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Original Article

Survival and prognostic factors in childhood medulloblastoma: A Brazilian single center experience from 1995 to 2016

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ABSTRACT

Background: Medulloblastoma is the most common malignant brain tumor in the pediatric population. Despite prognosis improvement in the past two decades, one-third of the patients still remain incurable. New evidence suggests that medulloblastoma comprises four distinct entities; therefore, treatment de-escalation is required. The aim of this article is to evaluate epidemiological data from patients treated at our institution. The primary objective is to analyze overall survival (OS) and event-free survival (EFS) and the secondary objective is to identify prognostic factor from this cohort.

Methods: We retrospectively analyzed 69 patients who underwent surgical resection for medulloblastoma among 423 children from the tumor registry data bank of Santo Antônio Children's Hospital from 1995 to 2016. Kaplan–Meier method and Cox regression analysis were used to identify OS, EFS, and prognostic factors.

Results: The 5-year OS and EFS rates found were 44.5% and 36.4%, respectively. The extent of resection and radiotherapy as adjuvant treatments was positively correlated to outcome while metastatic disease at diagnosis was negatively related to OS. Age younger than 3 years old did not have a worse outcome in our cohort.

Conclusion: Similar results to population-based studies were found, but we still face difficulties due to living in a developing country. In the near future, we look forward to new diagnostic techniques that will enable us to classify medulloblastomas according to molecular subgroups.

Keywords: Childhood medulloblastoma, Event-free survival, Gross total resection, Overall survival, Prognostic factors

INTRODUCTION

Medulloblastomas are the most common malignant tumor of the central nervous system (CNS) in children.[14] They account for 20% of the brain neoplasms in the pediatric population and are classified as embryonal tumors according to the World Health Organization (WHO) classification system. In the United States, medulloblastoma incidence is around 5.07 children per million and they have a bimodal peak at 3–4 years old, and then again at 8–7 years old.[12,16] Epidemiological data in Brazil are rare, and the real incidence of this tumor is not known. In a large series of pediatric tumors in an oncology reference center in São Paulo, medulloblastoma prevalence was around 13%.[19]

These tumors occur in the posterior fossa and they grow into the IV ventricle or in the cerebellar hemisphere leading to obstructive hydrocephalus.[2] Truncal ataxia and limb dysmetria may also occur in response to cerebellar involvement. Metastatic disease is frequent at diagnosis, especially in infants, occurring in around 30% of cases.

Since 1969, medulloblastoma risk stratification has undergone new modifications, and Chang's original system is currently still in use.[1] Patients younger than 3 years old, with metastatic disease at diagnosis or with a residual tumor >1.5 cm^2, are considered high-risk patients. More recently, other features have been added to the original stratification: the presence of large cell/anaplasia or MYC amplification, both being part of the high-risk group, and Wnt subgroup as part of the low/average risk group.[5]

Survival rates in medulloblastoma patients improved toward the end of the 90s. Craniospinal radiotherapy as an adjuvant treatment reached overall cure rates of around 70%–85%. This led to a reduction in the risk of death by approximately 30%.[6] Nowadays, current treatment protocols include maximal safe tumor resection followed by radiotherapy in children older than 3 years old, and chemotherapy (CT) with cytotoxic agents, both according to risk stratification. For children under 3 years old, only CT with potent agents is allowed due to the possible damage caused by irradiation on an immature brain.[2]

In this article, we reviewed our 21 years' experience in diagnosing and treating medulloblastomas at a children's hospital, in Southern Brazil, dedicated to the public national health system. The aim of our study was to evaluate epidemiological data on medulloblastoma population, determining the spectrum and frequency of the variants encountered as well as if the data correlate with the current literature. The analysis of overall survival (OS) and event-free survival (EFS) rates in our cohort will enable us to check our institution treatment results and to compare to scientific literature data. The secondary objective is the identification of prognostic factors for survival among the analyzed variables.

PATIENTS AND METHODS

We retrospectively analyzed patients presenting histological medulloblastoma diagnosis from the tumor registry data bank of Santo Antonio Children`s Hospital. Among 423 children operated on for brain tumors, we identified 69 patients with medulloblastoma, diagnosed and treated between January 1995 and June 2016; all were operated by the same surgeon (JWJB). Only those with complete medical records and follow-up were included. Exclusion criteria were supratentorial primitive neuroectodermal tumors (PNETs) and insufficient clinical data and follow-up information.

