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Ultrasound Evaluation of the Optic Nerve Sheath as a Predictor of Severity and Complications

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ABSTRACT

Objectives: Ultrasonography has the potential advantage of being a repeatable tool, safe at the bedside and low cost, without risks of radiation and side effects. Emerging as a tool with potential to promote the optimization of the prognosis of neurosurgical patients.

Methods: 31 participants diagnosed with expansive brain injury were selected, all over 18 years of age, after signing the free consent form and clarification, the postoperative evaluation was carried out at the time of hospital discharge and 3 months after surgery on an outpatient basis. The ultrasound evaluation of the optic nerve sheaths was performed by a team member, who was blind to the clinical and radiological information and using the same GE VERSANA ACTIVE ultrasound device.

Results: During the preoperative analysis of 31 patients, 41.9% were male (n=13) and 58.06% female (n=16), with a mean age of 50.64 +- 16.29. Regarding the functional analysis with KPS, it was found that 58% of patients (regardless of sex) had results >=70, equivalent to 18 patients. Regarding the diameter of the optic nerve sheath performed by ultrasound, the value of the preoperative BOD was greater than 6.1 mm, the value greater than 6.2 mm determined unfavorable prognosis in 3 months.

Discussion: In the present study, the cutoff point of the BNO measurement for favorable or unfavorable prognosis was 6.1 mm, and when we correlated this variable with the analyzed KPS variable, we can observe that they correlate, mainly with outcome, getting an unfavorable result.

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List of Acronyms
BNO: Sheath of the Optic Nerve
CAAE: Certificate of Presentation for Ethical Appreciation
ECG: Sao Paulo Coma Scale
CBTRUS: Central Brain Tumor Registry of the United States
INCA: National Institute of Health
KPS: Karnofsky Performance Scale
NCCN: National Comprehensive Cancer Network
PIC: Intracranial Pressure
CNS: Central Nervous System
UFAM: Federal University of Amazonas
USG: Ultrasonography
UST: Transorbital Ultrasonography

Introduction

Tumors that develop in the central nervous system, may be located in the brain and spinal cord, form through the growth of abnormal cells in tissues. This disease can be acquired through several causes that accumulate over time, such as genetic predisposition or exposure to ionizing radiation [1]. It is a growing and relevant global problem in terms of public health, especially in low and middle income countries [2].

Worldwide, the incidence of cancer of the central nervous system occupies the thirteenth position in men and the sixteenth position among women, in 2018, were estimated 162,000 new cases in men and 134,000 in women, corresponding to an estimated risk of 4,2/100 thousand men and 3.6/100 thousand women [3,4]. For Brazil, 5,870 new cases of central nervous system cancer are estimated in men and 5,220 in women, for each year of the 2020-2022 triennium. Corresponding to an estimated risk of 5.61 new cases per 100,000 men and 4.85 new cases per 100,000 women [1].

The advancement of neuroimaging technologies in recent decades such as computed tomography, magnetic resonance imaging and tomography has allowed physicians to diagnose tumors with greater certainty [5,6]. In this context, early diagnosis should aim not only to increase survival time but also to improve quality [7].

The method used for the safe diagnosis to measure the increase in intracranial pressure is through the monitoring of this intracranial pressure, being the method of choice [8]. However, transorbital ultrasonography with diameter measurement of the optic nerve sheath is an easily feasible non-invasive diagnostic tool, allowing the quantification of the diameters of the optic nerve and its sheaths [9]. It is a promising new diagnostic tool in neurology and intensive care medicine, the main areas of application are diseases with increased intracranial pressure, such as idiopathic intracranial hypertension, intracranial hemorrhage and neurotraumatological diseases [10,11].

Ultrasonography has the potential advantage of being a repeatable tool, safe at the bedside and low cost, without risks of radiation and side effects. However, it is important to carry out research using this device to relate the degree of distension of the optic nerve sheath with the real prognostic significance when applied in patients undergoing neurosurgical procedures diagnosed with expansive lesions correlation as a predictor of severity and post-complicationsoperatives. Emerging as a tool with potential to promote the optimization of the prognosis of neurosurgical patients.

