Effects of the growth pattern of medulloblastoma on short-term neurological impairments after surgery: results from the prospective multicenter HIT-SIOP PNET 4 study

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OBJECTIVE Extensive resection of a tumor in the posterior fossa in children is associated with the risk of neurological deficits. The objective of this study was to prospectively evaluate the short-term neurological morbidity in children after medulloblastoma surgery and relate this to the tumor's growth pattern and to the extent of resection.

METHODS In 160 patients taking part in the HIT-SIOP PNET 4 (Hyperfractionated Versus Conventionally Fractionated Radiotherapy in Standard Risk Medulloblastoma) trial, neurosurgeons prospectively responded to questions concerning the growth pattern of the tumor they had resected. The extent of resection (gross, near, or subtotal) was evaluated using MRI. The patients' neurological status before resection and around 30 days after resection was recorded.

RESULTS Invasive tumor growth, defined as local invasion in the brain or meninges, cranial nerve, or major vessel, was reported in 58% of the patients. After surgery almost 70% of all patients were affected by one or several neurological impairments (e.g., impaired vision, impaired extraocular movements, and ataxia). However, this figure was very similar to the preoperative findings. Invasive tumor growth implied a significantly higher number of impairments after surgery ($p = 0.03$) and greater deterioration regarding extraocular movements ($p = 0.012$), facial weakness ($p = 0.048$), and ataxia in the arms ($p = 0.014$) and trunk ($p = 0.025$) compared with noninvasive tumor growth. This deterioration was not dependent on the extent of resection performed. Progression-free survival (PFS) at 5 years was $80\% \pm 4\%$ and $76\% \pm 5\%$ for patients with invasive and noninvasive tumor growth, respectively, with no difference in the 5-year PFS for extent of resection.

ABBREVIATIONS CMS = cerebellar mutism syndrome; GTR = gross-total resection; NTR = near-total resection; PFS = progression-free survival; STR = subtotal resection.

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CONCLUSIONS Preoperative neurological impairments and invasive tumor growth were strong predictors of deterioration in short-term neurological outcome after medulloblastoma neurosurgery, whereas the extent of resection was not. Neither tumor invasiveness nor extent of resection influenced PFS. These findings support the continuation of maximal safe resection in medulloblastoma surgery where functional risks are not taken in areas with tumor invasion.

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KEYWORDS neurological sequelae; resection; growth pattern; medulloblastoma; pediatric neurosurgery; cerebellar mutism syndrome; CMS; oncology

MEDULLOBLASTOMA is the most common embryonal brain tumor in children, representing almost 20% of all childhood primary CNS tumors. Medulloblastoma originates in the posterior cranial fossa, most often from the cerebellar vermis in the roof of the fourth ventricle. The revised WHO classification of CNS tumors (2016) defined 4 medulloblastoma disease entities (WNT, SHH-TP53 wildtype, SHH-TP53 mutant, and non-WNT/non-SHH) with distinct cellular origin, localization, histopathological characteristics, molecular genetic features, and clinical behavior.^{21,23,30,34} The prognosis of nondisseminated medulloblastoma is, in addition to the histopathology, dependent on the genetic features of the tumor as well as clinical factors. The treatment of medulloblastoma involves surgery followed by radiotherapy and chemotherapy. Today the 5-year overall survival for standard-risk medulloblastoma is expected to be around 80%.²⁰

The prognostic importance of gross-total resection (GTR) versus near-total resection (NTR) or subtotal resection (STR) for survival is unclear.^{5,11,12,35} Recent publications have put more emphasis on the prognostic importance of the genetically defined entity of the tumor for survival^{24,29} and no benefit of GTR compared with NTR or STR on survival.^{35,36}

Concerning morbidity, extensive resection of a tumor in the posterior fossa may be associated with increased risk for neurological deficits, both short- and long-term.^{32,37} Children with medulloblastoma have been reported to encounter mutism, new cranial nerve palsies, and worsening of ataxia after surgery in 24%–44% of cases with increasing incidence when undergoing GTR.^{7,10} Extensive resection of medulloblastomas invasive into the brainstem causes a considerable neurological risk and no benefit in progression-free survival (PFS).¹⁰ Cerebellar mutism syndrome (CMS), characterized by mutism and emotional lability,^{14,25} is a negative prognostic factor for short- and long-term neurological outcome.^{17,33} Although its pathogenesis is most likely multifactorial,^{3,8} it might be increased after extensive resection compared with less complete resections.¹⁹

When neurosurgeons perform tumor resection, the final neuropathological diagnosis is not known, and the accomplished extent of resection is highly dependent on the growth pattern of the tumor as well as on the experience and skills of the surgeon. In the literature, there are few reports on the impact of the growth pattern of medulloblastoma on neurological morbidity after surgery.

