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Research Article

Surgical outcome and indicators of postoperative worsening in intra-axial thalamic and posterior fossa pediatric tumors: Preliminary results from a single tertiary referral center cohort

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ABSTRACT

Background: Shared indications about the best management of intra-axial thalamic (IAT) and posterior fossa (PF) pediatric tumors are still lacking. The aim of this study was to analyze neurosurgical outcome in these tumors and to investigate factors associated with postoperative worsening.
Methods: A retrospective single-center study on IAT and PF pediatric tumor patients treated surgically over a 7-year period was conducted. The Lansky Scale (LS) was used to assess patients' functional status. Surgical complexity was graded with the Milan Complexity Scale (MCS). The following analyses were performed: a longitudinal analysis of the preoperative, discharge, and 3 months' follow-up (FU) LS, a comparison between improved/unchanged and worsened patients, and an analysis of the predictive value of single MCS items.
Results: 37 cases were collected: 20 PF and 17 thalamic. Mean MCS score was 6 ± 1.7. Mean preoperative, discharge and FU LS were 80.8, 74.6 and 80.3 respectively. Surgical mortality was 0%.
The longitudinal analysis showed a neurological worsening at discharge compared to preoperative status ($p = 0.011$) and an improvement at FU compared to discharge ($p < 0.004$), both statistically significant. None of the variables analyzed showed a significant predictive value of early postoperative change; however, higher MCS scores were associated with a greater risk of worsening.
Conclusions: The surgical management of IAT and PF pediatric brain tumors remains challenging; early post-operative worsening is possible, but most deficits tend to improve at FU. The MCS seems to be a valuable tool to estimate the risk of early postoperative worsening and to facilitate parents' informed consent.

1. Introduction

Brain tumors (BT) are the most common solid tumors in children and the leading cause of death in this age group, more lethal than leukemias and any other type of cancer. Surgical removal is usually the recommended treatment option, followed by adjuvant therapies in selected cases [1,2].

Among all, deeply located tumors such as those in the thalamus and in the posterior fossa (PF), are considered the most difficult to treat, both from a medical and surgical point of view. These lesions, in fact, are not only very rare, but also difficult to reach and in close proximity, or right within, highly eloquent areas. These are the main reasons why no consensus still exists on the indications for their surgical removal, even though, at present, a more proactive approach has gained approval [3–8] over the more conservative strategy of the past [8–13].

As a matter of fact, the decision whether to operate on such complex

Abbreviations: BT, brain tumors; CHT, chemotherapy; CNS, central nervous system; CSF, cerebrospinal fluid; EOR, extent of resection; FU, follow-up; GTR, gross total resection; IAT, intra-axial thalamic; LS, Lansky Scale; MCS, Milan Complexity Scale; MR, Magnetic Resonance; OS, Overall Survival; PF, Posterior Fossa; PFS, Progression Free Survival; PR, partial resection; RT, radiotherapy; STR, subtotal resection; WHO, World Health Organization.

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tumors is influenced by several factors, which are both patient-specific and pathology-related. Among them, preoperative surgical complexity deserves special consideration because it can influence the surgical strategy and ultimately patient's outcome [14].

The aim of this work was to analyze neurosurgical outcome in pediatric patients with intra-axial tumors of the thalamus and PF, to compare patients clinically worsened after surgery with improved/unchanged ones and to investigate the presence of factors predictive of early postoperative worsening.

2. Methods

2.1. Study type and inclusion criteria

A retrospective study was conducted on all pediatric patients (<18 years old) affected by IAT and PF tumors that were surgically resected over a 7-years period (January 2013-December 2019) at a tertiary referral center (Fondazione IRCCS Istituto Neurologico Carlo Besta) in Milan, Italy. Only elective surgeries aimed at maximal safe tumor resection were considered [15–19] (i.e. needle and open biopsies were excluded). Among PF tumors, we included only those lesions (e.g. IV ventricle tumors), that required substantial intraoperative brainstem manipulation.

Patient records were reviewed by means of a dedicated, prospectively collected database containing details of the preoperative clinical presentation, histological diagnosis, surgical approach, complications' occurrence, clinical status at discharge and at 3-months follow-up (FU), and adjuvant chemo and/or radiotherapy (CHT and/or RT).

