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ORIGINAL ARTICLE

Spinal hemangioblastomas: analysis of surgical outcome and prognostic factors

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Abstract

The prognostic factors for surgically removed spinal hemangioblastomas, the impact of VHL disease on outcome, and the role of intraoperative neuromonitoring are still not completely clear. The aim of this study was to review our experience with spinal hemangioblastomas in order to assess potential predictors of neurological outcome after surgery. All cases of spinal hemangioblastomas removed at two Italian academic institutions from 1985 to 2020 were reviewed. Data about clinical presentation and symptom duration, diagnosis of VHL, surgical approach, use of IONM, duration of hospital stay, follow-up, and modified McCormick grade before and after surgery were extracted. Sixty-one patients (31 F, 30 M) underwent 69 surgeries to remove 74 spinal hemangioblastomas (37 cervical, 32 thoracic, 5 lumbar). Improvement was found in 32.3% of cases, neurological condition remained stable in 51.6% of cases, and deteriorated in 16.1% of patients. A worsening trend in VHL patients and an improvement trend in non-VHL patients were detected, despite the lack of statistical significance. Laminotomy and use of IONM were found to be associated with better outcome, although no association was found between surgery without IONM and worse outcome. In most cases, patients affected by spinal hemangioblastomas can expect a good long-term outcome. In our experience, laminotomy seems to be associated with better outcome compared to laminectomy. While its absence is not associated with worse outcome, IONM seems to be associated with a better neurological outcome. Our study suggests that the more impaired the preoperative neurological condition, the worse the outcome.

Keywords Hemangioblastoma · Spinal cord · VHL · Intramedullary · IONM · Outcome

Introduction

Hemangioblastomas (HBs) of the central nervous system are histologically benign entities that can present with symptoms due to mass effect and compression of neural structures, especially in the presence of associated edema, cyst, or syrinx. They are relatively uncommon, accounting for 2–6% of all spinal cord tumors and 2–15% of intramedullary tumors [1, 22, 39, 44, 46, 68]. They are sporadic in 70–80% of cases, while 20–30% of them are associated to von Hippel-Lindau (VHL) disease [34]. More than 50% have accompanying syringomyelia [10]. To date, only case reports and small series are available in the literature, with just a few large series having been published so far. Moreover, despite being biologically identical, sporadic and syndromic HBs pose specific issues in terms of decision of proper surgical timing and follow-up. Therefore, the optimal management strategy especially related to surgery timing, prognostic factors, and surgical outcome is still controversial. Similarly, surgery with the aid of intraoperative neurophysiological monitoring (IONM) may be favored but its impact is debated.

In this report, we review our experience with 74 spinal HBs removed during 69 procedures in 61 patients (24 of them affected by VHL disease) and provide a thorough review of the pertinent literature. We focused especially on

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the assessment of potential predictors of neurological outcome after surgery.

Methods

We reviewed all cases of spinal hemangioblastomas surgically removed at two Italian academic institutions from January 1985 to October 2020. Data about clinical presentation and symptom duration, diagnosis of VHL, presence of cyst or syrinx, surgical approach, use of IONM, duration of hospital stay, follow-up, and modified McCormick grade before and after surgery were extracted. All patients signed an informed consent before surgery, approved by the Ethical Board of both Institutions.

Clinical evaluation and medical history

The modified McCormick scale was used to evaluate the neurological status before surgery, after surgery, at discharge, and at follow-up. It was possible to retrieve specific onset symptoms for 44 patients.

Imaging evaluation

We reviewed all available preoperative and postoperative contrast-enhanced T1-weighted MRI in order to assess tumor location (cervical, thoracic, lumbar), presence of associated cyst or syrinx, extent of resection, and tumor residual or recurrence.

Surgical procedures

Surgery was performed as described elsewhere and commonly accepted [35]. After laminectomy or laminotomy, the feeding arteries were coagulated first, and the tumor-pial margin was progressively dissected to expose the tumor (Fig. 1). The major draining veins were the last vessels to be sacrificed, finally resecting the tumor en bloc. In selected, more recent cases, indocyanine green video-angiography (ICG-VA) was used during surgery to better distinguish between feeding arteries and draining veins, and to confirm complete resection with absence of residual tumor at the end of the procedure [16]. No patient underwent preoperative embolization or radiosurgery.

Intraoperative neurophysiological monitoring

The anesthesia protocol applied was total intravenous anesthesia (TIVA). More precisely, a continuous infusion of propofol (100–150 µg/kg/min) and fentanyl (1 µg/kg/min) was used, avoiding bolus.

Muscle MEPs were elicited by transcranial electrical stimulation (TES) via corkscrew-like electrodes (Ambu® Neuroline Corkscrew, Ambu, Copenhagen, Denmark) from the scalp. Short trains of 5 to 8 square-wave stimuli of 60–200-mA intensity, 0.5-ms duration, and interstimulus interval (ISI) of 4 ms were applied at a repetition rate up to 2 Hz through electrodes placed at C3-C4 scalp sites for upper limb muscles and C1-C2 for the lower limbs, according to the 10/20 EEG system [37]. To allow for monitoring producing less intense muscle twitching, sometimes a Cz-Fz

