperatively. If uncomplicated postoperative course an MRI is usually performed 1 year after surgery. Follow-up beyond one year is individualized.

2.3. Radiological variables

The following manual segmentations were performed: (1) the cross sectional area of the spinal cord at the level of maximum compression (cm^2); (2) the cross-sectional area of the spinal cord above and below the tumor (cm^2) where the shape of the spinal cord was regained; (3) the cross-sectional area of the tumor in the axial plane at the largest point of the meningioma; and (4) the cross-sectional area (cm^2) of the dural sac at maximal tumor compression level as a marker of the area of the spinal canal which is occupied by structures of interest in this study.

2.4. Surgical technique

The standard surgical technique in this time period was laminectomy without fusion with midline approach. The level of meningioma was identified with intraoperative fluoroscopy, both prior to opening and prior to laminectomy. Simpson grade 2 resection was attempted, thus the dural attachment was coagulated, but not removed [26]. The dural opening was closed with watertight sutures and usually with sealant patch and tissue glue. In more recent years, and in selected cases with one- or two-level meningioma, a hemilaminotomy with undercutting was performed. Laminoplasty was performed more rarely, mainly in younger patients.

2.5. Spinal cord compression and tumor occupancy percentage

As the cross-sectional area of the spinal cord varies, the SCC was calculated as the spinal cord area at the level of maximum compression in relation to the normal spinal cord area (mean of spinal cord area above and below the tumor). The resulting percentage represents the remaining spinal cord at maximal tumor compression. The cohort with assessable MRI scans (n = 83) was divided into three groups with intervals of SCC (<50%, 50–70%, and >70%) for further investigation. The cut-off was based upon distribution of the variable before exploring, where the intention was to create fairly balanced group sizes. The percentage of tumor occupation was calculated from the cross-sectional area of the meningioma at the level of maximal extent in relation to the cross-sectional area of the dural sac at the same level, multiplying the result by 100.

All segmentations were performed using the software Agfa XERO Viewer, version 8.1.4.110 and the integrated ROI-tool (see Fig. 1). T1-weighted sequences with contrast and/or T2-weighted sequences from the MRI scan closest to surgery were used. As patients were examined on clinical scanners at different hospitals over a long period of time examination parameters varied. Further, intramedullary signal hyperintensities on T2-weighted MR images were noted as well as the location in the spinal canal according to the classification system proposed by Bayoumi et al., which extends from small anterolateral meningiomas (Ia) to complete filling of the spinal canal (IVb) [27].

2.6. Statistics

All analyses were made using SPSS, version 24.0 (Chicago, IL, USA). Statistical significance level was set to $p < 0.05$ and all tests were two-sided. Data distribution was assessed with Q-Q plots which demonstrated a normal distribution for the cohort. Central tendencies were presented as mean ± standard deviation (SD), or median and interquartile range (IQR) if skewed. Fisher exact test was used in 2 × 2 tables. Other categorical data were analyzed with Pearson's chi square test. Independent sample *t*-test or Mann-Whitney *U* test were used when