Tumor volume was calculated using Horos v2.1.1 Medical Image Viewer (Horos ™) based on Magnetic Resonance (MR) volumetric T1-weighted sequences with IV contrast administration, T-2 weighted and FLAIR sequences. The extent of resection (EOR) was assessed through an early (within 48 h from surgery) MR with the aforementioned sequences; EOR was classified as total if 100% of the lesion was removed (gross total resection, GTR), subtotal if > 90% of the lesion was excised (subtotal resection, STR) and partial if < 90% of the lesion was removed (partial resection, PR). FU information was obtained at the outpatient visit performed 3 months after surgery.

The Lansky Scale (LS) [20] was used to evaluate patients' health and functional status before surgery, at discharge and at FU. This scale ranges from 0 to 100 and it is based on patients' independence regarding activities of daily living (Table 1).

Neurosurgical complications were classified according to two different systems: the Landriel-Ibanez classification, [21] which is based on the treatment required to address the complications, as well as an etiologic classification [14] that includes the following classes: traumatic (i.e. directly related to the surgical trauma/manipulation of a specific anatomical structure), cerebrospinal fluid (CSF)-related (i.e. leaks, hydrocephalus), septic, hemorrhagic, ischemic, epileptic, general (extra-Central Nervous System (CNS)) or other complications (i.e. not belonging to any of the other categories).

Complications were also recorded as major, [14] when they caused the patient a new deficit or disease, or as minor [14] when they required a prolonged hospital stay and even second surgery, but were not responsible for permanent new deficits or diseases.

Preoperatively, case complexity was assessed through the Milan Complexity Scale (MCS), which has been specifically designed for brain tumor surgery.[14] The MCS can predict the risk of postoperative clinical worsening after brain tumor surgery based on 5 preoperative parameters, named the Big Fives: involvement of major brain vessels, eloquent areas surgery, posterior fossa location, involvement of cranial nerves and tumor size>4 cm. The scale ranges from 0 to 8 points: the higher the score, the greater the case complexity and the higher the chance of clinical worsening after surgery. The MCS and the distribution of MCS parameters in the study population is reported in Table 2.

All LS assessments, as well as all MCS evaluations, were performed independently by three neurosurgeons with different levels of expertise (ZCM, BM, FP) and the final score was resolved by consensus.

The study was approved by the Ethical Committee of the Fondazione IRCSS Istituto Neurologico Carlo Besta and all patients' parents signed an informed consent form.

Some examples of the cases present in the series are shown in Figs. 1, 2 and 3.

2.2. Statistical analysis

The total number of cases (37) rather than the total number of patients (34) was considered for the analyses.

Descriptive statistics were employed to illustrate the distribution of socio-demographic and clinical data, as well as the classification of complications, EOR, tumor histology and location and LS scores.

Non-parametric tests were used, since the p-p plot showed that data were not normally distributed. All statistical analyses were performed using the SPSS v. 18.0 software (SPSS Institute, Cary, North Carolina, USA).

2.2.1. Longitudinal analysis

The longitudinal change in LS scores between preoperative period, discharge and FU was evaluated using Friedman's ANOVA with Wilcoxon post hoc test. Two-tailed significance level of $\alpha = 0.016$ was adopted due to Bonferroni adjustment to reduce type 1 error due to

Table 1
Lansky Scale.

Able to carry on normal activity; no special care is needed	
100	Fully active
90	Minor restriction in physically strenuous play
80	Restricted in strenuous play, tires more easily, otherwise active
Mild to moderate restriction	
70	Both greater restrictions of, and less time spent in active play
60	Ambulatory up to 50% of the time, limited active play with assistance/supervision
50	Considerable assistance required for any active play, fully able to engage in quiet play
Moderate to severe restriction	
40	Able to initiate quite activities
30	Needs considerable assistance for quiet activity
20	Limited to very passive activity initiated by others (e.g. TV)
10	Completely disabled, not even passive play
0	Dead

Table 2
Milan Complexity Scale[9] (MCS) and number of patients for each variable.