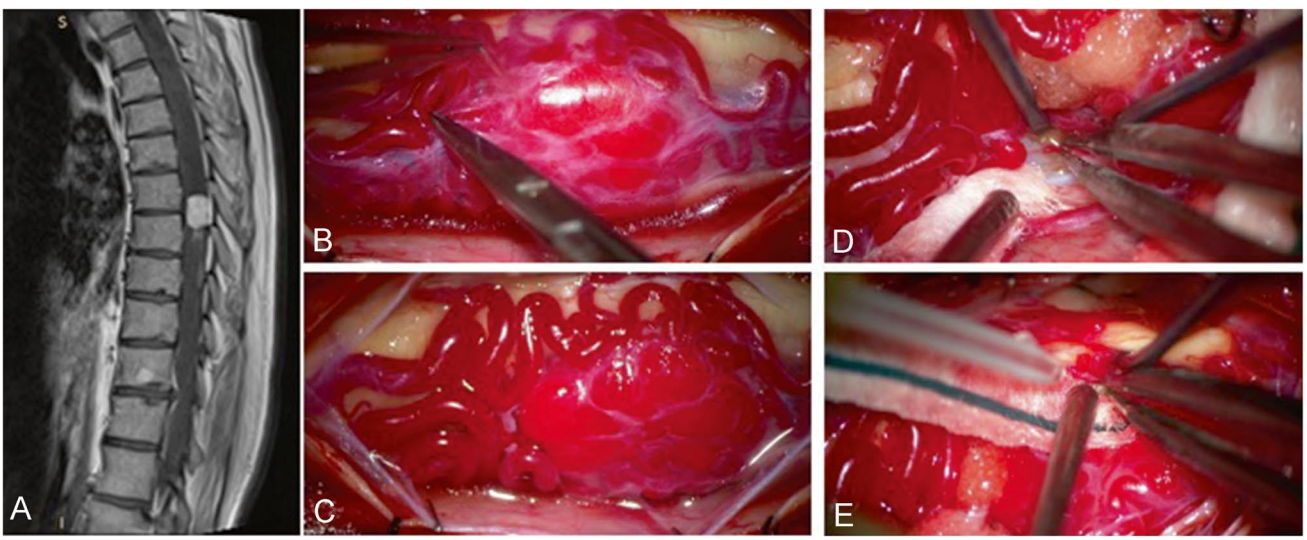

Fig. 1 **A** T1-weighted contrast-enhanced sagittal MRI showing the presence of a dorsal hemangioblastoma. **B** Intraoperative view of arachnoid dissection. **C** Evidence of the nodule and some feeders and draining veins. **D** Arterial feeders are coagulated and sectioned on the ventrolateral side of the hemangioblastoma. **E** Dissection of the pial layer separating the tumor from spinal cord

(leg muscles) or a C1-C2 montage (hand muscles) was preferred. Muscle responses were recorded via needle electrodes (Ambu® Neuroline Subdermal, Ambu, Copenhagen, Denmark) inserted in contralateral upper extremities (abductor pollicis brevis (APB), extensor digitorum longus (EXT), and biceps brachii (Biceps)) and lower extremities (tibialis anterior (TA) and abductor hallucis (AHB)). Somatosensory evoked potentials (SEPs) were evoked at the level of the median and the tibial nerve (20–40 mA, 0.2–0.3-ms duration, 4.3-Hz repetition) and recorded at the scalp via corkscrew electrodes inserted in the scalp at C1'/C2' (legs) and C3'/C4'. To conclude, D-wave monitoring was performed by applying a single TES stimulus with the same montages for muscle MEPs, to record from the epidural or subdural space of the spinal cord caudal to the tumor. Signals were amplified 10.000 times and the bandwidth was filtered 1.5 to 1700 Hz. Baseline D-waves were recorded after exposing the spinal cord. IONM systems used were an Axon Sentinel-4 (AXON Systems, Inc, Hauppage, NY, USA) or an ISIS-IOM (Inomed Medizintechnik GmbH, Emmendingen, Germany).

Literature review

We searched PubMed for previously published articles, with the terms "hemangioblastoma", "spinal", "spinal cord", "intramedullary" used in "AND" and "OR" combinations. Inclusion criteria were the following: (1) studies describing patients who were operated for the removal of spinal HBs, (2) studies reporting more than 1 patient, and (3) English language. Exclusion criteria were (1) case reports, (2) mixed series where no clear data about HBs could be extracted, and (3) cases published before year 2000.

Statistical analysis

We performed a statistical analysis to evaluate and identify potential predictors of neurological outcome. Categorical factors were summarized using frequencies and percentages, while continuous variables were summarized using means and standard deviations. Chi-square test and Student *t* test were implemented for the univariate analysis, and results were considered significant for p values < 0.05 in the contest of two-tailed test. The neurological status at follow-up defined by the modified McCormick score was the outcome variable of choice. Data were analyzed in the context of two different scenarios in which the outcome variable was dichotomized: the first aimed at assessing predictors of clinical improvement, the second at assessing predictors of either clinical stability or improvement. In the first scenario, patients were classified as having an optimal outcome if they had modified McCormick score of 1 and remained stable, or if they had modified McCormick score of 2 to 4 and improved of at least 1 point. Patients were classified as having a suboptimal outcome if a decline of one or more points was recorded on the modified McCormick scale or no improvement with preoperative modified McCormick score of 2 to 4 [66]. In the second scenario, patients were classified as having an optimal outcome if they had modified McCormick score of 1 and remained stable or if they had modified McCormick score of 2 to 4 and either improved or remained stable. Patients were classified as having poor outcome if a decline of one or more points was evidenced at follow-up on the modified McCormick scale. Factors that presented $p < 0.1$ in the univariate analysis were included in a multivariate logistic regression model. All statistical analysis were performed by using SPSS Windows version 26.0.

Results

Patient population

From January 1985 through October 2020, 61 patients (31 F, 30 M) underwent 69 surgeries to remove 74 spinal hemangioblastomas (37 cervical, 32 thoracic, 5 lumbar). All HBs were dorsally or laterally located. The average age at surgery was 35 years (range 2–74 years). Based on the different time and surgeons, we divided the series into two groups: patients operated in the period 1985–2000 (historical group) and those operated in the period 2000–2020 (recent group). Actually, some differences must be considered between the historical and the recent groups, mainly due to the improved tools and technical advancements. We started to routinely use IONM after year 2000, and for this reason, IONM operations are included only in the recent group. Similarly, ICG-VA was used in some cases only in the recent group.

