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Epidemiological Profile of Adult Patients with Surgically Treated Intracranial Neoplasms

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Authors' contributions

This work was carried out in collaboration among all authors. Author RTS, designed the study. Authors FD and LFMS, wrote the protocol. Author BRGMC, performed the statistical analysis. Author VKTF, managed the analyses of the study. Author JC, analyses of the study. Author JLR, analyses of the study. Author FLRD, wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The American Cancer Society,s estimates for brain and spinal cord tumors in the United States for 2023, include both adults and children,25,400 malignant tumors will be diagnosed. The objective of this study was to analyze the epidemiological profile, risk factors for complications and

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death in the in-hospital postoperative period, in addition to describing the histological type of intracranial tumors most frequently operated on in a private Brazilian institution.

Study Design: Retrospective cohort study.

Place and Duration of Study: Biocor Instituto/Rede D'Or, from 2018 to 2021

Methodology: Data were collected from the medical records of patients who underwent surgery for intracranial tumors. The variables analyzed in this study were demographic characteristics (age, sex, and comorbidities), histological types of primary and secondary neoplasms, anatomical location of the lesions, neurological deficits at admission and post-surgical treatment (at discharge), whether the surgery was urgent or elective, whether it was a reoperation, and whether there were deaths or complications during hospitalization.

Results: Of 242 patients, 11 patients were excluded, and 231 patients were included in the analysis. The most common histological type was meningioma, accounting for 28% of cases. The histological type most associated with the risk of death was hemangioblastoma; however, it was also the histological type that presented the lowest incidence of cases. 39 patients (17%) had some complication in the in-hospital postoperative period, and 14 patients (6%) died.

Conclusions: Meningiomas constituted the majority of cases, accounting for 28% of the sample. The rate of complications and mortality was higher when compared to data from the international literature because this series analyzed brain metastases together with the excision of primary tumors. Concerning in-hospital deaths, hemangioblastoma emerged as the histological type most associated with the risk of death. It is noteworthy, however, that hemangioblastoma also exhibited the lowest incidence among the various histological types.

Keywords: Intracranial tumors; neoplasms; brain metastases; brain tumor, spinal cord tumors, surgical resection.

1. INTRODUCTION

In adults, cerebral metastases are by far the most common intracranial tumors. The incidence of brain metastasis is difficult to determine with precision. It has been estimated to range from 21,000 to more than 100,000 new cases per year and nearly 70,000 new cases of primary malignant and benign brain and central nervous system are diagnosed in United States each year Primary malignant brain neoplasms are responsible for 2% of all cancers in adults in the United States and rarely metastasize outside of it [1,2]. It is estimated that 11,100 new cases of CNS tumors are diagnosed each year in Brazil: 5,870 in men and 5,230 in women [3].

There is no standard staging method for these patients, and surgical resection of the tumor is the basis of therapy. Glioblastoma is the most common example of these neoplasms and is classified as a tumor with a high degree of malignancy by the World Health Organization. This tumor has a very poor prognosis, with an incidence of approximately 3.19/100,000 inhabitants, and in patients with an average age of 64 years [4,5,6]. Among benign primary brain neoplasms, meningiomas are the most common subtype. This predominance is primarily attributed to their encapsulated nature, characterized by a low degree of genetic mutations [7,8,9]. More common in women than in men, they were the most frequently diagnosed neoplasms, accounting for 33.8% of all CNS tumors in the USA between 2002 and 2006. Regarding secondary CNS neoplasms, it is estimated that 10% to 45% of other primary cancers metastasize to brain tissue; the main primary tumors are lung, breast, melanoma, and colorectal carcinoma [10,11-12].

Usually, the prognosis of an intracranial neoplasm is unfavorable, with an overall five-year survival rate of 33.4% for primary intracranial tumors. If the diagnosis is glioblastoma multiforme, the average survival time is 15 months. In these cases, neurosurgical evaluation is essential to obtain tissue for diagnosis and consider possible tumor resection [4,6,9,11]. Progress in diagnostic and determination technologies, particularly for nonmalignant brain tumors, may account for much of the modest increase in incidence. Changes in tumor classification and coding are likely responsible for some of the increases in incidence for brain tumor histologies.

The objective of this study was to analyze the epidemiological profile, risk factors for complications, and death in the in-hospital postoperative period, in addition to describing the most common histological type of intracranial tumors operated on in a single Brazilian institution.

2. MATERIALS AND METHODS

This was a retrospective cohort study. Data was collected from the medical records of patients who underwent surgery for intracranial tumors at the Biocor Instituto/Rede D'Or between 2018 and 2021.