The present study was approved by the hospital's Research Ethics Committee in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments, under registration number CAAE 40232214.5.0000.5327.

Patient data were collected only from patients records on the following variables: age, sex, symptoms, prediagnostic symptomatic interval (PDSI), presence of hydrocephalus, tumor location, surgical approach, surgical resection, need of definitive hydrocephalus treatment, tumor histology, metastatic disease, tumor relapse, postoperative complication, and late sequelae.

Patient risk stratification was defined according to Chang's system.[1] From 1995 to 2002, the stratification risk was based on transoperative impression and postoperative head and spine CT. Only after 2002, magnetic resonance imaging (MRI) scan became available. The extent of resection was divided, for the purpose of data analysis, in total resection, where patients who underwent gross total and near-total resection were included, subtotal and biopsy groups.

Adjuvant conventional radiotherapy was performed according to current protocols so that high-risk patients received craniospinal irradiation of 36 Gy and a posterior fossa boost to complete 54 Gy. Standard risk patients instead received 24 Gy to the neuroaxis in addition to a posterior fossa boost to complete 54 Gy. CT standard protocol consisted of eight doses, once a week, of vincristine in a dose of 1.5 mg/m^2 during radiation therapy (RT). Subsequently, eight cycles of vincristine in a dose of 1.5 mg/m^2, 75 mg/m^2 of cisplatin, and also 75 mg/m^2 of lomustine were administered. A variation of this protocol was also used, with cyclophosphamide instead of lomustine, and in certain cases, etoposide was associated with these two described protocols. High-risk patients received a high-risk protocol known as head start, with high doses of methotrexate, vincristine, etoposide, cisplatin, and cyclophosphamide in five cycles followed by autologous stem cell rescue.[3]

The statistical analysis was performed with IBM SPSS® Statistics version 2.1. Quantitative variables were described by mean and standard deviation and interquartile range, depending on the distribution of data. Categorical variables were described by absolute and relative frequencies. OS and EFS were estimated with the Kaplan–Meier method. For OS, time was defined as the interval from the date of surgery to the date of death for all causes, with censoring at the date of the latest follow-up visit for live patients. For EFS, time was the interval also from the date of surgery to the date of an event such as relapse or death, with censoring at the latest follow-up visit for live patients and progression-free patients. For the prognostic effect of the variables, multivariate Cox regression analysis was applied. The criteria for entry of the variables into the multivariate model was that they had $P < 0.20$ value in the bivariate analysis and/or being relevant according to literature. The statistical significance level adopted was 5%.

RESULTS

Among the 69 patients enrolled from January 1995 to June 2016, only 61 patients had complete information in medical records, though two were excluded because they were not confirmed as medulloblastomas. From the 59 patients, 36 were male and 23 were female, a rate of 1.5:1.0. The mean age in this cohort was

6 years old, ranging from 5 months to 13 years old. Table 1 shows the sample clinical features in means and standard deviation or medium and interquartile interval.

All patients underwent surgery, with gross total resection achieved of 76.8%. The patient who only underwent a biopsy had M4 stage metastatic disease diagnosed at clinical presentation, with lung impairment. A second surgery was necessary for 17 patients due to local relapse or as a second-look surgery due to residual disease.

There were neither intraoperative nor surgical mortalities, considering this as death occurring within 30 days after the surgical procedure. Postoperative complications such as cerebrospinal fluid (CSF) leakage happened in only five cases. CSF increased cellularity was seen in 15 cases, and despite negative cultures, all of them were treated as meningitis. Posterior fossa syndrome was diagnosed in five (8.5%) patients. Tumor relapse occurred in 20 (34%) patients, in a mean time of 17 months, ranging from 5.5 to 39 months.

The 5-year OS and EFS were 44.5% and 36.4%, respectively, after a median follow-up time of 29 months, with an interquartile range of 10–79. The EFS and OS rates from this cohort according to the variables are shown in Figure 1.

Long-term survival according to treatment protocols

The impact of surgical resection, radiotherapy, and CT protocols on OS and EFS is shown in the Kaplan–Meier curves in Figures 2 and 3. CT protocols had no statistical significance among them. Although both adjuvant treatments had a positive impact on OS and EFS in bivariate analysis, only RT was significant when multivariate analysis was applied (OS $p_{adjusted}$ = 0.003 and EFS $p_{adjusted}$ = 0.005).