Material and Methods

A prospective, observational cohort study with longitudinal blind evaluation of clinical and functional outcomes was conducted. This study was approved by the ethics committee with CAAE: 38829020.7.0000.5020. We selected 31 participants with a diagnosis of expansive brain injury, all over 18 years, after signing the free consent form and clarification, the patients were evaluated by the same team member at the time of admission to the ward (preoperative evaluation) and submitted to elective surgical procedures, after surgery patients were followed up for three months. The postoperative evaluation was performed at the time of hospital discharge and after 3 months of surgery at the outpatient level, using the evaluation protocol, which included the following clinical information: motor deficit (monoparesis or monoparesthesia), sensory deficit (monoparesthesia or hemiparesthesia), evaluation of visual acuity (campimetry by confrontation), postural alteration (Romberg test) headache (pain grading) by visual analogue scale, pupillary reactivity (normal pupils or anisoceric), Glasgow coma scale and Karnofsky scale.

The ultrasonographic evaluation of the optic nerve sheath was performed by a team member, who was blind to clinical and radiological information and by the same GE VERSANA ACTIVE ultrasound device. A linear transducer with high frequency (7-10 MHtz) was used, configured to visualize structures up to 5-6 cm deep. The transducer was applied on the closed eyelid after applying the horizontal direction gel and performed three measurements in each eye reaching a final mean on each side. This examination was performed on all patients in this study within 24 hours before surgery, at hospital discharge and 3 months after surgery Two-dimensional ocular ultrasound. The brain magnetic resonance imaging tests were performed with contrast by the GE 1.5 Tesla machine, in the preoperative and postoperative periods (after 03 months, in the outpatient evaluation). The histopathological evaluation of brain lesions was performed by the pathology team of the Getúlio Vargas University Hospital in the city of Manaus-Amazonas, and the delivery of the results was made on average 30 days after the tests. The following classifications were used for brain tumors: Malígna (metastases or gliomas), Benigna (meningiomas or pituitary tumor).

For the statistical analysis, the primary dependent variable of the functional prognosis was analyzed in 03 months evaluated by the KPS dichotomized into favorable (>=70) and unfavorable (<70). The secondary outcome was assessed by death at 3 months. Data were expressed as mean standard deviation, median and interquartile range, or absolute frequency and percentage. The univariate analysis was performed using the Wilcoxon and Mann-Whitney test. The Spearman test was used to evaluate the primary outcome. P lower than 0.005 was considered significant. Data were analyzed using the program R 4.0.2.

Results

During the preoperative analysis of the 31 patients, it was observed that 41.9% were male (n=13) and 58.06% female (n=16), with a mean age of between 50.64 +- 16.29 (Table 1), as well as the results of the functional analysis with KPS, it was found that 58% of patients (regardless of gender) had results >=70, equivalent to 18 patients. However, 42% obtained results <70%, equivalent to 13 patients (Figure 2). This result is unfavorable, as the lower the classification on the Karnofsky scale, the worse the patient's expectation of recovery or return to normal activities.

Regarding the application of the Glasgow Coma Scale, used as a way of assessing the level of consciousness. It was observed (Figure 1) that more than 90% of patients had a Glasgow Coma Scale between 15 and 13 points, obtaining a favorable scale.

For the Radiological evaluation through preoperative magnetic resonance imaging (Table 1), in the evaluation of midline deviation (in 50% of patients there was deviation) and compression of the base cisterns (64.54% were normal and 35.48 % were compressed).