Variables	Score	n of patients (%)
Major Brain Vessels Manipulation*		
No	0	17 (45.9%)
Yes	1	20 (54.1%)
Posterior fossa		
No	0	13 (35.1%)
Yes	1	24 (64.9%)
Cranial Nerve Manipulation		
No	0	19 (51.4%)
Yes	2	18 (48.6%)
Eloquent Area†		
No	0	0 (0%)
Yes	3	37 (100%)
Tumor's size		
0–4 cm	0	15 (40.5%)
≥4,1 cm	1	22 (59.5%)
Total Score	0–8	

* Major arteries: ICA, ACA, MCA, Acomm, Pcomm, Anterior Choroidal, Ophtalmic, VA, BA, PICA, AICA, SCA, PCA. Major veins: Superior sagittal, transverse, sigmoid sinus, internal cerebral veins, vein of Galen.

† Motor, sensory, language or visual areas, hypothalamus, thalamus, internal capsule, brainstem, and pineal region.

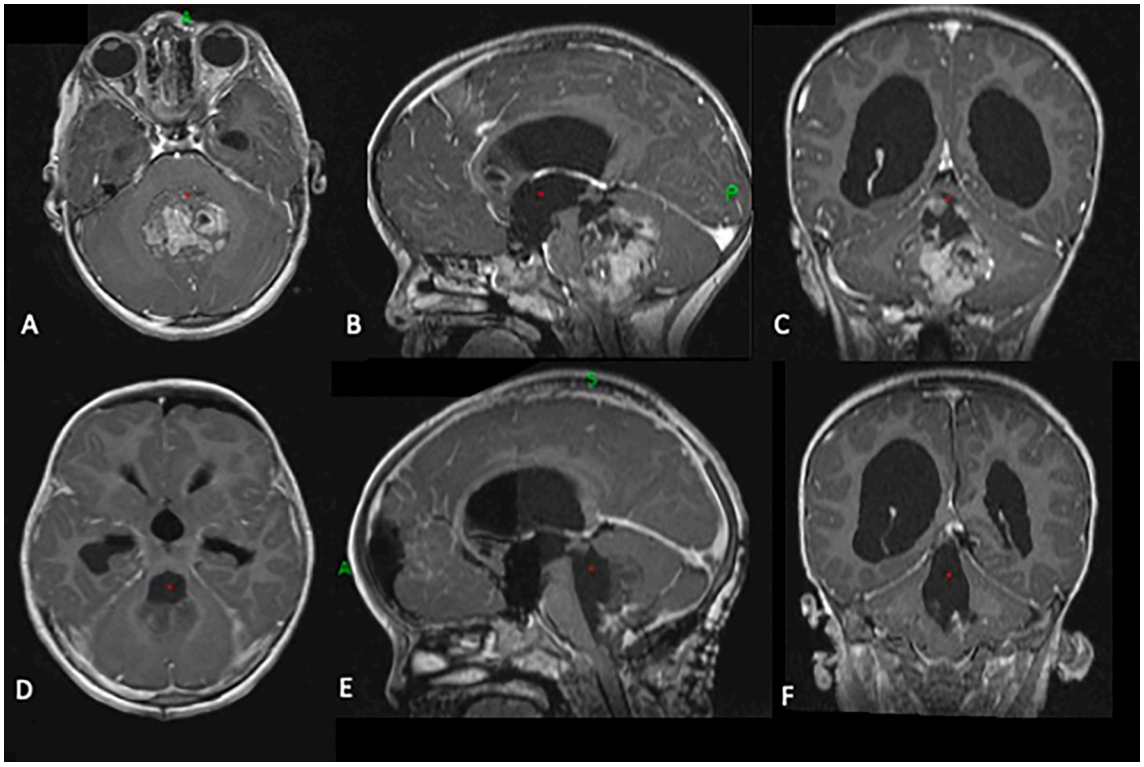

Fig. 1. Illustrative case 1 A, B, C: Preoperative axial, sagittal and coronal volumetric, T1-weighted MR images with intravenous contrast administration. The tumor is completely occluding the IV ventricle and is compressing the brainstem. The MCS score in this case was 6 (eloquent area = 3 points; tumor dimension > 4 cm = 1 point; major brain vessel manipulation (PICA) = 1 point; posterior fossa = 1 point) D, E, F: Postoperative axial, sagittal and coronal volumetric, T1-weighted MR images with intravenous contrast enhancement showing GTR of the tumor. Histopathologic examination revealed a medulloblastoma (grade IV WHO 2016).