For this study, all patients aged ≥ 18 years who underwent neurosurgery for intracranial tumors between 2018 and 2021 were included. Patients < 18 years of age, those without complete medical records, and those with pathological data incompatible with a tumor were excluded from the study.

2.1 Data Collection

The variables analyzed in this study were demographic characteristics (age, sex, and comorbidities), histological types of primary and secondary neoplasms, anatomical location of the lesions, neurological deficits at admission and after surgical treatment (at discharge), whether the surgery was urgent or elective, whether it was a reoperation, and whether there were deaths or complications during hospitalization.

To evaluate the histological types of neoplasms, anatomopathological reports were reviewed to evaluate demographic characteristics, lesion location, and clinical conditions, and data were collected directly from medical records. The identities of the patients were preserved, and there was no need for new consultations; all data were collected retrospectively.

2.2 Statistical Analysis

The data was analyzed using descriptive statistics techniques, with the construction of graphs, tables, and the calculation of measures such as means, standard deviations, and percentages, to summarize the data [13]. The occurrences of the primary outcome, intra-hospital postoperative complications, and secondary outcome (hospital death) were calculated using a point estimate and a 95% confidence interval [14].

Univariate analyses were performed to identify factors associated with both in-hospital death and in-hospital postoperative complications. Bilateral hypothesis tests were carried out, considering a significance level of 5% ($\alpha = 0.05$). Univariate analysis was conducted to evaluate the gross association between the independent variables of interest and each outcome. Categorical variables were evaluated using Pearson's chi-square test or exact tests (when necessary), and quantitative variables were evaluated using the non-parametric Mann–Whitney test [15].

Finally, multivariate analysis was performed using logistic regression for both in-hospital deaths and intra-hospital postoperative complications. The variables that constituted the model at this stage of the multivariate analysis were selected using univariate analysis ($P < 0.25$). To select the independent factors associated with the outcome, logistic regression methods with automatic variable selection or Forward Stepwise were applied [15].

This work was approved by the hospital board.

3. RESULTS

Of 242 patients who were operated on during the analyzed period, 11 were excluded (5 due to lack of data in the medical record, and 6 due to pathological findings not compatible with tumors). Thus, 231 adult patients with surgically treated intracranial neoplasms were evaluated. Regarding age, 64% were between 50 and 70 years old, with a mean and median of 57 + 15,3 years old. Regarding the Glasgow Coma Scale (GCS) at admission, most patients (87%) were admitted with a GCS of 14 or 15 points, with a mean of 14.8 + 0,5. Regarding neurological deficits at admission, most patients (84%) were admitted with at most one deficit, with a mean of 0.7. Male sex, motor deficit at admission, high WHO grade, and immediate postoperative complications were risk factors for death ($P <$ 0,005) (Table 1).

Thirty-nine patients (17%) had complications during the in-hospital postoperative period, and 14 (6%) progressed to death. Furthermore, older age, reduced GCS at admission, and increased total neurological deficits at admission were significantly associated with death (Table 2).

Other statistically significant risk factors for death were male sex, high total deficits on admission, and low GCS on admission (P = 0,009).

Table 1. Univariate analysis of categorical variables to identify factors associated with in-hospital death of adult patients with surgically treated intracranial neoplasms

Variable	Categories	Total sample (n = 231)	Deaths (n = 14)	Mortality rate	Relative Risk	p-value
Sex	Male	112 (48%)	12	10.7%	6.4	**0.005**
	Female	119 (52%)	2	1.7%		
Type of surgery	Elective	183 (79%)	8	4.4%	0.3	0.081
	Urgent	48 (21%)	6	12.5%		
ASA score	1	70 (30%)	2	2.9%	1.0	0.370
	2	109 (47%)	7	6.4%	2.2	
	3	48 (21%)	5	10.4%	3.6	
	4	4 (2%)	0	0.0%	0.0	
Motor deficit at admission	Yes	48 (21%)	10	20.8%	9.5	**0.000**
	No	183 (79%)	4	2.2%		
Sensory deficit at admission	Yes	11 (5%)	1	9.1%	1.5	0.505
	No	220 (95%)	13	5.9%		
Visual deficit at admission	Yes	46 (20%)	2	4.3%	0.7	0.742
	No	185 (80%)	12	6.5%		
Language deficit at admission	Yes	23 (10%)	2	8.7%	1.5	0.637
	No	207 (90%)	12	5.8%		
Other deficit at admission	Yes	49 (21%)	6	12.2%	2.8	0.083
	No	182 (79%)	8	4.4%		
Reoperation	Yes	50 (22%)	1	2.0%	0.3	0.313
	No	181 (78%)	13	7.2%		
Compartment	Infratentorial	58 (25%)	4	6.9%	1.2	0.754
	Supratentorial	173 (75%)	10	5.8%		
Approach	Craniotomy	202 (87%)	13	6.4%	1.9	1.000
	Transsphenoidal	29 (13%)	1	3.4%		
Base/Convexity	Base	66 (29%)	3	4.5%	1.0	0.509
	Convexity	114 (49%)	9	7.9%	1.7	
	Posterior fossa	51 (22%)	2	3.9%	0.9	
Side	Right	95 (41%)	7	7.4%	1.0	0.784
	Left	79 (34%)	4	5.1%	0.7	
	Midline	57 (25%)	3	5.3%	0.7	

