



# Spinal Cord Hemangioblastomas

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## 14.1 Introduction and Demographics

Hemangioblastomas are histologically benign but highly vascular tumors of the central nervous system (CNS) that can be either sporadic in nature, or in association with von Hippel-Lindau (VHL) syndrome. If VHL is present, the lesions can be multiple and distributed throughout the CNS. A recent meta-analysis of the available literature found that 60% of hemangioblastomas are sporadic in nature and 40% are associated with VHL [1].

Hemangioblastomas are classified as Grade I tumors according to the World Health Organization classification system [2, 3]. The most common location of occurrence is the posterior fossa [4], followed by the spinal cord [5]. Spinal cord hemangioblastoma is rare, accounting for only 2–6% of overall spinal cord tumors; however, they are the third most common primary spinal cord tumor following astrocytoma and ependymoma [6–10].

Spinal hemangioblastoma has been shown to have a male predominance with male-to-female ratios ranging from 1.6:1 to 5:1 in the literature [1, 10, 11]. Patients with

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sporadic hemangioblastoma typically present in the fourth decade of life, and those with VHL-associated hemangioblastoma present in the third decade of life [1, 10–12]. Spinal hemangioblastoma is most commonly found in the dorsum of the cervical spine, followed by the thoracic spine, and—more rarely—the lumbar spine [3, 9, 12–14]. This pattern is likely due to the distribution and quantity of embryonic precursor cells [15–17]. Some reports have shown that spinal hemangioblastomas associated with VHL have a tendency to be present in the caudal spine, compared with sporadic hemangioblastomas [14].

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## 14.2 Histopathology

All cases of VHL-associated hemangioblastoma—and about 50% of sporadic tumors [14, 18, 19]—are due to a malfunction of a tumor suppressor gene: VHL. This gene is located on chromosome 3p25-p26 and encodes pVHL, a protein that helps contribute to the formation of the ubiquitin ligase complex that downregulates hypoxia-induced growth factor (HIF-1). HIF-1 is a transcription factor that modulates the expression of growth factors, such as vascular endothelial growth factor, erythropoietin growth factor, and numerous other growth factors [20]. Some sporadic cases have been attributed to gain-of-function mutations of HIF-1 [21]. The above pathophysiology helps explain the polycythemia encountered in 10% of the patients with VHL.

Microscopically, these histologically benign lesions are composed of a vascular plexus surrounded by stromal cells, which have been shown to be the neoplastic cell of origin [19, 22].

Macroscopically, these tumors are well circumscribed and often in close proximity to the wall of a cyst. They are beefy red in appearance due to their vascular nature and are in striking contrast to their surrounding neural tissue. Lonser et al. [23] has shown that convective extravasation of plasma from the hemangioblastoma is the cause of the edema and subsequent cystic structures associated with these tumors.

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## 14.3 Clinical Presentation

The clinical presentation of spinal cord hemangioblastoma is dependent on the size and location of the tumor, and its effect on the spinal cord by direct growth of the tumor, edema, or an associated cyst or syrinx. The symptoms often include motor weakness in the form of hemiparesis, quadraparesis, or paraparesis at presentation. Sensory abnormalities and pain are often present and related to the dermatomes associated with the tumor or associated cyst and syrinx.

The presentation of patients with these tumors is often delayed due to their slow growth rate and indolent progression to clinical symptomatology [9]. Occasionally, asymptomatic patients have spinal hemangioblastoma lesions incidentally discovered on medical imaging.

The most devastating sequela of hemangioblastomas is hemorrhage and acute motor paresis [10], which can result secondary to bleeding from a spinal

hemangioblastoma. Additionally, lumbago, radiculopathy, and headache can occur due to subarachnoid hemorrhage secondary to this rare event [5, 24].

#### 14.4 Von Hippel–Lindau Disease Considerations

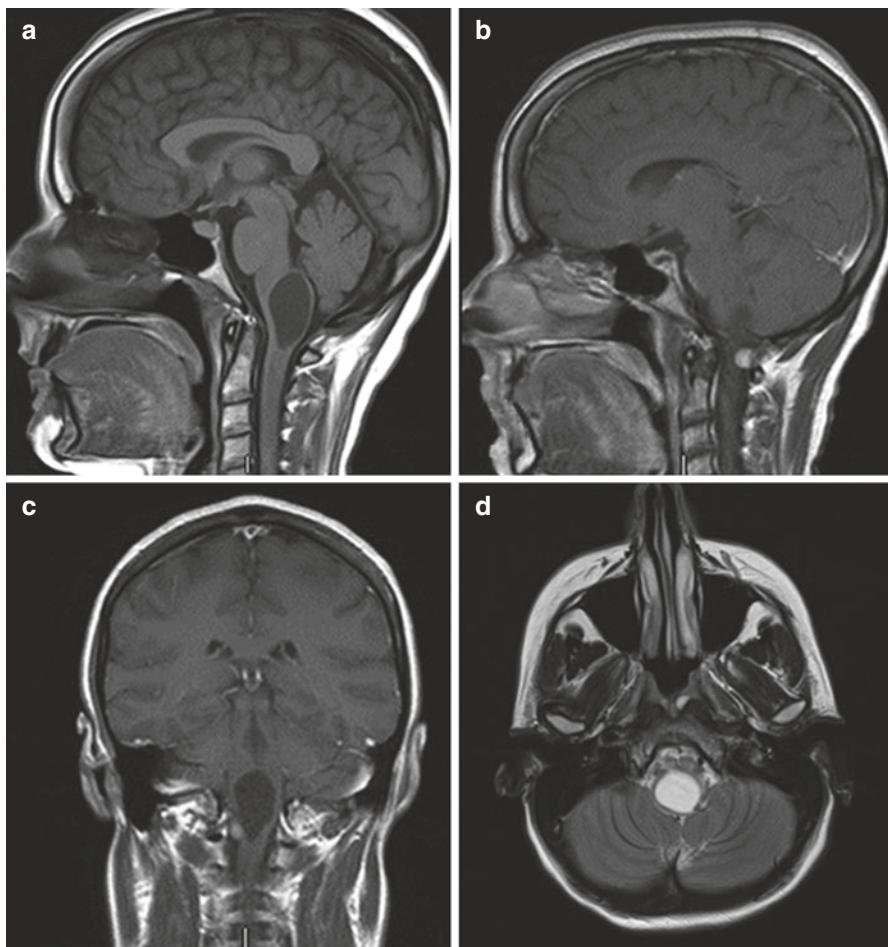
It is estimated that 10–40% of patients with hemangioblastomas harbor the genetic abnormalities of VHL disease [15]. The manifestations of VHL can include hemangioblastomas of the CNS and retina, endolymphatic sac tumors, pheochromocytomas, epididymal cystadenomas, and visceral cysts that commonly involve the kidneys and pancreas and are at increased risk for malignant transformation into carcinoma [25]. VHL is related to a germline mutation on the short arm of chromosome 3 (3p25.3) that is responsible for a tumor suppression gene inherited in an autosomal dominant fashion [26, 27]. Erythropoietin and vascular endothelial growth factor (VEGF) have been shown to be upregulated in hemangioblastomas and are likely related to the pathogenesis of these tumors [28]. Sporadic hemangioblastoma can also be associated with de novo mutations of the VHL gene [17].

The criteria for diagnosis of VHL are a positive family history and the presence of concomitant hemangioblastomas, *or*—in the absence of a family history—2 hemangioblastomas of the CNS, or 1 hemangioblastoma of the CNS and 1 of the following tumors: renal cell carcinoma, visceral cyst, pheochromocytoma, or a definitive mutation found in the VHL gene [4, 18]. It is recommended that all patients with spinal hemangioblastoma have undergo screening for VHL, which often includes entire neuraxis imaging, dedicated abdominal imaging, and fundoscopic eye examinations [3].

Most recommendations in the literature advocates only to operate on symptomatic VHL patients; however, some authors advocate for resection of asymptomatic lesions, which have shown progression and growth with impending neurological sequelae [18]. No study has shown a difference in outcome following surgical resection between VHL -associated and sporadic hemangioblastoma [29, 30]. However, since there is currently no curative treatment for VHL, a strategy of symptomatic palliation is followed and aggressive surgical resection of the lesions should be avoided as the extent of resection is less important than preservation of motor function [31].

#### 14.5 Radiologic Presentation

Magnetic resonance imaging (MRI) remains the most important diagnostic tool for hemangioblastomas (Figs. 14.1 and 14.2). The tumor nodule is hypointense on T2 weighted images. It enhances, homogenously or at times inhomogeneously after contrast application. Usually, there is associated cyst that has the cerebrospinal fluid (CSF) density. Finally, associated spinal cord syrinx may extend rostrally well beyond the location of the tumor nodule.

