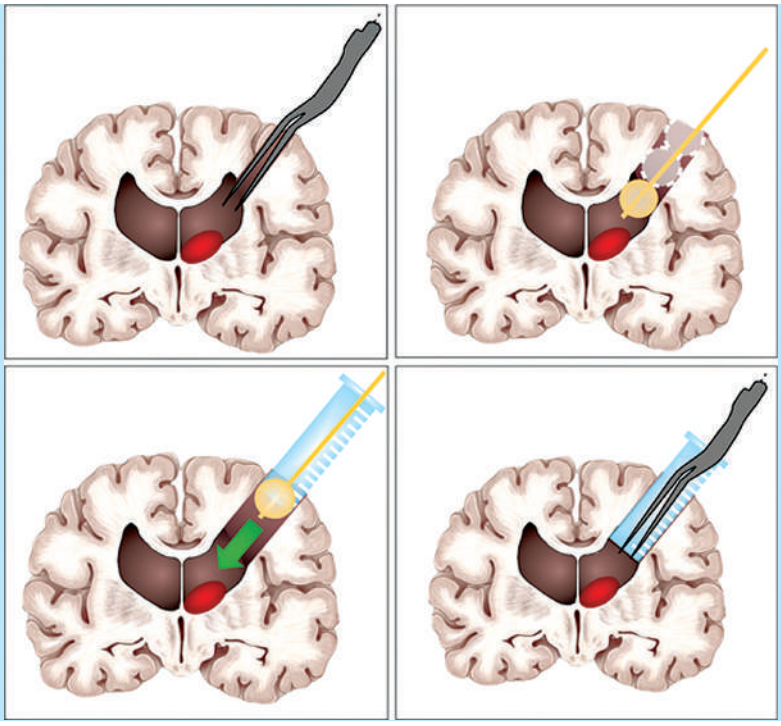
ISSN 0103-5355

Brazilian Neurosurgery

Arquivos Brasileiros de Neurocirurgia

Number 3 • Volume 43 • Pages 157–236 • September 2024



SBN
Sociedade Brasileira de Neurocirurgia

OPEN ACCESS

Thieme

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Volume 43, Number 3/2024

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Original Articles

Review Articles

Case Reports

Thieme Revinter Publicações Ltda

online www.thieme-connect.com/products

The colored content of this issue is available online at www.thieme.com/bns.

Cover design: © Thieme
Cover image source: © Sociedade Brasileira de Neurocirurgia
(Moraes CAVN, Neto JAGdS, Guedes BWM, Oliveira AMP, Santos BFdO. Syringe Port System as a Tubular Retractor Technique for Brain Lesions: Case Series and Review of the Literature. Arq Bras Neurocir 2024;43(3):226–236.)

 Arquivos Brasileiros de Neurocirurgia is published four times a year in March, June, September, and December by Thieme-Revinter Publicações Ltda, Rua do Matoso, 170, Rio de Janeiro, 20270-135, Brazil.

Editorial comments should be sent to **journals@thieme.com**. Articles may be submitted to this journal on an open-access basis. For further information, please send an e-mail to openaccess@thieme.com. The content of this journal is available online at **www.thieme-connect.com/products**. Visit our Web site at **www.thieme.com** and the direct link to this journal at w**ww.thieme.com/bns**.

Arquivos Brasileiros de Neurocirurgia is an official publication of the Brazilian Neurosurgery Society (Sociedade Brasileira de Neurocirurgia) and the Portuguese Language Neurosurgery Societies. It is listed in LILACS and LILACS-Express (Latin-American and Caribbean Center on Health Sciencies Information), and Latindex (Regional Cooperative Online Information System for Scholarly Journals from Latin America, the Caribbean, Spain and Portugal). Thieme Medical Publishers is a member of the CrossRef initiative.

ISSN 0103-5355

Evaluation of Admission Brain Computed Tomography Findings to Predict the Long-term Outcomes of Patients with Traumatic Brain Injury

Avaliação de achados em tomografia de crânio admissional para predizer o prognóstico a longo prazo de paciente com trauma cranioencefálico

Rafael de Souza Dantas[1] Thais Cristina de Souza Melo[1] Isabella Fontes de Santana Lins[1] Letícia Adrielle dos Santos[1] José Nolasco de Carvalho Neto[1] Bruno Fernandes de Oliveira Santos[1,2,3] Robson Luis Oliveira de Amorim[4] Arthur Maynart Pereira Oliveira[1,2]

[1] Department of Medicine, Fundação Universidade Federal de Sergipe, Lagarto, SE, Brazil
[2] Department of Medicine, Universidade Tiradentes, Aracaju, SE, Brazil
[3] Department of Neurosurgery, Hospital de Cirurgia, Aracaju, SE, Brazil
[4] Neurosurgery Service, Hopital Universitário Getúlio Vargas, Universidade Federal do Amazonas, Manaus, AM, Brazil

Address for correspondence Arthur Maynart Pereira Oliveira, MD, PhD, Department of Neurosurgery, Hospital de Cirurgia, Fundação de Beneficência Hospital de Cirurgia, Av. Desembargador Maynard 174, Aracaju, Sergipe, 49055-210, Brazil (e-mail: arthurmaynart@icloud.com).

Arq Bras Neurocir 2024;43(3):e157–e163.

Abstract

Objective To evaluate the admission brain computed tomography (CT) scan findings in patients with traumatic brain injury (TBI) in a low- and middle-income country (LMIC) to predict long-term neurological outcomes.

Materials and Methods Patients admitted to a tertiary emergency hospital between March 2017 and April 2018 who had suffered a TBI and had undergone a brain CT scan within 12 hours of the trauma were prospectively evaluated. All of the patients who were hospitalized for at least 24 hours were contacted by phone after 12 months to evaluate their neurological condition.

Results We achieved a 12-month follow-up with 180 patients, most of them male (93.33%). The brain changes identified by CT, such as brain contusion (BC; $p = 0.545$), epidural hemorrhage (EDH; $p = 0.968$) and skull base fracture (SBF; $p = 0.112$) were not associated with worse neurological outcomes; however, subdural hemorrhage (SDH; $p = 0.041$), subarachnoid hemorrhage (SAH; $p \leq 0.001$), brain swelling (BS; $p \leq 0.001$), effacement of cortical sulci (ECS; $p = 0.006$), effacement of basal cisterns (EBC; $p \leq 0.001$), depressed skull fracture (DSF; $p = 0.017$), and a brain midline shift > 5 mm ($p = 0.028$) were associated with worse outcomes.

Keywords
- traumatic brain injury
- computed tomography
- outcome
- developing countries

received
February 11, 2023
accepted
June 21, 2023
article published online
April 29, 2024

DOI https://doi.org/10.1055/s-0043-1776278.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Conclusion Findings such as SAH, BS and DSF were independent predictors of worse neurological outcomes. The rate of 70% of patients lost to follow-up shows the difficulties of conducting long-term research in LMICs.

Resumo

Objetivo Avaliar as variáveis de tomografia computadorizada (TC) cerebral admissional em pacientes com trauma cranioencefálico (TCE) em um país de baixa e média renda (PBMR) para prever os resultados neurológicos de longo prazo.

Materiais e Métodos Foram avaliados prospectivamente pacientes admitidos em um hospital terciário de emergência entre março de 2017 e abril de 2018, que sofreram TCE e realizaram tomografia de crânio em até 12 horas após o trauma. Todos os pacientes que permaneceram internados por pelo menos 24 horas foram contatados por telefone após 12 meses para avaliação de sua condição neurológica.

Resultados Conseguimos um acompanhamento de 12 meses com 180 pacientes, a maioria deles do sexo masculino (93,33%). As alterações cerebrais identificadas pela TC, como contusão cerebral (CC; $p = 0{,}545$), hemorragia peridural (HPD; $p = 0{,}968$) e fratura da base do crânio (FBC; $p = 0{,}112$) não foram associadas a piores desfechos neurológicos; no entanto, hemorragia subdural (HSD; $p = 0{,}041$), hemorragia subaracnóidea (HSA; $p \leq 0{,}001$), edema cerebral (EC; $p \leq 0{,}001$), apagamento de sulcos corticais (ASC; $p = 0{,}006$), apagamento de cisternas (AC; $p \leq 0{,}001$), fratura craniana deprimida (FCD; $p = 0{,}017$) e desvio da linha média do cérebro > 5 mm ($p = 0{,}028$) foram associados a piores resultados.

Conclusão Achados como HSA, EC e FCD foram preditores independentes de piores desfechos neurológicos. A taxa de perda de acompanhamento de 70% indica as dificuldades de se conduzir pesquisas de longo prazo em PBMRs.

Palavras-chave
- lesão cerebral traumática
- tomografia computadorizada
- prognóstico
- países em desenvolvimento

Introduction

Traumatic brain injury (TBI) is defined as a change in brain function or other evidence of encephalopathy caused by an external force.[1] These injuries can be caused by a bump, blow, or jolt to the head, or they may be penetrating head injuries that disrupt the normal function of the brain.[2] They represent an important public health problem, and are a significant cause of morbidity and mortality, especially among men and young adults.[3–5] Data from the TBI Model Systems National Data and Statistical Center (TBINDSC) in the United States, show that, in 2017, the cases among male patients greatly outnumbered those among female patients, accounting for more than 73% of all TBIs reported.[6] Patients who survive a moderate to severe TBI often experience a broad spectrum of cognitive and behavioral changes due to diffuse injury. These deficits include slow information processing, as well as impaired long-term memory, attention, functional memory, executive functions, social cognition, and self-awareness.[1]

Upon admission to the hospital, the severity of the TBI is commonly graded according to the Glasgow Coma Scale (GCS), a measure of the level of consciousness. This is purely a descriptive scale; it does not provide any structural information on potential intracranial lesions.[7,8] Due to its accessibility and speed, computed tomography (CT) is the routine imaging modality used to assess structural lesions in acute TBI;[8] it is important in the early identification of patients with significant intracranial damage at risk of deterioration, but CT can also identify lesions that are relevant to the patient's prognosis and rehabilitation but do not necessarily require neurosurgical intervention.[9] Knowledge of the relationship between the clinical signs presented by the patient in the first hours after trauma and the morphological changes identified by brain CT is important for the early diagnosis of TBI; however, CT has to be used with caution due to the increased risk of developing cancer resulting from exposure to ionizing radiation, especially in children.[10]

In 1991, Marshall et al.[11] used tomographic findings to classify patients with TBI. Initially, the purpose of the classification was descriptive; however, it also started to be used as a predictor of mortality. The study[11] used the term *diffuse brain injury*, which was divided into four categories: Marshall I, without any changes on brain CT; and Marshall II, III and IV, with certain degrees of brain damage. In the original study, the authors[11] noticed a direct relationship between the diagnosis of TBI and the mortality rate; however, other studies[12–15] have shown that the status of the basal cisterns, the midline shift, traumatic subarachnoid or intraventricular hemorrhage, and the presence of different types of mass lesions could produce a more accurate prognostic prediction. Other classifications were later created, such as the Rotterdam CT score (2005), which reweighted the components of the Marshall CT classification and added traumatic subarachnoid hemorrhage (tSAH)

and intraventricular hemorrhage, becoming part of the International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) outcome model for TBI patients.[12,13] More recently, new CT classifications have emerged, including the Stockholm CT score, in 2010,[14] and the Helsinki CT score, in 2014.[15] However, none of these scales have been extensively evaluated.