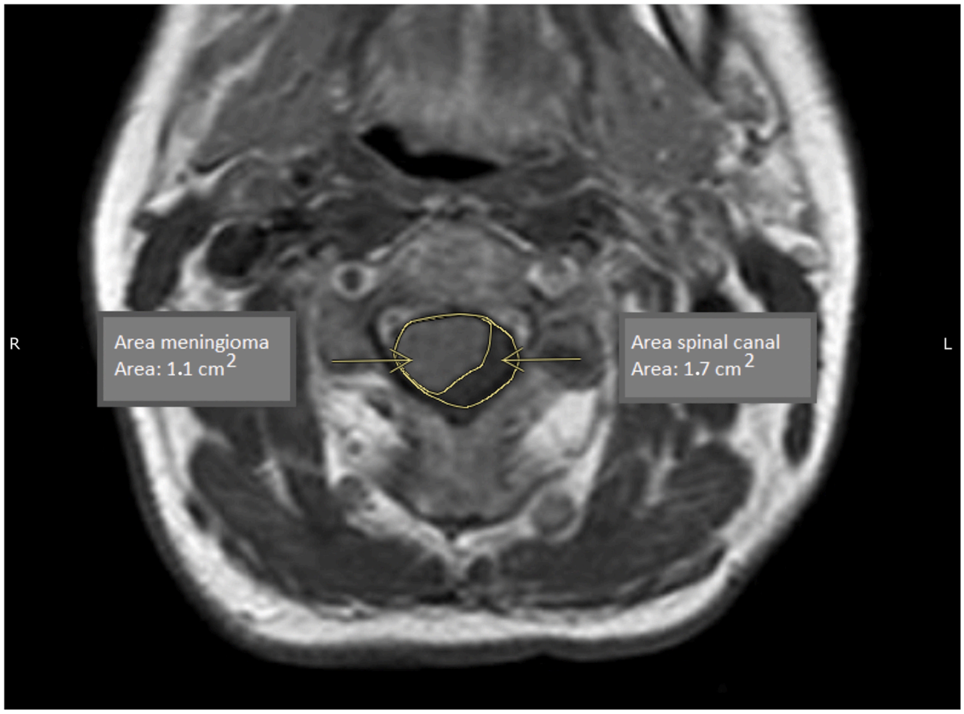

Fig. 1. Example of segmentation of a thoracic spinal meningioma, located predominantly to the patient's right side at level C2–3 and with a tumor occupancy percentage of 64.7%. Measurements were performed with the integrated ROI-tool in the radiological software Agfa XERO Viewer, version 8.1.4.110. The spinal cord is dislocated to the patient's left posterolateral side.

appropriate based on data type. ANOVA was used to analyze the relationship between categorical and continuous data. To further investigate the relationship between neurological deficit and the tumor size we performed an analysis to find a cutoff of percentage of tumor occupation in the spinal canal. The logistic regression was made using a randomized training subset (65%) of original data that was validated against the remaining test data subset (35%) to test the tumor occupancy percentage against motor deficit as the dependent variable. Error i.e. the percentage not correct predictions, is used for evaluation of the cutoff.

2.7. Ethical consideration

This project was approved by the regional ethical committee in Region Västra Götaland (DNR 1119–17).

3. Results

3.1. Cohort characteristics

Patient characteristics are given in Table 1. All but 6 patients (5.4%) experienced symptoms prior to surgery, with sensory disturbance (e.g. paresthesia), gait disturbance or radiculopathy being most common. However, 75.7% of the cohort presented prior to surgery with a Karnofsky score between 80 and 100 (normal activity), while 24.3% presented a score of 50–70 (cares for him/herself, but unable to work or perform normal activity). Main locations were the thoracic region (63.1%) and the cervical region (23.4%). The mean time to first follow-up postoperatively was 107 days (SD 108 days). The majority had a WHO grade 1 meningioma (95.2%) and 5 patients a WHO grade 2 meningioma (4.0%).

3.2. Spinal cord compression

In the 83 patients evaluated for SCC the mean tumor cross sectional area at the level of maximum compression was 1.42 cm^2 (SD 0.60) with larger tumors at the cervical level (mean 1.65 cm^2, SD 0.50) than the thoracic level (1.26 cm^2, SD 0.39). The mean cross-sectional area of the dural sac at maximal tumor area was 2.60 cm^2 (IQR 0.72) at the cervical level compared to 1.69 cm^2 (IQR 0.39) at the thoracic level. The mean extent of SCC was 50.6% (SD 22.7) and mean tumor occupancy percentage was 71.4% (SD 17.3).

Clinical data for patient groups with SCC of $< 50\%$, 50–70%, and $> 70\%$, respectively, are given in Table 2. In general group differences were scarce. As expected higher location classes according to Bayoumi et al. and high tumor occupancy percentage were more common among patients with high SCC. Group differences were also observed for motor deficit and gait disturbances or imbalance ($p = 0.05$, respectively $p = 0.03$).

3.3. Tumor occupancy percentage

A logistic regression model was used to identify a cut-off level of tumor occupancy percentage which causes motor deficit. With the cutoff set to the interval 49–65%, tumor occupancy percentage predicts motor deficit with 90% accuracy, with a sloping accuracy from 65% tumor occupancy (Fig. 2). Therefore, the cut-off level for tumor occupancy percentage to cause motor deficit was chosen to be 65%, see Fig. 1 as example of a 64.7% tumor occupancy.