Variable	**Categories**	**Total sample (n = 231)**	**Deaths (n = 14)**	**Mortality rate**	**Relative Risk**	**p-value**
WHO grade (n = 167)	1	109 (65%)	0	0.0%	0.0	**< 0.001**
	2	15 (9%)	1	6.7%	0.4	
	3	8 (5%)	0	0.0%	0.0	
	4	35 (21%)	6	17.1%	1.0	
Type of tumor	Pituitary adenoma	36 (16%)	1	2.8%	1.0	0.065
	Cavernous malformation	4 (2%)	0	0.0%	0.0	
	High grade glioma	41 (18%)	6	14.6%	5.3	
	Low grade glioma	13 (6%)	1	7.7%	2.8	
	Hemangioblastoma	4 (2%)	1	25.0%	9.0	
	Meningioma	64 (28%)	0	0.0%	0.0	
	Metastasis	41 (18%)	4	9.8%	3.5	
	Other	16 (7%)	1	6.3%	2.3	
	Schwannoma	12 (5%)	0	0.0%	0.0	
Immediate postoperative complication	Yes	39 (17%)	14	35.9%	-	**0.000**
	No	192 (83%)	0	0.0%		
Comorbidity	Hypertension	102 (44%)	8	7.8%	1.7	0.407
	Diabetes	45 (19%)	5	11.1%	2.3	0.156
	Smoking	24 (10%)	1	4.2%	0.7	1.000
	Other tumors	42 (18%)	3	7.1%	1.2	1.000
	Others	78 (34%)	5	6.4%	1.1	1.000

Table 2. Univariate analysis of categorical variables to identify factors associated with in-hospital complications of adult patients with surgically treated intracranial neoplasms

Variable	Categories	Total sample (n = 231)	Postoperative complications (n = 39)	Complication rate	Relative Risk	p-value
Sex	Male	112 (48%)	26	23.2%	2.1	**0.014**
	Female	119 (52%)	13	10.9%	0.7	
Type of surgery	Elective	183 (79%)	28	15.3%		0.278
	Urgency	48 (21%)	11	22.9%		
ASA score	1	70 (30%)	7	10.0%	1.0	0.182
	2	109 (47%)	21	19.3%	1.9	
	3	48 (21%)	11	22.9%	2.3	
	4	4 (2%)	0	0.0%	0.0	
Motor deficits at admission	Yes	48 (21%)	13	27.1%	1.9	**0.049**
	No	183 (79%)	26	14.2%		
Sensory deficits at admission	Yes	11 (5%)	3	27.3%	1.7	0.596
	No	220 (95%)	36	16.4%		
Visual deficits at admission	Yes	46 (20%)	8	17.4%	1.0	1.000
	No	185 (80%)	31	16.8%		
Language deficits at admission	Yes	23 (10%)	7	30.4%	2.0	0.110
	No	207 (90%)	31	15.0%		
Other deficits at admission	Yes	49 (21%)	10	20.4%	1.3	0.519
	No	182 (79%)	29	15.9%		
Reoperation	Yes	50 (22%)	8	16.0%	0.9	1.000
	No	181 (78%)	31	17.1%		
Compartment	Infratentorial	58 (25%)	10	17.2%	1.0	1.000
	Supratentorial	173 (75%)	29	16.8%		
Approach	Craniotomy	202 (87%)	32	15.8%	0.7	0.289
	TNE	29 (13%)	7	24.1%		
Base/Convexity	Base	66 (29%)	13	19.7%	1.0	0.770
	Convexity	114 (49%)	18	15.8%	0.8	
	Posterior fossa	51 (22%)	8	15.7%	0.8	
Side	R	95 (41%)	17	17.9%	1.0	0.883
	L	79 (34%)	12	15.2%	0.8	
	M	57 (25%)	10	17.5%	1.0	