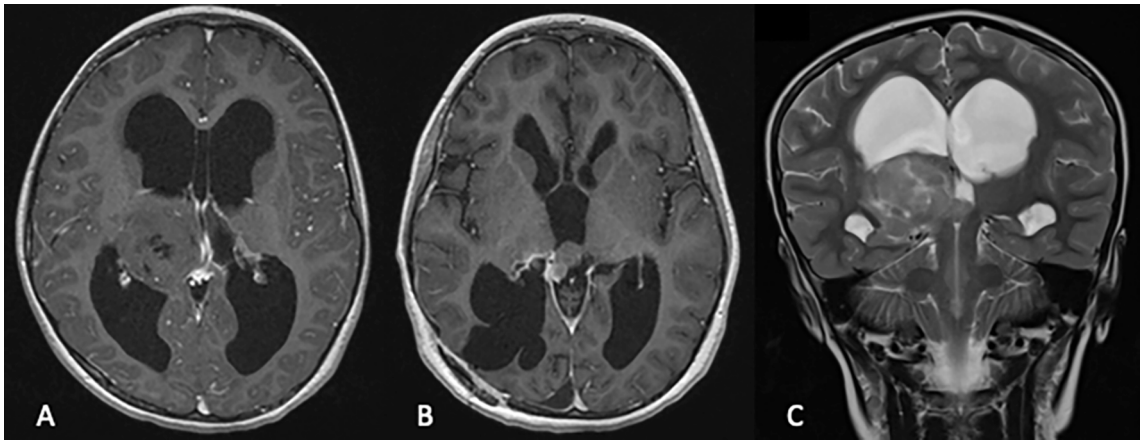

Fig. 2. Illustrative case 2 A, C: Preoperative axial 3D, T1-weighted with intravenous contrast administration and coronal T2-weighted MR images, showing a right thalamic pilocytic astrocytoma (grade I WHO 2016). The MCS score in this case was 4 (eloquent area = 3 points; major brain vessel manipulation (internal cerebral veins) = 1 point). B: Postoperative axial 3D, T1-weighted MR image with intravenous contrast enhancement showing GTR of the tumor.

multiple comparisons.

2.2.2. Comparison of variables between two groups

For each of the three timepoints we analyzed (i.e. preoperative, discharge and follow-up), the sample was dichotomized into two groups, improved/unchanged versus worsened patients, based on the differences in LS. Regarding the LS, it is important to recognize that there is no established "minimum clinically important difference" in score after neuro-oncological surgery, and that a 10-point change on the upper LS is not as meaningful to a patient as a 10-point change on the lower LS. Thus, for our analysis, we adapted the definition for "significant change" as a decrease of $\geq$ 20 points if baseline LS $\geq$ 80, or a decrease of $\geq$ 10 points if baseline LS $<$ 80.

The comparison between these two groups was performed using the chi-squared test or the Fischer exact test for tumor location (posterior fossa vs thalamus), World Health Organization (WHO) grade (Grade I and II vs Grade III and IV), complications occurrence (yes vs no) and EOR (total or subtotal vs partial). The Mann Whitney test was used when comparing MCS scores. Two-tailed type I error level was set at α value equal to 0.01 after Bonferroni's correction to address statistical significance.