Further analysis was performed where the patients were divided into two groups depending on tumor occupancy percentage; those with a tumor occupancy of $\leq 65\%$ and those above 65%, see Table 3. Patients with meningiomas with a tumor occupancy of $\leq 65\%$ are more often asymptomatic ($p < 0.01$) prior to surgery. In patients with tumor occupancy $> 65\%$ urinary or fecal incontinence was found in 44.3% of patients compared to 9.1% in those with a tumor occupancy of $\leq 65\%$ ($p < 0.01$). Motor deficit was found in 90.2% of those with high tumor occupancy compared with 59.1% of those with $\leq 65\%$ tumor occupancy percentage ($p < 0.01$).

Table 1
Demographics, clinical presentation, and postoperative complications according to the Clavien-Dindo classification of postoperative complications for the complete cohort of 111 patients.

Variables	
Age, years (SD)	62.5 (13.9)
Female, n patients (%)	86 (77.5)
Time to first follow-up postoperatively, days (SD)	107 (108)
Preoperative symptoms, n patients (%)	
Sensory disturbance	101 (91.0)
Motor deficit	89 (80.2)
Gait disturbance or imbalance	75 (67.6)
Back pain	49 (44.1)
Urinary or fecal incontinence	37 (33.3)
Asymptomatic	6 (5.4)
Location in spinal canal, n patients (%)	
Craniocervical	9 (8.1)
Cervical	26 (23.4)
Thoracic	70 (63.1)
Lumbar	11 (9.9)
Sacral	1 (0.9)
Karnofsky score, n patients (%)	
80–100	84 (75.7)
50–70	27 (24.3)
Complications according to Clavien-Dindo classification[a], n patients (%)	
Grade Ia	3 (2.7)
Grade II[b]	11 (9.9)
Grade IIIa[c]	2 (1.8)
Grade IIIb[d]	7 (6.3)
Grade IVa	0 (0.0)
Grade IVb	0 (0.0)

[a] Number of reported complications counting all complications per patient and not only the most severe one.
[b] Included anaemia, pneumonia, urinary tract infection, wound infection, and stroke;
[c] Included CSF leakage (sutures), liquid accumulation in laminectomy area, and severe pain requiring pain pump;
[d] Included CSF cyst, CSF leakage and infection, implantation of VP-shunt, infection and abscess, burn from lamp leading to necrosis and revision, and immediate postoperative paralysis in legs (although no hematoma at surgical exploration, caused permanent deficit, McCormick score V at follow up).

3.4. Postoperative complications

A total of 21 patients experienced 24 complications, with Clavien-Dindo grade II being the most common, including CSF leakage, severe pain, and accumulation of fluid in the laminectomy area (Table 1). Three patients (2.7%) suffered from CSF leakage postoperatively, and one patient (0.9%) needed reoperation due to the leakage. Three patients (2.7%) were operated due to tumor recurrence (all WHO grade 1), mean time from primary surgery to surgery for recurrence was 71.7 months (SD 60.0). The individual time periods for these three patients from first surgery to operation of recurrence were 11, 73 and 131 months.

3.5. Functional outcome

The change of the McCormick score between before and after surgery for the whole cohort (n = 111) is illustrated in a Sankey diagram, see Fig. 3. McCormick score II was most common prior to surgery (44 patients, 39.6%) followed by grade III (29 patients, 26.1%). Postoperatively, 59 patients (53.2%) experienced improvement in their level of deficit, three patients (2.7%) experienced worsening and an unchanged McCormick score was found in 48 patients (43.2%). Changes in McCormick score was not statistically relevant when diving into group of SCC (see Table 2). However, when studying tumor occupancy percentage with cut, improvement in McCormick score was seen in 66.7% in the group with tumor occupancy > 65%, and 31.8% in those with occupancy < 65% ($p < 0.01$). Additionally, more patients were unchanged in the group with lower tumor occupancy compared with those with occupancy > 65% (68.2%, respectively 31.7%, $p < 0.01$).

Table 2
Patient cohort characteristics in relation to extent of SCC (excluding extradural meningiomas and those without assessable MRI scans), n = 83.