Variable	**Categories**	**Total sample (n = 231)**	**Postoperative complications (n = 39)**	**Complication rate**	**Relative Risk**	**p-value**
WHO grade (n = 167)	1	109 (65%)	12	11.0%	0.4	0.022
	2	15 (9%)	1	6.7%	0.2	
	3	8 (5%)	1	12.5%	0.4	
	4	35 (21%)	11	31.4%	1.0	
Type of tumor	Pituitary adenoma	36 (16%)	8	22.2%	1.0	**0.005**
	Cavernous malformation	4 (2%)	1	25.0%	1.1	
	High grade glioma	41 (18%)	12	29.3%	1.3	
	Low grade glioma	13 (6%)	1	7.7%	0.3	
	Hemangioblastoma	4 (2%)	3	75.0%	3.4	
	Meningioma	64 (28%)	5	7.8%	0.4	
	Metastasis	41 (18%)	7	17.1%	0.8	
	Others	16 (7%)	2	12.5%	0.6	
	Schwannoma	12 (5%)	0	0.0%	0.0	
Comorbidities	Hypertension	102 (44%)	24	23.5%	1.7	**0.021**
	Diabetes	45 (19%)	8	17.8%	2.3	0.827
	Smoking	24 (10%)	4	16.7%	0.7	1.000
	Other tumors	42 (18%)	4	9.5%	1.2	0.238
	Other comorbidities	78 (34%)	17	21.8%	1.1	0.193

Patients who died were older than those discharged from the hospital. They had a lower postoperative GCS than discharged patients and a greater pattern of total deficits on admission than discharged patients. There was no significant difference between deaths and surgeons.

Regarding neurological deficits at discharge, there was a new postoperative deficit in 8.8% of patients.

Male sex, motor deficits at admission, tumor category, and hypertension were risk factors for in-hospital postoperative complications. A low GCS on admission and high total neurological deficits on admission were significantly associated with complications during the in-hospital postoperative period.

Regarding the histological types operated on, meningioma (28%) was the most common tumor (Fig. 1), followed by high-grade glioma (18%) (Fig. 2), metastasis (18%) (Fig. 3), and pituitary adenoma (16%).

There was no significant difference in the complication rate during the in-hospital postoperative period stratified by the surgeon.

There was a statistical relevance regarding low GCS and a greater number of deficits on admission associated with risk factors for in-hospital postoperative complications.

In this series, the histological type most associated with the risk of death was hemangioblastoma; however, it was also the histological type that presented the lowest incidence of cases.

Regarding complications in the in-hospital postoperative period, it is possible to highlight that the most frequent complication was CSF leak, representing 21% of cases, followed by sepsis (18%), hydrocephaly (5%), and uncal herniation in 5% of cases (Fig. 4).

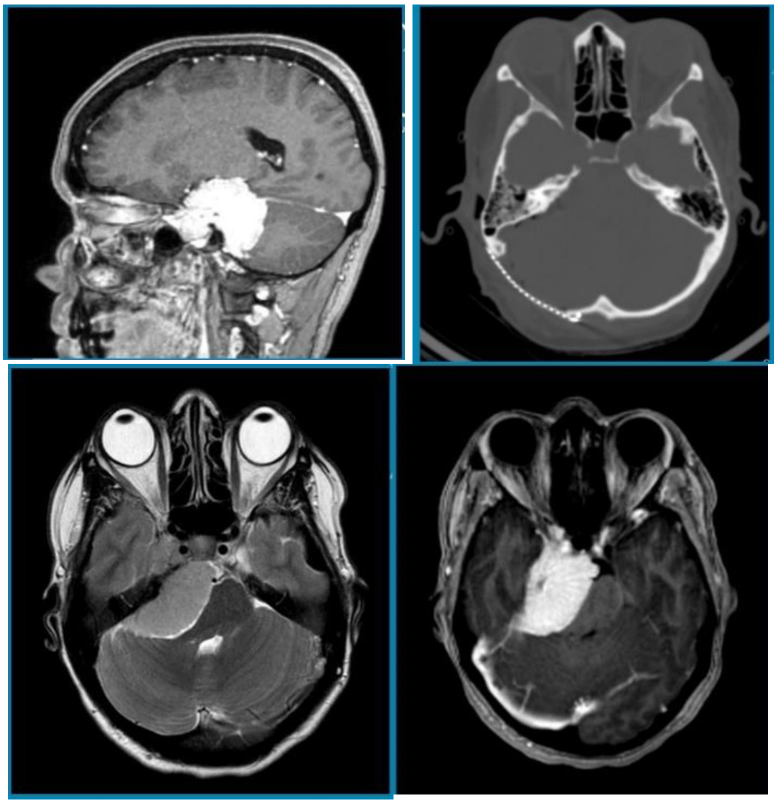

Fig. 1. Clinical case: Female patient, 46 years old, presented with a headache with a different pattern than usual, in addition to mild right hearing loss. Skull Magnetic Resonance Imaging (MRI) showed an expansive lesion in the petroclival region on the right, suggestive of meningioma. The approach was performed using a retrosigmoid approach, with subsequent cranioplasty with a titanium plate