The aim of the present study was to investigate the

short-term neurological deficits in children who underwent surgery for medulloblastoma and relate this to the growth pattern and the extent of resection as well as to PFS. This information was prospectively collected in the multicenter HIT-SIOP PNET 4 (Hyperfractionated Versus Conventionally Fractionated Radiotherapy in Standard Risk Medulloblastoma) study.

Methods

The international phase 3 multicenter study HIT-SIOP PNET 4 recruited 338 patients with standard-risk medulloblastoma from 10 European countries between 2001 and 2006 (clinical trial registration no. NCT01351870, clinicaltrials.gov).²⁰ The patients were 4–21 years of age at inclusion. Standard-risk medulloblastoma was defined as no sign of metastatic disease on preoperative MRI or cerebrospinal fluid cytology. Postoperative residual tumors of any size were allowed. At diagnosis, tumor material was centrally reviewed by experienced neuropathologists, confirming the diagnosis and the histological medulloblastoma entity. Epigenetic subgroup analysis and cytogenetic evaluation were performed later but only in a fraction of the cohort.¹¹ The randomized question concerned the use of conventional or hyperfractionated radiotherapy and showed no difference in survival rate.²⁰

The treatment protocol included a prospective collection of neurosurgical data with pre- and postoperative neurological status evaluation. Seventy different neurosurgical centers in 9 European countries took part in this substudy. The study was approved by each national/institutional review board, and informed consent was obtained from all patients, parents, and/or guardians.

After surgery, the neurosurgeons filled out a questionnaire concerning the growth pattern of the tumor regarding the presence of local brain or leptomeningeal invasion or involvement of a cranial nerve or major vessels. Thus, invasive tumor growth was defined by the neurosurgeon as the presence of any of these factors. The neurosurgeons were also asked about the techniques employed (e.g., use of an ultrasonic aspirator or operating microscope and management of hydrocephalus). The hydrocephalus issue included yes or no answers to the use of preoperative steroids, pre- or intraoperative external ventricular drain, ventricular shunt or puncture, or neuroendoscopic third ventriculostomy. No information about the surgical approach was collected. Intraoperative limiting factors such as blood loss, brain swelling, cardiovascular changes, inadequate access, and premature halting of the operation

were reported as a yes or no answer. Operation time was recorded.

Data collected on preoperative MRI included the tumor size but not the growth pattern of the tumor or the more precise localization of the tumor. Postoperative MRI was performed, most often within 72 hours postsurgery in all patients but one, who underwent CT scanning instead. The images were centrally reviewed in each participating country, and the extent of resection was reported. GTR was defined as there being no sign of residual tumor, NTR as a residual tumor less than or equal to 1.5 cm² (largest diameter in the axial plane according to protocol), and STR as a residual tumor more than 1.5 cm².²⁰

The following general complications within 30 days after surgery were recorded: seizures, CMS, intracranial hemorrhage, hydrocephalus requiring operation, CNS infection, other infection, subcutaneous CSF collection, and readmission to intensive care. These complications were reported by a yes or no answer on the questionnaire. Time to regain full consciousness was also recorded.

Neurological status before and around 30 days after surgery (before the start of radiotherapy) was recorded by a physician. The neurological record stated whether the patient had full or impaired consciousness, whether vision was impaired, and whether the patient had impairment of extraocular movements or palate or tongue movements. The presence of facial weakness, ataxia of the arms and trunk, and limb weakness was also recorded. In this present study, 2 ways of studying neurological deficits were used. First, the number of impairments for each patient was added and compared before and after surgery; and second, to analyze which neurological functions were most likely to be affected by surgery, we compared each patient's neurological deficits before and after tumor resection and graded the change in each neurological impairment as better, same, or worse.

Patient follow-up is part of the HIT-SIOP PNET 4 study. Events are continuously registered in the database by each national study group.