In this study, after analyzing the histological type of tumors, they were classified as benign tumors for patients diagnosed with meningiomas and pituitary tumors, with 13 patients diagnosed as meningiomas, corresponding to 41.93% of patients and 04 diagnosed as tumors. pituitary glands, malignant tumors in patients diagnosed with gliomas (low and high grade) and metastases were diagnosed in 58.06%, 11 gliomas and 03 metastases (Table 1). Most of these patients underwent a surgical procedure and subtotal excision was performed, totaling 86.67% of patients and only 13.33% had total excision performed.

In relation to the diameter of the optic nerve sheath performed by ultrasound, the preoperative DBNO value was greater than 6.1 mm (Figure 3) and obtained an unfavorable prediction with the outcome at 3 months ($p<0.0001$). a value greater than 6.2 mm determined an unfavorable prognosis at 3 months with a sensitivity of 87.5% and a specificity of 94.7%, with an accuracy of 92.6% (Figure 4).

Table 1: Variables analyzed in the 31 patients who were part of the study

Variables		Quantity	Percentage (%)
Male	Men Women	13 16	41,90 58,06
Old	50.64 +- 16.29		
KPS	>=70 <70	18 13	58,00 42,00
ECG	15-13 12-09 <09	28 03 00	90,30 9,60 0,0
Motor deficit	Yes No	07 24	22,58 77,42
Sensory deficit	Yes No	04 27	12,90 87,10
Postural alteration	Yes No	29 02	93,55 6,45
Visual alteration	Yes No	06 25	19,35 80,65
Histological type	Malignant Benign	18 13	58,06 41,93
Midline deviation	Yes No	15 15	50,00 50,00
Basal cistern	Compressed Normal	11 20	35,48 64,54
Degree of tumor resection	Total Subtotal	04 26	13,33 86,67
Preoperative usg	<0,57 cm >0,57 cm<0,6 cm >0,6 cm	00 09 22	0,0 29,00 71,00