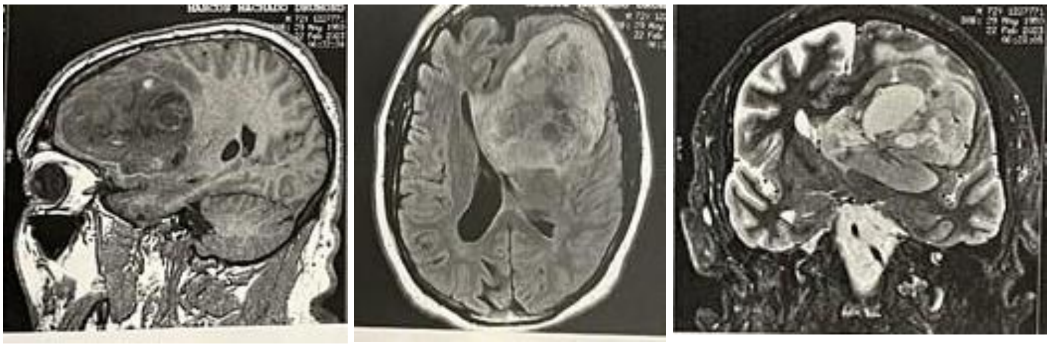

Fig. 2. Clinical case: 72-year-old male patient with bradypsychism and motor aphasia. A workup revealed an expansive left frontotemporal lesion with mass effect and adjacent edema. Patient underwent partial excision of the lesion in the emergency room. Anatomopathological examination confirmed that it was glioblastoma

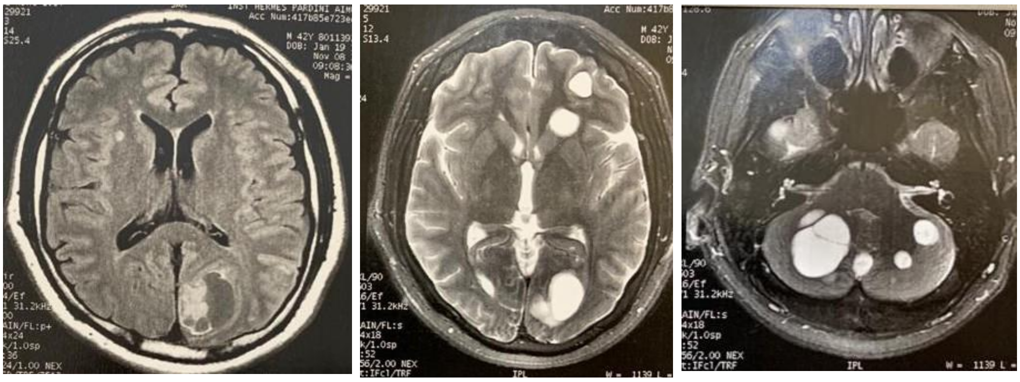

Fig. 3. Clinical case: MRI of the brain in a female patient with lung adenocarcinoma that developed dysmetria and imbalance. The workup revealed multiple brain lesions, which after excision confirmed that they were pulmonary metastases