To objectively assess the functionality of patients with TBI, Jennett and Bond[16] (1975) developed the Glasgow Outcome Scale (GOS),[7,16,17] which was modified over time to provide a more detailed categorization, becoming the Glasgow Outcome Scale-Extended (GOSE),[17,18] a global scale for the functional evaluation of TBI patients.[19]

The purpose of the present study was to evaluate the potential association between morphological brain changes identified through CT and the long-term functional neurological outcomes of patients with TBI.

Materials and Methods

Study Design

We conducted a prospective cohort study of TBI patients admitted to a Brazilian tertiary hospital – Hospital de Urgências de Sergipe Governador João Alves Filho. Patients were recruited between March 2017 and April 2018 and were followed up until 12 months after the injury.

Sample

The study included patients who had suffered a TBI, were referred to the emergency unit to undergo a brain CT scan within 12 hours of the injury, and were then admitted to the hospital for at least 24 hours. After 12 months, we attempted to contact all the patients by phone.

Exclusion Criteria

We excluded patients who: reported or presented CT changes from a previous TBI; had other neurological or neurosurgical conditions, were aged $\leq$ 18 years; did not agree to participate in the study (or whose legal guardian/next of kin did not agree); and had suffered the head trauma more than 12 hours before the Brain CT scan.

Data Collection

All data about the admission brain CT scan were collected during the study period, including the grade on the Marshall classification and 12 radiological variables (brain contusion, epidural hemorrhage, subdural acute hemorrhage, subarachnoid hemorrhage, brain swelling, basal cistern effacement, cortical sulci effacement, brain midline shift $>$ 5 mm, brain midline shift $<$ 5 mm, skull fracture, depressed skull fracture, and skull base fracture). Twelve months later, the patients/next of kin were contacted by phone and assessed through a structured questionnaire to obtain the GOSE score: 1–death; 2–vegetative state; 3–severe disability (low); 4–severe disability (high); 5–moderate disability (low); 6–moderate disability (high); 7–good recovery (low); and 8–good recovery (high). They were then divided into 2 groups: good recovery (GOSE score $\geq$ 7) and poor recovery (GOSE score $<$ 7).

Statistical Analysis

Data were systematized, analyzed, and statistically tested using the IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, United State) software, version 23.0. The variables were expressed as absolute and relative frequencies, and median, arithmetic mean, and standard deviation (SD) values. The results of interest were analyzed using the Chi-squared (χ^2) test and logistic regression. A multivariate analysis was performed to create a model of the CT variables regarding the functional outcomes at the 12-month follow-up. Values of $p < 0.05$ were considered statistically significant.

Results

From the initial 600 subjects who had suffered a TBI and had undergone CT, we achieved a 12-month follow up with 180 (30%) patients (►**Fig. 1**). Most patients were male (93.3%), with a mean age of 36 (SD: $\pm$ 16.2) years. As aforementioned, the patients were divided into two groups: good recovery (42.7%), defined by a GOSE score $\geq$ 7; and poor recovery (56.3%), defined by a GOSE score $<$ 7 (38.9% had moderate to severe disability, 0.56% were in a vegetative state, and 17.8% had died). At baseline, 168 patients (93.3%) presented pathological findings on the brain CT and 12 (6.7%) prresented completely normal images. Among the patients with TBI-related CT alterations, 99 (58.9%) had a good recovery (GOSE score $\geq$ 7), while 69 patients had disability or death (GOSE score $<$ 7). The distribution of the patients in terms of functionality is shown in ►**Table 1**.

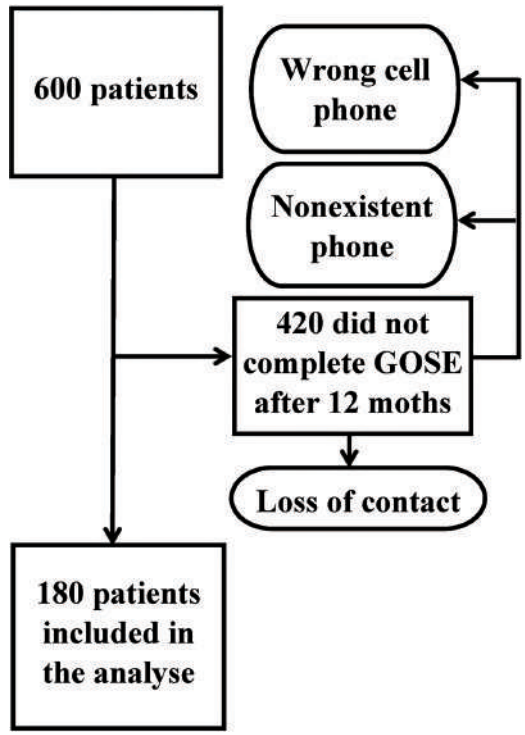


Fig. 1 Flowchart of the data cohort and the 180 patients included in the study.

Table 1 Demographics, changes in computer tomography in the patients included, and associations with neurological outcomes

Variable	Included patients: GOSE score < 7 ($n = 103$)	Included patients: GOSE score ≥ 7 ($n = 77$)	*p*-value
Ages in years: mean ± standard deviation	36.6 ± 16.2)	36.06 ± 16.2)	0.738
Sex: n (%)			0.637
Male	87 (84)	63 (82)	
Female	16 (16)	14 (18)	
Changes on CT: n (%)	99 (96)	69 (90)	0.083
Contusion	57 (56)	39 (51)	0.545
EDH	23 (22)	17 (22)	0.968
SDH	33 (32)	14 (18)	**0.041**
SAH	69 (67)	30 (39)	**< 0.001**
Swelling	23 (22)	03 (04)	**< 0.001**
Effacement of cortical sulci	44 (43)	18 (23)	**0.006**
Effacement of basal cisterns	17 (17)	01 (01)	**< 0.001**
Brain midline shift > 5 mm	20 (19)	06 (08)	**0.028**
Brain midline shift < 5 mm	15 (15)	05 (07)	0.084
Skull fracture	65 (63)	34 (44)	**0.011**
Depressed skull fracture	17 (17)	04 (05)	**0.017**
Skull base fracture	60 (59)	36 (47)	0.112
Marshall grade 1	13 (13)	15 (19)	0.219
Marshall grade 2	51 (50)	52 (67)	**0.019**
Marshall grade 3	21 (20)	04 (05)	**0.003**
Marshall grade 4	17 (17)	11 (15)	**0.040**

Abbreviations: CT, computed tomography; EDH, epidural hemorrhage; GOSE, Glasgow Outcome Scale-Extended; SDH, subdural hemorrhage; SAH, subarachnoid hemorrhage.
Note: *p*-values in bold indicate statistical significance.

Brain CT and Neurological Prognosis

There were no significant associations regarding brain contusions ($p = 0.545$), epidural hemorrhage ($p = 0.968$), skull base fractures ($p = 0.112$), and a worse outcome. In patients with a GOSE score < 7 there was an increased frequency of subdural hemorrhage ($p = 0.041$) and subarachnoid hemorrhage ($p \leq 0.001$). Conditions that are related with increased intracranial pressure and a worse neurological prognosis, such as brain swelling ($p \leq 0.001$), effacement of cortical sulci ($p = 0.006$), effacement of basal cisterns ($p \leq 0.001$), and brain midline shift > 5 mm ($p = 0.028$) were also observed. Skull fracture ($p = 0.011$) and depressed skull fracture ($p = 0.017$) were also associated with worse outcomes at 12 months. A summary of all changes in the brain CT scans (including the Marshall grade) and the associations with neurological outcomes are shown in ►**Table 1**.

After a multivariate analysis of the CT variables, only the presence of subarachnoid hemorrhage, swelling, and depressed skull fracture were independent predictors of outcomes (►**Table 2**).

Secondary Analysis

Age, baseline GOSE scores, and the main baseline CT variables were analyzed for the group of patients lost to follow-up, and no statistically significant differences were found (►**Table 3**).