Of the total number of patients who underwent CT, 15 had the protocol interrupted due to treatment complications (n = 1), death due to therapy complications (n = 6), or death due to disease progression (n = 8). All patients who underwent RT completed the protocol.

Multivariable analysis of clinical risk factors

Neither age, PDSI, need of hydrocephalus definitive treatment, nor tumor relapse had a prognostic impact. Postoperative complications were statistically significant on bivariate analysis, although multivariate analysis suggested the opposite ($p_{adjusted}$ = 0.415). Metastatic disease at diagnosis was the only variable identified in this cohort that had significance (P = 0.022, HR 2.76; IC 1.16–6.58). Histology was not assessed in this cohort due to lack of information on histological subclassification and central pathology review. Only seven tumor specimens were categorized according to the WHO histological subclassification. Tables 2 and 3 describe Cox regression for OS and EFS and the variables used in this analysis.

Table 1: Clinical features.

Quantitative variables	**Mean±SD (minimum-maximum)/Md (P25–P75)**
Age (months)	70±39.4 (5–165)
PDSI (days)	30 (20–60)
Relapse meantime (months)	17 (5.5–39)
Categorical variables	***n* (%)**
Age	
<3 years old	14 (23.7)
>3 years old	45 (76.3)
Symptoms	
Intracranial hypertension	50 (90.9)
Cerebellar syndrome	23 (42.6)
Cranial nerve impairment	14 (25.5)
Tumor location	
Midline (IV ventricle/vermis)	44 (81.5)
Cerebellar hemisphere	10 (18.5)
Presence of hydrocephalus	48 (84.2)
EVD insertion	46 (83.6)
Definitive treatment for hydrocephalus	28 (47.5)
Surgical approach	
Suboccipital craniotomy	54 (91.5)
Others	5 (8.5)
Surgical resection	
Total	43 (76.8)
Subtotal	12 (21.4)
Biopsy	1 (1.8)
Metastatic disease at diagnose	10 (18.2)
Risk stratification	
Standard risk	33 (55.9)
High risk	26 (44.1)
RT	
No	18 (31.6)
Standard risk	29 (50.9)
High risk	10 (17.5)
CT	
No	5 (8.5)
Standard	22 (37.3)
Headstart I/II	14 (23.7)
Etoposide protocols	10 (16.9)
Others	5 (8.5)
Tumor relapse	21 (35.6)
Relapse location	20
Local	11 (55)
Mass at spine cord/brain	3 (15)
CSF dissemination	6 (30)
Late sequelae	39
Without late sequelae	26 (66.7)
Hypothyroidism	10 (25.6)
Growth deficiency	5 (12.8)
Hearing loss	4 (10.3)

SD: Standard deviation, PDSI: Prediagnostic symptomatic interval, EVD: External ventricular drain, RT: Radiation therapy, CT: Chemotherapy, CSF: Cerebrospinal fluid

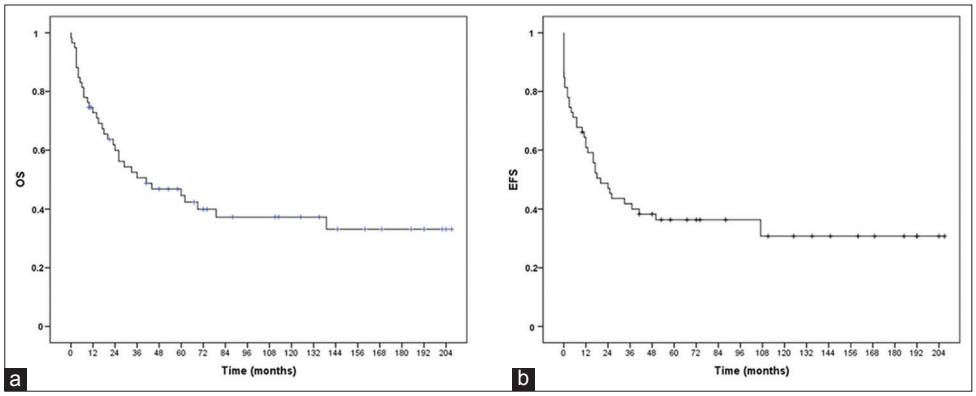

Figure 1: (a) Overall survival in 5 years of 44.5% and 10 years of 37.3%. (b) Event-free survival in 5 years of 36.4% and 10 years of 30.8%.