Clinical and radiological features

Motor impairment was most commonly encountered (32 cases), followed by pain (26), sensory impairment (21), and sphincter deficit (18). Symptoms started on average 2 years before diagnosis (20.5 months, range 0–240 months). In the historical group, symptoms lasted on average 28.8 months (range 0–240); in the recent group, they lasted just more than 1 year (15.1 months, range 0–103 months). In 24 patients (39%), a diagnosis of VHL was made by molecular analysis. An associated cyst or syrinx was found in 24 (34.7%) and 30 (43.5%) cases, respectively. Demographic data of patients, tumor characteristics, and preoperative and postoperative modified McCormick grade are summarized in Table 1. In this series, 28 patients were operated on with a modified McCormick grade I. The reason why we decided to operate them was pain in 12 cases, dysesthesias in 11 cases, and subjective motor impediment without any clear motor impairment in 3 cases. Two patients were asymptomatic: in one

Table 1 Case series

Group	Procedure	Patient	Age	Gender	VHL	Level	Symptoms	Symptoms duration (mos)	Surgery type	IOM
Historical group	1	1	26	F	1	C	M, S	9	Laminectomy	
	2	2	26	F	0	T	M, S	12	Laminectomy	
	3	3	63	M	0	C	P	5	Laminectomy	
	4	4	14	M	0	T	P	6	Laminotomy	
	5	5	10	F	0	T	P, M	0	Laminotomy	
	6	6	51	M	0	T	S	9	Laminotomy	
	7	7	24	M	1	C	M	1	Laminectomy	
	8	8	22	M	0	T	P, M	2	Laminectomy	
	9	9	18	M	0	C	P, M	18	Laminectomy	
	10	10	25	F	1	C	S	40	Laminotomy	
	11	11	37	F	0	L	P	30	Laminotomy	
	12	12	22	M	0	C	S	36	Laminectomy	
	13	13	41	F	0	C	P	10	Laminectomy	
	14	14	37	M	1	C	M	14	Laminectomy	
	15	15	19	M	0	T	M, S	2	Laminotomy	
	16	16	2	M	0	C	P	13	Laminotomy	
	17	17	60	M	0	T	M	146	Laminectomy	
	18	18	22	M	0	C	S	1	Laminectomy	
	19	19	43	F	0	C	P	240	Laminotomy	
	20	20	34	M	0	C	P	39	Laminotomy	
	21	21	33	F	0	T	P, M, S	40	Laminotomy	
	22	22	38	F	0	T	S	25	Laminectomy	
	23	23	49	M	0	L	P	6	Laminectomy	
	24	24	24	F	0	C	S	12	Laminotomy	
	25	25	21	F	0	C	M	3	Laminectomy	
	26	26	74	F		T	M	31	Laminectomy	

Table 1 (continued)

Group	Procedure	Patient	Age	Gender	VHL	Level	Symptoms	Symptoms duration (mos)	Surgery type	IOM
Recent group	27	27	18	F	0	T	P	24	Laminotomy	yes
	28	28	16	M	0	T	A		Laminotomy	yes
	29	29	76	M	0	C	S	36	Laminotomy	yes
	30	30	72	F		C	P	5	Laminotomy	yes
	31	31	42	M		T	M	66	Laminectomy	yes
	32	32	35	F	0	T	P	5	Laminotomy	yes
	33	33	46	M		C	M	24	Laminectomy	yes
	34	34	68	M		C	P	10	Laminectomy	yes
	35	35	24	F	0	T	S	10	Laminotomy	yes
	36	36	34	F	0	C	S	4	Laminectomy	yes
	37	37	29	M	0	C	S	6	Laminectomy	yes
	38	38	66	M		C	P, S	36	Laminectomy	yes
	39	39	25	M		T	S	10	Laminotomy	yes
	40	40	17	F	1	T	A		Laminotomy	yes
	41	41	45	F	1	T	M	6	Laminotomy	yes
	42	42	32	M	1	T	M		Laminotomy	yes
	43	43	30	F	1	T	M	12	Laminectomy	no
	44		47			T	P, M	36	Laminectomy	yes
	45	44	48	F	1	T	P, M	5	Laminotomy	yes
	46	45	37	M	0	T	M	6	Laminectomy	yes
	47	46	30	M	1	C	S	12	Laminotomy	yes
	48	47	24	M	1	C	M	6	Laminotomy	yes
	49	48	24	M	1	L	P, M	1	Laminotomy	yes
	50		27			T	P	6	Laminotomy	yes
	51		27			T	P	0	Laminectomy	no
	52	49	30	F	1	C	M	6	Laminectomy	yes
	53	50	28	F	1	C	M	1	Laminectomy	no
	54		31			C	M	12	Laminectomy	no

Table 1 (continued)

Group	Procedure	Patient	Age	Gender	VHL	Level	Symptoms	Symptoms duration (mos)	Surgery type	IOM
	55	51	24	F	1	C	P	7	Laminectomy	no
	56		43			C	M	103	Laminectomy	yes
	57	52	23	M	1	T	P	6	Laminotomy	no
	58	53	32	F	1	C	S	6	Laminectomy	no
	59		34			L	P	3	Laminectomy	no
	60		34			C	M	12	Laminectomy	no
	61	54	45	F	1	C	M	24	Laminectomy	no
	62	55	52	F	1	C	M	36	Laminectomy	no
	63	56	28	F	1	T	S	12	Laminectomy	no
	64		30			T	S	12	Laminectomy	no
	65	57	39	F	1	T	S	8	Laminectomy	no
	66	58	47	F	1	L	P	3	Laminectomy	no
	67	59	36	F	1	C	M	12	Laminectomy	no
	68	60	45	M	1	C	M	6	Laminectomy	no
	69	61	40	M	1	T	M	10	Laminectomy	no

-Group	-Inpatient time (days)	-Cyst or syringe	-Modified McCormick grade				-Last follow up (mos)	-Rec	-Res
			-Preop	**-Postop**	**-Discharge**	**-Last follow-up**			
Historical group	27	1	4		4	4	8	1	
	34	1	3		3	3	7	0	
	11		1		2	2	6	0	
	19	1	2		1	1	12	0	
	21		4		4	2	65	0	
	18	0	2		2	3	2	0	
	19		4		4			0	
	66		4		4	3	23	0	
	72		4		4				1
	68	1	2		2	2	68	0	
	21	1	1		1	1	34		1
	8	1	1		1	1	6		1
	23	0	2		2	1	84	0	
		1	4						1
	63	1	2		3	2	7		1
	42	1	2		2	1	73	0	
	105		4		4	3	21		1
	25		2		2	1	9	0	
	10	1	2		2	2	15	0	

Table 1 (continued)