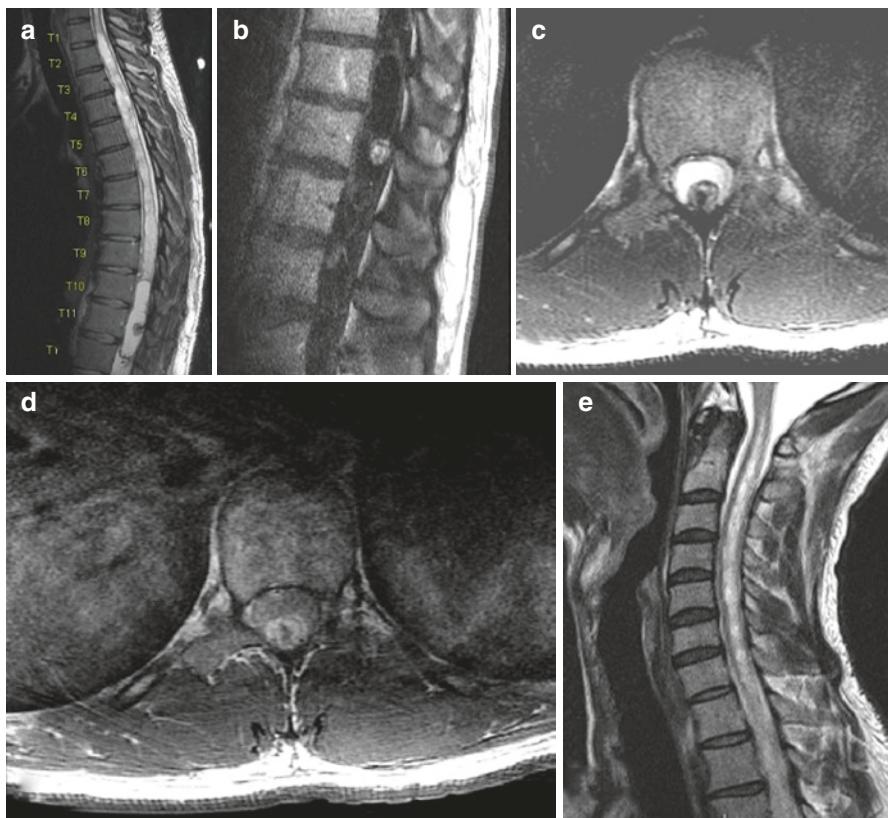


**Fig. 14.1** Medulla oblongata/brain stem hemangioblastoma (Patient 1: VHL disease, female patient operated by the senior author, KIA) [57]. (a) Preoperative MRI of brain. (b) Sagittal pre-contrast T1- weighted MRI showing medulla oblongata cyst. (c) Sagittal post-contrast T1-weighted MRI showing enhancing nodule. (d) Coronal post-contrast T1-weighted MRI showing enhancing nodule and adjacent cyst. (e) Axial T2-weighted MRI showing medullae oblongata cyst

We always obtain plain X-rays in anterior-posterior, lateral, flexion and extension to evaluate spinal alignment and stability for preoperative surgical planning.

## 14.6 Surgical Management

Due to the slow growth rate and benign characteristics of hemangioblastomas, asymptomatic patients with spinal hemangioblastoma may be observed initially—especially in the setting of VHL—in order to avoid an excessive number



**Fig. 14.2** Thoracic spinal cord hemangioblastoma (Patient 2: non-VHL disease, male patient operated by the senior author, KIA) [58]. (a) Preoperative MRI of spine. (b) T2-weighted sagittal MRI showing holocord spinal syrinx (above the lesion) and hypointense spinal cord hemangioblastoma at T11 surrounded by cyst. (c) T1 post-contrast sagittal MRI showing enhancing tumor nodule. (d) T2-weighted axial scan showing a tumor nodule. (e) T1 post-contrast axial MRI showing an enhancing tumor nodule. (f) Sagittal T2-weighted MRI showing syrinx extension to the brain stem

of surgical interventions [3, 17, 24]. Sporadic tumors not associated with VHL are curable by complete surgical excision, and are often present with symptoms that necessitate surgery. The current National Comprehensive Cancer Network guidelines suggest that primary spinal tumors undergo observation if they are asymptomatic, and undergo microsurgical resection if symptomatic [3, 18, 21, 32].

The goal of surgical treatment is complete removal of the tumor. Treatment of an associated cyst is usually not necessary as most improve with time with removal of the tumor [9, 33, 34]. The associated cystic cavity collapses upon nodule resection and pial opening. Additionally, associated edema and cord swelling usually resolves with time, following complete surgical excision [1]. The approach is often dependent upon the location of the tumor within the spinal canal. The posterior midline

approach with spinal laminectomy (or laminoplasty) and complete resection of the tumor is the most common and recommended approach [30].

The resection of a spinal hemangioblastoma should follow several surgical principles:

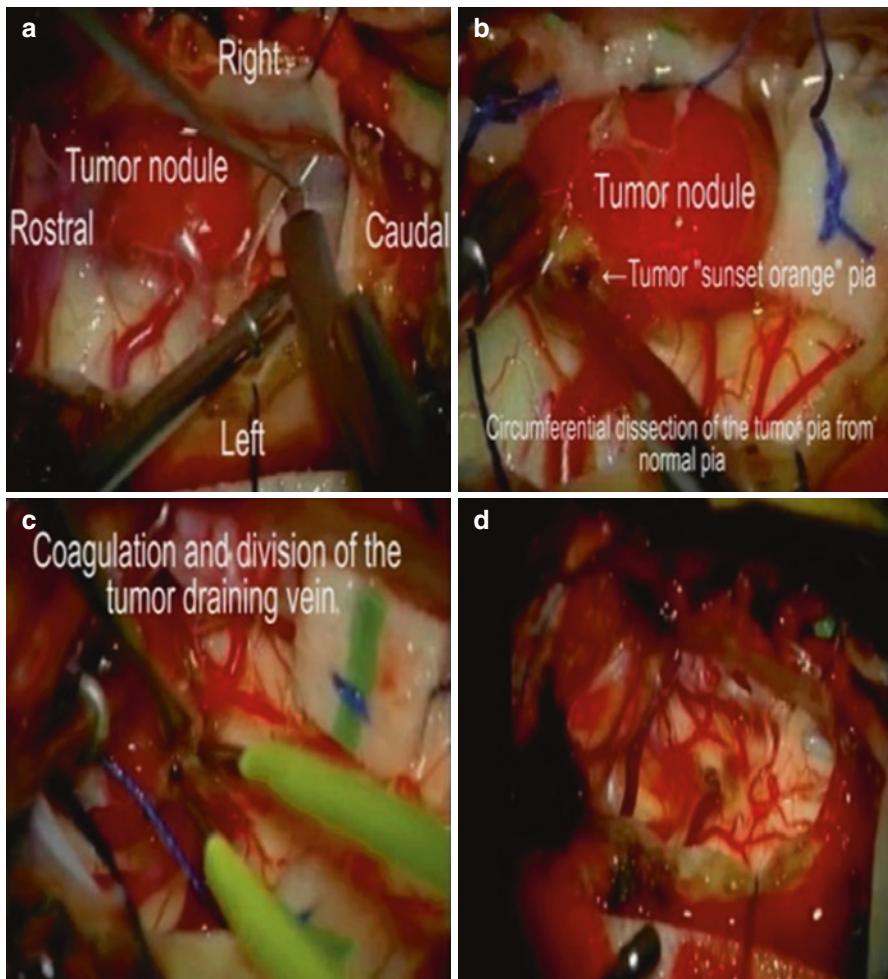
- Avoid entering the tumor nodule and causing significant hemorrhage
- Keep manipulation of neural tissue at a minimum and avoid any spinal vasculature not involved with the tumor nodule
- Use circumferential dissection in the plane between the tumor nodule and gliotic spinal cord
- Look for the junction of normal glistening white spinal cord pia and the sunset orange-yellow pia of the hemangioblastoma nodule with the microsurgical opening of the pia
- Treat the tumor like an arteriovenous malformation with low intensity bipolar coagulation of afferent vessels leading to the tumor nodule, and coagulate vessels close to the tumor in order to avoid damage to the spinal cord; coagulate the efferent veins last
- Shrink the nodule (if necessary) with low intensity coagulation

Due to the vast majority of spinal cord hemangioblastomas being located in the dorsum of the spinal cord, we describe our posterior approach to these tumors. Those tumors located anterior to the dentate ligament may be approached using an anterior or anterolateral approach.