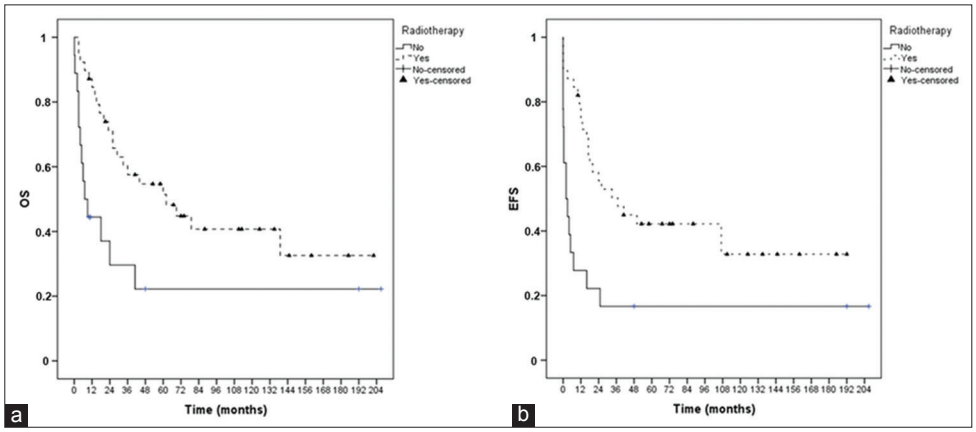

Figure 2: (a and b) Overall survival and event-free survival for radiotherapy.

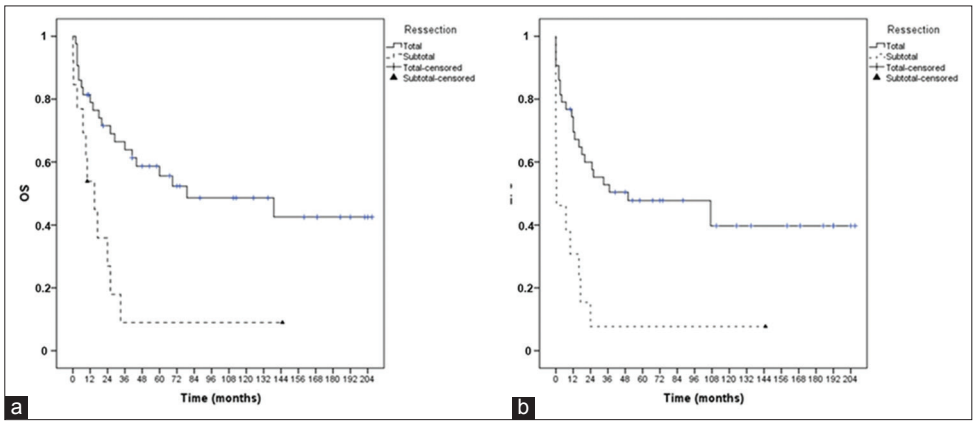

Figure 3: (a and b) Overall survival and event-free survival for gross total resection.

DISCUSSION

During the 90s, OS in medulloblastomas improved with the inclusion of routine craniospinal radiation and CT protocols. At that time, several multicentric trials assessing treatment results on medulloblastoma began and are still in progress. The evaluation of the described OS and EFS can achieve rates as high as 90% in some trials.[9,17,24] Table 4 lists the trials and OS/EFS results.[7,11,18,23,24]

Most publications on medulloblastoma patients' survival describe the results of clinical trials, which have stringent eligibility criteria that necessarily influence the survival data.[19] Therefore, they may not be representative of the general population.[25] Most papers analyze children older than 3 years old and with no evidence of metastatic disease at diagnosis, two clinical data point that was previously recognized as a prognostic factor in other series.[13]

Table 2: Overall survival – Cox regression analysis.