2.2.3. Predictors of postoperative worsening

A logistic regression model was built to investigate the strength of

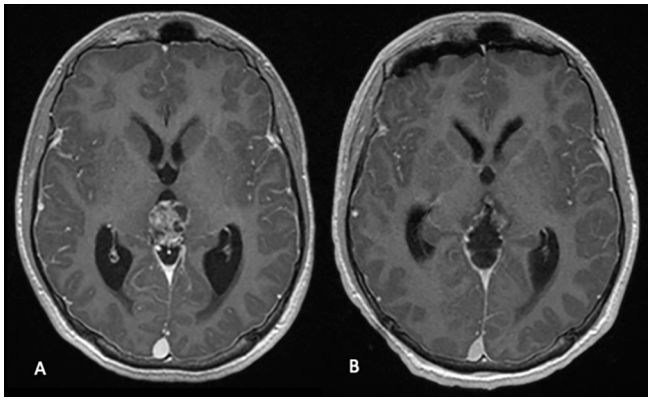

Fig. 3. Illustrative case 3 A: Preoperative axial 3D, T1-weighted MR image with intravenous contrast administration, showing a pineal gland mass in close relationship with the internal cerebral veins system. The MCS score in this case was 5 (eloquent area = 3 points; major brain vessel manipulation = 1 point; posterior fossa = 1 point). B: Postoperative axial 3D, T1-weighted MR image with intravenous contrast enhancement showing STR of the tumor with a small remnant in the left thalamus. Histopathologic examination revealed a papillary tumor of the pineal region (grade III WHO 2016).

the relationship between the worsening change in LS scores at discharge and the following variables: posterior fossa, cranial nerve manipulation, tumor dimension, major blood vessel manipulation and MCS total score (eloquent area was not included since all tumors were located in an eloquent area). Odds ratio and Nagelkerke R^2 were used to evaluate the goodness of fit of the model.

3. Results

3.1. Demographic and neurosurgical variables

A total of 34 patients were enrolled in the study. There were 9 (26.5%) males and 25 (73.5%) females. Mean age at surgery was 7 ± 4.55 years and the age ranged from 10 months to 17 years. Three patients had to be re-operated for disease recurrence, so that, eventually, the total number of cases was 37.

Tumors were located as follows: 14 (37.8%) in the thalamus, 12 (32.4%) in the IV ventricle, 8 (21.6%) in the brainstem (3 in the mesencephalon, 3 in the pons and 2 in the medulla) and 3 (8.1%) in the pineal region.

Histological analysis of tissue samples obtained during surgery revealed a heterogeneous group of tumors. There were 15 (40.5%) pilocytic astrocytomas, 8 (21.6%) medulloblastomas, 5 (13.5%) ependymomas, 2 (5.4%) germ cell tumors, 2 (5.4%) glioblastomas multiforme, 2 (5.4%) pineal tumors, 1 (2.7%) low-grade glioma, 1 anaplastic astrocytoma (2.7%) and 1 embryonal tumor, other than medulloblastoma (2.7%).

EOR was GTR in 23 (62.1%) cases, STR in 10 (27%) and PR in 4 (10.8%) cases.

Demographic, clinical and histological data, tumor location, surgical approaches, EOR and adjuvant therapies data are summarized in Table 3.

Surgical mortality in this series was 0%. At the 3-months FU, all 34 patients (37 cases, since 3 patients were operated twice for tumor recurrence) were alive. Neurosurgical complications of any kind were recorded in 25 patients (67.6%): of these 10 were major complications (27% overall) and 15 were minor complications (40.5% overall). Mortality and complications data are summarized in Table 4.

Regarding the change in LS scores, compared to the preoperative status, at discharge there were 20 (54.1%) improved/unchanged and 17 (45.9%) worsened patients, while at FU there were 26 (70.3%) and 11 (29.7%), respectively. Finally, at FU, compared to discharge, there were

Table 3
Demographic, clinical, histological data, tumor location, surgical approaches, extent of resection (EOR) and adjuvant therapies data.