Our surgical technique (senior author, KIA) (Figs. 14.3 and 14.4) involves prone positioning of the patient with laminectomies performed to provide exposure about 1–2 cm above and below the tumor. If tumor location involves cervical-thoracic or cervicolumbar junction, posterior sublimation should be considered. In younger patients and/or patients with tumor spanning several levels, laminoplasty should be considered. Ultrasound may be used to distinguish the tumor location once laminectomies are performed to aid in determining if further removal of the bone is needed. Bleeding from the edges of the bone laminectomy is easily controlled using Gelfoam Powder (Pfizer, New York, NY). We utilize Yasargil bipolar forceps with different, progressive lengths and different tip sizes which we use commensurate with intraoperative distances and surgical situation. Also, we use Yasargil controlled suctions of different sizes, where we can dial the strength of the suction according to intraoperative needs. Micro scissors of different sizes, straight and curved, with blunt and sharp tips in different lengths are used according to intraoperative situation and tactic.

The dura is incised in the midline with care to preserve the arachnoid plane. Retaining sutures are then placed to fasten the dura to surrounding soft tissues. The arachnoid membrane is opened (Figs. 14.3a and 14.4a) and retained to the dura using Ligaclips (Ethicon US, LLC, Somerville, NJ). An operative microscope is used to identify and dissect the hemangioblastoma nodule and free it from the supplying vessels. It is not necessary to enter the cyst cavity, if one is present, as complete tumor removal will eliminate and collapse the syrinx cavity.

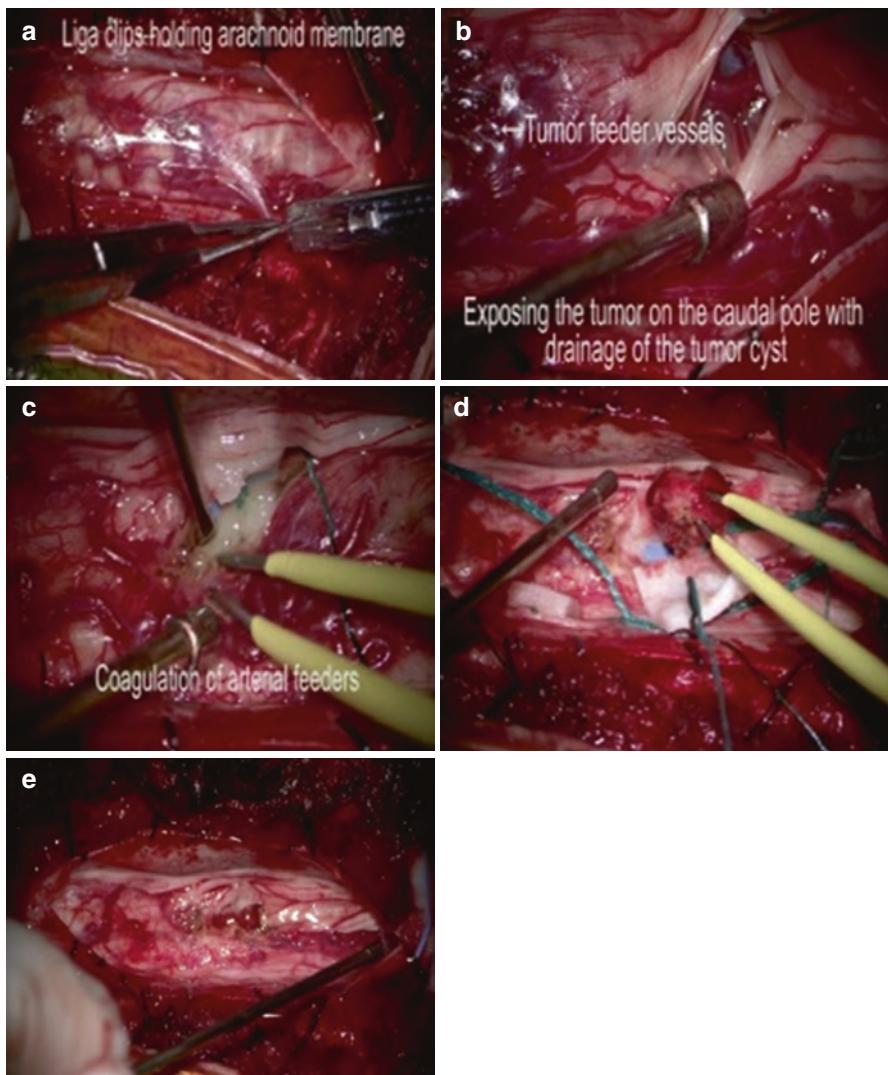
The vasculature (perforators) that abuts the tumor margin is coagulated at low intensity with bipolar cautery; bipolar power is usually at 20–25 watts (Figs. 14.3b



**Fig. 14.3** Intraoperative microsurgical pictures of Patient 1 [57]. (a) Opening of arachnoid membrane. (b) De-vascularization of tumor nodule by coagulation of arterial feeders and division of the “sunset orange” pia of the nodule from white, “glistening” pia of the medulla. (c) Final coagulation of the tumor nodule draining vein before its division and delivery of the nodule. (d) Postoperative view of medulla oblongata after tumor nodule resection

and 14.4c). Care is taken to avoid violating the tumor capsule as this could cause unexpected bleeding. The pia is incised at the tumor margin to identify the gliotic plane between the tumor nodule and the spinal cord. There is often the clear margin between the white, glistening pia of the normal spinal cord and the orange-yellow pia of the tumor nodule. The pia is opened right at the junction between the 2.

The nodule is then circumferentially dissected using bipolar forceps and micro scissors to coagulate and divide the arterial feeder vessels that enter the tumor nodule. The draining vein of the nodule is kept intact until the very end, much like

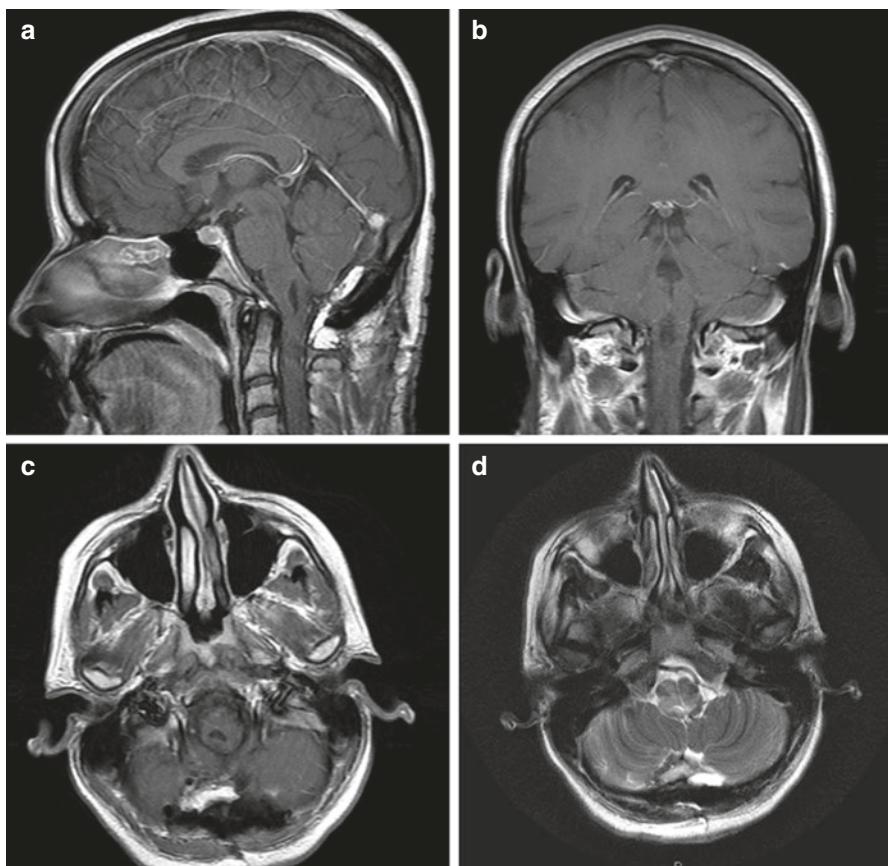


**Fig. 14.4** Intraoperative microsurgical pictures of Patient 2 [58]. (a) Dura is opened. Arachnoid membrane tacked up to the dura with small Ligaclips. (b) Midline myelotomy below the tumor nodule with draining of the adjacent cyst. (c) Coagulation and division of arterial feeders to the nodule. (d) Delivery of the tumor nodule after coagulating and dividing the draining vein. (e) Spinal cord after tumor resection