Variables	*n*	OS (md)	OS 5 year old %	OS 10 year old %	HR (IC 95%) (crude)	*P* value	$HR_{adjusted}$ (IC 95%)	$p_{adjusted}$
Age								
<3 years old	14	26	45.9	45.9	0.96 (0.42–2.20)	0.920	0.49 (0.12–1.92)	0.304
≥3 years old 45	45	41	44.5	35.5	1		1	
PDSI					1.00 (0.99–1.01)	0.300		
Hydrocephalus treatment							-	
No	31	-	68.9	59	1		1	
Yes	28	18	18.9	14.2	3.88 (1.87–8.07)	<0.001	1.96 (0.72–5.36)	0.188
Resection								
Total	43	79	55.6	48.6	1		1	
Subtotal	13	15	9	9	3.29 (1.54–7.03)	0.002	2.77 (1.14–6.68)	0.024
Metastasis								
No	45	62	51.2	42.2	1		1	
Yes	10	12	18	18	2.76 (1.16–6.58)	0.022	3.45 (1.24–9.54)	0.017
Risk stratification								
Standard	33	79	59	47	1			
High risk	26	23	24	24	2.27 (1.15–4.48)	0.018	-	
RT protocol								
No	18	7	22.2	22.2	2.56 (1.21–5.39)	0.014	-	
Low risk	29	62	52.8	39.1	1		-	
High risk	10	26	45.7	22.9	1.14 (0.45–2.93)	0.782	-	
RT								
No	18	7	22.2	22.2	2.47 (1.23–4.96)	0.011	5.71 (1.80–18.1)	0.003
Yes	39	62	51.4	40.7	1		1	
CT								
No	5	3	20.0	20.0	3.92 (1.50–10.2)	0.005	2.46 (0.66–9.17)	0.179
Yes	53	44	45.6	37.2	1		1	
CT protocol								
No	5	3	20.0	20.0	5.49 (1.86–16.2)	0.002	1.79 (0.45–7.06)	0.405
Standard	22	-	62.6	50.6	1		1	
Headstart	14	12	23.8	23.8	2.40 (0.96–6.03)	0.062	0.51 (0.12–2.24)	0.374
Variations including etoposide	10	41	40.0	40.0	1.18 (0.43–3.25)	0.750	0.40 (0.09–1.71)	0.215
Others	5	18	0	0	2.39 (0.74–7.73)	0.144	0.92 (0.18–4.65)	0.916
Relapse								
No	38	-	53.5	53.5	1		1	
Yes	21	36	33.3	17.9	1.62 (0.83–3.16)	0.156	1.76 (0.62–5.01)	0.291
Postoperative complications								
No	36	69	55.7	43.9			1	
Yes	23	12	26.1	26.1	2.42 (1.24–4.74)	0.010	1.49 (0.57–3.88)	0.415

PDSI: Prediagnostic symptomatic interval, OS: Overall survival, RT: Radiation therapy, CT: Chemotherapy

In regard to epidemiological data, population-based studies are more reliable. Weil *et al.*, analyzing the SEER data (Surveillance, Epidemiology, and End Results Program – a central cancer registry of the U.S.), identified the year of 1990 as a critical time-point. They labeled two cohorts, the historic one (1973–1989) and the contemporary one (1990–2012), and compared their 5-year OS. They observed that OS ranged from 51% to 69% among both, thus being statistically significant ($P < 0.001$).[25] Johnston *et al.* also described this 5-year OS uplift, from 60% to 73%, in their cohort in Canada. For both authors, medulloblastoma incidence remained stable.[8] The probable cause of this improvement in outcome is unclear, though one should consider a number of points: better access to health care, faster initial diagnosis, greater recruitment into clinical trials, alternatives of adjuvant therapy, aggressiveness of management initially and at relapse, and better supportive care and improvement in RT and imaging technology.

The 5-year OS and EFS rates gathered from this cohort analysis were lower than those in the current scientific literature, despite the fact the extent of resection was 76.8% in accordance with the

Table 3: Event free survival – Cox regression analysis.