Methylation Analysis

Epigenetic subgrouping of the tumors was performed in all patients with sufficient remaining tumor material left ($n = 74$), as previously described.^{11,28}

Statistical Analysis

Kaplan-Meier survival plots and logistic regression were performed in R using the survival and stats packages. For all other statistical analyses, IBM SPSS (version 25, IBM Corp.) was used. Comparisons of categorical variables between groups were performed using McNemar's test, chi-square test, and Fisher's exact test where appropriate. Prognostic factors for neurological deficits after surgery were evaluated using logistic regression analysis, with sex, age, tumor size, tumor growth pattern, extent of resection, and a categorical variable denoting whether there were fewer than 2 or 2 or more deficits before surgery as covariates. Complete data for the logistic regression analysis was available for 120 patients. The PFS was estimated using the Kaplan-Meier method, and differences

in outcome between patient groups were tested using the log-rank method; $p < 0.05$ was considered significant.

Results

Patients

A total of 160 eligible patients with standard-risk medulloblastoma and neurosurgical data were identified. Patient characteristics are listed in Table 1. There were 99 male and 61 female patients with a sex ratio of 1.6. The mean age at diagnosis was 9.4 years (range 3.2–19.3 years). The tumor size was between 1.9 and 9.5 cm in its largest diameter (mean 4.3 cm). The mean operation time was 4 hours, 30 minutes (range 1 hour, 40 minutes to 8 hours, 30 minutes). The operation techniques used were very similar in all centers; for example, 95% used an operating microscope and 80% an ultrasonic aspirator. Very few intraoperative limiting factors were reported (data not shown).

The vast majority of centers reported 1–2 patients to the study. Eight centers reported 5–13 patients, each who together composed one-third of the study population.

Tumor Growth and Resection

The surgeon's description of the tumor's growth pattern was available for 158 patients. It was reported as invasive in 91 patients (58%) and noninvasive in 67 patients (42%) (Table 1). The majority of invasive tumors (in 72 of 91 patients) had local brain invasion reported as the only sign of invasive growth. Nineteen patients had a combination of growth in a major vessel or cranial nerve or local invasiveness (local brain or leptomeningeal) reported. The 5 most invasive tumors exhibited local brain invasion as well as growth in a cranial nerve and involvement of a major vessel.

A GTR was performed in 129 (80%) patients, an NTR in 25 (16%), and an STR in 6 (4%). As shown in Table 1, the extent of resection was similarly distributed in invasive and noninvasive tumors. Eight patients underwent secondary surgery due to a residual tumor, and postoperative MRI thereafter showed GTR in 6 patients and NTR in 2.

General Complications Within 30 Days Postresection

General complications were reported in 19% of the patients (Table 2). The time to full recovery of consciousness after surgery showed great variation (0–48 days); however, 75% of patients had fully recovered within 1 day. The patient with the longest recovery time, 48 days, had CMS and is a long-term survivor.

Neurological Deficits as a Result of Tumor Growth Pattern and Resection

Both pre- and postresection, 68% and 69% of patients were affected by at least 1 neurological impairment, respectively. Thus, 30% of the patients had no neurological impairment either before or after surgery. The frequency of the most common preoperative impairments, such as vision impairment and ataxia of arms and trunk, remained essentially unchanged after surgery (Table 3). Improve-

TABLE 1. Clinical and tumor characteristics in 160 children treated for medulloblastoma in the HIT-SIOP PNET 4 study

	Value
Male	99 (62)
Female	61 (38)
Mean age at diagnosis, yrs (range)	9.4 (3.2–19.3)
Mean tumor size, cm (range)	4.3 (1.9–9.5)
Operation time, range	1 hr, 40 mins to 8 hrs, 30 mins
Extent of resection*	
GTR	129 (80)
NTR (≤ 1.5 -cm ² residual tumor)	25 (16)
STR (> 1.5 -cm ² residual tumor)	6 (4)
Growth pattern†	
Invasive signs (≥ 1 per patient)	91 (58)
Local brain invasion	87 (55)
Leptomeningeal invasion	7 (4.4)
Major vessel involvement	15 (9.5)
CN invasion	9 (6)
Noninvasive	67 (42)
Growth pattern & extent of resection	
Invasive growth	
GTR	73 (80)
NTR	14 (15)
STR	4 (4)
Noninvasive growth	
GTR	54 (81)
NTR	11 (16)
STR	2 (3)
Preop steroids	115 (77)
Molecular subgroups	74 (46)
WNT	10 (14)
SHH	16 (22)
Non-WNT/non-SHH	48 (65)

CN = cranial nerve.

Values are presented as the number of patients (%) unless stated otherwise.

* As noted on postoperative radiology.