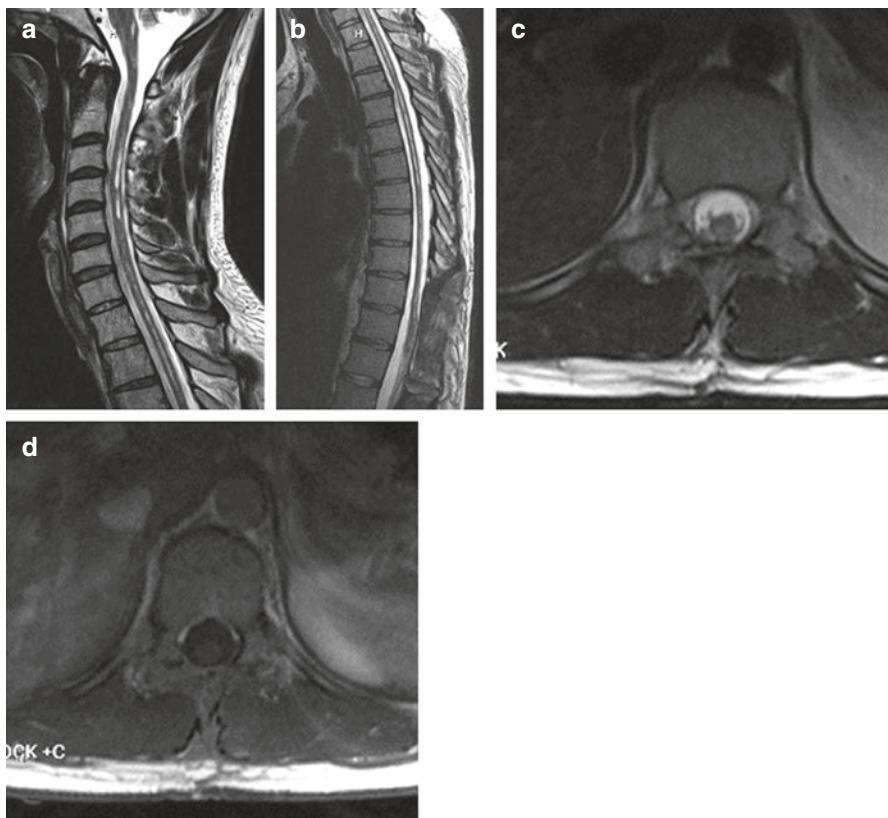
resection of an arteriovenous malformation (Figs. 14.3c and 14.4c–d). Dynamic retraction can be performed by gentle use of the suction accompanied by microcotton pledges as needed. Sensory nerve rootlets embedded in the tumor may be incised at thoracic levels; however, every effort should be made to preserve all neural tissue. Hemostasis is obtained using bipolar cautery (Figs. 14.3d and 14.4e).

The dura is closed in a simple running continuous watertight fashion and the remainder of the wound is closed in the standard fashion. We use a layer of fat tissue harvested from abdominal site at the beginning of surgery to cover the dura, obliterate any remaining “dead space,” and avoid cerebrospinal fluid leak or pseudomeningocele formation [7]. Figures 14.3 and 14.4 show intraoperative photographs of surgical removal of hemangioblastoma while Figs. 14.5 and 14.6 show postoperative MRIs; Videos 14.1 and 14.2 also shows tumor removal.

We strongly recommend—and agree—with the literature that advocates for the routine use of neurophysiological monitoring during any surgery that involves the spinal cord by using somatosensory evoked potentials (SSEPs), motor evoked potential (MEPs), and nerve action potentials (NAP) stimulation [9, 36]. Additionally,



**Fig. 14.5** Postoperative MRI of brain of Patient 1 [57]. (a) Post-contrast sagittal T1-weighted MRI showing cyst collapse after nodule resection. Note the fat graft dorsal to the dura to avoid CSF leak or pseudomeningocele formation. (b) Post-contrast coronal T1-weighted MRI showing cyst collapse after nodule resection. (c) Post-contrast axial T1-weighted MRI showing cyst collapse after nodule resection. Note the fat graft dorsal to the dura to avoid CSF leak or pseudomeningocele formation. (d) T2-weighted axial MRI showing cyst collapse after nodule resection



**Fig. 14.6** Postoperative MRI of brain of Patient 2 [58]. (a) Sagittal T2-weighted MRI of cervical spine showing syrinx collapse after tumor resection. (b) Sagittal T2-weighted MRI of thoracic spine showing syrinx collapse after tumor resection. (c) Axial T2-weighted MRI showing postoperative thoracic spinal cord after tumor resection. (d) Axial T1-weighted post-contrast MRI showing postoperative thoracic spinal cord after tumor resection

temporary artery clipping of the main feeding artery when coupled with SEPs and MEPs can provide additional information to the surgeon on the safety of sacrificing vessels that are adjacent to and supply the tumor in order to facilitate safe removal of the nodule [37].

There are several common types of hemangioblastomas described that have special relevance to the technical aspects of surgical excision (Table 14.1).

## 14.7 Considerations in Pregnancy

The progression or presentation of spinal hemangioblastomas is known to occur during pregnancy and may be due to the increased blood volume and changing hormonal milieu [11, 38, 39]. Surgical resection has been noted to be the preferred

**Table 14.1** Types of spinal hemangioblastoma and preferred approaches<sup>a</sup>

Type	Details	Surgical approach
Dorsal intramedullary	Most common; covered by a layer of pia mater and requires a midline myelotomy; located near dorsal nerve root entry zone.	Posterior approach Midline Myelotomy
Ventral intramedullary	Rare; outcomes worse due to difficulty of surgical excision.	Anterior or anterolateral approach [35]
Exophytic	Reaches the surface and can be directly removed; obviates the need for a midline myelotomy.	Posterior approach
Intradural Extramedullary	Does not have a direct attachment to cord parenchyma; can be directly removed.	Posterior approach
Extradural	Commonly arises from spinal nerves.	Posterior approach

<sup>a</sup>Adapted from Sun et al. [1].

treatment in order to prevent progression of neurological deficits, and has been noted to be safely performed in the second and third trimesters without increased risks of abortion or preterm labor. However, it is advisable to postpone surgery until after delivery with close observation of the patient and the patient's neurological condition, if clinically appropriate.

Careful consideration should be taken to prevent radiation to the fetus from diagnostic or intraoperative tests [39–42]. It is advised that a team-based approach with obstetric, anesthetic, and neurosurgical physicians should be used in the care of these patients.

## 14.8 Medical Management

Several medical therapies have been evaluated in the literature for treatment of difficult to resect spinal hemangioblastoma. Bevacizumab is a monoclonal antibody that blocks angiogenesis due to its effect on vascular endothelial growth factor A. There have been case reports of bevacizumab treatment causing significant tumor regression in a patient with an unresectable spinal cord hemangioblastoma [43]. Thalidomide has recently been shown to be effective in some cases of unresectable hemangioblastoma [44, 45]. However, the role of adjuvant chemotherapy in the treatment of hemangioblastoma remains controversial [2].

## 14.9 Radiosurgery

There have been reports of patients with spinal hemangioblastomas being treated with radiosurgery for unresectable tumors. However, radiosurgery has been reported to be associated with unfavorable outcomes, such as radiation necrosis, and often does not address the underlying symptom-causing syrinx [2, 46].

## 14.10 Preoperative Embolization

Preoperative embolization has been used in some reports in the literature to decrease vascularity. However, this often does not completely address the vascularity of the tumor and often requires super-selective catheterization, which can place the normal spinal parenchyma at risk and is usually not needed for complete resection [11]. It is, therefore, not used in the majority of patients undergoing surgical excision [37, 47–49], and in our opinion is mostly unnecessary.

## 14.11 Outcomes

The first excision of a spinal cord hemangioblastoma was described by Schultze in 1912 [20]. The neurological morbidity of spinal cord tumor surgery was poor until improvements in microsurgery and imaging arrived in the 1960s and 1970s [49–53]. We have compiled a summary of the available data in the literature showing outcomes of surgical resection of spinal hemangioblastomas in Table 14.2.

### 14.11.1 Neurological Outcome

Tumor location and size have been shown to affect outcome, with larger ventral and ventrolateral tumors associated with worse surgical outcomes [17, 30]. The McCormick functional status scale (Table 14.3) has been used in the literature to grade the neurological outcome of intrinsic spinal cord tumor surgery [54].

This scale, while not validated, has been used extensively in research of spinal cord tumors and hemangioblastomas. Several studies have shown that preoperative neurological status has a tendency to predict the postoperative neurological status of patients following resection of hemangioblastoma [31]. Microsurgical removal of tumors can result in favorable neurological outcomes, if good technique is applied and the conditions of the tumor are favorable (i.e., location, size, vascularity, and plane between tumor and spinal cord). The majority of patients operated on remain neurologically stable with a small subset who undergo neurological deterioration in the intraoperative period, but who eventually improve over time [17]. While not common, permanent neurological deterioration does occur and is often related to larger tumors that are not located in the dorsum of the spinal cord. Table 14.2 describes the outcomes of all of the case series that we could find available in the English literature as of October 2017.