Table 2 Computed tomography variables that were independent predictors of outcome after a multivariate analysis

Variable	Odds ratio	95% confidence interval	*p*-value
Subarachnoid hemorrhage	2.38	1.24–4.55	0.009
Swelling	4.39	1.20–15.99	0.025
Depressed skull fracture	3.30	1.02–10.70	0.046

Table 3 Comparison of baseline clinical and radiological findings of the patients recruited regarding loss or not to follow-up

Variable	Not lost to follow-up ($n = 180$)	Lost to follow-up ($n = 420$)	*p*-value
Ages in years: mean ± standard deviation	36.5 ± 16.1)	34.75 ± 16.5)	0.23
Sex: n (%)			0.77
Male	354 (84.3)	150 (83.3)	
Severe traumatic brain injury: n (%)	159 (37.9)	66 (36.7)	0.81
Changes on computed tomography: n (%)			
Subdural hemorrhage	119 (28.3)	47 (26.2)	0.70
Subarachnoid hemorrhage	217 (51.7)	99 (55.0)	0.45
Swelling	50 (11.9)	26 (14.4)	0.56
Effacement of cortical sulci	148 (35.2)	62 (34.4)	0.79
Effacement of basal cisterns	77 (18.3)	39 (21.7)	0.59
Brain midline shift > 5 mm	49 (11.67)	26 (14.4)	0.52
Skull fracture	233 (55.5)	99 (55.0)	0.79
Depressed skull fracture	62 (14.8)	22 (12.2)	0.46
Marshall grade 1	72 (17.1)	28 (15.56)	0.89
Marshall grade 2	250 (59.52)	103 (57.22)	0.78
Marshall grade 3	47 (11.2)	25 (13.9)	0.72
Marshall grade 4	50 (11.9)	22 (12.2)	0.93

Discussion

The present study investigated the associations involving morphological changes in the brain identified by CT and the functional outcomes after 12 months measured through the GOSE, which was chosen because it is the most cited and accepted scale to measure functional outcomes following TBI. A simplified Portuguese version of the scale has been validated for use in Brazil.[20–22] It is a very flexible scale that can help to improve follow-up, as it can be applied face to face or by telephone. McMillan et al.[19] found no differences between these two interview modalities in terms of results. Rainer et al.,[23] in 5-year prospective cohort, reported that the best functional improvement occurs 6 to 12 months after the TBI, data that supports the time chosen by us to conduct the follow-up. In the present study, 12 months after the TBI, we found that 42.7% of the patients had good recovery, a figure that is in agreement with the results of the study by Samanamalee et al.[24]

Regarding the Marshall CT classification in a study with a large sample ($n = 2269$), Mass et al.[13] (2005) confirmed that it had a good predictive value, although they recommended making more use of the characteristics underlying the classification and including other predictors, such as intraventricular and traumatic subarachnoid hemorrhage, as well as a clearer differentiation between basal and mass lesions, to produce a better prognostic tool. The results of the present study are in line with most of the results found by Mass et al.,[13] showing the importance of including the effacement of basal cisterns ($p < 0.001$), midline shift > 5 mm ($p < 0.028$) and subarachnoid hemorrhage ($p < 0.001$); however, unlike Mass et al.,[13] we did not find epidural hemorrhage to be associated with better outcomes and intravascular hemorrhage to be related to worse outcomes. In fact, we found a similar percentage of patients with these abnormalities in both groups in the present study, with no association with the outcomes.[13] According to Gennarelli et al.,[25] the worst TBI they observed was subdural hematoma, as it was not only responsible for the majority of all deaths in their series of patients, but it was associated with the greatest impact on quality of life among the survivors. Another study, also conducted in Brazil, Amorim et al.[26] reported an associations regarding epidural, subdural, subarachnoid, and intracerebral hemorrhage and higher levels of mortality in 14 days, as well as with worse GCS scores, findings similar to those of the present study.

Increased intracranial pressure due to a mass effect from swelling or hematoma can lead to displacement of the brain parenchyma into a different compartment, resulting in a worse prognosis. The signs of increased pressure that were analyzed on the CT scans in the present study included brain swelling, effacement of cortical sulci and basal cisterns, and brain midline shift > 5 mm. These alterations were related to functional decline, especially basal cistern effacement, which was the variable most associated with poor recovery. Cordobés et al.[27] found a mortality rate of 76% in the presence of basal cistern effacement. Murphy et al.[28] showed that basal cistern effacement had a close relationship with increased intracranial pressure, being an important independent prognosis factor in first hours after a TBI.

Vascular injury with hemorrhage is an important complication in TBI, and it can be caused by several mechanisms.

Arterial lesions as a result of a direct laceration or skull base fracture are among the most common causes, leading to other complications, such as cerebrospinal fluid leak, which increases the risk of developing meningitis or orthostatic headaches months to years after the lesion.[29] Although a basilar skull fracture was not associated with either good or poor recovery in the data ($p = 0.112$) of the present study, we found that depressed skull fracture, which could indicate a high-energy trauma and a possible parenchyma lesion, was associated with poor recovery ($p = 0.017$). Most of the studies on TBI prognosis[10,11,13] do not report skull fracture as an important indicator of neurological prognosis. In the present study, among the CT variables, depressed skull fracture was found to be an independent predictor of outcome; however, this anomalous finding should be interpreted with caution, and needs to be better evaluated in future studies.

The present cohort study has some limitations which could reduce the impact of our findings. The successful follow-up rates were lower than expected when compared with other studies, such as that the one by Rainer et al.,[23] which reported a loss of only 56% with the same follow-up period, against the rate of 70% observed in the present study. The main reason for the low level of successful follow-up in the present study was the lack of correct contact information in medical records and difficulty accessing the patients' data in general. In low- middle-income countries (LMICs), long-term follow-up may be more challenging than in high-income countries, since telecommunication networks, including mobile phone use and the internet, are not as developed.[26] Moreover, the regular contact that may be maintained by patients visiting rehabilitation centers in countries with better resources is more difficult in LMICs such as Brazil, where the health infrastructure is less developed, as described by Conforto et al.[30,31] Despite the rate of patients lost to follow-up, no statistically significant differences were observed regarding the baseline characteristics of the individuals in the follow-up group and lost to follow-up group. A final limitation is the fact that external factors, such as socioeconomic condition, level of schooling, access to a multidisciplinary team (physiotherapist, physiatrist, or occupational therapist), which could affect functional recovery in the long term, were not assessed in the present study. These important variables could be included in future studies. One important strength of the study was the fact that we used self-reported measures, such as the GOSE, in the follow-up. These are important, as they introduce the direct perspective of the patients, which is often missing in studies which only include provider-driven measures, thus introducing a potential bias.

Conclusion

The present study showed that subarachnoid hemorrhage, brain swelling, and depressed skull fracture were the main morphological abnormalities identified on admission CT scans and the strongest independent predictors of functional outcomes measured at follow-up 12 months after the TBI. Although there was an important rate of patients lost to follow-up, a common difficulty in studies in LMICs, there were no statistically significant differences at baseline regarding the characteristics of the overall sample and the follow-up group. Further studies with larger samples and longer follow-up are warranted to provide a higher level of evidence regarding the important variables identified in the present study.

Ethical Considerations

The present study was approved by the Ethics Committee of Fundação Universidade Federal de Sergipe (in accordance with the Helsinki Declaration, revised in 1983), and all patients or their legal guardian/next of kin signed an informed consent form.

Authors Contribution

All authors contributed to the conception and design of the study. Material preparation and data collection and analysis were performed by RSD, TCSM, IFSL, JNCN, LAS, BFOS,RLOA, and AMPO. The first draft of the manuscript was written by RSD, and all authors commented on previous versions of the manuscript. The final draft of the manuscript was written by LAS. All authors read and approved the final manuscript.

Funding

The authors declare that they have received no funding for the performance of the present study.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgments

We would like to thank Cassandra Schaly for her contribution in reviewing the language used in the article, and the Research Coordination Department (Coordenação de Pesquisa, COPES, in Portuguese) at Fundação Universidade Federal de Sergipe for the encouragement to complete the study.

References

1 Azouvi P, Arnould A, Dromer E, Vallat-Azouvi C. Neuropsychology of traumatic brain injury: An expert overview. Rev Neurol (Paris) 2017;173(7-8):461–472
2 Capizzi A, Woo J, Verduzco-Gutierrez M. Traumatic Brain Injury: An Overview of Epidemiology, Pathophysiology, and Medical Management. Med Clin North Am 2020;104(02):213–238
3 Gaudêncio TG, Leão Gde MA epidemiologia do Traumatismo Crânio-Encefálico: Um Levantamento bibliográfico no Brasil. Revista Neurociencias. 2013;21(03):427–434
4 Feitas JPP, Ribeiro LA, Jorge MT. Vítimas de acidentes de trânsito na faixa etária pediátrica atendidas em um hospital universitário: aspectos epidemiológicos e clínicos. Cad Saude Publica 2007;23 (12):3055–3060
5 Melo JRT, de Santana DLP, Pereira JLB, Ribeiro TF. Traumatismo cranioencefálico em crianças e adolescentes na cidade do Salvador - Bahia. Arq Neuropsiquiatr 2006;64(04):994–996
6 National database: 2017 profile of people within the traumatic brain injury model systems. Traumatic brain injury model systems National Data and Statistical Center. Center. Available at: https://msktc.org/lib/docs/Data_Sheets_/2017_TBIMS_ National_Databa.