† Based on the neurosurgical report.

ment after surgery was seen for impaired consciousness. Deterioration was seen mainly for extraocular movements ($p = 0.03$), facial weakness ($p < 0.01$), and limb weakness ($p < 0.01$).

Half of all patients had no impairment or only a single neurological impairment before and after surgery, which in individual patients could mean deterioration or improvement (see below). The other half had 2 or more impairments. Before resection, there was no difference in the number of neurological deficits in the 91 patients with invasive tumor growth compared with those with noninvasive growth. After resection, there was a significantly higher percentage of patients with 2 or more impairments in the patients with invasive tumor growth compared with those with noninvasive growth (57% and 37%, respectively; $p = 0.03$) (Table 4), giving an OR of 2.15. This differ-

TABLE 2. General complications within 30 days postresection

	Value
CMS	19 (13)
Subcutaneous CSF collection	10 (7)
Readmission to intensive care	9 (6)
CNS infection	7 (5)
Other infection	7 (5)
Hydrocephalus requiring operation postresection	8 (5)
Seizures	4 (3)
Intracranial hemorrhage	4 (3)
Mean days btwn surgery & full recovery of consciousness (range)	2.2 (0–48)

Data are presented as number of patients (%) unless stated otherwise.

ence in number of postoperative neurological impairments was not seen when comparing the extent of resection performed (Table 4).

Looking at specific neurological impairments in the 91 patients with an invasive tumor, the evolution of these was significantly worsened postresection compared with the patients in whom the tumor was noninvasive. This was true for extraocular movements ($p = 0.012$), facial weakness ($p = 0.048$), ataxia of the arms ($p = 0.014$), and truncal ataxia ($p = 0.025$) (Table 5). This worsening in neurological outcome after surgery was independent of the extent of surgical resection (data not shown).

A multivariate analysis was performed for all patients with complete data of the preoperative factors: age, sex, number of preoperative neurological impairments, tumor size, tumor growth pattern, and extent of resection. The number of postoperative impairments was positively associated with the number of preoperative impairments and the degree of tumor invasiveness ($p < 0.05$ for both, OR 7 and 3, respectively) but not with the extent of resection ($p = 0.5$). Every increase in centimeters of the tumor size also increased the risk of having more postoperative deficits, with an OR of 1.75.

Molecular Subgroup Analysis

In 74 patients, tumor material was available for molecular subgroup analysis (Table 1). In the 24 tumors with subgroups WNT and SHH, invasive tumor growth was seen in 50% and 43%, respectively, and in non-WNT/non-SHH in 58%. In tumors with subgroup WNT and SHH, a GTR was performed in 90%–100% of patients, and in non-WNT/non-SHH it was performed in 77% of patients (not significant). There was no correlation between subgroup and number of impairments.

Cerebellar Mutism Syndrome

Cerebellar mutism syndrome was recorded to be present in 13% of the children. In patients with invasive tumor 13% developed CMS and in patients with noninvasive tumor growth 10%. CMS was only present in patients who underwent GTR or NTR but not in the 6 patients with STR.

TABLE 3. Occurrence of pre- and postoperative neurological impairments within 30 days postresection

Neurological Impairment	Preresection, %	Postresection, %	p Value*	95% CI
Impaired consciousness (n = 148)	8	2	0.02	0.01 to 0.1
Impaired vision for age (n = 145)	24	25	>0.99	
Impaired extraocular movements (n = 143)	25	36	0.03	-0.2 to -0.02
Facial weakness (n = 141)	3	10	<0.01	-0.1 to -0.03
Impaired palate/tongue movements (n = 140)	<1	4	0.2	
Limb weakness (n = 140)	10	26	<0.01	-0.2 to -0.09
Ataxia arms (n = 136)	37	46	0.09	
Ataxia trunk (n = 135)	39	39	0.86	

* McNemar's chi-square test; statistical analysis excluded nonpaired data.

Management of Hydrocephalus

Seventy-seven percent of all patients received preoperative steroids. Of the 153 patients for which we had information about the management of hydrocephalus, 74 (48%) required an operation for hydrocephalus (ventriculostomy, ventricular shunt, or external drainage preoperatively or intraoperatively).

Long-Term PFS

At 5 years from diagnosis, PFS was $80\% \pm 4\%$ and $76\% \pm 5\%$ for patients with invasive and noninvasive tumor growth, respectively, with no significant difference between the groups ($p = 0.8$) (Fig. 1). The 5-year PFS was $77\% \pm 4\%$ for GTR, $88\% \pm 7\%$ for NTR, and $83\% \pm 15\%$ for STR with no significant difference between the groups.