### 14.11.2 Tumor Recurrence

Tumor recurrence can be due to either regrowth of new tumor, incomplete resection, or growth of new tumors in both VHL associated and sporadic hemangioblastoma. Young age, short duration of symptoms, multiple CNS tumors, and having VHL

**Table 14.2** Literature review on studies evaluating spinal cord hemangioblastoma (both sporadic and VHL)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Browne TR (1975) USA Retrospective cohort and literature review	N = 85 Male = 42 Female = 38 VHL: 36 (33%) Male = n/a Female = n/a	71 patients underwent surgeries, 7 patients had surgery followed by radiation, and only 2 received radiation therapy	Not formally documented	Not formally documented	Symptoms persisted with incomplete resection whereas almost complete resolution caused symptoms. If incompletely resected, symptoms eventually recurred even if the cystic component had been removed with radiation for the residual tumor.
Guidetti B (1979) Italy Retrospective cohort	N = 6 Male = 3 Female = 3 VHL: 0 Male = n/a Female = n/a	6 patients underwent 6 surgeries	1 patient had intra-operative cardiac arrest and died after 24 h. 5 patients (83%) improved neurologically with phased return to work.	Mean, 28.5 (range, 2 months–11 years)	Patients undergoing complete surgical resection showed good neurological recovery compared with those who had incomplete resection or palliative procedures. Total removal is possible if a good plane is found between the tumor and the cord.

(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Pluta RM (2003) USA Retrospective cohort	N = 8 Male = 6 Female = 2 VHL: n/a Male = n/a Female = n/a	9 patients underwent surgery for ventral tumors: A posterior approach was selected to treat 5 patients (laminectomy and posterior myelotomy) in 4 patients, and the posterolateral approach in 1 patient; an anterior approach (corpectomy and arthrodesis) was selected to treat the remaining 3 patients.	Immediately after surgery, the ability to ambulate remained unchanged in patients in whom an anterior approach had been performed, but deteriorated significantly in patients in whom a posterior approach had been used, because of motor weakness (4 of 5 patients) and/or proprioceptive sensory loss (3 of 5 patients). This difference in ambulation remained significant 6 months after surgery.	Mean for anterior approach, 28 +/− 9.2 months Mean for posterior approach, 79.6 +/− 38.6 months	The presence of an intraspinal syrinx should not influence the choice of surgical approach used to remove ventral spinal hemangioblastomas. In selected cases, the immediate and long-term results are appreciably better when surgery is performed using an anterior approach rather than a posterior or posterolateral approach.
Lee DK (2003) Korea Retrospective cohort	N = 14 Male = 11 Female = 3 VHL: n/a Male = n/a Female = n/a	14 patients underwent surgery with pre-operative angiography performed in 11 and pre-operative embolization performed in 4.	In 4 patients with preoperative embolization, intraoperative bleeding was minimal and total resection was possible. In 3 of 4 patients without total resection, their functional outcomes were aggravated postoperatively. At the last follow-up 8 patients were improved, 3 were stationary, and 3 deteriorated. All patients who showed improvements underwent total resection.	Mean, 47 months.	Total resection resulted in a better outcome. Preoperative embolization could be effective in the reduction of intraoperative bleeding and facilitate total resection with an improved surgical outcome.

Lonser RR (2003) USA Retrospective cohort	N = 44 VHL:44 (100%) Male = 26 Female = 18	44 patients with VHL underwent 55 operations with resection of 86 spinal cord hemangioblastomas.	84% of patients remained at the same McCormick grade, 7% improved (1 grade), and 9% worsened (1 or more grades) as of the final clinical assessment.	Mean, 44 months	Surgery improves McCormick status but having a ventral or ventrolateral lesion and the lesion being larger than 500mm <sup>3</sup> is associated with poor outcomes. The presence of a syrinx does not influence outcomes and the removal of a tumor associated with a syrinx leads to its resolution, alleviating the need for entering the syrinx, and doing so has strongly been discouraged.
Lonser RR (2005) USA Description of surgical technique	>190 operations (almost all were VHL patients)	More than 190 operations using microsurgical technique for resection	n/a	n/a	Hemangioblastomas, in contrast to other spinal cord tumors, are benign tumors that can be excised en bloc. Their technique uses administration of steroids at induction, a direct posterior approach to the tumor, ultrasound-guided identification of tumor site, development of a precise dissection plane, and relatively bloodless surgical field with no need to enter the syrinx associated with the tumor.

(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Biondi A (2005) France Retrospective cohort	N = 4 Male = 2 Female = 2 VHL: 1	4 patients with lower spinal hemangioblastomas underwent embolization followed by surgery. Male = n/a Female = n/a	Embolization caused no permanent complications, although 1 patient with a cauda equina hemangioblastoma mildly worsened after the endovascular procedure, but recovered before surgery. At surgery, the tumor was completely removed in all cases. At 1-year postsurgical follow-up, 2 patients recovered completely from neurologic deficits, and 2 showed significant recovery.	Mean, 3.5 years	Pre-op embolization ensures less blood loss and easier manipulation of the tumor. It is therefore a useful procedure in aiding surgical resection.
Sharma BS (2007) India Retrospective cohort	N = 22 Male = 13 Female = 9 VHL:3	22 patients underwent surgery Male = n/a Female = n/a	20 patients (91%) showed post-operative improvement or stability in their neurological deficits.	Mean, 4.6 years	Microsurgical resection is the treatment of choice even in the presence of gross pre-op neurological deficits.
Na JH (2007) Korea Retrospective cohort	N = 9 Male = 4 Female = 5 VHL: 5	9 patients underwent surgery Male = n/a Female = n/a	All patients showed improvement or stability in their neurological deficits and there were no complications.	Mean, 22.4	Complete microsurgical resection in all cases of spinal hemangioblastomas provided good post-operative outcomes, and syrinxes associated with these tumors spontaneously resolved post-operatively.

<p>Na JH (2007) Korea Retrospective cohort</p> <p>N = 9 Male = 4 Female = 5 VHL: 3 Male = 2 Female = 3</p>	<p>9 patients underwent surgery</p> <p>All patients remained stable post-operatively at 6-month follow-up whereas 3 (33%) improved by 1 grade at final follow-up with the remainder staying at their pre-operative grade. There were no complications or post-operative worsening of neurological symptoms.</p>	<p>Mean, 22.4 months</p>	<p>The posterior approach is safe and effective. Postoperatively, edema and syrinx resolved spontaneously. For early diagnosis and family consultation, the VHL mutation analysis was useful in patients with family history and in those with multiple hemangioblastomas.</p>
<p>Bostrom A (2008) Germany Retrospective cohort</p> <p>N = 23 Male = n/a Female = n/a VHL: 8 (35%) Male = n/a Female = n/a</p>	<p>23 patients underwent surgery</p> <p>18 patients remained neurologically stable and 5 patients improved post-operatively. There was 1 case of tumor recurrence (even though the patient improved post-operatively) and 1 case of cerebrospinal fluid leak.</p>	<p>6 months</p>	<p>DSA is mandatory for pre-operative work-up, and en bloc resection by occlusion of the arteries and using bipolar coagulation is crucial. Radiographic progression and/or symptomatic progression prompts resection in VHL patients, but radiographic progression is a rarely-used an indication for surgery in patients with sporadic hemangioblastomas.</p>

(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Shin DA (2009) Korea Retrospective cohort	N = 20 Male = 12 Female = 8 VHL: 2 (10%) Male = n/a F:n/a	20 patients underwent 24 operations	18 (90%) patients remained at the same grade or improved post-operatively; 2 patients progressed to a higher grade post-operatively; 5 had recurrence, 3 of whom had revision; 1 had radiation and 1 was observed.	Mean, 5.6 years	Pre-operative motor weakness and paraesthesia are more commonly present in those with cystic components; syrinxes shrank in 86% after tumor removal. En bloc resection is the fundamental surgical principle, aided by the tumor having a well-defined capsule.
Mandigo CE (2009) USA Retrospective cohort	N = 15 Male = 7 Female = 8 VHL: 4 Male = n/a Female = n/a	15 patients underwent 17 surgeries for the removal of 18 hemangioblastomas	1 patient worsened by 1 grade post-operatively; 1 improved by 1 grade; all others (87%) stayed at the same grade.	Mean, 35 months	Pregnancy can exacerbate the symptoms of these tumors— But microsurgical en bloc resection remains the treatment of choice in all cases. A technique that has been perfected over almost a century, it causes minimal blood loss and most importantly, minimal neurological morbidity.