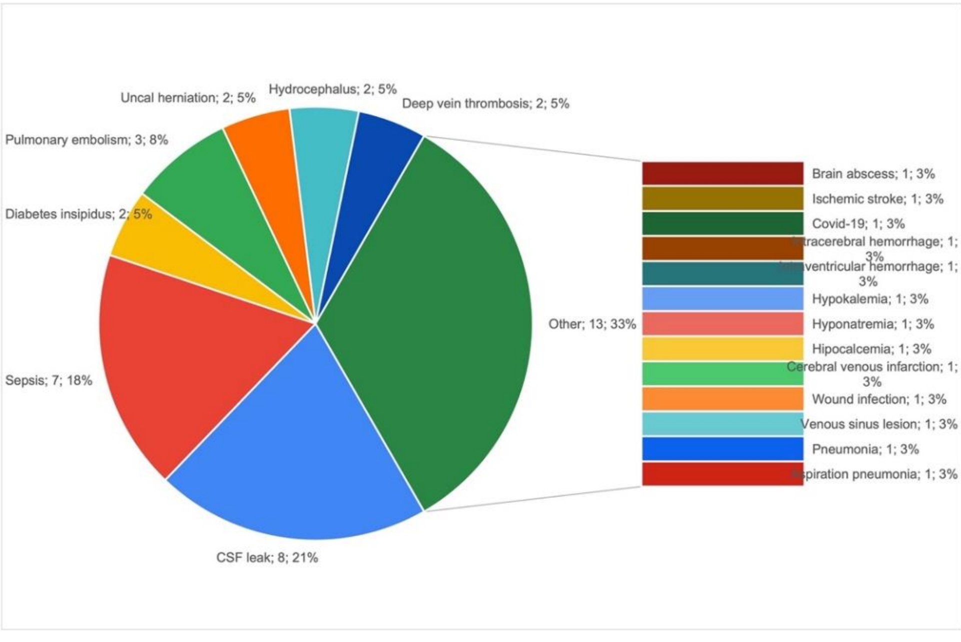

Fig. 4. Postoperative complications in the immediate postoperative period

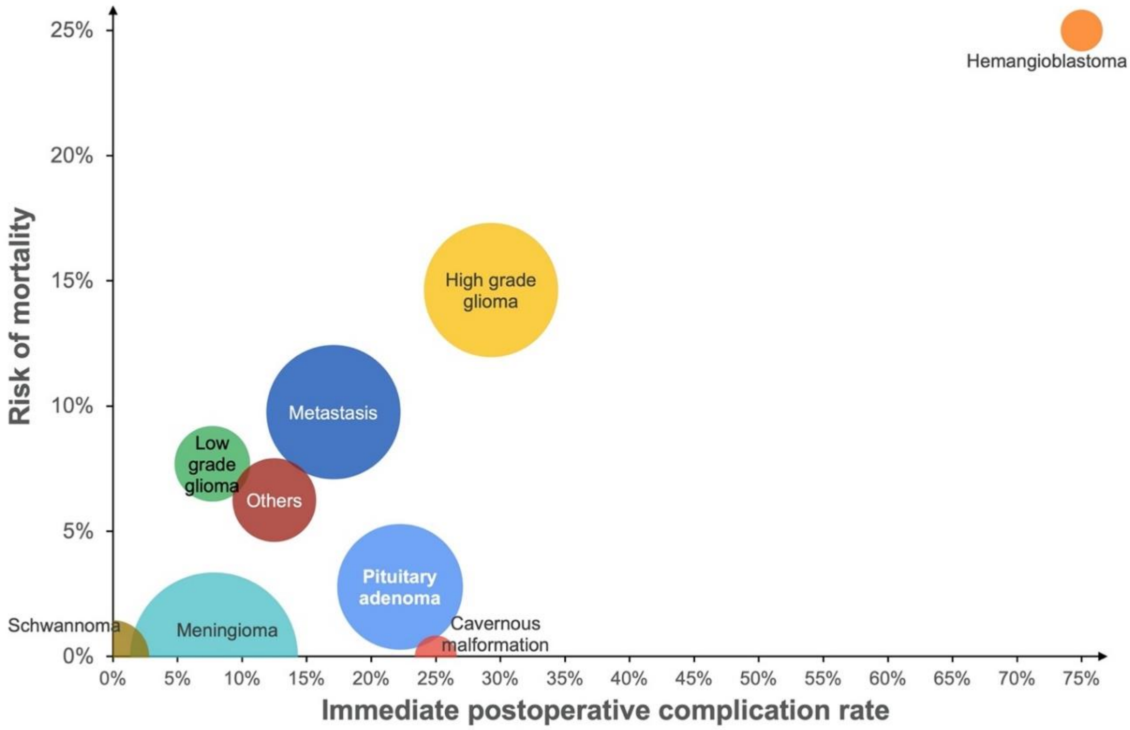

Fig. 5. Relation between risk of mortality to each histological type and immediate postoperative complication rate

Finally, there was a significant reduction in the number of neurological deficits after surgery regardless of the histological type. There was also a difference in the pattern of the number of deficits at discharge compared with that at admission between the histological types analyzed.

The Fig. 5 shows the risk of mortality and immediate postoperative complication rate for each histological type of tumor.

4. DISCUSSION

Most patients in this series (64%) were aged between 50 and 70 years (mean 57 + 15,3 years). Age alone was not a risk factor for a worse prognosis. This finding aligns with the study by Rogne et al. [16] that evaluated patients over 70 years of age surgically treated for intracranial tumors, specifically surgeries for lesion excision and biopsies. The study showed that even older patients benefited from surgery and that there was no statistical difference in the prognosis of older patients [16].

The overall complication rate in our series was 17% and the in-hospital mortality rate was 6%. The rates of complications and mortality were higher when compared to data from the international literature because this series analyzed brain metastases together with the excision of primary brain tumors. Using the international data, Bekelis et al. [17] obtained a mortality rate of 2.4% considering only primary CNS tumors [17]. Ambekar et al. [18] reported a rate of 1.3% considering only surgically treated meningiomas [18].