Discussion

When discussing the 3 cornerstones in the treatment for medulloblastoma (surgery, radiotherapy, and chemotherapy) and their propensities to cause morbidity, the least focus has been on surgery. Therefore, we studied neurological status before and after surgery related to neurosurgical conditions, which were prospectively collected in the international multicenter study HIT-SIOP PNET 4. Our main finding is that patients with an invasive tumor growth were more likely to experience deterioration in

their neurological impairments between pre- and postoperative evaluations.

In this study, we report on short-term neurological findings after surgery. Many studies have shown that patients undergoing treatment for medulloblastoma, including neurosurgery, have long-term neurological and neurocognitive problems.^{22,38} Most of these findings have been attributed to treatment with radiotherapy. In the HIT-SIOP PNET 4 study, younger children who underwent hyperfractionated compared with conventional radiotherapy had better executive function and marginally higher verbal IQ but without accompanying change in health status, behavior, or quality of life.^{6,18} Apart from studies looking at the long-term effects of CMS,^{17,33} there are only a few studies linking long-term neurological sequelae also to surgery-related factors.¹³ Naturally surgical short-term damage has bearing on the long-term neurological outcome.

To our knowledge, there have been no studies on the impact of tumor invasiveness on neurological morbidity. In this study, when comparing the *number* of neurological impairments pre- and postresection we found that patients with invasive tumor growth had a more than 2-fold-higher risk of having 2 or more neurological deficits after surgery compared with patients with noninvasive tumor growth. When looking at the *changes* (better, same, worse) in neurological symptoms postresection, patients with invasive tumor growth had a significant deterioration of sev-

TABLE 4. Neurological impairments postresection in patients with a tumor with an invasive or noninvasive growth pattern and GTR, NTR, or STR

	No. of Neurological Impairments*		p Value†	95% CI
	0 or 1	≥2		
Invasive tumor growth (n = 83)	43	57	0.03	0.02–0.37
Noninvasive tumor growth (n = 62)	63	37		
GTR (n = 120)	52	48	>0.99	
NTR (n = 21)	52	48		
STR (n = 6)	50	50		

* Values are presented as the percentage of patients.

† Pearson's chi-square test.

TABLE 5. Change in neurological impairment related to invasive tumor growth or noninvasive tumor growth

	Invasive Tumor Growth, % (n = 91)	Noninvasive Tumor Growth, % (n = 67)	p Value*
Vision for age			0.523
Worse	10.7	5.4	
Same	82.7	85.7	
Better	6.7	8.9	
CN palsy of III, IV, or VI			0.012
Worse	24.7	8.2	
Same	65.4	86.9	
Better	9.9	4.9	
CN palsy of IX, X, or XI			0.076
Worse	0	5.1	
Same	100	94.6	
Better	0	0	
Facial weakness			0.048
Worse	12.5	3.3	
Same	87.5	95	
Better	0	1.7	
Arm ataxia			0.014
Worse	23.4	6.9	
Same	71.4	79.3	
Better	5.2	13.8	
Truncal ataxia			0.025
Worse	20.3	5.3	
Same	70.9	78.6	
Better	8.9	15.8	
Limb weakness			0.124
Worse	23.5	11.7	
Same	72.8	86.7	
Better	3.7	1.7	

* Chi-square test.

eral neurological impairments postsurgery compared with noninvasive tumors. This deterioration was not dependent on the extent of resection performed. There was also no difference regarding the number of or worsening of neurological deficits if tumors with invasive growth were resected totally or near/subtotally. It thus seems that the invasiveness of the tumor growth per se could be important for the outcome of neurological deficits. This finding was confirmed in a multivariate analysis. Certainly, this result may suggest that the neurosurgeons made the appropriate decision concerning the extent of resection in the individual cases. Many medulloblastomas grow adherent to the floor of the fourth ventricle and to the brainstem where neurosurgeons have made decisions to resect with caution. This may have contributed to the finding of no clear relationship between extent of resection and postsurgical neurological status.

However, the patient's postoperative status was to the highest degree dependent on the preoperative status, which in turn was not different in invasive and noninvasive

tumors. In fact, in our study, when looking at all patients, we found the same percentage of patients (68% and 69%, respectively) affected by at least 1 neurological impairment before and after surgery. This high percentage after short-term follow-up has also been noted in previous studies for posterior fossa tumors in general.¹⁶ However, despite this overall stable finding of pre- and postsurgery deficits, some patients improved and some deteriorated. Not surprisingly, ataxia of the trunk and arms as well as impaired vision and palsy of cranial nerves III, IV, and VI were the most common neurological deficits before and a short time after surgery.