Clark A.J (2010) USA Retrospective cohort	N = 20 Male = n/a Female = n/a VHL: 11 (55%) Male = n/a Female = n/a	20 patients underwent surgery, 5 of whom had additional intra-operative temporal artery occlusion with concurrent neuromonitoring.	Of the 20 patients, 5 improved, 13 remained stable, and 2 worsened. Of the 5 treated with TAO, 2 improved, 3 remained stable, and none worsened. Median McCormick's functional grade of patients treated with TAO was II and improved to I after the operation, whereas the grade of those not treated with TAO remained unchanged at II.	Mean, 19 weeks	Temporary arterial occlusion with concurrent neuromonitoring is a fast, safe, and efficient method that may assist the surgeon in difficult cases in differentiating tumor vessels from those supplying the spinal cord.
Mehtha GU (2010) USA retrospective cohort	N = 108 Male = 57 Female = 51 VHL: 108 (100%) Male = 57 Female = 51	108 patients underwent 156 operations for resection of 218 spinal cord hemangioblastomas.	At 6-month follow-up, patients were stable or improved after 149 operations (96%) and worse after 7 operations (4%). The proportion of patients remaining functionally stable at 2, 5, 10, and 15 years' follow-up Was 93, 86, 78, and 78%, respectively.	Mean, 7 years +/- 5 years	Ventral or completely intramedullary tumors were associated with an increased risk of post-operative worsening. Symptom progression and not radiological progression alone should prompt surgical resection in VHL patients, which is a strategy that permits long-term stability of neurological status in most cases.

(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Kim TY (2012) Korea Retrospective cohort	N = 12 Male = 9 Female = 3 VHL: 12 (100%) Male = 9 Female = 3	12 patients with 24 spinal cord hemangioblastomas were divided into 3 treatment groups: Group 1 (13 tumors), asymptomatic tumors at initial diagnosis followed with serial imaging studies; group 2 (4 tumors), asymptomatic tumors at initial diagnosis that were subsequently resected; and group 3 (7 tumors), symptomatic tumors at initial diagnosis, all of which were resected.	7 tumors exhibited symptoms when diagnosed, and 17 did not. Among these 17 tumors, 9 tumors (53%) were ultimately resected. The 5 asymptomatic patients (42%) were McCormick grade I and remained at the same grade post-operatively. Among the symptomatic patients, 3 showed a 1-point reduction in functional status (25%), and 1 worsened from grade I to grade IV (8%).	Mean, 49.3 months	VHL patients with a large tumor and an extensive syrinx were at a greater risk of neurological deficits, some of which may be irreversible. Thus, the functional outcomes of patients with a large tumor are affected more by the presence of neurological symptoms and deficits than by the tumor volume itself, and thus resection of significantly large asymptomatic tumors might bring about better outcomes.
Harati A (2012) Finland Retrospective cohort	N = 17 Male = 10 Female = 7 VHL: 11 Male = N/A Female = N/A	17 patients underwent microsurgical resection of 20 tumors.	No patient had neurological decline on long-term follow-up. Among the patients with VHL, 5 patients with pre-operative sensorimotor deficits showed improvement of their symptoms but never regained full function. One patient who presented with tetraplegia remained the same.	Mean, 57 months	Asymptomatic patients with VHL benefit from early resection as well as those with a tumor size larger than 55mm <sup>3</sup> .

Park C.H (2012) Korea Retrospective cohort	Total: 16 Male = 12 Female = 4 VHL: 4 Male = n/a Female = n/a	16 patients underwent 30 operations; of these, 10 patients had pre-operative angiography and 3 had pre-operative embolization.	10 patients had total resection whereas 6 had subtotal resection. Postoperatively, improvement was noted in 18.7%, stability in 56.3%, but 25% were worse. Stable postoperative neurological functions were found in 83% of patients with preoperative McCormick grade I, and total resection was achieved In 75% of these patients.	Mean, 90 months	Capsule of the tumor is fragile, which is why pre-operative angiography is mandatory for knowledge of feeders and to avoid intra-operative bleeding and subtotal resection. In addition, the feeding artery should be dissected before the draining vein is coagulated. Preoperative mild deficit and fastidious microsurgical technique are associated with favorable outcomes, whereas age over 70 is a predictor of poor outcome. There is no correlation between postoperative functional outcomes and other variable factors, such as tumor size or location, the extent of resection, the recurrence or progression of the lesion, and the number of repeated surgeries. In addition, a non-aggressive surgical approach is the optimal strategy to preserve the neurological function in spinal cord hemangioblastomas associated with VHL disease.
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(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Deng X (2014) China Retrospective cohort	N = 92 Male = 59 Female = 33 VHL: 32 (34.8%) Male = n/a Female = n/a	92 patients underwent 102 operations for resection of 116 intraspinal hemangioblastomas. Preoperatively, 13 patients underwent DSA, 15 patients underwent 3D CTA.	Gross-total resection was achieved for 109 tumors (94.0%), and subtotal resection for 7 tumors. Functional outcome improved for 38 patients (41.3%), remained stable for 40 (43.5%), and deteriorated for 14 (15.2%).	Mean, 50 months	Gross-total resection leads to better outcomes. Subtotal resection is a risk factor for poor outcomes. Compared with spinal DSA, 3D CTA is a promising technique because it is noninvasive, takes less time to perform, requires lower X-ray doses and less contrast media, results in fewer complications, and offers high accuracy for delineating the feeding arteries.
Sun H.I (2014) Turkey Retrospective cohort	N = 14 Male = 8 Female = 6 VHL: 0 Male = n/a Female = n/a	14 patients with sporadic spinal hemangioblastoma underwent 15 operations during a span of 23 years.	Symptoms improved after 8 (53.3%) of 15 operations, remained the same after 5 (33.3%), and worsened after 2 (13.3%). Gross total resection was achieved in all cases, and there was 1 recurrence in 15 years.	Mean, 4 years	Sporadic spinal hemangioblastomas occur slightly more often than those associated with VHL disease, are most commonly encountered as solitary lesions, and are most frequently located in the upper spinal cord. Excellent surgical results can be achieved with microsurgery without the use of preoperative or postoperative adjuvant therapies, and the long-term outcome is good with only rare recurrences.

Joaquin AF (2015) USA Retrospective cohort	N = 16 Male = 10 Female = 6 VHL: 7 Male = n/a Female = n/a	16 patients underwent 17 surgeries.	Total resection was achieved in all cases; 4 patients had some functional worsening immediately after surgery but at 6 month follow-up, 1 patient remained functionally worse, 2 improved, and the remainder (81%) remained stable.	Mean, 48 months	The use of neurophysiological monitoring, accompanied with a meticulous surgical technique that avoids disruption of the spinal cord outside the tumor boundaries, can almost work as a guarantee that postoperative deficits will not occur—Surgery generally maintains the patient's preoperative neurological status.
Liu A (2016) USA Retrospective cohort	N = 21 Male = 14 Female = 7 VHL: 0 Male = n/a Female = n/a	21 patients with sporadic intramedullary spinal hemangioblastomas underwent 23 surgeries.	Total resection was achieved in all but 1 surgery, and no cases involved intraoperative complications. However, postoperative complications occurred after 5 cases; 12 patients (57%) experienced long-term dysfunction after surgery, and 2 patients experienced recurrence requiring a second surgery.	Mean, 12 months	Total resection can be achieved successfully with surgery and effectively improve neurological function with rare recurrences.

(continued)

**Table 14.2** (continued)

Authors (Year) Location Study Type	Patients (No.)	Treatment	Outcome	Follow up	Findings
Pan J (2016) USA Retrospective cohort	N = 28 Male = 14 Female = 14 VHL: 14 (50%) Male = n/a Female = n/a	28 patients with 48 tumors were treated using CyberKnife image-guided radiosurgery.	Radiographic follow-up was available for 19 patients with 34 tumors; 32 (94.1%) tumors were radiographically stable or displayed signs of regression. Actuarial control rates at 1, 3, and 5 years were 96.1%, 92.3%, and 92.3%, respectively. Clinical evaluation on follow-up was available for 13 patients with 16 tumors; 13 (81.2%) tumors in 10 patients had symptomatic improvement. No patient developed any complications related to radiosurgery.	Mean, 54.3 months	Stereotactic radiosurgery allows for excellent local control and symptomatic management of spinal hemangioblastomas in both VHL and sporadic lesions with an optimal safety profile.
Das JM (2017) India Retrospective cohort	N = 14 Male = 6 Female = 8 VHL: 7 (50%) Male = 3 Female = 4	14 patients underwent 18 surgeries.	8 patients had neurological deterioration in postoperative period (5 recovered); 11 (79%) patients had good functional outcome at 5 years.	Mean, 5 years	Microsurgical removal of spinal hemangioblastoma can result in postoperative neurological deterioration, however, complete microsurgical excision can result in good functional outcomes at 5 years.