	variable		value
Sex	male		9 (26.5%)
	female		25 (73.5%)
Age	mean +/-SD		7 ± 4.55
	range		1–17
Tumour location	thalamus		14 (37.8%)
	4th ventricle		12 (32.4%)
	brainstem		8 (21.6%)
		midbrain	3
		pons	3
		medulla	2
	pineal region		3 (8.1%)
Tumour histology	pilocytic astrocytomas		15 (40.5%)
		pilomyxoid	2
	medulloblastomas		8 (21.6%)
	ependymomas		5 (13.5%)
		anaplastic	3
		ependimoblastoma	1
	germinal tumours		2 (5.4%)
	glioblastomas		2 (5.4%)
	pineal tumours		2 (5.4%)
	Other embryonal tumors		1 (2.7%)
	Anaplastic astrocytoma		1 (2.7%)
	LGG		1 (2.7%)
Clinical presentation	CN deficits		15
	motor disturbances		14
	cerebellar symptoms		13
	intracranial hypertension		9
	slowing of cognitive function		5
	epilepsy		2
Adjuvant treatment (CHT/RT)	Total		19 (51.4%)
	only CHT		6 (16.2%)
	only RT		2 (5.4%)
	CHT + RT		11 (29.7%)
Surgical approaches	Median suboccipital		14 (37.8%)
	Transcerebral/ transcortical image-guided		11 (29.7%)
	Supracerebellar infratentorial		4 (10.8%)
	Interhemispheric transcallosal		3 (8.1%)
	Retrosigmoid		2 (5.4%)
	Pterional		2 (5.4%)
	Combined		1 (2.7%)
Extent of tumour resection	Complete		23 (62.1%)
		Low grade	12/18
		High grade	11/19
	Subtotal (>90%)		10 (27%)
		Low grade	5/18
		High grade	5/19
	Partial (<90%)		4 (10.8%)
		Low grade	1/18
		High grade	3/19

CPA: cerebellopontine angle; LGG: low grade glioma; CN: cranial nerves; CHT: chemotherapy; RT: radiotherapy; FOZ: fronto-orbito-zygomatic.

Table 4
Complications rate and mortality. Classification of complications according to the Landriel-Ibanez classification[13] and the etiological classification[9].

	variable		value
Surgical mortality			0 (0%)
Complications	No complications		12 (32.4%)
	Complications		25 (67.6%)
		major*	10 (27%)
		minor†	15 (40.5%)
	Landriel-Ibanez classification‡		
	Grade I		8 (32%)
		Grade Ia	2
		Grade Ib	6
	Grade II		13 (52%)
		Grade IIa	3
		Grade IIb	10
	Grade III		4 (16%)
		Grade IIIa	3
		Grade IIIb	1
	Grade IV		0 (0%)
	Etiological classification§		
	Traumatic		9
	CSF-related		13
	Septic		9
	General medicine (extra CNS)		4
	Haemorrhagic		2
	Epilepsy		2
	Others		1
	Haemorrhagic/ischemic stroke		0

*Major complications: new or worse impaired neurological function (e.g., hemiparesis, hemianopia), cranial nerve palsies, stroke, sepsis, "major" re-craniotomy (e.g., blood clot/subdural/extradural hematoma removal, decompressive craniectomy for brain swelling, surgical CSF leak repair), and life-threatening medical complications (e.g. heart complications, pulmonary embolism)
† Minor complications: wound infection, subgaleal fluid collection, subjective neurological disturbances (e.g., visual disturbances, dizziness, sense of confusion), postoperative meningitis, seizures, postoperative fever or minor infections (e.g. urinary tract infections), and "minor" re-craniotomy (e.g., wound revision, external ventricular drainage, ventriculo-peritoneal (VP) shunt, external spinal drainage for CSF leak repair).
‡ Landriel-Ibanez classification:
Grade I = any non-life-threatening deviation from normal postoperative course that did not require invasive treatment (Ia = non requiring drug treatment; Ib requiring drug treatment)
Grade II = complication requiring invasive interventions, such as surgical, endoscopic or endovascular treatment (IIa = without general anaesthesia; IIb = with general anaesthesia)
Grade III = life-threatening interventions requiring ICU management (IIIa = complication involving single organ failure; IIIb = complications involving multiple organ failure)
Grade IV = complications resulting in death
§The number of complications based on the etiological category was higher than those based on the Landriel Ibañez classification due to the fact that a complication may have multiple etiologies.
FU: follow-up; CSF: cerebrospinal fluid; CNS: central nervous system.

34 (91.9%) improved/unchanged and 3 (8.1%) worsened patients (Table 5).

Concerning preoperative surgical complexity, all patients had a minimum MCS score of 3, since all the lesions were located in eloquent areas. Four (10.8%) patients had a score of 3, six (16.2%) had a score of 4, eight (21.6%) had a score of 5, four (10.8%) had a score of 6, five (13.5%) had a score of 7 and ten (27%) had a score of 8. Mean MCS score for all cases was 6 ± 1.7.