Variables	Spinal cord compression at level of maximal tumor compression			P-value
	< 50% (n = 38)	50–70% (n = 24)	> 70% (n = 21)	
Age in years, mean (SD)	61.6 (11.8)	65.0 (14.7)	63.8 (13.9)	0.59
Female gender, n (%)	27 (71.1)	20 (83.3)	17 (81.0)	0.47
Symptoms at presentation[a]**, n (%)**				
Sensory disturbance	34 (89.5)	23 (95.8)	21 (100.0)	0.24
Motor deficit	27 (71.1)	21 (87.5)	20 (95.2)	**0.05**
Gait disturbance or imbalance	22 (57.9)	18 (75.0)	19 (90.5)	**0.03**
Back pain	18 (47.4)	9 (37.5)	8 (38.1)	0.68
Urinary or fecal incontinence	10 (26.3)	8 (33.3)	11 (52.4)	0.13
Asymptomatic	4 (10.5)	0 (0.0)	1 (4.8)	0.23
Karnofsky status preoperatively, n (%)				
Karnofsky score 80–100	25 (65.8)	20 (83.3)	13 (61.9)	0.22
Tumor location in spinal canal, n (%)				
Craniocervical junction	5 (13.2)	3 (12.5)	0 (0.0)	0.22
Cervical	15 (39.5)	3 (12.5)	3 (14.3)	**0.02**
Thoracic	18 (47.4)	18 (75.0)	17 (81.0)	**0.02**
Location according to Bayoumi et al., n (%)				
Small anterolateral – class Ia	1 (2.6)	0 (0.0)	0 (0.0)	0.55
Small posterolateral – class Ib	3 (7.9)	0 (0.0)	0 (0.0)	0.16
Midline anterior – class IIa	0 (0.0)	0 (0.0)	0 (0.0)	–
Midline posterior – class IIb	1 (2.6)	1 (4.2)	0 (0.0)	0.66
Lateral – class IIc	7 (18.4)	2 (8.3)	1 (4.8)	0.24
Large anterolateral – class IIIa	13 (34.2)	2 (8.3)	0 (0.0)	**< 0.01**
Large posterolateral – class IIIb	9 (23.7)	2 (8.3)	0 (0.0)	**0.03**
Partially filling – class IVa	4 (10.5)	16 (66.7)	14 (66.7)	**< 0.01**
Completely filling – class IVb	0 (0.0)	1 (4.2)	6 (28.6)	**< 0.01**
Mainly left	19 (50.5)	11 (45.8)	14 (66.7)	0.33
Mainly right	18 (47.4)	9 (37.5)	7 (33.3)	0.53
Central	1 (3.6)	4 (16.7)	0 (0.0)	**0.03**
Calcifications on MRI	7 (18.4)	2 (8.3)	4 (19.0)	0.50
Spinal cord edema	1 (2.6)	1 (4.2)	0 (0.0)	0.66
Tumor occupancy percentage, mean % (SD)	59.9 (17.4)	77.1 (8.9)	85.6 (8.8)	**< 0.01**
Percentage SCC, mean in % (SD)	30.5 (13.0)	56.2 (4.8)	80.6 (5.4)	**< 0.01**
WHO grade, n (%)				
Grade 1	43 (100.0)	23 (100.0)	17 (100.0)	
Postoperative McCormick, n (%)				
McCormick postoperative improved	18 (48.6)	13 (54.2)	16 (76.2)	0.12
McCormick postoperative unchanged	19 (51.4)	10 (41.7)	5 (23.8)	0.12
McCormick postoperative worsened	0 (0.0)	1 (4.2)	0 (0.0)	0.29

[a] More than one symptom at presentation possible.

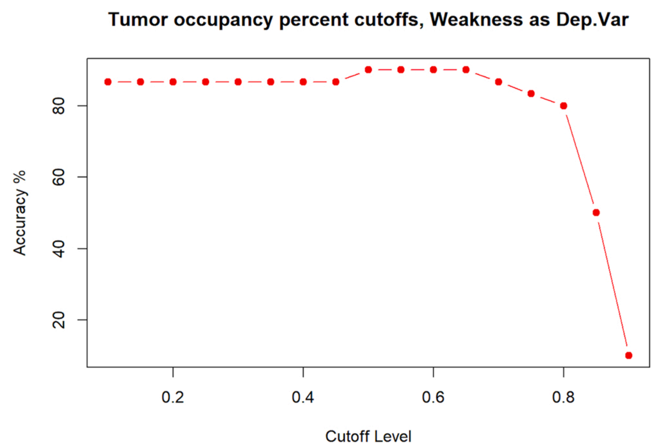

Fig. 2. Accuracy for the prediction of motor deficit depending on the cut-off value for tumor occupancy percentage. When the cut-off is set in the interval 49–65% the tumor occupancy percentage predicts motor deficit with 90% accuracy.