Thus, it seems that for this cohort, surgery did not put the patients at risk for increased neurological morbidity. In individual patients exceptions occurred in both ways. An exception was CMS, which is never present before surgery. This study showed a relatively low frequency of CMS,^{15,26} which may be due to the fact that the definition of CMS was made by each center and could have been underreported in the absence of a standardized scale. Still, we did

FIG. 1. Long-term probability of PFS (Kaplan-Meier, log-rank test) in relation to invasive or noninvasive medulloblastoma tumor growth, as defined by the neurosurgeon intraoperatively (n = 158).

not find that tumor invasiveness or extent of resection was related to an increased risk of CMS.

Tumor invasiveness did not affect cure in this study. Tumors with invasive tumor growth had a 5-year PFS of $80\% \pm 4\%$, which is in line with previous publications from the HIT SIOP-PNET 4.^{20,27}

The importance of resection for cure in patients with medulloblastomas is widely established. We also found, in a study of relapse in this patient cohort, that surgery for relapse was associated with a higher survival rate than other therapies at relapse.²⁷ However, medulloblastoma is a radio- and chemosensitive tumor, and cure may occasionally be achieved even without surgery. For a long time, it has been accepted that GTR and NTR allowing a residual tumor $\leq 1.5 \text{ cm}^2$ do not differ with respect to survival outcome. The PNET 4 study confirmed this finding²⁰ but showed that a residual tumor $> 1.5 \text{ cm}^2$, i.e., STR, implied a higher risk for relapse in the PNET 4 study,²⁰ similar to the older studies of Albright and Zeltzer.^{1,39} No difference in 5-year PFS was seen comparing the extent of resection in this PNET 4 substudy where the great majority had no or a small residual tumor. However, a recent study on all medulloblastoma risk groups including large residuals did not show a significant benefit in overall survival associated with GTR when incorporating the molecular subgroup analyses.³⁶ In our study, molecular subgroup analysis was performed in less than half of the patients. From this limited cohort, we could not draw meaningful conclusions on subgroups and tumor invasiveness or resection. In non-WNT/non-SHH standard-risk medulloblastomas, chromosomal signatures were found to be highly predictive for survival, while its variants “group 3” and “group 4” showed no difference.¹¹

In individual patients, this question is important. Patients with STR may undergo second-look surgery to achieve GTR/NTR, or their treatment may be intensified to high-risk therapy, with increased risk of long-term side effects.^{2,4,9,31} With more knowledge of the distinct genetically defined medulloblastoma entities²¹ this decision may be easier to make. However, at the time of surgery, biological factors are not known and neurosurgical decisions have to be made based on tumor growth and location.

Study Strengths and Limitations

The strength of this study is the prospective collection of tumor growth pattern in a multicenter setting, which should support its universality. Also, the postoperative tumor status was centrally reviewed by MR. Although we do not have information on every type of neurological complication, we cover those most important after posterior fossa surgery.

The limitations of this study are a lack of consensus on the tumor growth definitions before the study start. The neurosurgeons may have judged this differently, and we had no information on tumor invasiveness from preoperative MRI. We cannot exclude that tumors with a cumbersome and long operation more often could be reported with invasive growth. On the other hand, judgments were made by a large group of neurosurgeons, which should limit bias. There was no information about the neurosurgical approach or the presence of pre- and postoperative hydrocephalus, albeit the need for hydrocephalus management was recorded. These factors may have had an impact on postoperative complications. Finally, the occurrence of CMS was clinically determined, without the use of a systematic scale, which could have underestimated the incidence of milder forms of CMS.

Conclusions

In this multicenter prospective study, the overall frequency of neurological impairments secondary to medulloblastoma surgery remained stable, both pre- and postoperatively, at 70%. Interestingly, postoperative neurological damage was mainly due to preoperative factors, including invasive tumor growth. This affected short-term neurological outcome, whereas the extent of resection did not. This somewhat unexpected finding needs to be confirmed in other studies but may be the result of the current recommendations with maximal safe resection where functional risks are not taken in areas with tumor invasion.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Schepke, Lannering, Tisell. Analysis and

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Supplemental Information

Previous Presentations

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