7 Teasdale G, Jennett B. Assessment and prognosis of coma after head injury. Acta Neurochir (Wien) 1976;34(1-4):45–55
8 Thelin EP, Nelson DW, Vehviläinen J, et al. Evaluation of novel computerized tomography scoring systems in human traumatic brain injury: An observational, multicenter study. PLoS Med 2017;14(08):e1002368
9 Kolias AG, Guilfoyle MR, Helmy A, Allanson J, Hutchinson PJ. Traumatic brain injury in adults. Pract Neurol 2013;13(04):228–235
10 Zhu H, Gao Q, Xia X, Xiang J, Yao H, Shao J. Clinically-important brain injury and CT findings in pediatric mild traumatic brain injuries: a prospective study in a Chinese reference hospital. Int J Environ Res Public Health 2014;11(04):3493–3506
11 Marshall LF, Marshall SB, Klauber MR, et al. A new classification of head injury based on computerized tomography. J Neurosurg 1991;75(Supplement):S14–S20
12 Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. PLoS Med 2008;5(08):e165, discussion e165
13 Maas AIR, Hukkelhoven CWPM, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. Neurosurgery 2005;57(06):1173–1182, discussion 1173–1182
14 Nelson DW, Nyström H, MacCallum RM, et al. Extended analysis of early computed tomography scans of traumatic brain injured patients and relations to outcome. J Neurotrauma 2010;27(01): 51–64
15 Raj R, Siironen J, Skrifvars MB, Hernesniemi J, Kivisaari R. Predicting outcome in traumatic brain injury: development of a novel computerized tomography classification system (Helsinki computerized tomography score). Neurosurgery 2014;75(06):632–646, discussion 646–647
16 Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1(7905):480–484
17 Jennett B, Snoek J, Bond MR, Brooks N. Disability after severe head injury: observations on the use of the Glasgow Outcome Scale. J Neurol Neurosurg Psychiatry 1981;44(04):285–293
18 Wilson JTL, Pettigrew LEL, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. J Neurotrauma 1998;15(08): 573–585
19 McMillan T, Wilson L, Ponsford J, Levin H, Teasdale G, Bond M. The Glasgow Outcome Scale - 40 years of application and refinement. Nat Rev Neurol 2016;12(08):477–485
20 de Sousa RM. Comparação entre instrumentos de mensuração das consequências do trauma crânio-encefálico. Rev Esc Enferm USP 2006;40(02):203–213
21 de Sousa RM, Koizumi MS. Recuperação das vítimas de traumatismo crânio-encefálico no período de 1 ano após o trauma. Rev Esc Enferm USP 1996;30(03):484–500
22 de Sousa RMC, Koizumi MS. Recuperação das vítimas de trauma cranioencefálico entre 6 meses a 1 ano. Braz Neurosurg 1998;17 (02):72–80
23 Rainer TH, Hung KKC, Yeung JHH, et al. Trajectory of functional outcome and health status after moderate-to-major trauma in Hong Kong: A prospective 5 year cohort study. Injury 2019;50 (05):1111–1117
24 Samanamalee S, Sigera PC, De Silva AP, et al. Traumatic brain injury (TBI) outcomes in an LMIC tertiary care centre and performance of trauma scores. BMC Anesthesiol 2018;18(01):4
25 Gennarelli TA, Spielman GM, Langfitt TW, et al. Influence of the type of intracranial lesion on outcome from severe head injury. J Neurosurg 1982;56(01):26–32
26 Amorim RL, Oliveira LM, Malbouisson LM, et al. Prediction of Early TBI Mortality Using a Machine Learning Approach in a LMIC Population. Front Neurol 2020;10(01):1366
27 Cordobés F, de la Fuente M, Lobato RD, et al. Intraventricular hemorrhage in severe head injury. J Neurosurg 1983;58(02): 217–222
28 Murphy S, Thomas NJ, Gertz SJ, et al; Investigators of the Approaches and Decisions in Acute Pediatric Traumatic Brain Injury (ADAPT) Study. Tripartite Stratification of the Glasgow Coma Scale in Children with Severe Traumatic Brain Injury and Mortality: An Analysis from a Multi-Center Comparative Effectiveness Study. J Neurotrauma 2017;34(14):2220–2229
29 Vella MA, Crandall ML, Patel MB. Acute Management of Traumatic Brain Injury. Surg Clin North Am 2017;97(05):1015–1030
30 Conforto AB, Anjos SM, Saposnik G, et al. Transcranial magnetic stimulation in mild to severe hemiparesis early after stroke: a proof of principle and novel approach to improve motor function. J Neurol 2012;259(07):1399–1405
31 Conforto AB, Paulo RB, Patroclo CB, et al. Stroke management in a university hospital in the largest South American city. Arq Neuropsiquiatr 2008;66(2B):308–311

Traumatic Brain Injury: in-hospital Survival Rates and the Main Predictors of in-hospital Mortality in Northeastern Brazil*

Traumatismo cranioencefálico: taxas de sobrevida intrahospitalar e os principais preditores de mortalidade intrahospitalar no nordeste do Brasil

Diego Henrique Gois Pereira[1] José Nolasco de Carvalho Neto[2] Thaís Cristina de Souza Melo[3] Catharine Natielle Oliveira Dias Belarmino dos Santos[1] Elisa Ribeiro Carvalho Silva[1] Arthur Maynart Pereira Oliveira[2,4,5] Bruno Fernandes de Oliveira Santos[1,2,4,5]

[1] Faculdade de Medicina, Universidade Tiradentes, Aracaju, SE, Brazil
[2] Faculdade de Medicina, Universidade Federal de Sergipe, Aracaju, SE, Brazil
[3] Universidade Federal de São Paulo, São Paulo, SP, Brazil
[4] Fundação de Beneficência Hospital de Cirurgia, Aracaju, SE, Brazil
[5] Hospital de Urgência de Sergipe, Aracaju, SE, Brazil

Address for correspondence Diego Henrique Gois Pereira, Faculdade de Medicina, Universidade Tiradentes, Aracaju, Sergipe 49020-090, Brazil (e-mail: diegohenrique952@gmail.com).

Arq Bras Neurocir 2024;43(3):e164–e171.

Abstract

Introduction Upper middle-income countries have epidemiological peculiarities that should be considered to identify the main predictive factors of intrahospital mortality regarding traumatic brain injury (TBI) to address modifiable problems.

Objective To assess the in-hospital survival of patients with TBI and to identify the predictors of in-hospital death.

Methods This is a retrospective dynamic cohort study of victims of TBI who were admitted to the Hospital de Urgência de Sergipe (HUSE, in the Portuguese acronym) between March 1, 2017 and April 29, 2018. The outcome considered was in-hospital death from any cause. Cox regression was used to assess predictors of in-hospital mortality.

Results The sample comprised 596 patients, with a median age of 31.0 (12–94) years old, 504 (84%) of whom were men. Regarding TBI severity, 250 had mild TBI; 121 had moderate TBI; and 225 had severe TBI. The average follow-up was 20.6 ± 4.0 days, with 60 in-hospital deaths and a 30-day mortality of 22.9%. Four independent predictors of in-hospital death were identified: acute subdural hemorrhage (ASDH) (risk ratio [RR] = 1.926; 95% confidence interval [CI] = 1.15–3.22; $p = 0.013$), swelling (risk ratio

Keywords
- developing country
- mortality
- survival
- traumatic brain injury

* *Hospital de Urgência de Sergipe, Aracaju, SE, Brazil.*

received
February 3, 2022
accepted
June 21, 2023
article published online
October 31, 2023

DOI https://doi.org/10.1055/s-0043-1776272.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

[RR] = 3.706; 95%CI = 2.21–6.19; $p < 0.001$), skull fracture (RR = 2.551; 95%CI = 1.36–4.75; $p = 0.003$), and severe TBI (RR = 2.039; 95%CI = 1.29–4.12; $p = 0.005$).

Conclusions Acute subdural hemorrhage, swelling, skull cap fracture, and a Glasgow Coma Scale score of < 9 at admission were independent predictors of in-hospital mortality in patients with TBI.

Resumo

Introdução Os países de renda média alta possuem peculiaridades epidemiológicas que devem ser levadas em consideração para identificar os principais fatores preditivos de mortalidade intrahospitalar por traumatismo cranioencefálico (TCE) a fim de abordar problemas modificáveis.

Objetivo Avaliar a sobrevida hospitalar de pacientes com TCE e identificar os preditores de óbito hospitalar.

Métodos Trata-se de um estudo de coorte dinâmico retrospectivo de vítimas de TCE que deram entrada no Hospital de Urgência de Sergipe (HUSE) entre 1° de março de 2017 e 29 de abril de 2018. O desfecho considerado foi óbito hospitalar por qualquer causa. A regressão de Cox foi usada para avaliar os preditores de mortalidade hospitalar.

Resultados A amostra foi composta por 596 pacientes, com idade mediana de 31,0 (12–94) anos, sendo 504 (84%) homens. Em relação à gravidade do TCE, 250 tiveram TCE leve; 121 tiveram TCE moderado, e 225 tiveram TCE grave. O seguimento médio foi de 20,6 ± 4,0 dias, com 60 óbitos hospitalares e mortalidade em 30 dias de 22,9%. Quatro preditores independentes de morte hospitalar foram identificados: hemorragia subdural aguda (ASDH, na sigla em inglês) (risk ratio [RR] = 1,926; intervalo de confiança [IC] 95% = 1,15–3,22; $p = 0,013$), inchaço (RR = 3,706; IC95% = 2,21–6,19; $p < 0,001$), fratura de crânio (RR = 2,551; IC95% = 1,36–4,75; $p = 0,003$) e TCE grave (RR = 2,039, IC95% = 1,29–4,12; $p = 0,005$).

Conclusões Hemorragia subdural aguda, edema, fratura da calota craniana e pontuação na Escala de Coma de Glasgow < 9 na admissão foram preditores independentes de mortalidade hospitalar em pacientes com TCE.

Palavras-chave
- país em desenvolvimento
- mortalidade
- sobrevivência
- traumatismo cranioencefálico

Introduction

Trauma is one of the main causes of global morbidity and mortality, and traumatic brain injury (TBI) is responsible for more global death and disability than any other traumatic injury,[1] especially among adolescents and young adults.[2,3] The rates are highest in low- and middle income countries (LMICs), such as Brazil, mainly for socioeconomic reasons.[3] Moreover, TBI victims put great pressure on health services, not only regarding their initial emergency treatment, but also the treatment of long-term sequelae such as motor and cognitive deficits. In Brazil, the estimated incidence of TBI ranges from 26.2 to 65.7 per 100,000 inhabitants, with overall lethality rate estimated at 7.7%, and 33.3% for those with severe TBI.[4] Hospital mortality has been estimated to be 5.1 per 100,000 inhabitants per year.[3]

The hospital considered in the present study is located in the Northeast of Brazil, an area which is marked by poor education, poverty, and increased levels of violence. The incidence of traffic accidents in the region is high and is the main cause of TBI. Frequent cases of driving while intoxicated by alcohol or riding a motorcycle without a helmet result in significant levels of severe TBI cases. Despite efforts to reduce these behaviors, limited resources mean that the oversight of traffic is still poor. Furthermore, the Northeast of Brazil is the most violent region in the country, which results in more cases of TBI caused by aggression and the use of firearms.

Another important factor in LMICs is the lack of resources in health units, such as the equipment required to undertake a computed tomography (CT) scan, especially outside major urban centers, where there is less access to healthcare and emergency medical services. Patients, therefore, have to be transferred to referral hospitals, which can delay treatment, resulting in reduced survival rates when compared with high-income countries.

In general, there is a lack of studies on TBI in LMICs, including in Brazil. The present study, therefore, aims to assess the in-hospital survival of patients with TBI and to identify the predictors of in-hospital death from any cause in a reference hospital in Northeastern Brazil.

Methods

Study Design

This is a dynamic retrospective cohort study comprising 596 TBI patients admitted to the Hospital de Urgência de Sergipe (HUSE, in the Portuguese acronym), a tertiary care center in the city of Aracaju, state of Sergipe, in Northeastern Brazil, between March 1, 2017, and April 29, 2018. The survival of patients suffering from acute TBI was investigated using demographic, clinical, and tomographic parameters. The outcome was in-hospital death from any cause. Patients were censored at discharge.