-Group	-Inpatient time (days)	-Cyst or syringe	-Modified McCormick grade				-Last follow up (mos)	-Rec	-Res
			-Preop	**-Postop**	**-Discharge**	**-Last follow-up**			
	27	1	1		1	1	6	0	
	26	1	3		3	2	82	0	
			2		2	2	73	1	
	17	1	1		1	2	28	1	
	30	1	2		2			0	
	41		4		4			0	
	25		3		3			0	
Recent group	14	1	2	2	2	1	6	0	0
	9	1	1	1	1	1	12	0	0
	8	1	1	2	1	1	13	0	0
	10	1	3	3	3	2	48	0	0
	8	1	2	2	2	1	6	0	0
	7	1	1	1	1	1	11	0	0
	13	1	3	4	3	2	4	0	0
	8	0	2	2	2	1	119	0	0
	7	1	1	2	1	1	39	0	0
	7	0	1	2	1	1	8	0	0
	14	1	1	2	1	1	48	1	0
	35	1	1	3	3			0	0
	8	1	1	2	1	1	180	0	0
	9	1	1	2	1	1	6	0	0
	6	1	4	3	3	3	5	0	0
		1	2	2	2	1	36	0	0
	20	1	1	1	1	3	112	1	0
	28	1	3	3	3	3	2	0	0
	14	1	2	2	2	1	7	0	0
	14	0	1	3	3	2	40	0	0
	8	1	1	1	1	1	38	0	0
	10	1	2	2	1	1	24	0	0
	4	0	1	1	1	1	32	0	0
	6	0	1	1	1	1	1	0	0
	12	0	1	2	2	1	24	0	0
	7	1	2	2	2	1	18	0	0
	10	1	4	5	5	3	36	0	0
	18	1	4	4	4	3	12	0	0
	12	0	2	2	2	4	228	0	0
	6	1	4	5	5	5	12	0	0
	7	0	1	1	1	1	12	0	0
	10	1	1	1	1	1	24	0	0
	7	1	1	1	1	3	6	0	0
	20	1	3	3	3	3	12	0	0
	21	0	5	5	5	5	2	0	1
	20	0	4	4	4	4	100	0	1
	12	0	1	1	1	1	24	0	0
	12	0	1	1	1	2	24	0	0
	11	0	1	1	1	1	32	0	0
	12	0	1	1	1	1	30	0	0

Table 1 (continued)

-Group	-Inpatient time (days)	-Cyst or syringe	-Modified McCormick grade				-Last follow up (mos)	-Rec	-Res
			-Preop	**-Postop**	**-Discharge**	**-Last follow-up**			
	70	1	4	4	4	4	12	0	0
	30	0	3	3	3	4	192	0	0
	13	0	1	1	1	1	150	0	1

C cervical, *T* thoracic, *L* lumbar, *P* pain, *S* sensitive dysfunction, *M* motor dysfunction, *A* asymptomatic, *Rec* recurrence, *Res* residual

case, the tumor was an occasional finding, while the second patient was affected by VHL disease and there was radiological evidence of progressive tumor and cyst enlargement.

Surgery and resection

In 42 cases (60.8%), a laminectomy was performed, while laminotomy was preferred in 27 cases (39.1%), based on the surgeon's preference. In 25/69 cases (36%), intraoperative neurophysiological monitoring was used. In 4 patients affected by VHL disease, more than 1 HB was resected in a single operation (2 thoracic, 1 cervical + 1 thoracic, 2 cervical, 3 cervical, respectively). Patients were discharged after a mean period of 21 days (range 4–105 days); however, the "recent group" presented a significantly lower hospital stay compared to the "historical group" (average 13.7 vs 34.1 days, $p < 0.001$). Overall, 5 cases of recurrence of an apparently totally resected tumor and 9 cases of residual tumor were registered. Among the 9 patients who had an incomplete resection, 2 were lost at follow-up, 6 remained stable (mean follow-up 49.8 months, range 2–150), and 1 improved at 21 months follow-up. Due to the satisfactory clinical evolution, none of them underwent second surgery nor adjuvant therapy.

Literature review

A thorough review of the literature after year 2000 identified 55 articles with a total of 1199 patients (622 males, 463 females; mean age 38.7 years) and 1432 HBs. Overall, 551 patients were affected by VHL disease. Cervical (45.6%) and thoracic (43.8%) were the most frequent locations. Use of IONM was reported in 18 studies (in 1 study, only SEPs were used; in 1 study, IONM was used only during positioning) (Table 2).

Follow-up and outcome

Modified McCormick grading was available in all cases (69) in the preoperative setting, 43 cases in the immediate postoperative evaluation, 68 cases at discharge. Seven patients were lost at follow-up; therefore, recent follow-up examinations were available for 54 patients. Patients were followed up for an average of 46 months (range 1–228 months). In the early (2–3 days) postoperative period, improvement was found in 2.3% of cases, neurological condition remained stable in 67.4% of cases, and deteriorated in 30.2% of cases. At discharge, improvement was found in 4.4% of cases, neurological condition remained stable in 85.3% of cases, and deteriorated in 10.3% of cases. At the last follow-up, improvement was found in 32.3% of cases, neurological condition remained stable in 51.6% of cases, and deteriorated in 16.1% of cases (Fig. 2).

There was no statistical difference between change in modified McCormick score before and after surgery between VHL and non-VHL patients ($p = 0.17$). However, comparing the mean values of modified McCormick changes, there is a worsening trend in VHL patients (mean difference + 0.06) and an improvement trend in non-VHL patients (mean difference − 0.23).

When considering the first scenario, the univariate analysis showed a significant association between type of surgical approach and outcome, where laminotomy favors optimal outcome ($p = 0.03$, OR 5.4, 95% CI 1.6–16.7). Similarly, surgery with IONM favors optimal outcome ($p = 0.017$, OR 5.23, 95% CI 1.42–21.7). Having a preoperative modified McCormick score of I or II, although not significant, showed a trend towards association to better outcome ($p = 0.08$) (Table 3).

No association was found between outcome and age, gender, VHL diagnosis, symptoms duration, presence of cyst or syrinx, and HB location.