3.2. Statistical analysis

3.2.1. Longitudinal analysis

The longitudinal analysis showed a worsening in LS scores between the preoperative and discharge time (p = 0.011), but also an improvement of the LS at FU compared to discharge (p = 0.004).

Mean LS score for the preoperative period was 80.8 ± 13.4, for the postoperative period was 74.6 ± 18.3 and for the FU was 80.3 ± 17.6. These data are reported in Table 5.

Table 5
LS (Lansky Scale) score descriptive statistics and longitudinal analysis.

Descriptive statistics of LS			
	variable		n of patients
Change in LS score after surgery (discharge vs preop)	Improved/ unchanged		20 (54.1%)
	Worsened		17 (45.9%)
Change in LS score at 3 months FU (FU vs preop)	Improved/ unchanged		26 (70.3%)
	Worsened		11 (29.7%)
Change in LS score at 3 months FU (FU vs discharge)	Improved/ unchanged		34 (91.9%)
	Worsened		3 (8.1%)
	Preoperative	Discharge	Follow-up
Mean LS score	80.8 ± 13.4	74.6 ± 18.3	80.3 ± 17.5
	Discharge-Preop	Follow up-Preop	Follow up-Discharge
LS change	−6.22	−1.62	+5.68
P-values (p < 0.016)	+0.011	+0.852	+0.004

3.2.2. Comparison of variables between two groups

Regarding the comparison between improved/unchanged and worsened patients at discharge and FU compared to preoperative status, the worsened group had a significantly higher percentage of complications (p = 0.000 and p = 0.007, respectively), while no other statistically significant differences were detected.

3.2.3. Predictors of postoperative worsening

None of the five analyzed MCS items (tumor dimension > 4 cm, posterior fossa surgery, cranial nerve manipulation, major brain vessel manipulation and MCS total score) was found to be a significant predictor of early postoperative change/worsening. However, the percentages of worsened patients between discharge and the preoperative period for each MCS score were calculated and a trend toward an increase in the number of worsened patients as the MCS score increases was evident. The worsening percentages were distributed as follows: 25% (1/4) of MCS 3 patients, 33% (2/6) of MCS 4 patients, 50% (4/8) of MCS 5 patients, 50% (2/4) of MCS 6 patients, 60% (3/5) of MCS 7 patients and 70% (7/10) of MCS 8 patients (Table 6).

4. Discussion

In the present series of intra-axial thalamic and PF pediatric tumors, treated surgically according to a maximal safe resection attitude, [15–19] there was a statistically significant clinical worsening at

Table 6
Percentages of worsened patients at discharge for each MCS (Milan Complexity Scale) score.

Percentages of worsened patients at discharge for each MCS score	variable	percentage
	1*	\
	2*	
	3	25%
	4	33%
	5	50%
	6	50%
	7	60%
	8	70%

*In the present study no patient had an MCS score of 1 or 2.

discharge, followed by a significant improvement at FU. The majority of the complications developed by patients following surgery were transient and improved with time and physiotherapy.

Our case series was histologically heterogeneous, which implied a variety of biological behaviors and degrees of resectability. Surgery was used alone in half of the cases, while the other half also received adjuvant therapies (CHT, RT or both), in line with the most recent publications and established guidelines. [1,22,23]

The early post-operative complication rate (at discharge) was 67.6%, of which less than half were major complications. Nevertheless, most postoperative new deficits revealed to be transient in nature, as patients were able to recover or even improve their condition, either spontaneously or through physiotherapy. Accordingly, the mean LS score at FU improved compared to discharge (from 74.6 to 80.3), thus returning back to the preoperative baseline (80.8).

Historically, surgery of this kind of BT in children was considered too risky to be performed and, usually, only biopsies followed by CHT or RT were offered. [9–13] However, even though long term progression free survival (PFS) and overall survival (OS) were not the focus of the present study and therefore were not analyzed, several recent reports, claim that surgical resection, as the initial management strategy for these kinds of lesions, positively impacts OS and PFS, [24–27] especially if it is as radical as possible. Surely the risks of surgery in such deeply seated areas are high and the balance between surgical prudence and surgical aggressiveness is extremely delicate. Nonetheless, recent improvements in preoperative and intraoperative technologies, as well as in surgical techniques, have allowed a shift toward a more proactive approach in surgical removal. [3–8] Moreover, other studies have also postulated that postoperative deficits in children with deep-seated tumors are most of the times fully recoverable: in a study by Baroncini et al., 16 pediatric patients treated for thalamic tumors between 1992 and 2006 were reviewed and among the results, no permanent worsening of the patients' neurological status was recorded in the long-term FU. This was attributed to the extraordinary plasticity of the pediatric nervous system. [28] Similarly, Cinalli et al. also presented their case series of pediatric thalamic tumors and they also came to the conclusion that postoperative deficits are likely to occur, but tend to improve rapidly and significantly during the FU period. [29]