Table 3
Tumor occupancy percentage and neurological deficits, n = 83.

	Tumor occupancy percentage		
	≤ 65% (n = 22)	> 65% (n = 61)	P-value
Symptoms at presentation*, n patients (%)			
Sensory disturbance	19 (86.4)	59 (96.7)	0.07
Motor deficit	13 (59.1)	55 (90.2)	**< 0.01**
Gait disturbance or imbalance	8 (36.4)	51 (83.6)	**< 0.01**
Back pain	10 (45.5)	25 (41.0)	0.72
Urinary or fecal incontinence	2 (9.1)	27 (44.3)	**< 0.01**
Asymptomatic	4 (18.2)	1 (1.6)	**< 0.01**
Postoperative McCormick score change, n patients (%)[a]			
McCormick postoperative improved	7 (31.8)	40 (66.7)	**< 0.01**
McCormick postoperative unchanged	15 (68.2)	19 (31.7)	**< 0.01**
McCormick postoperative worsened	0 (0.0)	1 (1.7)	0.54

[a] One patient missing follow-up

4. Discussion

A tumor occupancy of > 65% was associated higher risk for symptoms such as motor deficit, gait disturbance and urinary or fecal incontinence, and a subsequent functional improvement after surgery. For asymptomatic patients with an incidental meningioma approaching a tumor occupancy percentage of 65%, surgery should be considered. The current study does, however, lack non-operated cases, and comparisons between surgery and natural course of the disease cannot be performed. Even patients with a high tumor occupancy and poor McCormick score preoperatively may benefit from surgery.

Our findings did show a relationship between both higher extent of SCC and higher tumor occupancy (>65%) and motor deficit, with higher amount of patients have motor deficit at presentation, similar to literature [18]. Prior to surgery McCormick score II was the most common in the whole cohort. A majority of the patients experienced improvement of their preoperative deficit (51.4%), even those with the higher McCormick scores IV and V (corresponding to severe motor deficit or sensory disturbance, and para- or quadriplegia, respectively). Literature have shown that higher spinal cord compression may show a worse clinical outcome [18]. This finding is, however, not supported in our material. Pettersson-Segerlind et al. showed a similar finding and speculated in when no irreparable damage to the spinal cord has occurred, patients have the potential of improvement [8]. In our cohort 4.5% of patients experienced worsening at follow-up postoperatively, similar to previous literature [12,28].

The tumor occupancy percentage in our data is similar to the findings by Yamaguchi et al., who found a tumor occupancy of 63.68% as a threshold to cause motor deficit [17]. In our material that threshold was identified to be at 65%. From a clinical perspective tumor occupancy percentage might thus be a more important biomarker indicating the need of surgery than the level of SCC, a parameter often more focused on in radiology. Indication for surgery needs to be based on an individual patient evaluation considering symptoms and radiology findings. This study adds evidence on how to interpret preoperative imaging findings regarding clinical outcome, and can be useful in asymptomatic patients which are increasingly more common [19].

In our data the group of tumor occupancy percentage of ≤ 65% have a higher number of patients unchanged after surgery, which can be explained by the fact that only patients with functional impairment can show an improvement. But in an otherwise fit patient, even if asymptomatic, if tumor occupancy ratio is approaching 60–65%, surgery should be considered, as symptoms are very likely to occur at this point. Despite having a meningioma occupying a large part of the spinal canal, there is hope for improvement also for the group of patients suffering from functional impairment prior to surgery.

Postoperative CSF leakage was identified in 2.7% of the cohort. One patient needed surgery due to the CSF leakage. Previously reported incidence of CSF leakage for both intra- and extradural tumors was 6.6% ± 5.8%, placing our data in the lower range [18,29]. We observed that 2.7% were operated on due to tumor recurrence, also in line with current literature [8,30–34]. However, the time of follow-up of the patients operated in the later part of the inclusion period may not yet have reached time point for recurrence.