Data Collection

For each patient, their clinical and tomographic records at admission and during hospitalization were evaluated. Epidemiological data and information on the trauma mechanism were also collected. The Glasgow Coma Scale (GCS) assessment was performed by the neurosurgeon at the initial assessment and TBI was considered mild when the GCS score was 14 to 15, moderate when between 9 and 13, and severe when ≤ 8.

Headache, nausea, vomiting, and dizziness were not evaluated in patients who arrived at the hospital with an altered level of consciousness and without companions, unless it was reported in the prehospital evaluation record. Alcohol and drug intoxication were considered positive when reported by the patient or described in the medical record by a companion. Hypoxia at admission was measured by pulse oximeter and only considered when saturation was $< 92\%$.

Data that could not be obtained in the initial interview or from medical records were considered missing values. Mild cases who did not require hospitalization or patients who lacked tomographic data were excluded from the study.

Statistical Analysis

Categorical variables were presented as percentages and continuous variables were represented by means $\pm$ standard deviation (SD). Cox regression in a univariate and multivariate manner was used to assess the risks factors for in-hospital death from any cause. The variables included in the multivariate model were all those with $p < 0.05$ in the univariate analysis. Any multicollinearity problems were solved before the variables were inserted in the model. The backward method of variable selection was used. The variables that remained in the model were tested for possible interactions. The risk proportionality assumption was tested using Schoenfeld residues for each of the variables that remained in the final model. The method that was used to estimate the probabilities of survival was the Kaplan-Meier method. Values of $p < 0.05$ were considered significant. IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis.

Results

The median age of the patients was 31.0 (12–94) years old, 504 (84%) being male. Out of the total of 596 patients, 225 were considered severe on admission (►**Table 1**).

The direct photomotor reflex (DPR) was absent in at least 1 eye in 76 (12.7%) cases, but it was not an independent predictor of in-hospital mortality (►**Table 2**).

Regarding tomographic data, there were 316 (52.5%) cases of traumatic subarachnoid hemorrhage (SAH), 125 (20.9%) cases of epidural hematoma (EDH), 166 (27.8%) cases of acute subdural hematoma (ASDH), 76 (12.7%) cases of swelling, 332 (55.3%) of skull cap fractures, and 315 (52.8%) skull base fractures.

Using Cox regression, potential risk factors for in-hospital death from any cause were identified (►**Table 2**). After multivariate analysis, the study identified 4 independent predictors of in-hospital death in this cohort: ASDH (risk ratio [RR] = 1.926; 95% confidence interval [CI] = 1.15–3.22; $p = 0.013$); swelling (RR = 3.706; 95%CI = 2.21–6.19; $p < 0.001$), skull cap fracture (RR = 2.551; 95%CI = 1.36–4.75; $p = 0.003$), and severe TBI (RR = 2.039; 95%CI = 1.29–4.12; $p = 0.005$) (►**Table 3**).

Most clinical data were not independent predictors of death, except for severe TBI. The mean follow-up was 20.6 ± 4.0 days, with a death rate in 30 days of 22.9%. At the end of the period, there were 60 in-hospital deaths. (►**Fig. 1**). The median survival of patients suffering from ASDH was 58 days with a standard error of 49 days (►**Fig. 2**); from skull cap fracture, it was 172 days with a standard error of 82 days (►**Fig. 3**); from swelling, it was 41 days with a standard error of 20 days (►**Fig. 4**); and from severe TBI, it was 172 days with a standard error of 62 days (►**Fig. 5**).

Discussion

The present dynamic cohort study aimed to analyze the in-hospital survival of TBI victims, as well as the main predictors of in-hospital mortality from any cause. The 30-day survival rate was 22.9%. Independent predictors of death were both variables associated with primary damage (skull cap fracture and ASDH), and characteristics related to secondary injury (swelling). In addition, severe TBI proved to be a predictor of death in these patients, being an important indicator of severity on admission.

The number of cases of TBI increases each year in Brazil; the main cause is automobile accidents, both in adolescents and young adults,[1,5] and in the age group from 21 to 60 years old. Falls are the second major cause, affecting mainly the pediatric and geriatric population.[5] Some studies indicate that there is a relationship between older age and higher mortality,[6,7] even in cases of mild TBI.[6] However, there is no consensus on an appropriate cutoff; an age between 45 and 50 years old is generally suggested, with higher mortality in the first 14 days in this age group.[8,9] In other studies, age has been more related to functional recovery than mortality.[10] In the present cohort, age was not a significant predictor of mortality, even when different extracts were explored. This may result from the limitations of the power of the study', or it may correspond to particular characteristics of the population. In Northeastern Brazil, it is common for young people to drive at high speed, to drive when intoxicated, and to not use a helmet when riding a motorbike; this is reflected in the

Table 1 Characteristics of the population hospitalized by TBI

Characteristics	Value
Number of patients	596
Age (median)	31.0 (12–94) Years old
Sex	
Male	504
Female	92
GCS at admission	
Mild (14–15)	250 (41,7%)
Moderate (9–13)	121 (20,2%)
Severe (3–8)	225 (37,5%)
Pupillary reactivity	
Absence of DPR	76 (12,7%)
Anisocoria	68 (11,3%)
Alcohol	246 (41,0%)
Loss of consciousness	481 (80,2%)
Hypoxemia	275 (46,1%)
OTI	250 (41,7%)
Racoon Sign	119 (19,8%)
Battle Sign	31 (5,2%)
Eyelid edema	307 (51,2%)
Otorrhagia	153 (25,5%)
Rhinorrhagia	192 (32,0%)
CT findings	
EDH	125 (20,9%)
AHSD	166 (27,8%)
SAH	316 (52,5%)
Swelling	76 (12,7%)
Skull cap fracture	332 (55,3%)
Skull base fracture	315 (52,8%)
Depressed skull fracture	83 (13,8%)
MLS $>$ 5mm	75 (12,5%)
Unlit Cisterns	61 (10,2%)
Unlit Sulcus	210 (35,0%)
Marshall	
I	100 (16,7%)
II	353 (58,8%)
III	72 (12,0%)
IV	72 (12,0%)
Neurological surgery	110 (18,3%)

Abbreviations: ASDH, acute subdural hemorrhage; CT, computed tomography; DPR, direct photomotor reflex; EDH, epidural hematoma; GCS, glasgow coma scale; MLS, midline shift; OTI, orotracheal intubation; SAH, subarachnoid hemorrhage.

cohort of the present study, with 41% of the patients being intoxicated at the time of admission. This may lead to more severe traumas than those caused by falls in older adults. Otherwise, the elderly seem to have the worst recovery from TBI.[11]

Traumatic brain injury is responsible for 30% of trauma deaths, and those who survive may remain extremely debilitated.[1] Survival and life expectancy in patients suffering from TBI are reported as being significantly reduced when compared with the general population.[12] It depends on prehospitalization and treatments that can control intracerebral pressure.[13,14] A study in Finland that included 5 neurosurgery intensive care units (ICUs), showed 30-day mortality rates after TBI of 18%,[15] ranging from 23 to 26% in cases of moderate-to-severe TBI. Falls were the main cause of trauma in this study, followed by traffic accidents. Age and GCS scores were the strongest predictors of mortality rates.[15] A study that used data from the Brain Trauma Foundation database in New York showed that 23% of the patients died within 14 days of the TBI,[16] with older age, unreactive pupils, and poor GCS motor scores being associated with mortality. In contrast, a study of a Chinese cohort of 13,138 patients showed that the overall 30-day mortality rate was 5%, and 20% in cases of severe TBI.[17] A study performed in São Paulo, Brazil's largest city, located in the Southeastern region of the country, showed intrahospital mortality rates from TBI of 10.2%,[18] with 1-to-7-day mortality of 60.9%, with falls being the main cause. In the present study, the mortality rates were of 10.6%, and the 30-day mortality was of 22.9%, with mortality being associated with four factors: ASDH, swelling, skull cap fracture, and severe TBI with swelling being the factor with the strongest association with mortality. Severe TBI may be more related to traffic accidents and violence, factors that are more prevalent in the Northeast region of Brazil. This can be seen in another study from the state of Maranhão, in which 58.1% of hospital admissions were for TBI resulting from a traffic accident, and 14.5% resulting from aggression.[19]

The incidence of TBI is around five times higher in men than in women.[1,3] This is because men have greater risk behaviors for TBI, such as traffic accidents and violence.[20] However, some studies show that women have higher mortality rates.[21] The influence of gender on survival remains controversial, and does not appear to be a significant predictor of mortality, as was found in the present study. Likewise, despite the well-known association between intoxication and TBI, the use of drugs and alcohol was not reflected in increased mortality, which was also reported in a study by Signorini[9] undertaken in the United Kingdom.

Among the clinical prognostic factors, pupillary reaction, hypoxemia, and arterial hypotension have previously been shown to be significant prognostic factors in several studies.[8,22–24] These factors are highly prevalent, occurring in $\sim$ 80% of cases, both before and after hospital admission.[24] The absence of pupillary reaction, for example, is an important sign of severity in clinical practice,[23,24] being a clinical indication of intracranial hypertension. This is especially significant in cases of bilateral mydriasis, which is associated with increased mortality at 48 hours, 6 months, and 1 year.[25]

Hypoxemia is also related to higher mortality. This, perhaps, is due to the fact that it is frequently accompanied by

Table 2 Univariate analysis of predictors of in-hospital death from any cause (Cox regression)

Variable	RR	CI 95%	*p-value*
GCS	0.87	0.82–0.92	< 0.001
Severity	1.91	1.36–2.67	< 0.001
Hypoxemia	3.27	1.72–6.24	< 0.001
OTI	3.51	1.91–6.42	< 0.001
Face trauma	0.62	0.40–0.96	0.034
Presence of DPR	0.27	0.16–0.43	< 0.001
Contusion	1.91	1.20–3.05	0.006
ASDH	1.92	1.15–3.22	0.013
SAH	2.56	1.50–4.38	0.001
Skull cap fracture	2.55	1.36–4.75	0.003
Depressed skull fracture	1.71	1.02–2.88	0.041
MLS > 5mm	3.24	2.05–5.12	< 0.001
Unlit sulcus	2.46	1.55–3.91	< 0.001
Swelling	3.70	2.21–6.19	< 0.001
Conduct	1.67	1.05–2.65	0.028
Neurosurgical conduct	1.65	1.03–2.63	0.036
Severe TBI	2.03	1.29–4.12	0.005

Abbreviations: ASDH, acute subdural hemorrhage; CT, computed tomography; DPR, direct photomotor reflex; EDH, epidural hematoma; GCS, glasgow coma scale; MLS, midline shift; OTI, orotracheal intubation; SAH, subarachnoid hemorrhage; TBI, traumatic brain injury.

hypercapnia, which, in turn, promotes cerebral edema, and consequently increases intracranial pressure.[24] A previous study showed that patients who are submitted to endotracheal intubation have higher mortality rates compared with patients who do not need such measure.[26]

Arterial hypotension was not evaluated in the present cohort, but has been shown to be a relevant predictor of survival in other studies, and is strongly associated with worse outcomes.[7] In some studies, it has been reported to be the clinical parameter most strongly associated with mortality.[23,24] In our study, the absence of DPR and hypoxemia were predictors of mortality in the univariate analysis, but did not remain as such in the multivariate analysis. This may be due to the fact that the absence of DPR and hypoxemia are closely related to the severity of TBI variable, which ended up performing better in the statistical model. In other words, DPR and hypoxemia, in this population, did not confer an additional mortality risk to the proposed statistical model.