Even though the difference was close to significance ($p = 0.06$), optimal and suboptimal groups did not present a significant difference in pre-operative modified McCormick score. A significant difference was however found in

the post-op modified McCormick score ($p = 0.016$, 2.92 VS 1.93), mean difference of − 0.9 (95% CI − 1.7 to − 0.19), at discharge ($p < 0.009$, 2.67 VS 1.83), mean difference of − 0.8 (95% CI − 1.4 to − 0.2) and at follow-up ($p < 0.001$, 1.34 VS 3.05), and mean difference − 1.7 (95% CI − 2.14 to − 1.2).

Univariate analysis in the second scenario confirmed a significant association between type of surgical approach and outcome, where laminectomy correlated with a poorer outcome ($p = 0.02$) (Table 3). No association was found between surgery without IONM and worse outcome ($p = 0.094$).

In the multivariate analysis for both scenarios, surgical approach was the only variable that retained significance (respectively $p = 0.01$ and $p = 0.019$). In the first scenario, preoperative modified McCormick score almost reached statistical significance ($p = 0.056$). In the second scenario, the presence of syrinx almost reached statistical significance ($p = 0.083$).

Discussion

HBs are not commonly encountered by neurosurgeons; however, they are not rare, accounting for 2 to 15% of primary intramedullary spinal cord tumors in reported series. The reported male-to female ratio is 1.6:1 to 5.5:1 [39]. Similar to the literature data, the majority of the HBs in our patients occurred in the cervical and dorsal spinal cord. A reason for this may be the predominant distribution of embryonic precursor cells in these areas of the spinal cord [36, 52, 55]. Overall, onset symptoms in our series recapitulate those commonly reported in other studies: sensory and motor deficits, pain, urinary dysfunction, and occasionally bulbar symptoms.

It is well known that the postoperative neurological outcome typically correlates with the preoperative functional status in patients with intramedullary tumors, and HBs are not an exception [41, 57]. Also, large tumors, and those ventrally located, have been associated with a worse neurological outcome [36], possibly because of a more ventral location of corticospinal fibers.

Postoperatively, 50 to 80% of patients experience a worsening of their neurological status [39]. However, these deficits are usually transient, and patients recover to the baseline after some weeks/months. Almost one-third of our patients experienced postoperative neurological worsening. Nonetheless, consistent with the reported trend, just 1 patient did not recover to the baseline at last follow-up. Assessing the neurological status at the last follow-up is therefore more interesting and reliable than the immediate postoperative outcome.

To assess potential predictors of neurological outcome, we dichotomized outcome in two different ways. The second scenario, in which good outcome includes both improvement and stability, is the most realistic, as simply avoiding symptoms worsening is usually considered a success in this kind of surgery. However, patients experiencing motor or sensitive preoperative symptoms obviously aim to have a complete recovery or at least an improvement, and they often ask how big the chances are to get such a result. Therefore, it would be useful to know also potential predictive factors for improving the patients' neurological condition after surgery. For this reason, we designed the first scenario, where good outcome includes only improvement and neurological stability in case of preoperative modified McCormick grade 1. While the first scenario helps define potential predictors associated with improvement, the second one aims to find possible factors to avoid neurological worsening.

HB outcome and preoperative neurological status

The importance of the neurological condition at admission has been already shown to have an impact on the final outcome [47, 57]. Although our study failed to find a clear statistical significance, our data confirm that preoperative modified McCormick score of I or II tends to be associated with a better outcome, compared to those patients presenting with more severely impaired neurological condition. In case of intramedullary spinal cord tumors, and in general in neurosurgical diseases, it is a general experience that preoperative functional status is the most important predictor of neurological outcome [23, 54, 57]. This is particularly important in case of VHL-associated HBs. In these patients, it is certainly wise to wait until spinal HB becomes symptomatic before indicating surgical removal in order to avoid unnecessary operations, but not too long in order to guarantee the best neurological outcome to the patient. There is a strong association between VHL disease and HBs, and especially spinal HBs. About one-third of patients with spinal HBs are affected by VHL disease, and up to 40% of VHL-related CNS HBs develop in the spinal cord [34, 50]. The management of HBs in VHL patients can be challenging, due to the presence not only of other tumor types as pheochromocytoma, but also of multiple HBs. In 3 of our VHL-affected patients, 2 spinal HBs were resected in a single operation, and in one patient, 3 spinal HBs were removed during the same surgery. These patients were admitted with severe neurological status (modified McCormick 3 and 4), and had a modified McCormick 3 at the last follow-up, confirming that the multifocality of VHL lesions can severely impact on postoperative outcome. Moreover, it is remarkable that the rate of patients with deteriorated neurological condition at discharge (10.3%) is lower than at follow-up (16.1%). After analyzing more carefully the data, we found that VHL-affected patients among those who worsened their neurological condition at discharge and at last follow-up were 43% and

Table 2 Spinal hemangioblastomas: review of the literature since year 2000. Series with more than 1 case were included