The most common histological type was meningioma, accounting for 28% of cases. In a study published by Barnholtz-Sloan et al. [19], meningiomas accounted for 36.3% of cases and were also the most common histological type [19]. In the same Harvard study, the incidence of high-grade gliomas was 25.5%, slightly higher than in the present study, which comprised 18% of cases. It is important to highlight that in the American study, only primary CNS tumors were included in the analysis, and metastases were excluded, which justifies the slightly higher percentage values than those in this study [19].

Regarding postoperative neurological deficits, this series showed that there was a significant reduction in the number of neurological deficits after surgery, regardless of the histological type, with statistical relevance.

When analyzing in-hospital postoperative complications, it is possible to highlight that the most frequent complication was CSF leak, representing 21% of cases, followed by sepsis, which accounted for 18% of cases. Unlike other case series in which surgical site infection represents a large percentage of complications [16], the absence of post-hospital follow-up in this series explains why such complication was not included, as it typically manifests after hospital discharge [19,20]. The variables with statistical significance associated with complications were male sex, presence of motor deficit at admission, tumor type (high-grade gliomas cause more complications), and hypertension.

There was also a statistical relevance regarding lower GCS and a higher number of deficits on admission, both of which were associated with risk factors for complications in the in-hospital postoperative period.

Schiavolin et al. (2020), in a study carried out in Italy, evaluated the risk factors associated with worse outcomes in patients surgically treated for brain tumors. In this study, they found that males have a higher risk of unfavorable outcomes, as evidenced in this series. Furthermore, concerning pre-operative neurological deficits, they found that high-grade gliomas and language deficits were associated with worse outcomes. In this study, the pre-operative deficit associated with the worst outcome was motor deficit [20].

Regarding the preoperative ASA score, in the present study, there was no statistical value in the prognosis of operated patients. Rogne et al. [16] also showed that the ASA score was not statistically significant in the prognosis of these patients [16].

Regarding in-hospital death, the histological type most associated with the risk of death was hemangioblastoma; however, this was also the histological type that presented the lowest incidence of cases and was the only case that progressed to death, making a more careful analysis difficult.

Other risk factors associated with in-hospital death were male sex, motor deficit on admission, high WHO grade, and presence of postoperative complications (all with statistically significant p-values). Increased age, low GCS, and increased total neurological deficits on admission were also significantly associated with mortality.

In a study conducted by the American College of Surgeons, Bekelis et al. [17] found that the presence of any neurological deficit upon admission was associated with a higher mortality rate in these patients. It is important to highlight that in this study there was also no influence of older ages on the prognosis [17].

Therefore, a thorough analysis of the risk factors for increased complications and death is necessary to improve modifiable factors. For patients with non-modifiable factors, evaluation of more effective treatment alternatives and improvement in the quality of surgical services are needed.

This study has some limitations. It was a retrospective study, conducted in a single institution, and did not consider the length of hospital stay of patients. Future studies will be necessary to confirm these findings. Due to the relative rarity of any histological type of brain tumor, communication between investigators through collaborative studies will be essential to allow information to be compared.