Our analysis included investigation of five items - namely tumour location, WHO grade, complication development, EOR and MCS score - in association with clinical outcome after surgery. This was done by comparing the improved/unchanged LS group to the worsened LS group. A significant relationship between the development of complications and a worsening of the LS score, both at discharge and FU, was recorded. Although rather intuitive, the literature still lacks studies on the presence of factors associated to postoperative clinical decline for tumors in these areas. On the other hand, it was not possible to find a statistically significant association between the other items and postoperative worsening. This is probably due to the small sample size of our cohort, as well as the biased data distribution secondary to the high baseline MCS scores. In fact, the mean MCS scores in the improved/unchanged group versus the worsened group were very similar, when comparing both discharge with preoperative, and FU with preoperative status. Conversely, in a previous work published by our group, [14] which first established the MCS as an effective predictive tool of clinical worsening, the 746 cases were distributed among all brain regions and had MCS scores ranging from the minimum to the maximum grade, maximizing the difference between the two groups.

In the surgical care of IAT and PF pediatric tumors, predictive factors to assess the risk of clinical decline after surgery are unfortunately still lacking. In an attempt to find any such factors, we investigated the strength of the relationship between the drop in LS scores at discharge and four MCS items (posterior fossa, cranial nerve manipulation, major brain vessel manipulation and tumor dimension) plus the total MCS score. The item "eloquent area" was excluded from this analysis since all tumors in the series were located in highly functional brain regions, thus confirming a high case complexity in this series. None of these factors were individually found to be significant predictors of early postoperative worsening. Nonetheless, by calculating the percentage of worsened patients for each of the MCS scores, a trend toward aggravation at the higher end of the scale was evident, confirming the fact that, at least from a descriptive point of view, higher MCS grades are associated with postoperative clinical worsening (Table 6). In this sense, even though the MSC was not found to be significantly predictive of clinical decline after surgery, the scale might still be useful in the surgical decision-making process when discriminating between cases that would benefit from surgical resection versus cases where surgical risks outweigh the benefits. Moreover, we also believe the MCS to be a helpful tool when discussing a patient's clinical situation and the risks of surgery with parents. In such a psychologically, emotionally and physically demanding moment, the MCS can provide a more objective view of the situation and it may help parents understand a condition which they are most likely not familiar with.

There are several limitations to this study that must be considered: first and foremost, this is a single-center retrospective study. Multicentric data collection and analysis are warranted to validate these results. The small sample size could also have affected our results on significant differences among groups and on longitudinal differences. However, considering that these kinds of tumors are rare entities, the present series of 34 patients denotes a high degree of specialization of our center for these kinds of pathologies. We are also aware that the factors we analyzed in association with clinical outcome after surgery are far from being the only ones possibly involved. Nevertheless, they were deemed some of the most significant ones after a careful evaluation of the existing literature and our study population. The sample is also very heterogeneous and future studies using larger and more homogenous groups are recommended.

5. Conclusions

Surgical resection of IAT and posterior fossa tumors in pediatric patients is surely challenging, but it is nonetheless feasible and worthwhile. To date, GTR is still the strongest predictor of outcome for these patients. Therefore, new deficits, secondary to surgical resection pushed to the boundaries of involved eloquent areas, might indeed be a price worth paying, especially since most of them are transient and tend to improve at FU. We were not able to identify significant factors to predict the risk of clinical decline after surgery; however, the MCS and its items seem valuable tools to broadly estimate early postoperative worsening, thus improving parents' informed consent, the decision-making process and the whole management of these challenging lesions.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inat.2020.101054.

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