Variables	*n*	EFS (md)	EFS 5 year old (%)	EFS 10 year old (%)	HR (IC 95%) (crude)	*P* value	$HR_{adjusted}$ (IC 95%)	$p_{adjusted}$
Age								
<3 years old	14	4	35.7	35.7	0.83 (0.39–1.74)	0.614	0.66 (0.24–1.77)	0.404
≥3 years old 45	45	25	36.5	29.2	1		1	
PDSI					1.00 (0.99–1.01)	0.277		
Hydrocephalus definitive treatment							-	
No	31	-	56.8	51.1	1		1	
Yes	28	13	14.3	9.5	2.89 (1.49–5.61)	0.002	2.88 (1.27–6.52)	0.011
Resection								
Total	43	50	47.7	39.8	1		1	
Subtotal	13	0,5	7.7	7.7	3.38 (1.65–6.93)	0.001	2.83 (1.26–6.39)	0.012
Metastasis								
No	45	37	43.2	36	1		1	
Yes	10	2	10	10	3.49 (1.59–7.66)	0.002	4.23 (1.62–11)	0.003
Risk stratification								
Standard	33	107	50.1	40.1	1			
High risk	26	5	19.2	19.2	2.51 (1.32–4.76)	0.005	-	
RT Protocol								
No	18	2	16.7	16.7	2.76 (1.36–5.60)	0.005	-	
Low risk	29	41	42.9	36.8	1		-	
High risk	10	18	40	20	1.25 (0.52–3.03)	0.615	-	
RT								
No	18	2	16.7	16.7	2.59 (1.34–5.02)	0.005	3.85 (1.50–9.88)	0.005
Yes	39	37	42.2	32.8	1		1	
CT								
No	5	0,1	20	0	3.09 (1.19–8.04)	0.020	1.84 (0.57–5.90)	0.307
Yes	53	24	36.6	33.3	1		1	
CT Protocol								
No	5	0,1	20.0	0	4.70 (1.61–13.7)	0.005	1.78 (0.45–7.01)	0.411
Standard	22	107	52.5	45	1		1	
Headstart	14	5	14.3	14.3	3.17 (1.38–7.26)	0.007	1.04 (0.32–3.39)	0.954
Variation including etoposide	10	25	40.0	40.0	1.13 (0.42–3.05)	0.817	0.67 (0.19–2.28)	0.526
Others	5	12	20	20	2.65 (0.83–8.41)	0.099	1.40 (0.34–5.73)	0.636
Postoperative complications								
No	36	37	44.1	39.2			1	
Yes	23	7	24.2	18.1	2.04 (1.08–3.85)	0.029	1.02 (0.45–2.34)	0.958

EFS: Event-free survival, PDSI: Prediagnostic symptomatic interval, RT: Radiation therapy, CT: Chemotherapy

Table 4: Medulloblastoma trials.

Author/year	Trial	Sample	Age	Evaluation	5 years OS/EFS
Taylor *et al.*[23]	SIOP-PNET 3	179	>3 years old/no MTx	PreRT chemotherapy with highly active agents	OS 70%/EFS 67%
Gajjar *et al.*[7]	ST-Jude Medulloblastoma 96	134	>3 years old	Risk-adapted craniospinal RT followed by high dose CT and stem cell rescue	OS AR 85% HR 70% EFS AR 83% HR 70%
von Hoff 2009[24]	HIT91	187	>3 years old	Compared preradiation and post radiation protocols	OS 63% EFS 57%
Lannering *et al.*[11]	HIT-SIOP PNET 4	340	>4 years old	Compared hyperfractionated RT versus conventional RT	OS 85–87% EFS 77–78%
Packer *et al.*[18]	coga9961	379	>3 years old/no MTx	Survival and incidence of secondary tumors in patients treated with RT and CT	OS 87% EFS 81%

PNET: Primitive neuroectodermal tumors, RT: Radiation therapy, EFS: Event-free survival, OS: Overall survival, CT: Chemotherapy

data reported in literature.[2,16] Undoubtedly, three factors might have influenced the findings: (1) the acquisition of the MRI by the studied institution happened in 2002, (2) there were numerous pediatric oncology teams performing in the same institution, and (3) the three-dimensional radiotherapy planning began to be implemented in 2005. Furthermore, it is proper to assume that the gross total resection rate could have been improved provided the use of a better quality microscope and ultrasonic aspirator. Taken together, these may be classified as everyday dilemmas in public health systems to economically developing countries.

The average time interval between symptom onset and diagnosis in our review has a median time of 30 days, in accordance with current data. Reulecke *et al.* reported an interval of 24 days in a German center, while Dobrovoljac *et al.* reported a higher interval of 60 days.[4,20] According to Kukal *et al.*, who compared PDSI to patient's age, tumor histology, tumor location, and OS, an association was found between tumor histology and location, though there was no correlation between PDSI and outcome in their series. Higher-grade tumors tend to have a smaller PDSI than lower-grade tumors, which may explain their finding.[10]

In contrast, our series comprises patients at high-risk stratification, including those younger than 3 years old. We also observed that among patients under CT protocols (n = 53), 15 had treatment interruption due to medical complications or death, meaning a loss of 30%. Von Hoff *et al.* reported that 70% of the patients under Packer CT protocol in the HIT91 cohort needed CT dose reduction due to toxicity, though all of them completed at least four cycles. Their analysis did not find any negative influence on survival rates.[24] Furthermore, patients who were submitted to the headstart protocol had a tendency to worse prognosis (EFS P = 0.007) which was not confirmed in multivariate analysis (P = 0.954). Overall, we did not find any difference between CT protocols, nor that CT in our series was a prognostic factor.