5. CONCLUSION

Based on this retrospective cohort, we concluded that the most common histological type was meningioma, followed by high-grade gliomas and metastases. There was an improvement in the number of neurological deficits at discharge after the surgical approach compared with that at admission. The most common postoperative complications were cerebrospinal fluid leaks, followed by sepsis, hydrocephalus and uncal hernia. The risk factors associated with death in surgically treated patients were male sex, motor deficit at admission, high WHO grade, immediate postoperative complications, increased age, low GCS at admission, and increased total neurological deficits at admission.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. PDQ Adult Treatment editorial board. adult central nervous system tumors treatment (PDQ®): Health Professional Version. 2023 Jan 20. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002. Available:https://www.ncbi.nlm.nih.gov/books/NBK65982/
2. American Cancer Society. Cancer Facts & Figures 2023. Atlanta: American Cancer Society; 2023
3. Instituto Nacional do Câncer (INCA), Ministério da Saúde. Access on February 26,2024 Available:https://www.gov.br/inca/pt-br/assuntos/cancer/numeros
4. Chandana SR, Movva S, Arora M, Singh T. Primary brain tumors in adults. Am Fam Physician. 2008;77(10):1423-30. PMID:18533376
5. Lah Novak M, Breznik B. Brain malignancies: Glioblastoma and brain metastases. Sem Cancer Biol.2021;60:262-273. DOI: 10.1016/j.semcancer.2019.10010. Epub 2019 Oct 22. PMID:31654711
6. Perjins A, Liu G. Primary brain tumors in adults: diagnosis and treatment. Am Fam Physician. 2016;93(3):211-7. PMID 26926614
7. Wielmels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. J Neurooncol. 2010;99(3):307-14. DOI: 10.1007/s11060-010-0386-3. Epub 2010 Sep 7. PMID:20821343; PMCID: PMC2945461
8. Englot DJ, Magill ST, Han SJ, Chang EF, Berger MS, McDermott MW. Seizures in supratentorial meningioma: A systematic review and meta-analysis. J Neurosurg. 2016;124(6):1552-61. DOI: 10.3171/2015.4.JNS142742. Epub 2015 Dec 4. PMID: 26636386; PMCID: PMC4889504.
9. Pandey R, Caflisch L, Lodi A, Brenner AJ, Tiziani S. Metabolomic signature of brain cancer. Mol Carcinog. 2017;56(11):2355-2371. DOI: 10.1002/mc.22694. Epub 2017 Jul 17. PMID: 28618012; PMCID: PMC5708886.
10. Zumel-Marne A, Castano-Vinyals G, Kundi M, Alguacil J, Cardis E. Environmental factors and the risk of brain tumours in young people: A systematic review. Neuroepidemiology. 2019;53(3-4):121-141. DOI: .1159/000500601. Epub 2019 Jun 5. PMID: 31167200.
11. Thakkar JP, Dolecek TA, Horbinski C, Ostrom QT, Lightner DD, Barnholtz-Sloan JS, Villano JL. Epidemiologic and molecular prognostic review of glioblastoma. Cancer Epidemiol Biomarkers Prev. 2014;23(10):1985-96. DOI: 10.1158/1055-9965.EPI-14-0275. Epub 2014 Jul 22. PMID: 25053711; PMCID: PMC4185005.
12. Ostrom QT, Bauchet L, Davis FG, Deltour I, Fisher JL, Langer CE, Pekmezci M, Schwartzbaum JA, Turner MC, Walsh KM, Wrensch MR, Barnholtz-Sloan JS. The epidemiology of glioma in adults: a "state of the science" review. Neuro Oncol. 2014;16(7):896-913. DOI: 10.1093/neuonc/nou087. PMID: 24842956; PMCID: PMC4057143.
13. Soares, JF; Siqueira, AL. Introdução à estatística médica. 2.a ed. Coopmed Editora Médica. Belo Horizonte. 2002;300.
14. Practical Statistics for Medical Research (Chapman & Hall/CRC Texts in Statistical Science) 1st Edition by Douglas G. Altman; 1991.
15. Field A. Discovering statistics using SPSS. 3rd Edition, Sage Publications Ltd., London; 2009.
16. Rogne SG, Konglund A, Meling TR, Scheie D, Johannesen TB, Rønning P, Helseth E. Intracranial tumor surgery in patients >70 years of age: is clinical practice worthwhile or futile? Acta Neurol Scand. 2009; 120(5):288-94. DOI: 10.1111/j.1600-0404.2009.01157. x Epub 2009 Sep 8. Erratum in: Acta Neurol Scand. 2009 Dec;120(6):453. PMID: 19737154.
17. Bekelis K, Bakhoum SF, Desai A, Mackenzie TA, Roberts DW. Outcome prediction in intracranial tumor surgery:

The National Surgical Quality Improvement Program 2005-2010. J Neurooncol. 2013;113(1):57-64.
DOI: 10.1007/s11060-013-1089-3.
Epub 2013 Feb 24.
PMID: 23436132;
PMCID: PMC5617728.

18. Ambekar S, Sharma M, Madhugiri VS, Nanda A. Trends in intracranial meningioma surgery and outcome: a Nationwide Inpatient Sample database analysis from 2001 to 2010. J Neurooncol. 2013;114(3):299-307.
DOI: 10.1007/s11060- 013-1183-6.
Epub 2013 Jul 13.
PMID: 23852621.

19. Barnholtz-Sloan JS, Ostrom QT, Cote D. Epidemiology of brain tumors. neurol clin. 2018;36(3):395-419.
DOI: 10.1016/j.ncl.2018.04.001.
Epub 2018 Jun 15.
PMID: 30072062.

20. Schiavolin S, Raggi A, Scaratti C, Toppo C, Silvaggi F, Sattin D, Broggi M, Ferroli P, Leonardi M. Outcome prediction in brain tumor surgery: A literature review on the influence of nonmedical factors. Neurosurg Rev. 2021;44(2):807-819.
DOI: 10.1007/s10143-020-01289-0.
Epub 2020 May 7.
PMID: 32377881.

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