Author	Period	Patients	Tumors	VHL	Mean age	Sex	Level	IOM	Outcome	Follow-up	McCormick
Pietilä et al., 2000[58]	1995–1999	15	30	13	27	1 M, 14F		SEPs	6 improved, 17 stable	20 mos	No
Conway et al., 2001[8]	1973–1999	10		7				No			No
Roonprapunt et al., 2001[62]		19	19	0	32	13 M, 6F	13C, 6 T	Yes	13 improved, 6 stable	50 mos	No
Malis, 2002[38]	1967–1990	19	19	0			14C, 5 T	Only during positioning	All recovered or improved	Minimum 8 years	No
Xu et al., 2002[79]		21							20 improved, 1 deteriorated		
Pai & Krishna, 2003[53]		2	2		26	2 M	1 T, 1L	No	2 improved	9.5 mos	No
Lee et al., 2003[31]	1986–2000	14	16	6	37.2	11 M, 3F	8C, 7 T, 1L	No	8 improved, 3 stable, 3 deteriorated	47 mos	No
Huang et al.,2003[19]	1993–2003	10		5	33	3 M, 7F			4 improved, 6 stable	3 mos	Yes
Van Velthoven et al., 2003[73]	1991–2001	22	22	18	38	14 M, 14F	14C, 7 T, 1L	Yes	28.6% improved, 71.4% stable	31 mos	Yes
Lonser et al., 2003[36]	1988–1997	44	86	44	34	26 M, 18F	44C, 33 T, 9L	No	9% deteriorated	44 mos	Yes
Pluta et al., 2003[59]		8	9	8	34	6 M, 2F	5C, 4 T		3 stable, 5 deteriorated	6 mos	
Escott et al., 2004[12]		3	3	0	59	3 M	1C, 2L	No	2 improved, 1 stable		No
Glasker et al., 2005[14]		6	6	3	44	3 M, 3F	1C, 3 T, 2L	No	5 improved, 1 stable		No
Glasker & Van Velthoven, 2005[15]		5	5	2	46	5F	3C, 2 T	No		14 years	No
Biondi et al., 2005[2]		4	4	1	43	2 M, 2F	4L	No	4 improved	3 years	No
Vougioukas et al., 2006[75]		5	5	5	13.6		2C, 3 T	Yes	5 stable		No
Na et al., 2007[48]	1994–2006	9	9	5	37.8	4 M, 5F	5C, 4 T	No	3 improved, 6 stable	22.4 mos	Yes
Boström et al., 2008[3]	1990–2005	23		8			10C, 15 T, 2L	No	5 improved, 18 stable	27 mos	Yes
Dwarakanath et al., 2008[11]	1992–2006	22	22		35.9	13 M, 9F	15C, 1CT, 6 T	No	20 improved or stable, 2 deteriorated	4.6 years	No
Shin et al., 2008[69]	1991–2005	20	24	2	49.4	12 M, 8F	C8, T12, L4	No	7 improved, 14 stable, 3 deteriorated	5.6 years	No
Pavesi et al., 2008[57]	2000–2008	7	19	7			7C, 6 T, 6L	No	4 improved, 3 stable	36.7 mos	No
Kanno et al., 2008[24]	2000–2002	48	74	48	33.5	21 M, 27F	30C, 40 T, 4L	No	83% improved or stable, 17% deteriorated	6.5 years	Yes
Wang, 2008[76]	1991–2002	68	90	20	36.6	44 M, 24F	50C, 32 T, 8L	No	Better outcome for single lesions and cervical location compared to multiple HBs and thoracic location		No
Mandigo et al., 2009[39]	2002–2007	15	18	2	43	7 M, 8F	3C, 13 T, 2L	Often	1 improved, 12 stable, 2 deteriorated	35 mos	yes

Table 2 (continued)

Author	Period	Patients	Tumors	VHL	Mean age	Sex	Level	IOM	Outcome	Follow-up	McCormick
Parker et al., 2009[56]	1985–2002	34	34	25	41	15 M, 19F	28C, 25 T, 7L	No	11 improved, 17 stable, 6 deteriorated	60 mos	Yes
Mehta et al., 2010[44]	1984–2008	108	218	108	33	57 M, 51F	102C, 96 T, 20L	No	6 improved, 86 stable, 16 deteriorated	7 years	Yes
Takai et al., 2010[72]	1988–2008	35		18	39	25 M, 10F	22C, 17 T, 13L	No	3 improved, 16 stable, 11 deteriorated	70 mos	Yes
Clark et al., 2010[7]	1995–2008	20	33	11	49	13 M, 7F	19C, 9 T, 5L	Yes	5 improved, 13 stable, 2 deteriorated	19 weeks	Yes
Kim et al., 2012[26]	1999–2009	12	24	12	42.3	9 M, 3F	6C, 14 T, 4L	Yes	8 stable, 4 deteriorated	49.3 mos	Yes
Park et al., 2012[54]	2003–2012	16	30	4	45.2	12 M, 4F	12C, 14 T, 2L	No	3 improved, 9 stable, 4 deteriorated	90 mos	Yes
Harati et al., 2012[17]	1997–2011	17	20	11	43	10 M, 7F	13C, 5 T, 2L	No	4 improved, 13 stable	57mos	Yes
Hao et al., 2013[16]	2011	7	7	2	34	6 M, 1F	4C, 3 T	Yes	7 stable		yes
Serban & Exergian, 2013[68]	2003–2009	5	5	2	40		2C, 3 T	No	4 stable, 1 deteriorated		No
Sun et al., 2014[71]	23 years	14	15	0	41.5	8 M, 6F	9C, 3 T, 1L	No	53.3% improved, 33.3% stable, 13.3% deteriorated	4 years	No
Boström et al., 2014[4]	1987–2007	5	5					Yes	1 improved, 3 stable, 1 deteriorated	55 mos	Yes
Hojo et al., 2014[18]		3	3		51	2 M, 1F	1 T, 2L	No			No
Deng et al., 2014[10]	2007–2011	92	116	32	33	58 M, 33F	58C, 49 T, 9L	No	38 improved, 40 stable, 14 deteriorated	50 mos	yes
Joaquim et al., 2015[22]	2000–2014	16	16	7	34	10 M, 6F	11C, 5 T	Yes (7)	2 improved, 13 stable, 1 deteriorated	48 mos	Yes
Li et al., 2016[32]	2008–2013	25	25	16	37	17 M, 8F	12C, 8 T, 2L	No	100% McCormick I or II	21 mos	Yes
Liu et al., 2016[33]	1996–2014	21	23	0	45	14 M, 7F	13C, 9 T	Yes (16)	9 improved, 12 long-term dysfunction	17 mos	
Westwick et al., 2016[78]	2000–2010	133	133		48	62 M, 71F					
Kim et al., 2016[25]	2009–2014	6	6		35	5 M, 1F	3C, 3 T	Yes			
Prokopienko et al., 2016[60]		12	12	6	34	5 M, 7F	6C, 2CT, 4 T	Yes	6 improved, 6 stable	5 years	Yes
Yasuda et al., 2016[80]	2010–2013	11	11	1	53.9	8 M, 3F	4C, 5 T, 2L				Yes
Siller et al., 2017[70]	2000–2013	24	27	7	36.8	12 M, 12F	21C, 5 T, 1L	Yes	88.2% improved or stable	7.9 years	Yes
Imagama et al., 2017[21]	1993–2013	28	28	6	43	17 M, 11F	12C, 10 T, 6L	Yes	Probability of good outcome: 79% if preop McCormick grade I and II. 22% if preop grade III, IV, V	10 years	Yes