Although GCS is one of the main tools for assessing patients with |TBI, some studies suggest that it is not a good predictor of mortality, with an area under the receiver operating characteristic (ROC) curve of 0.64.[8] However, some studies show that the GCS has an almost linear relationship with mortality in the first 14 days of TBI,[8] and there seems to be a clear association between a decreased GCS score and lethality in polytrauma patients.[9,27] A GCS of 15 would be equivalent to 1% lethality. In those with an GCS of 4, we would have a lethality of 27%,[27] with an increase in continuous and almost linear lethality over the entire scale.[7] In our cohort, GCS severity proved to be an independent predictor of mortality and was an easy clinical parameter to obtain. Patients who had a GCS score < 9 had a 2-fold greater risk of dying during hospitalization.

Tomographic aspects have also been shown to be good predictors of mortality in the literature.[7] The appearance of the subarachnoid cisterns, the number of contusions, the appearance of the 4th ventricle, swelling, midline deviation, the presence of subdural hematoma, subarachnoid hemorrhage or intraventricular hemorrhage, and the volume of cranial injury have already been described as predictors of death

Table 3 Multivariate analysis of predictors of in-hospital death from any cause (Cox regression)

Variable	RR	95%CI	*p-value*
ASDH	1.926	1.150–3.224	0.013
Skull cap fracture	2.551	1.368–4.755	0.003
Swelling	3.706	2.218–6.192	< 0.001
Severe TBI	2.039	1.292–4.127	0.005

Abbreviations: ASDH, acute subdural hemorrhage; CI, confidence interval; RR, risk ratio; TBI, traumatic brain injury.

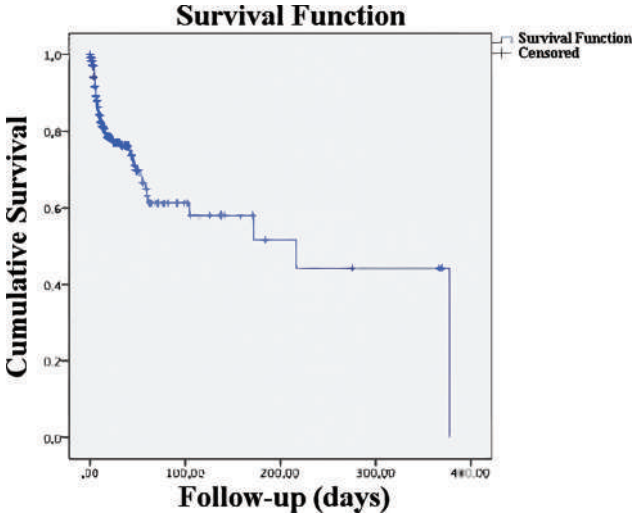


Fig. 1

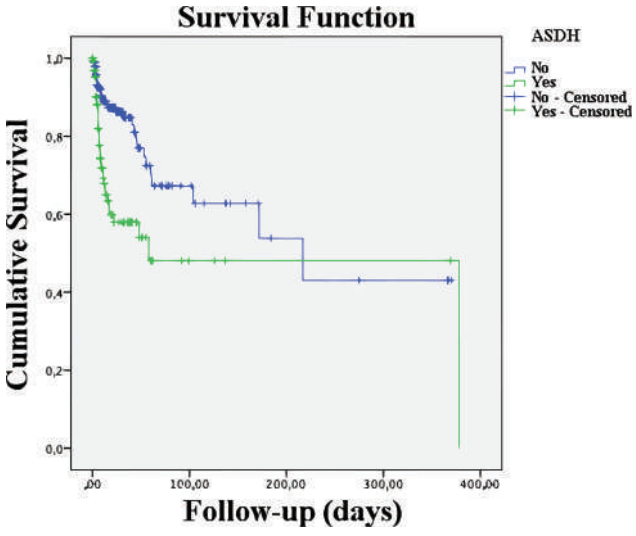


Fig. 2

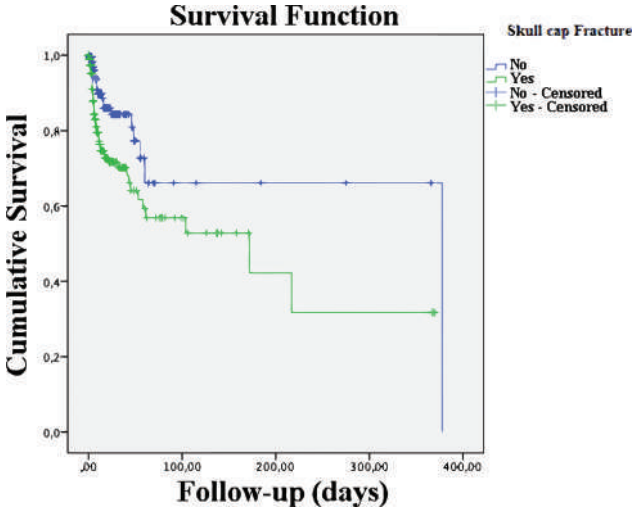


Fig. 3

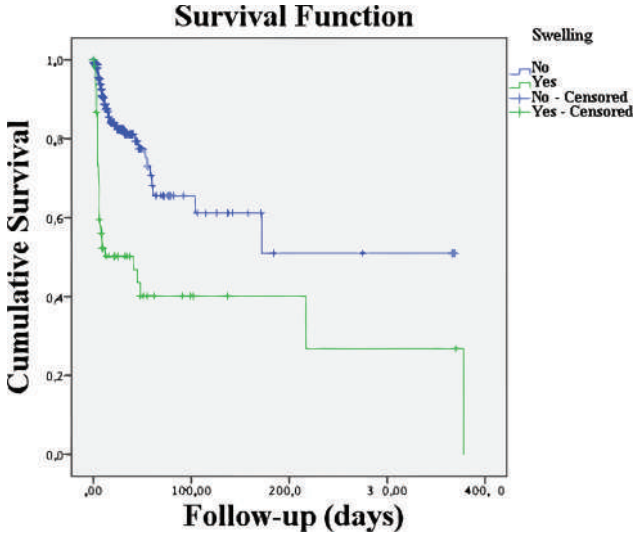


Fig. 4

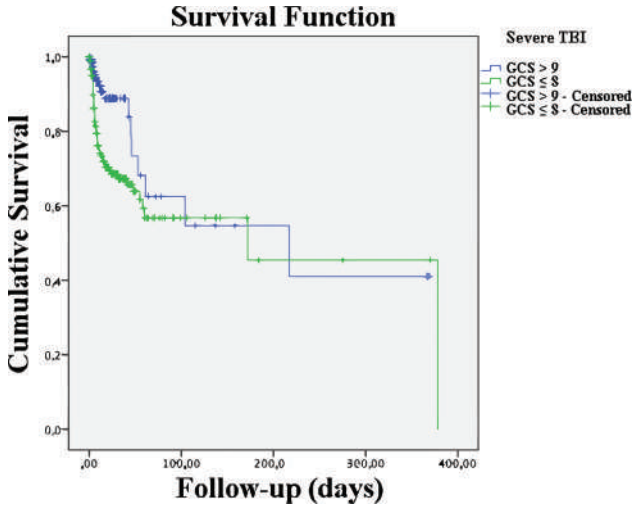


Fig. 5

associated with higher mortality in the first 48 hours after the injury.[8,9] In addition, cerebral edema detected on initial CT is considered an independent predictor of intrahospital mortality.[28] In the current study, skull cap fracture, swelling, and ASDH were important independent predictors of mortality in the multivariate analysis that were identified by tomography. Probably the skull cap fracture implies a worse prognosis, as a factor equivalent to a trauma of greater energy.

Other predictors of outcome scores are available, such as the Injury Severity Score (ISS), the CRASH basic score and the IMPACT core score, which have already proved effective in other populations. The ISS has been shown to present great sensitivity and specificity to predict in-hospital death in patients suffering from severe TBI, with AUC of 0.76 on the ROC curve.[25] Regarding the CRASH and IMPACT scores, a study by Maeda et al., which researched the applicability of these scores in the Japanese population in victims of severe TBI, found that they were both effective, with AUC scores of 0.86 and 0.81, respectively.[29]

De Silva et al. showed in their study using the CRASH score that patients in LMICs had a greater chance to die following a TBI than patients in high-income countries, with patients with severe TBI being twice (OR 2,23; 95%CI) as likely to die.[30] Unfortunately, a lack of information made it impossible to use these scores in this cohort. The applicability of these scores in northeastern Brazil must be tested in future studies.