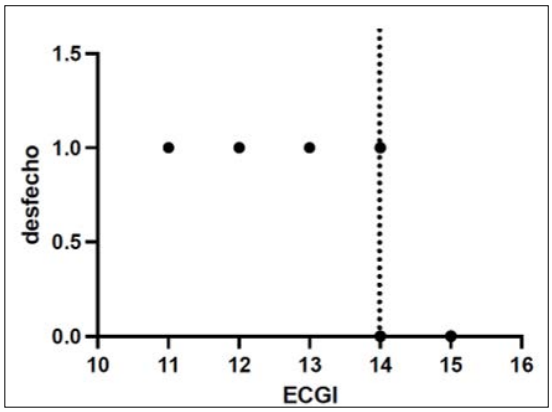

Figure 1: Glasgow Coma Scale vs Lag

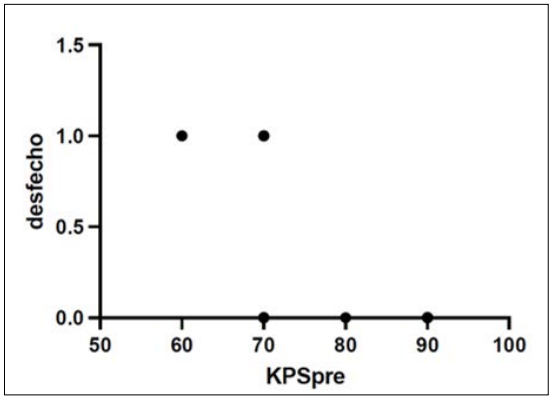

Figure 2: Karnofsky vs outdated scale

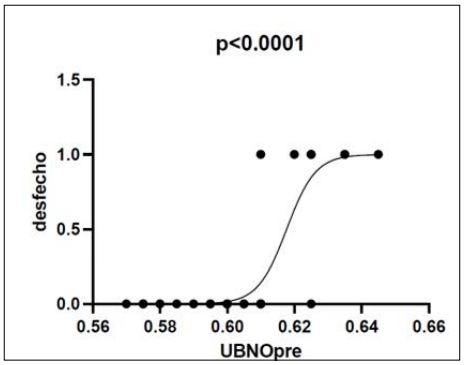

Figure 3: Diameter of the preoperative optic nerve sheath vc outcome

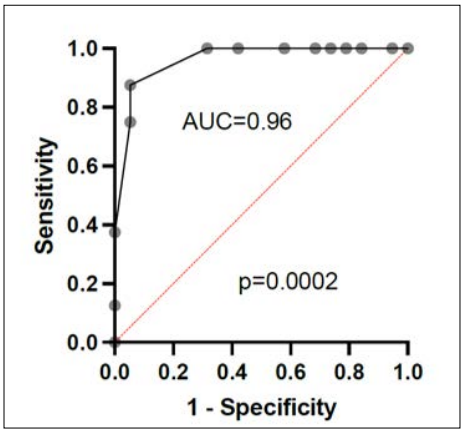

Figure 4: Sensitivity vs specificity

Discussion

Of the 31 patients analyzed preoperatively, 41.9% were male (n=13) and 58.06% were female (n=16), with a mean age of 50.64 +- 16.29. This corroborates Sandes et al. in which brain tumors were more common in women, accounting for 54.5% of cases, compared to 45.5% in men, noting the predominance of females in all major histological types. However, this disagrees with the relatively equal proportions of brain tumors between genders commonly reported in the literature, since CNS cancer in men appears as the seventh most frequent in the North and Central-West regions and among women, it ranks ninth in the North [1]. In general, one of the predominant tumors in women is meningioma, with age groups in the third and fourth decades of life, and may occur in childhood [12-15]. Its incidence is approximately twice as high in women as in men. Studies suggest that endogenous hormones may be involved in the development or progression of meningiomas; the predominance in women is described in the proportion 3:1, suggesting a hormonal influence on tumor pathogenesis, with a peak of highest incidence between the fifth and sixth decades of life [16]. Higher levels of estrogen and growth factors in obese women may increase tumor growth. The association between high body mass index (BMI) and the risk of meningiomas has also been described, suggesting a relationship between high adiposity and activation of aromatase, an enzyme essential in estrogen production, which may justify the results found. However, in this study, no data were collected that correlate the predominance of brain tumors in females with weight or hormone levels [17].

Regarding the functional analysis data with KPS (Table 1), the results found in this study are considered favorable, since with results above 70, patients are able to perform activities without needing special care and, depending on the classification on the Karnofsky scale (80, 90, 100), many return to their normal routine of activities and work.

However, 42% obtained results <70%, equivalent to 13 patients (Figure 2). This result is unfavorable, since the lower the classification on the Karnofsky scale, the worse the expectation of the patient's recovery or return to normal activities. The Karnofsky Performance Scale (KPS) is a scale considered objective and practical, with the level of functionality assessed by the health professional with a percentage ranging from 100% (normal, no complaints, no evidence of disease) to 0% (death); because it is strictly related to levels of symptom distress, the KPS is often used as a prognostic tool to predict life expectancy. Patients with low Karnofsky Performance Scale (KPS) scores, multiple neurological deficits or advanced or treatment-refractory systemic disease will generally have a poor prognosis even with multidisciplinary treatment. The symptoms of these patients should be alleviated in addition to exclusive palliative support [18].

The results found for the application of the Glasgow Coma Scale (Figure 1) showed that more than 90% of patients had a Glasgow Coma Scale score between 15 and 13 points, resulting in a favorable scale. The Glasgow Coma Scale (GCS) is widely used to assess neurological impairment in patients with traumatic brain injury. Total GCS scores range from low, such as three (worst), to high, such as 15 (best), when three items are assessed, such as: best verbal response (range one to five), best motor response (range one to six), and best eye opening response (range one to four).