Siller S (2017) Germany Retrospective cohort	N = 24 Male = 12 Female = 12 VHL: 10 Male = n/a Female = n/a	24 patients underwent 26 operations for 27 spinal cord hemangioblastomas with intra-operative neurophysiology	Long-term follow-up evaluation revealed a stable or improved McCormick myelopathy grade in 88.2% of the patients, and 88.2% reported a stable or improved overall outcome, according to Odom's criteria. Long-term general performance was excellent with 88.2% having a ECOG performance status grade ≤ 1.	Mean, 7 +/- 4 years
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CTA computed tomography angiography, DSA digital subtraction angiography, ECOG Eastern Cooperative Oncology Group, IONM intraoperative neuromonitoring, n/a not applicable, TAO temporary arterial occlusion, VHL von Hippel-Landau

**Table 14.3** McCormick functional status scale

Grade	Description
I	Neurologically intact, may have minimal dysesthesia, normal gait
II	Mild motor or sensory deficit, patient maintains functional independence
III	Moderate deficit, limitation of function, independent with external aid
IV	Severe motor or sensory deficit, limited function, dependent
V	Paraplegia or quadriplegia, even with flickering movement

disease have been associated with increased tumor recurrence [55]. Sporadic hemangioblastomas have been reported to have a recurrence rate of 6–7% following surgical excision and often occur many years after surgical resection illustrating the need for continued long-term follow-up of these patients [1]. Hemangioblastomas associated with vHL have been classified into three different growth patterns: saltatory, linear, or exponential with tumor growth rates of 4mm<sup>3</sup>/y, 24mm<sup>3</sup>/y, and 79mm<sup>3</sup>/y respectively [56]. Additionally, hemangioblastomas occurring in the spinal cord and cauda equina grew at slower rates compared with those found elsewhere in the CNS (median 0.3mm<sup>3</sup>/y and 0mm<sup>3</sup>/y respectively) and higher growth rates were observed in males compared to females [56].

## References

1. Sun HI, Ozduman K, Usseli MI, Ozgen S, Pamir MN. Sporadic spinal hemangioblastomas can be effectively treated by microsurgery alone. *World Neurosurg.* 2014;82(5):836–47. <https://doi.org/10.1016/j.wneu.2014.05.024>.
2. Chang SD, Meisel JA, Hancock SL, Martin DP, McManus M, Adler JR Jr. Treatment of hemangioblastomas in von Hippel-Lindau disease with linear accelerator-based radiosurgery. *Neurosurgery.* 1998;43(1):28–34. discussion 34–25
3. Joaquim AF, Ghizoni E, dos Santos MJ, Valadares MG, da Silva FS, Tedeschi H. Intramedullary hemangioblastomas: surgical results in 16 patients. *Neurosurg Focus.* 2015;39(2):E18. <https://doi.org/10.3171/2015.5.FOCUS15171>.
4. Neumann HP, Eggert HR, Weigel K, Friedburg H, Wiestler OD, Schollmeyer P. Hemangioblastomas of the central nervous system. A 10-year study with special reference to von Hippel-Lindau syndrome. *J Neurosurg.* 1989;70(1):24–30. <https://doi.org/10.3171/jns.1989.70.1.0024>.
5. Murota T, Symon L. Surgical management of hemangioblastoma of the spinal cord: a report of 18 cases. *Neurosurgery.* 1989;25(5):699–707. discussion 708
6. Arnautovic K, Arnautovic A (2009) Extramedullary intradural spinal tumors: a review of modern diagnostic and treatment options and a report of a series. *Bosnian journal of basic medical sciences/Udruzenje basicnih medicinskih znanosti = Association of Basic Medical Sciences 9 Suppl* 1:40–45.
7. Arnautovic KI, Kovacevic M. CSF-related complications after Intradural spinal tumor surgery: utility of an autologous fat graft. *Med Arch.* 2016;70(6):460–5. <https://doi.org/10.5455/mendarh.2016.70.460-465>.

8. Garces-Ambrossi GL, McGirt MJ, Mehta VA, Sciubba DM, Witham TF, Bydon A, Wolinsky JP, Jallo GI, Gokaslan ZL. Factors associated with progression-free survival and long-term neurological outcome after resection of intramedullary spinal cord tumors: analysis of 101 consecutive cases. *J Neurosurg Spine*. 2009;11(5):591–9. <https://doi.org/10.3171/2009.4.SPINE08159>.
9. Liu A, Jain A, Sankey EW, Jallo GI, Bettegowda C. Sporadic intramedullary hemangioblastoma of the spine: a single institutional review of 21 cases. *Neurol Res*. 2016;38(3):205–9. <https://doi.org/10.1179/1743132815Y.0000000097>.
10. Mehta GU, Asthagiri AR, Bakhtian KD, Auh S, Oldfield EH, Lonser RR. Functional outcome after resection of spinal cord hemangioblastomas associated with von Hippel-Lindau disease. *J Neurosurg Spine*. 2010;12(3):233–42. <https://doi.org/10.3171/2009.10.SPINE09592>.
11. Mandigo CE, Ogden AT, Angevine PD, McCormick PC. Operative management of spinal hemangioblastoma. *Neurosurgery*. 2009;65(6):1166–77. <https://doi.org/10.1227/01.NEU.0000359306.74674.C4>.
12. Kanno H, Yamamoto I, Nishikawa R, Matsutani M, Wakabayashi T, Yoshida J, Shitara N, Yamasaki I, Shuin T, Clinical VHLRGiJ (2009) Spinal cord hemangioblastomas in von Hippel-Lindau disease. *Spinal Cord* 47 (6):447–452. <https://doi.org/10.1038/sc.2008.151>.
13. Roonprapunt C, Silvera VM, Setton A, Freed D, Epstein FJ, Jallo GI. Surgical management of isolated hemangioblastomas of the spinal cord. *Neurosurgery*. 2001;49(2):321–7. discussion 327–328.
14. Takai K, Taniguchi M, Takahashi H, Usui M, Saito N. Comparative analysis of spinal hemangioblastomas in sporadic disease and Von Hippel-Lindau syndrome. *Neurol Med Chir*. 2010;50(7):560–7.
15. Lonser RR, Glenn GM, Walther M, Chew EY, Libutti SK, Linehan WM, Oldfield EH. von Hippel-Lindau disease. *Lancet*. 2003;361(9374):2059–67. [https://doi.org/10.1016/S0140-6736\(03\)13643-4](https://doi.org/10.1016/S0140-6736(03)13643-4).
16. Lonser RR, Wait SD, Butman JA, Vortmeyer AO, Walther MM, Governale LS, Oldfield EH. Surgical management of lumbosacral nerve root hemangioblastomas in von Hippel-Lindau syndrome. *J Neurosurg*. 2003;99(1 Suppl):64–9.
17. Lonser RR, Weil RJ, Wanebo JE, Devroom HL, Oldfield EH. Surgical management of spinal cord hemangioblastomas in patients with von Hippel-Lindau disease. *J Neurosurg*. 2003;98(1):106–16. <https://doi.org/10.3171/jns.2003.98.1.0106>.
18. Van Velthoven V, Reinacher PC, Klisch J, Neumann HP, Glasker S. Treatment of intramedullary hemangioblastomas, with special attention to von Hippel-Lindau disease. *Neurosurgery*. 2003;53(6):1306–13. discussion 1313–1304
19. Vortmeyer AO, Gnarra JR, Emmert-Buck MR, Katz D, Linehan WM, Oldfield EH, Zhuang Z. von Hippel-Lindau gene deletion detected in the stromal cell component of a cerebellar hemangioblastoma associated with von Hippel-Lindau disease. *Hum Pathol*. 1997;28(5):540–3.
20. Shultze F. Further contribution to diagnosis and surgical treatment of tumors of the spinal cord and the spinal cord. *Deutsch Med*. 1912;38:1676–9.
21. Wang C, Zhang J, Liu A, Sun B. Surgical management of medullary hemangioblastoma. Report of 47 cases. *Surg Neurol*. 2001;56(4):218–26. discussion 226–217
22. Berkman RA, Merrill MJ, Reinhold WC, Monacci WT, Saxena A, Clark WC, Robertson JT, Ali IU, Oldfield EH. Expression of the vascular permeability factor/vascular endothelial growth factor gene in central nervous system neoplasms. *J Clin Invest*. 1993;91(1):153–9. <https://doi.org/10.1172/JCI116165>.
23. Lonser RR, Oldfield EH. Microsurgical resection of spinal cord hemangioblastomas. *Neurosurgery*. 2005;57(4 Suppl):372–6. discussion 372–376
24. Miller DJ, McCutcheon IE. Hemangioblastomas and other uncommon intramedullary tumors. *J Neuro-Oncol*. 2000;47(3):253–70.
25. Butman JA, Linehan WM, Lonser RR. Neurologic manifestations of von Hippel-Lindau disease. *JAMA*. 2008;300(11):1334–42. <https://doi.org/10.1001/jama.300.11.1334>.