Despite not being investigated in this cohort, laboratory parameters deserve due attention, since serum glucose, platelet count, and hemoglobin levels have also been shown to be independent predictors of survival.[23]

Conclusion

Understanding the independent predictors of mortality is of fundamental importance for the survival of patients suffering from TBI, in addition to serving as a substrate for clinical practices and informing public health policies. Acute subdural hematoma, swelling, skull cap fracture, and a GCS score < 9 at admission were independent predictors of intrahospital mortality from any cause in in patients hospitalized for TBI at the HUSE.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Rodrigues Mde SEpidemiologia de traumatismo cranienceфálico em um hospital. Rev Soc Bras Clin Med 2018;16:21–24
2 Morgado FL, Rossi LA. Correlação entre a escala de coma de Glasgow e os achados de imagem de tomografia computadorizada em pacientes vítimas de traumatismo cranioencefálico. Radiol Bras 2011;44(01):35–41. Doi: 10.1590/S0100-39842011000100010
3 de Almeida CER, de Sousa Filho JL, Dourado JC, Gontijo PAM, Dellaretti MA, Costa BS. Traumatic Brain Injury Epidemiology in Brazil. World Neurosurg 2016;87:540–547. Doi: 10.1016/j.wneu.2015.10.020
4 Soares de Souza R, Pessoa Pinheiro P, Ferreira de Lima Silva JM, Leite Rolim Neto M, Machado Filho JA. Traumatic brain injury (TBI): morbidity, mortality and economic implications. Int Arch Med. Doi: 10.3823/1672
5 Gaudêncio T, Leão G. A Epidemiologia do Traumatismo Crânio-Encefálico: Um Levantamento Bibliográfico no Brasil. RNC 2013; 21(03):427–434. Doi: 10.4181/RNC.2013.21.814.8p
6 Thompson HJ, McCormick WC, Kagan SH. Traumatic brain injury in older adults: epidemiology, outcomes, and future implications. J Am Geriatr Soc 2006;54(10):1590–1595. Doi: 10.1111/j.1532-5415.2006.00894.x
7 Hernández AV, Steyerberg EW, Butcher I, et al. Adjustment for strong predictors of outcome in traumatic brain injury trials: 25% reduction in sample size requirements in the IMPACT study. J Neurotrauma 2006;23(09):1295–1303. Doi: 10.1089/neu.2006.23.1295
8 Perel P, Arango M, Clayton T, et al; MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. BMJ 2008;336(7641):425–429. Doi: 10.1136/bmj.39461.643438.25
9 Signorini DF, Andrews PJD, Jones PA, Wardlaw JM, Miller JD. Predicting survival using simple clinical variables: a case study in traumatic brain injury.:6.
10 Cremer OL, Moons KGM, van Dijk GW, van Balen P, Kalkman CJ. Prognosis following severe head injury: Development and validation of a model for prediction of death, disability, and functional recovery. J Trauma 2006;61(06):1484–1491. Doi: 10.1097/01.ta.0000195981.63776.ba
11 Dhandapani S, Manju D, Sharma B, Mahapatra A. Prognostic significance of age in traumatic brain injury. J Neurosci Rural Pract 2012;3(02):131–135. Doi: 10.4103/0976-3147.98208
12 Brown AW, Leibson CL, Mandrekar J, Ransom JE, Malec JF. Long-term survival after traumatic brain injury: a population-based analysis controlled for nonhead trauma. J Head Trauma Rehabil 2014;29(01):E1–E8. Doi: 10.1097/HTR.0b013e318280d3e6
13 Shackelford SA, Del Junco DJ, Reade MC, et al. Association of time to craniectomy with survival in patients with severe combat-related brain injury. Neurosurg Focus 2018;45(06):E2. Doi: 10.3171/2018.9.FOCUS18404
14 Cooper DJ, Rosenfeld JV, Murray L, et al; DECRA Trial Investigators Australian and New Zealand Intensive Care Society Clinical Trials Group. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med 2011;364(16):1493–1502. Doi: 10.1056/NEJMoa1102077
15 Raj R, Bendel S, Reinikainen M, et al. Traumatic brain injury patient volume and mortality in neurosurgical intensive care units: a Finnish nationwide study. Scand J Trauma Resusc Emerg Med 2016;24(01):133. Doi: 10.1186/s13049-016-0320-6
16 Roozenbeek B, Chiu YL, Lingsma HF, et al. Predicting 14-day mortality after severe traumatic brain injury: application of the IMPACT models in the brain trauma foundation TBI-trac® New York State database. J Neurotrauma 2012;29(07):1306–1312. Doi: 10.1089/neu.2011.1988
17 Gao G, Wu X, Feng J, et al; China CENTER-TBI Registry Participants. Clinical characteristics and outcomes in patients with traumatic brain injury in China: a prospective, multicentre, longitudinal, observational study. Lancet Neurol 2020;19(08):670–677. Doi: 10.1016/S1474-4422(20)30182-4
18 Koizumi MS, Lebrão ML, Mello-Jorge MHPD, Primerano V. Morbimortalidade por traumatismo crânio-encefálico no município de São Paulo, 1997. Arq Neuropsiquiatr 2000;58(01):81–89. Doi: 10.1590/S0004-282. Doi: × 2000000100013
19 Santos MF, de Carvalho FR, Barbosa RL. TCE EM UTI: EPIDEMIOLOGIA, TRATAMENTO E MORTALIDADE NO MARANHÃO, BRASIL. Published online 2019:11.
20 Colantonio A. Sex, Gender, and Traumatic Brain Injury: A Commentary. Arch Phys Med Rehabil 2016;97(02):S1–S4. Doi: 10.1016/j.apmr.2015.12.002
21 Ottochian M, Salim A, Berry C, Chan LS, Wilson MT, Margulies DR. Severe traumatic brain injury: is there a gender difference in mortality? Am J Surg 2009;197(02):155–158. Doi: 10.1016/j.amjsurg.2008.09.008
22 Lingsma HF, Roozenbeek B, Steyerberg EW, Murray GD, Maas AI. Early prognosis in traumatic brain injury: from prophecies to predictions. Lancet Neurol 2010;9(05):543–554. Doi: 10.1016/S1474-4422(10)70065-X
23 Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting Outcome after Traumatic Brain Injury: Development and International Validation of Prognostic Scores Based on Admission Characteristics. Singer M, ed. PLoS Med. 2008;5(08):e165 Doi: 10.1371/journal.pmed.0050165
24 Volpi PC, Robba C, Rota M, Vargiolu A, Citerio G. Trajectories of early secondary insults correlate to outcomes of traumatic brain injury: results from a large, single centre, observational study. BMC Emerg Med 2018;18(01):52. Doi: 10.1186/s12873-018-0197-y
25 Strnad M, Borovnik Lesjak V, Vujanović V, Križmarić M Predictors of mortality in patients with isolated severe traumatic brain injury. Wien Klin Wochenschr 2017;129(3-4):110–114. Doi: 10.1007/s00508-016-0974-0
26 Davis DP, Peay J, Sise MJ, et al. The impact of prehospital endotracheal intubation on outcome in moderate to severe traumatic brain injury. J Trauma 2005;58(05):933–939. Doi: 10.1097/01.TA.0000162731.53812.58

27 Teasdale G, Maas A, Lecky F, Manley G, Stocchetti N, Murray G. The Glasgow Coma Scale at 40 years: standing the test of time. Lancet Neurol 2014;13(08):844–854. Doi: 10.1016/S1474-4422(14)70120-6
28 Tucker B, Aston J, Dines M, et al. Early Brain Edema is a Predictor of In-Hospital Mortality in Traumatic Brain Injury. J Emerg Med 2017;53(01):18–29. Doi: 10.1016/j.jemermed.2017.02.010
29 Maeda Y, Ichikawa R, Misawa J, et al. External validation of the TRISS, CRASH, and IMPACT prognostic models in severe traumatic brain injury in Japan. Balogh ZJ, ed. PLoS ONE. 2019;14(08): e0221791 Doi: 10.1371/journal.pone.0221791
30 De Silva MJ, Roberts I, Perel P, et al; CRASH Trial Collaborators. Patient outcome after traumatic brain injury in high-, middle- and low-income countries: analysis of data on 8927 patients in 46 countries. Int J Epidemiol 2009;38(02):452–458. Doi: 10.1093/ije/dyn189

Alcohol Consumption and Helmet Use in Patients with Traumatic Brain Injury due to Motorcycle Accident

Consumo de álcool e uso de capacete em pacientes com traumatismo cranioencefálico por acidente de motocicleta

Vitor de Deus da Rocha Ribeiro Gonçalves[1] Carlos Eduardo Cordeiro Cavalcante[2] Ana Luiza Ribeiro Barroso Maia[3] Raimundo Nonato Campos Sousa[4] Arquimedes Cavalcante Cardoso[4] Kelson James Silva de Almeida[4,5]

[1] Neurosurgery Division, Santa Casa de Misericórdia de Belo Horizonte, SCMBH, Belo Horizonte, MG, Brazil
[2] Faculdade de Medicina, Universidade Federal do Piauí, Teresina, PI, Brazil
[3] Faculdade de Medicina, Centro Universitário Facid Wyden/Intituto de Educação Médica (UniFacid/Idomed), Teresina, PI, Brazil
[4] Department of Neurology, Faculdade de Medicina, Universidade Federal do Piauí, Teresina, PI, Brazil
[5] Department of Neurology, Faculdade de Medicina, Centro Universitário Facid Wyden (UniFacid), Teresina, PI, Brazil

Address for correspondence Vitor de Deus da Rocha Ribeiro Gonçalves, Neurosurgery Division, Santa Casa de Misericórdia de Belo Horizonte, SCMBH, Rua Dr. Anísio Maia 1.264, Ininga, Teresina, PI, 64049810, Brazil (e-mail: vrocha_@hotmail.com).

Arq Bras Neurocir 2024;43(3):e172–e178.

Abstract

Alcohol consumption is an important risk factor for traumatic brain injury (TBI), and it has a great impact on its incidence and severity. However, studies suggest potential beneficial effects of alcohol during hospitalization and in the prognosis of moderate or severe TBI, with conflicting results. The objective of the present study was to associate alcohol consumption and helmet use in TBI patients, as well as the prognostic variables and patterns of injuries secondary to TBI. We analyzed 109 medical records of patients who suffered TBI due to a motorcycle accident. We evaluated data on alcohol consumption, helmet use, TBI severity, and tomographic findings on admission. The subjects with moderate or severe TBI were evaluated regarding hospitalization, mortality and prognosis variables. Patients who wore a helmet at the time of trauma had lower rates of skull fracture and extradural hematoma (EDH), but an increased incidence of subarachnoid hemorrhage (SAH). Furthermore, patients with moderate or severe TBI who were those under alcohol intoxication had a greater need for Intensive Care Unit (ICU) admission and a tendency to have a lower in-hospital mortality rate and a higher score on the Glasgow Prognostic Score (GPS). Thus, although the consumption

Keywords
- traumatic brain injury
- helmet
- alcohol
- motorcyclist
- prognosis

received
August 24, 2022
accepted
June 21, 2023
article published online
October 31, 2023

DOI https://doi.org/10.1055/s-0043-1776274.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

of alcohol has an impact on the incidence and severity of TBI at admission, it seems to be related to a lower in-hospital mortality rate and a better prognosis. In addition, helmet use is essential to prevent injuries from direct head-to-shield impact, but no similar reduction in the incidence of injuries caused by indirect forces was observed.