When we analyzed data according to stratification risk, the achieved rates in our cohort were more similar to other population-based studies. Fairley *et al.* found an OS of 54% in 5 years for children under 14 years old in the U.K.[6] Similarly, Smoll, in 2012, calculating the cumulative relative survival estimate, found a 5-year OS and 10-year OS of 25%/25% and 56%/52% for infants and children, respectively.[22] The lack of information from Brazilian cohorts does not allow internal comparisons.

Focusing on children younger than 3 years old, we observed an OS rate in 5 and 10 years of 45.9%. None of them underwent radiotherapy protocols, receiving only high dose CT. Rutkowski *et al.*, in a meta-analysis evaluating survival and prognostic factors in children under 5 years old, found OS in 8 years of 56%. Prognostic factors included the extent of resection, metastatic stage, and the presence of desmoplasia/extensive nodularity and anaplasia/large cell tumor in histology.[21] Johnston *et al.* analyzed 96 children under 5 years old treated in Canadian pediatric oncology centers between 1990 and 2005. In this population-based study, the 5-year OS rate was 45.7%; however, 20% of their population was treated with CNS irradiation. As prognostic factors, radiotherapy and CT were statistically significant in their evaluation.[8]

In our analysis, we did not prove that younger children had a worse prognosis. On the contrary, our 5-year survival rates are similar in both groups (P = 0.92). Comparing our 5-year and 10-year OS, as well as EFS rates, especially in the youngest population, we observed minimal differences between them. Our case losses, therefore, occurred mostly before the 5-year follow-up period. As for the death in our cohort, we found that only one happened 6 years after the diagnosis. Another series found that 8 years following the initial diagnosis is a critical time point after which the odds of mortality from medulloblastoma are much lower when compared to all other-cause mortality.[25]

We achieved gross total resection in 76.8% of the children in our series. This number is in accordance with the current scientific literature.[2,16] Twelve children underwent subtotal resection and one had just a biopsy. Multivariate analysis showed that these two groups have a 177% greater chance of dying from medulloblastoma than those who had a total resection (P = 0.024). Gajjar *et al.* did not find an advantage in gross total resection in their series, nor an association between the extent of resection and the occurrence of posterior fossa syndrome.[7] Taylor *et al.* in the PNET 3 study also did not find this association.[15-23] Nonetheless, there are articles that do correlate the extent of resection with a better outcome.[26]

Curiously, hydrocephalus definitive treatment and postoperative complications were correlated to worse outcome in bivariate analysis. Shunt placement or endoscopic third ventriculostomy was needed in almost 50% of patients and those had a 188% greater chance of dying from the tumor. However, on multivariate analysis, it was not statistically significant for OS (P = 0.188). This might be related to the clinical presentation, but further studies are necessary.

There are several limitations to this study. It was not possible to perform both central pathological and radiological reviews due to the lack of access to the paraffin-embedded tissue blocks, as well as to the neuroaxis exams pre-MRI era. Furthermore, metastatic stage analysis was not possible due to the small number of patients in M2/M3 groups, as well as bias from false negative neuroimaging exams from the preMRI era and incomplete information from CSF sample acquisition. Finally, this study is subject to all the potential biases of a retrospective cohort.

CONCLUSION

As far as we know, this retrospective cohort is the largest one in Brazil that has evaluated medulloblastoma treatment outcome. Available information in literature is commonly derived from

multicenter clinical randomized trials that include several countries, and sample sizes can reach hundreds of patients. Despite a limited sample, we were able to analyze OS and EFS rates in our institution, a typical public health system hospital in Brazil. The results that we have found are similar to population-based studies from the past two decades. Nevertheless, one should consider that working in a developing country, not rarely we face more difficulties in promoting the more appropriate treatment for medulloblastomas patients.

Similarly to other series, we found prognostic factors to be the extent of resection, the presence of metastatic disease, and posterior fossa and craniospinal irradiation. On the other hand, children younger than 3 years old were not correlated to a worse prognosis.

Finally, the study of this cohort of medulloblastoma epidemiological data provides the main features of this significant pathology in Southern Brazil, and we soon hope to be able to perform the molecular classification, which will provide the best treatment advances for our patients.

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Conflicts of interest

There are no conflicts of interest.

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