26. Catapano D, Muscarella LA, Guarneri V, Zelante L, D'Angelo VA, D'Agruma L. Hemangioblastomas of central nervous system: molecular genetic analysis and clinical management. *Neurosurgery*. 2005;56(6):1215–21. discussion 1221
27. Latif F, Tory K, Gnarra J, Yao M, Duh FM, Orcutt ML, Stackhouse T, Kuzmin I, Modi W, Geil L, et al. Identification of the von Hippel-Lindau disease tumor suppressor gene. *Science*. 1993;260(5112):1317–20.
28. Krieg M, Marti HH, Plate KH. Coexpression of erythropoietin and vascular endothelial growth factor in nervous system tumors associated with von Hippel-Lindau tumor suppressor gene loss of function. *Blood*. 1998;92(9):3388–93.
29. Conway JE, Chou D, Clatterbuck RE, Brem H, Long DM, Rigamonti D. Hemangioblastomas of the central nervous system in von Hippel-Lindau syndrome and sporadic disease. *Neurosurgery*. 2001;48(1):55–62. discussion 62–53
30. Das JM, Kesavapany K, Sadasivam S, Nair SN. Microsurgical treatment of sporadic and von Hippel-Lindau disease associated spinal Hemangioblastomas: a single-institution experience. *Asian Spine J*. 2017;11(4):548–55. <https://doi.org/10.4184/asj.2017.11.4.548>.
31. Park CH, Lee CH, Hyun SJ, Jahng TA, Kim HJ, Kim KJ. Surgical outcome of spinal cord hemangioblastomas. *J Korean Neurosurg Soc*. 2012;52(3):221–7. <https://doi.org/10.3340/jkns.2012.52.3.221>.
32. Yang S, Yang X, Hong G. Surgical treatment of one hundred seventy-four intramedullary spinal cord tumors. *Spine*. 2009;34(24):2705–10. <https://doi.org/10.1097/BRS.0b013e3181b43484>.
33. Na JH, Kim HS, Eoh W, Kim JH, Kim JS, Kim ES. Spinal cord hemangioblastoma : diagnosis and clinical outcome after surgical treatment. *J Korean Neurosurg Soc*. 2007;42(6):436–40. <https://doi.org/10.3340/jkns.2007.42.6.436>.
34. Oppenlander ME, Spetzler RF. Advances in spinal hemangioblastoma surgery. *World Neurosurg*. 2010;74(1):116–7. <https://doi.org/10.1016/j.wneu.2010.04.018>.
35. Pluta RM, Iuliano B, DeVroom HL, Nguyen T, Oldfield EH. Comparison of anterior and posterior surgical approaches in the treatment of ventral spinal hemangioblastomas in patients with von Hippel-Lindau disease. *J Neurosurg*. 2003;98(1):117–24. <https://doi.org/10.3171/jns.2003.98.1.0117>.
36. Hsu W, Bettogowda C, Jallo GI. Intramedullary spinal cord tumor surgery: can we do it without intraoperative neurophysiological monitoring? *Child's Nerv Syst*. 2010;26(2):241–5. <https://doi.org/10.1007/s00381-009-1022-4>.
37. Clark AJ, Lu DC, Richardson RM, Tihan T, Parsa AT, Chou D, Barbaro NM, Kunwar S, Weinstein PR, Lawton MT, Berger MS, McDermott MW. Surgical technique of temporary arterial occlusion in the operative management of spinal hemangioblastomas. *World Neurosurg*. 2010;74(1):200–5. <https://doi.org/10.1016/j.wneu.2010.03.016>.
38. Cushing HBP (1928) Tumors arising from the blood vessels of the brain: Angiomatous malformations and Hemangioblastomas. Springfield,
39. Delisle MF, Valimohamed F, Money D, Douglas MJ. Central nervous system complications of von Hippel-Lindau disease and pregnancy: perinatal considerations: case report and literature review. *J Matern Fetal Med*. 2000;9(4):242–7. [https://doi.org/10.1002/1520-6661\(200007/08\)9:4<242::AID-MFM11>3.0.CO;2-5](https://doi.org/10.1002/1520-6661(200007/08)9:4<242::AID-MFM11>3.0.CO;2-5).
40. Kurne A, Bakar B, Arsava EM, Tan E. Pregnancy associated quadripareisis in a patient with Von-Hippel Lindau disease. *J Neurol*. 2003;250(2):234–5.
41. Ogasawara KK, Ogasawara EM, Hirata G. Pregnancy complicated by von Hippel-Lindau disease. *Obstet Gynecol*. 1995;85(5 Pt 2):829–31.
42. Ortega-Martinez M, Cabezudo JM, Fernandez-Portales I, Pineda-Palomo M, Rodriguez-Sanchez JA, Bernal-Garcia LM. Multiple filum terminale hemangioblastomas symptomatic during pregnancy. Case report *Journal of neurosurgery Spine*. 2007;7(2):254–8. <https://doi.org/10.3171/SPI-07/08/254>.
43. Omar AI. Bevacizumab for the treatment of surgically unresectable cervical cord hemangioblastoma: a case report. *J Med Case Rep*. 2012;6:238. <https://doi.org/10.1186/1752-1947-6-238>.
44. Capitanio JF, Mazza E, Motta M, Mortini P, Reni M. Mechanisms, indications and results of salvage systemic therapy for sporadic and von Hippel-Lindau related hemangioblasto-

- mas of the central nervous system. Crit Rev Oncol Hematol. 2013;86(1):69–84. <https://doi.org/10.1016/j.critrevonc.2012.10.001>.
45. Sardi I, Sanzo M, Giordano F, Buccoliero AM, Mussa F, Arico M, Genitori L. Monotherapy with thalidomide for treatment of spinal cord hemangioblastomas in a patient with von Hippel-Lindau disease. Pediatr Blood Cancer. 2009;53(3):464–7. <https://doi.org/10.1002/pbc.22065>.
  46. Patrice SJ, Snead PK, Flickinger JC, Shrieve DC, Pollock BE, Alexander E 3rd, Larson DA, Kondziolka DS, Gutin PH, Wara WM, McDermott MW, Lunsford LD, Loeffler JS. Radiosurgery for hemangioblastoma: results of a multiinstitutional experience. Int J Radiat Oncol Biol Phys. 1996;35(3):493–9.
  47. Cornelius JF, Saint-Maurice JP, Bresson D, George B, Houdart E. Hemorrhage after particle embolization of hemangioblastomas: comparison of outcomes in spinal and cerebellar lesions. J Neurosurg. 2007;106(6):994–8. <https://doi.org/10.3171/jns.2007.106.6.994>.
  48. Rodesch G, Gaillard S, Loiseau H, Brotchi J. Embolization of intradural vascular spinal cord tumors : report of five cases and review of the literature. Neuroradiology. 2008;50(2):145–51. <https://doi.org/10.1007/s00234-007-0308-z>.
  49. Shin DA, Kim SH, Kim KN, Shin HC, Yoon DH. Surgical management of spinal cord haemangioblastoma. Acta Neurochir. 2008;150(3):215–20.; discussion 220. <https://doi.org/10.1007/s00701-008-1396-6>.
  50. Browne TR, Adams RD, Roberson GH. Hemangioblastoma of the spinal cord. Review and report of five cases. Arch Neurol. 1976;33(6):435–41.
  51. Cristante L, Herrmann HD. Surgical management of intramedullary hemangioblastoma of the spinal cord. Acta Neurochir. 1999;141(4):333–9. discussion 339-340
  52. Guidetti B, Fortuna A. Surgical treatment of intramedullary hemangioblastoma of the spinal cord. Report of six cases. J Neurosurg. 1967;27(6):530–40. <https://doi.org/10.3171/jns.1967.27.6.0530>.
  53. Kuharic M, Jankovic D, Splavski B, Boop FA, Arnautovic KI. Hemangioblastomas of the posterior cranial fossa in adults: demographics, clinical, morphologic, pathologic, surgical features, and outcomes. a systematic review. World Neurosurg. 2018;110:e1049–62.
  54. McCormick PC, Torres R, Post KD, Stein BM. Intramedullary ependymoma of the spinal cord. J Neurosurg. 1990;72(4):523–32. <https://doi.org/10.3171/jns.1990.72.4.0523>.
  55. Niemela M, Lemeta S, Summanen P, Bohling T, Sainio M, Kere J, Poussa K, Sankila R, Haapasalo H, Kaariainen H, Pukkala E, Jaaskelainen J. Long-term prognosis of haemangioblastoma of the CNS: impact of von Hippel-Lindau disease. Acta Neurochir. 1999;141(11):1147–56.
  56. Lonser RR, Butman JA, Huntoon K, Asthagiri AR, Wu T, Bakhtian KD, Chew EY, Zhuang Z, Linehan WM, Oldfield EH. Prospective natural history study of central nervous system hemangioblastomas in von Hippel-Lindau disease. J Neurosurg. 2014;120(5):1055–62. <https://doi.org/10.3171/2014.1.JNS131431>.
  57. Pojskić M, Arnautović KI. Microsurgical resection of medulla oblongata hemangioblastoma: 2-dimensional operative video. Oper Neurosurg. 2018;15(5):E64–5.
  58. Pojskić M, Arnautović KI. Microsurgical resection of spinal cord hemangioblastoma: 2-dimensional operative video. Oper Neurosurg. 2018. <https://doi.org/10.1093/ons/opy123>