This scale is used in a simple, objective manner and is highly accurate and reliable, since it uses similar concepts and facilitates communication between the team. Thus, some studies have proposed the use of simplified components of the GCS as an alternative to the full use of the scale [19]. There is a direct and negative relationship between pupillary reactivity and the GCS and when compared, they show that: as the GCS score decreases, pupillary reactivity decreases and mortality worsens [20]. In this study, after analyzing the histological type of tumors (Table 1), patients diagnosed with meningiomas and pituitary tumors were classified as benign tumors. The results found are in agreement with a study by, who reported that of the symptomatic primary brain tumors: gliomas (mainly astrocytomas) account for approximately 30% of cases; and meningiomas for 35 to 40%; pituitary tumors for 15% to 20%; primary CNS lymphoma by 2% to 3%; and craniopharyngioma by 1% [21].

Malignant tumors in patients diagnosed with gliomas (low and high grade) and metastases were diagnosed in 58.06%, with 11 gliomas and 03 metastases. Most of these patients underwent surgical procedures and subtotal excision was performed, totaling 86.67% of patients, and only 13.33% underwent total excision. The treatment of choice for malignant glioma is surgical resection, to alleviate mass symptoms, achieve cellular reduction and provide adequate tissue for histological and molecular characterization of the tumor [22,23].

Therefore, to achieve a balance between surgical cytoreduction and reducing the risks of intervention, it is necessary to evaluate the patient's preoperative prognosis, mainly through KPS and tumor location, to provide maximum survival associated with functional benefit [24]. Therefore, the extent of resections becomes extremely variable and changes according to the case of each individual affected by the tumor. In the scientific literature, we can find numerous studies that aim to correlate different extents of surgical resection and minimally invasive procedures with patient survival [24,25].

The findings of this study are in agreement with most of the literature regarding the prevalence of malignant brain tumors. The literature reports gliomas as the most prevalent type of tumor, followed by meningiomas. These are the most common tumors in elderly people between 60 and 80 years of age, and the number of patients is expected to increase as the population ages [26]. A possible explanation for this increase in the rates of malignant brain tumors in the CNS may be related to the increase in life expectancy of the population around the world [27]. Regarding the diameter of the optic nerve sheath (Figure 3) measured by ultrasound, studies suggest that the DBNO cutoff value that provides the best accuracy for predicting intracranial hypertension (ICP = 20 mmHg) is 5.7 to 6.0 mm and that DBNO values above this limit should alert the physician to the presence of elevated ICP [28,29]. In this study, the preoperative DBNO value was greater than 6.1 mm and obtained an unfavorable prediction with the outcome at 3 months ($p<0.0001$). Measurement of the optic nerve sheath by tomography is also a method used. In a study with 40 patients, with a cutoff point of 6.35 mm, sensitivity of 0.93 (95% CI 0.84-1.00), specificity of 0.80 (95% CI 0.50-1.00) and AUC of 0.87 (95% CI 0.69-1.00) were obtained, corroborating this study, obtaining a preoperative NODB ROC curve of 0.96 (95% CI 0.89-1, $p=0.0002$). However, a value greater than 6.2 mm determined an unfavorable prognosis at 3 months with a sensitivity of 87.5% and specificity of 94.7%, with an accuracy of 92.6% (Figure 4) [30].

In a study that evaluated 100 patients, the case group consisting of 50 individuals with CT alterations suggestive of ICH and the control group consisting of 50 normal individuals, all of whom underwent

USG of the NOBD, it was observed that USG is a useful method for determining increased ICP, thus defining the cutoff value for the NOBD diameter of 5.3 mm for detecting deviation of structures from the median line, corresponding to 70% sensitivity and 74% specificity [31].

Conclusions

The preoperative measurement of BMB through ultrasonography is associated with the functional outcome and mortality in 3 months of patients undergoing brain tumor resection. In the present study, the cutoff point of the BNO measurement for favorable or unfavorable prognosis was 6.1 mm, and when we correlated this variable with the analyzed KPS variable, we can observe that they correlate, mainly with outcome, getting an unfavorable result. However, more studies are needed using this tool as an outcome predictor and with a larger sample N than used in this study, thus obtaining more accurate results and with good significance and accuracy.

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