4.1. Strengths and limitations

Strengths of this study include the population-based cohort with a long inclusion period and few missing data. Limitations include those associated with a retrospective study design and the lack of assessable imaging data for all cases. Our data have high external validity regarding gender and tumor location, as 78% of patients were female, and the thoracic region was the most common location, similar to previous studies [4,5,18]. Additionally, as no preoperative longitudinal data were available, our material lacks data regarding rate of meningioma growth, a likely important factor in the development of neurological deficit. Finally, we lack data regarding non-operated cases and therefore is a comparison between natural history of spinal meningiomas and operated cases not possible to perform.

5. Conclusion

Patients with an intradural tumor occupancy percentage of > 65% are more likely to have a preoperative symptom and deficit, validating previous findings. Therefore, we suggest that even in asymptomatic, otherwise fit, patients with tumor occupancy approaching 65% should be considered for surgery since there is a high risk of developing deficit with even minimal growth. Concerning recovery, patients with tumor both high tumor occupancy and significantly impaired function tended to improve their functional level postoperatively.

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CRediT authorship contribution statement

Alba Corell: Methodology, Formal analysis, Investigation,

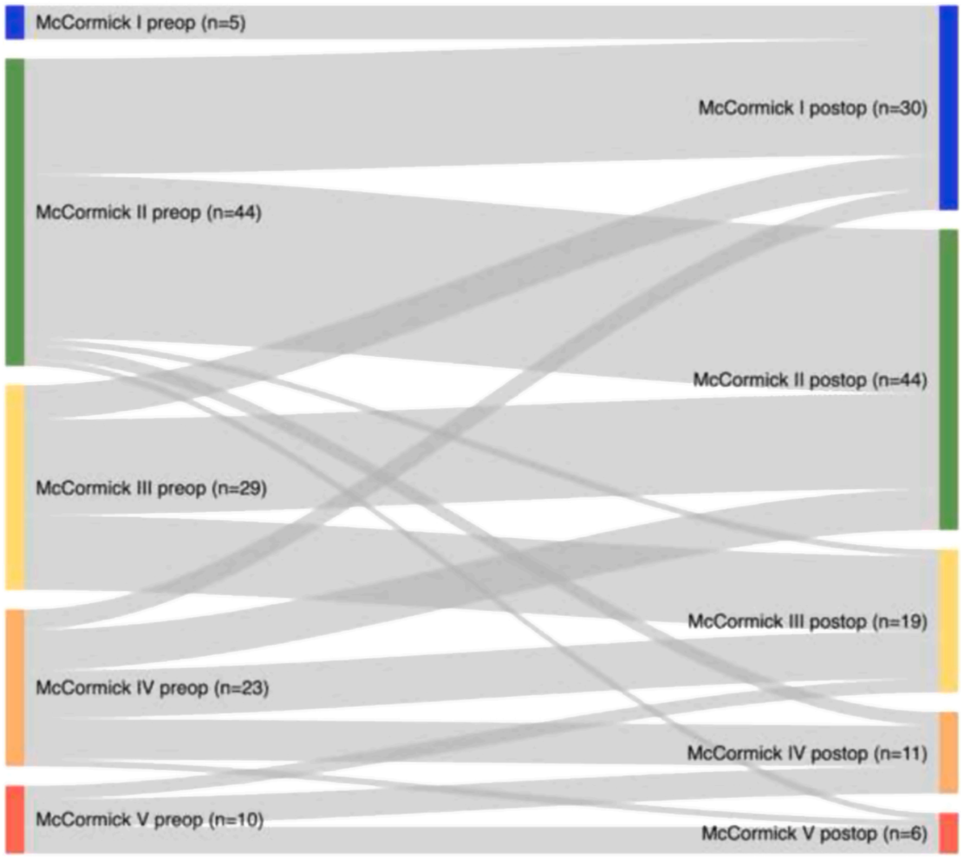

Fig. 3. Sankey chart over preoperative and postoperative McCormick scores (n = 111).

Resources, Writing – original draft. **Charlotte Cerbach:** Investigation, Writing – original draft. **Nickoleta Hoefling:** Writing – review & editing. **Isabella M. Björkman-Burtscher:** Writing – original draft, Writing – review & editing. **Asgeir Store Jakola:** Conceptualization, Methodology, Formal analysis, Supervision.

Declaration of Competing Interest

None.

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