Table 2 (continued)

Author	Period	Patients	Tumors	VHL	Mean age	Sex	Level	IOM	Outcome	Follow-up	McCormick
Das et al., 2017[9]	2000–2013	14	15	7	33.7	6 M, 8F	8C, 5 T, 1L	No	11 good functional outcome	5 years	Yes
Nemeiko et al., 2019[49]	2010–2015	4			39	3 M, 1F	4C				
Yousef et al., 2019[82]	1997–2016	42		20	44	31 M, 11F	47.6%C, 26.2%T, 9.5%CT		38 improved	20.9 mos	No
Krüger et al., 2019[30]	2010–2018	18	19	16					17 improved or stable, 1 deteriorated		Yes
Sadashivam et al., 2020[63]	2001–2014	15	23	8	33.8	7 M, 8F	9C, 13 T, 1L		80% favorable	5 years	Yes
Wang et al., 2020[77]	2008–2018		3					Yes			
Chang et al., 2020[5]	2005–2015	11	11	0	28.5	8 M, 3F	11C	No	8 improved, 3 stable	6–48 mos	Yes
Richards et al., 2020[61]	2008–2017	6	6	2							Yes
Vergauwen et al., 2020[74]	1996–2013	26	82	26		17 M, 9F	26C, 28 T, 5L	Yes			Yes
Present study	1985–2020	60	68	24	35	30 M, 30F	37C, 32 T, 5L	Yes (25)	20 improved, 32 stable, 10 deteriorated	46 mos	Yes

C cervical, *CT* cervicothoracic, *T* thoracic, *L* lumbar

60%, respectively. Therefore, one possible explanation is the fact that VHL patients can develop new symptoms due to the progression of their disease.

HBs and surgical approach

The association of surgical approach with neurological outcome in spinal surgery has been debated for a long time. Our study showed that laminotomy is significantly associated with a better outcome compared to laminectomy, both in univariate and multivariate logistic regression models. This is in contrast with some studies, which failed to show any correlation between surgical approach and neurological outcome [43]. It is not easy to find a reason to interpret this result. It has been shown that bilateral disruption of paraspinal ligaments, muscles, and the spinous process may cause not only spinal instability, but also pain and neurological and functional compromise [40, 51, 81]. Moreover, laminotomy has been shown to achieve more favorable outcomes than laminectomy in some studies, especially in children and young adults [42]. Besides eventual motor and sensory deficits, the removal of posterior structures may therefore have a role in delaying postoperative recovery. In fact, outcome in our study was measured with the modified McCormick scale, which is a functional scale, not a grading of neurological motor or sensory functions per se. It assesses the ambulatory ability and the independence of patients in daily life, which are affected not only by neurological deficits. Therefore, while motor and sensitive functions depend mainly on the preservation of neural pathways, mobility and functional independence can be affected also by other factors such as paraspinal muscles and osteoligamentous conditions. We hypothesize that laminotomy may guarantee a better preservation of osteoligamentous and muscular connections, thus facilitating postoperative improvement. Nevertheless, the small number of patients is a clear limitation, which can possibly invalidate the results and explain the alleged different outcome in laminotomy vs laminectomy groups.

HBs and IONM

Over the last 20 years, several studies have shown that monitoring spinal cord function during resection of intramedullary spinal cord tumors may not only reassure the surgeon during the procedure, but also potentially lead to improved outcomes [64]. Actually, most of intraoperative neurophysiological derangements are reversible and for this reason, IONM is a valuable tool not only to predict, but also to prevent neurological injury [64]. A combined mMEP and D-wave monitoring protocol during surgery for intramedullary spinal cord tumors proved to significantly improve motor outcome [27, 65, 67]. Despite this evidence, the use of IONM during surgery to remove spinal HBs is still

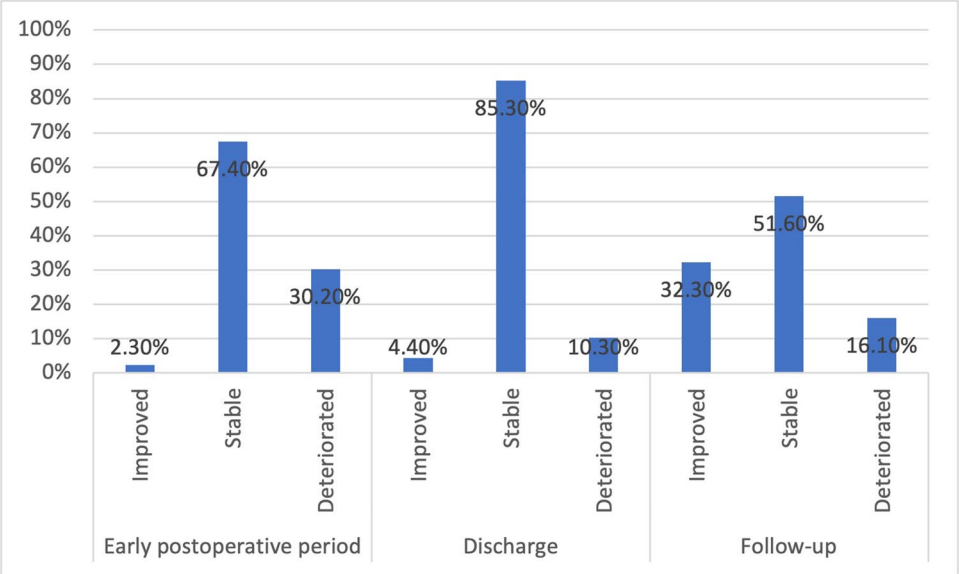

Fig. 2 Outcome of operated patients in the early postoperative period, at discharge, and at last follow-up

considered controversial. Since HBs have normally a clear border separating them from the spinal cord, monitoring is considered by some authors not useful to increase safety in surgical resection [39]. In some cases, the studies focusing on the value of IONM in intramedullary spinal cord tumors include HBs along with other tumor histotypes, making it difficult to assess the role of IONM in the specific case of HBs [4, 6, 13, 20, 29, 65]. Clark et al. published the use of IONM in 20 patients with spinal HBs, focusing on temporary arterial occlusion (7). However, in the last 20 years, the use of IONM during the resection of spinal HBs has become more and more common, with an increasing number of authors showing the importance of such method also in HB removal, both for surgical strategy and for prognostic reasons [21, 25, 45, 60, 70, 74, 77].

In our results, the use of IONM was also associated with optimal outcome. There are a number of reasons which may support this result, which is in line with previous literature [4, 6, 13, 20, 29, 65, 70]. In our clinical setting, it is common practice to abandon surgery if D-wave amplitude decreases over 50% and does not recover with corrective measures such as irrigation, papaverine, and hypertension, as it has been shown to predict persistent motor deficit [47]. Another benefit may have been related to MEP monitoring. Although SEPs are generally considered useful for spinal cord preservation in scoliosis surgery, MEPs are more reliable in monitoring corticospinal tract function, particularly in the short term [28]. Even if they do not appear to be correlated with long-term outcome, they may provide timely information of initial damage to part of the motor system since a decrease of MEPs during surgery normally anticipates a reduction in D-wave amplitude. This may be very useful to modify surgical strategy and timing accordingly. A decrease of MEP amplitudes might suggest the need of making a pause during pial dissection, or at least move to a different side of the tumor, irrigating the spinal cord with warm saline solution to allow amplitudes to recover. This strategy might potentially be beneficial to the spinal cord, which is stressed not only by tumor compression but also by the even cautious microsurgical maneuvers. In any case, it is worth noting that the univariate analysis of our data in the second scenario revealed that the absence of IONM is not associated with a poorer outcome. However, although it is not possible to say that the absence of IONM increases the odds for a poor outcome, our analysis shows that their use may increase the chances for a postoperative improvement of neurological function in the long-term follow-up. Certainly, the results about the use of IONM are related to the study design, which includes two different scenarios. However, these results are not necessarily contradictory. In fact, if we look for factors predicting an improvement after surgery (first scenario), our data show that the use of IONM is associated with postoperative improvement of neurological function at the long-term follow-up. If we look for factors associated with worsening after surgery (second scenario), our results show that the absence of IONM is not associated with postoperative neurological worsening.

VHL vs sporadic HBs

We showed that surgery offers high chances to improve neurological condition or at least to avoid further deterioration due to the HB. Our data suggest that VHL patients may have a poorer outcome compared to those with sporadic HBs. This is in contrast with some published series [9, 63], but in line with others [70, 72, 74], and further research is certainly needed to clarify this issue. However, we expect poorer long-term outcome in VHL patients to be due to disease

Table 3 Univariate analysis of outcome predictors in scenarios 1 and 2

Variable	Scenario 1		Scenario 2	
	Rate of optimal outcome (%)	*p* value	Rate of optimal outcome (%)	*p* value
Gender		0.06		NS
M	78.6		82.1	
F	55.9		85.3	
VHL		NS		NS
Yes	58.1		80.6	
NO	69.2		84.6	
Location		NS		NS
Cervical	60.7		85.7	
Dorsal	73.3		86.7	
Lumbar	60		60	
Laminotomy		**0.009**		**0.02**
Yes	84.6		96.2	
No	52.8		75	
IONM		**0.008**		0.09
Yes	87.5		91.7	
No	50		72.1	
Cyst		NS		NS
Yes	65.2		91.3	
No	65.6		78.1	
Syringe		NS		**0.008**
Yes	70.4		96.3	
No	54.5		68.2	
Modified McCormick pre		0.086		NS
≤ 2	72.7		81.8	
> 2	50		88.9	

VHL, von Hippel Lindau disease; *IOM*, intraoperative monitoring; *NS*, not significant. Statistically significant differences are indicated by bold entries

progression and cumulative functional morbidity rather than the single surgical operation per se, as the growth of multiple HBs may multiply the risk of preoperative neurological deficits and related sequelae from cumulative surgeries, as already pointed out in other studies [74].

Limitations

Our study has several limitations. First, there are limitations due to the study design, which is retrospective and includes a limited number of patients. Second, neurological outcome was not consistently available for all patients due to losses at follow-up. Third, this series is composed by patients who were operated during a long-spanned time period, when different surgical tools and devices were available. Moreover, this series includes patients treated in two different institutions, with a possible bias due to potentially different surgical strategies.

Conclusions

Spinal hemangioblastomas are uncommon, though not rare, benign vascular tumors. Surgery can be curative if no remnants are left. Laminotomy seems to be associated with better outcome compared to laminectomy. While its absence is not associated with worse outcome, IONM seems to be associated with a better neurological outcome. Our study suggests that the more impaired the preoperative neurological condition, the worse the outcome. This finding should prompt neurosurgeons to balance very carefully the timing for surgery, especially in case of VHL-affected patients.

Author contribution Alberto Feletti: conception and design of the work, analysis and interpretation of data, draft of the work, approval of the final version. Alessandro Boaro: analysis and interpretation of data, draft of the work, approval of the final version. Davide Giampiccolo: acquisition and interpretation of data, draft of the work, approval of the final version. Giorgio Casoli: acquisition of data, approval of the final version. Fabio Moscolo: acquisition of data, approval of the final version. Massimiliano Ferrara: acquisition of data, approval of the final version. Francesco Sala: design of the work, interpretation of data, critical revision, approval of the final version. Giacomo Pavesi: design of the work, interpretation of data, critical revision, approval of the final version.

Availability of data and material The corresponding author has full access to all data and material.

Code availability Not applicable.

Declarations

Ethics approval As this is a retrospective study, no approval was required by the Institutional Ethics Board.

Consent to participate Consent to participate was not required because of the retrospective nature of the study, and because patients cannot be identified.

Consent for publication Consent for publication was not required because of the retrospective nature of the study, and because patients cannot be identified.

Conflict of interest The authors declare no competing interests.

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