Resumo

O consumo de álcool é um importante fator de risco para o traumatismo cranioencefálico (TCE), e tem grande impacto em sua incidência e gravidade. Entretanto, estudos sugerem potenciais efeitos benéficos do álcool durante a internação e no prognóstico do TCE moderado ou grave, com resultados conflitantes. Neste estudo, objetivou-se associar o consumo de álcool e o uso de capacetes em pacientes com TC, além das variáveis prognósticas e dos padrões de lesões secundárias ao TCE. Analisamos 109 prontuários de pacientes com TCE por acidente de motocicleta. Avaliamos dados relativos ao consumo de álcool, uso do capacete, gravidade do TCE, e achados tomográficos admissionais. Os pacientes com TCE moderado ou grave foram avaliados em termos das variáveis de internação, mortalidade e prognóstico. Os pacientes que utilizavam capacete no momento do trauma apresentaram menores índices de fraturas cranianas e hematoma extradural (HED), e aumento da incidência de hemorragia subaracnóidea (HSA). Além disso, os pacientes com TCE moderado ou grave que haviam consumido álcool apresentaram maior necessidade de internação em Unidade de Tratamento Intensivo (UTI) e tendência a apresentar menor taxa de mortalidade intra-hospitalar e maior pontuação no Escore Prognóstico de Glasgow (EPG). Assim, apesar de o consumo de álcool ter um impacto na incidência e na gravidade do TCE à admissão, ele parece estar relacionado a uma menor taxa de mortalidade intra-hospitalar e a um melhor prognóstico. Além disso, o uso do capacete é fundamental para a prevenção de lesões por contato direto cabeça–anteparo, mas não foi observada similar redução da incidência das lesões por forças indiretas.

Palavras-chave
- traumatismo cranioencefálico
- capacete
- álcool
- motociclista
- prognóstico

Introduction

Traumatic brain injury (TBI) consists of any aggression that causes anatomical or functional injury to the scalp, skull, meninges, or brain. According to the World Health Organization (WHO), this type of trauma is the main determinant of death and sequelae in polytrauma patients.[1] It has a high socioeconomic impact and is responsible for high rates of morbidity, mortality and disability.[2] In Brazil, $\sim$ 100 thousand hospitalizations due to TBI were registered in the Unified Health System (Sistema Único de Saúde, SUS, in Portuguese) in 2020.[3]

The etiology of TBI is diverse and varies according to age group. In children, there is a prevalence of domestic accidents, sports accidents, and falls; among adolescents and young adults, traffic accidents prevail – especially motorcycle accidents –, as well as aggressions, whereas in the elderly, falls and domestic accidents are the main causes.[4] There is still a territorial distribution in Brazil in relation to the etiology of the trauma even in the adult population: the Northeastern region of the country has the second highest number of accidents involving motorcyclists, only behind the Southeastern region.[3]

Among the several risk factors for TBI, the consumption of alcohol has a great impact on its incidence and severity. In relation to traffic accidents, mainly involving motorcycles, alcohol consumption is associated with high driving speed and reduced ability to process information, such as road signs and traffic lights. Although it constitutes a crime under Brazilian legislation, driving under the influence of alcohol remains one of the main factors responsible for the high incidence of accidents with victims, and for $\sim$ 70% of fatal accidents.[1]

Despite the association involving alcohol consumption and the incidence and severity of TBI, some studies[5,6] suggest that alcohol has a beneficial effect on patients with moderate or severe TBI, reducing the incidence of complications and in-hospital mortality. Therefore, the literature is conflicting regarding such associations; hence, cross-sectional studies can enrich knowledge on this field of study.

The first reports of the neuroprotective effects of alcohol after TBI were highlighted in animal and laboratory studies.[7–9] Other studies[10,11] contradict this thesis, and claim that the neuroprotective role of alcohol in TBI needs further clarification.

Thus, there is a need to know the real impact of alcohol during hospitalization and on the prognosis of patients with moderate or severe TBI. Thus, the present study aims to associate alcohol consumption and the use of helmets in TBI patients, as well as the prognostic variables and patterns of

injuries secondary to moderate and severe TBI in a subgroup analysis.

Materials and Methods

The present is a descriptive, quantitative, observational, and retrospective study conducted through a review of the medical records of patients with TBI due to motorcycle accidents admitted to a reference emergency hospital in the city of Teresina, state of Piauí, Northeastern Brazil.

The study sample was calculated according to the formula for finite populations:

$$n = \frac{N \cdot \sigma^2 \cdot (Z_{\alpha/2})^2}{(N-1) \cdot E^2 + \sigma^2 \cdot (Z_{\alpha/2})^2}$$

in which "n" is the number of individuals in the sample; "N" is the population size (355 individuals; we performed a survey on the admission of patients with TBI due to motorcycle accidents in 2019 at the hospital where the study was conducted); "Zα/2" is the critical value corresponding to the 95% confidence level (1.96); "σ" is the population standard deviation of the studied variable (σ ≈ amplitude/4); and "E" is the margin of error (15). The calculation yielded a sample of ~ 98 patients.

The number of patients found exceeded the sample initially stipulated, and we included 109 patients with TBI due to motorcycle accident, aged between 18 and 70 years, who were admitted to a referral emergency hospital in the city of Teresina. Patients who did not report alcohol consumption, helmet use, and for whom there was no data on the Glasgow Coma Scale (GCS) score on admission were excluded from the study, as well as those with associated systemic trauma or who had previous neurological diseases.

The medical records of the patients were evaluated regarding alcohol consumption, helmet use, TBI severity on admission (GCS score), and tomographic findings on admission.

A subgroup of patients with moderate (GCS score between 9 and 12) and severe TBI (GCS score $\leq$ 8, or who had a reduction in the score $\geq$ 3 points during hospitalization) was established for secondary analyses. These were evaluated regarding the need for intensive care unit (ICU) admission, mean length of ICU stay, mean length of hospital stay, and in-hospital mortality rate.

For the prognostic analysis of the subgroup of patients with moderate to severe TBI, a prospective evaluation was performed. The prognosis of these patients was assessed using the Glasgow Prognostic Score (GPS): the patients who were discharged were contacted by telephone between the twelfth and fifteenth months after admission.

Regarding the tomographic findings on admission, the patients were stratified into 4 groups according to the dependent variables: helmet use and alcohol consumption (present or absent for each). This enabled the individual analysis of the correlation of these dependent variables with the need for ICU stay, the mean length of stay in the ICU and hospital, the in-hospital mortality rate, and the mean GPS as independent variables.

The statistical analysis was performed using the SPSS Statistics for Windows (SPSS Inc., Chicago, IL, United States) software, version 17.0. The Chi-squared test (χ^2) was used to test the significance of the association regarding the categorical independent variables (use of helmet at the time of trauma and alcohol consumption before TBI) and categorical dependent variables (tomographic findings on admission, need for ICU on admission). The Student *t*-test was used to assess the significance of the association involving the categorical independent variables (helmet use at the time of trauma and alcohol consumption before TBI) and quantitative dependent variables (length of ICU and hospital stays, in-hospital mortality, and GPS). The significance level was set as $p < 0.05$. Graphs were developed using the Minitab statistical software (Minitab, LLC, State College, PA, United States).

Results

The study included 109 patients with TBI due to a motorcycle accident; 93 (85.3%) of them were not wearing a helmet, and 63 (57.8%) were drunk at the time of the accident. The subgroup of patients with moderate to severe TBI who could be followed for 12 to 15 months was composed of 39 patients, 23 of whom were intoxicated at the time of the accident.

When evaluating the impact of these variables alone on the tomographic findings on admission, we observed that head-to-shield direct-impact injuries corresponding to fractures ($p = 0.025$) and extradural hematoma (EDH; $p = 0.042$) presented the highest rates among patients who did not wear a helmet (►**Table 1** and Graph 1A).

When comparing the presence of bruises in motorcycle accidents according to the use or not of helmets, we found that subjects who were negligent had a higher rate of EDH than of acute subdural hematoma (SDH), at a proportion of 1:0.7. In patients who were wearing helmets during the TBI, this proportion was reduced to 1:3 (►**Table 1** and Graph 1A). In addition, a higher incidence of subarachnoid hemorrhage (SAH) was observed in patients who were wearing a helmet at the time of trauma ($p = 0.033$)

Regarding alcohol consumption, intoxicated patients had proportionally higher rates of tomographic findings on admission in all categories, except for EDHs, when compared with those who were not intoxicated (Graph 1B). We could identify a trend, despite the lack of statistical relevance in the data presented ($p > 0.05$).

Regarding the data on hospitalization and prognosis of patients with moderate or severe TBI, the group who was intoxicated had a higher severity index in relation to the greater need for ICU admission among the group of patients who were not using a helmet (65.2% versus 62.5% respectively; Graph 2A). However, they had a lower in-hospital mortality rate (34.7% versus 43.7% respectively; Graph 2D) and a higher GPS (2.7 versus 2.5 respectively; Graph 2E). It is worth mentioning the lack of statistical relevance in the data presented ($p > 0.05$).

Table 1 Correlation regarding tomographic findings on admission, helmet use, and alcohol consumption before a TBI

Variables	Helmet (+); N = 16–n (%)	Helmet (-); N = 93–n (%)	OR (*p*-value)	Alcohol (+); N = 63–n (%)	Alcohol (-); N = 46–n (%)	OR (*p*-value)
Skull fracture	7 (43.8%)	67 (72%)	0.3 (0.025)	44 (69.8%)	30 (65.2%)	1.2 (0.610)
Contusion	7 (43.8%)	43 (46.2%)	0.9 (0.854)	31 (49.2%)	19 (41.3%)	1.8 (0.414)
EDH	2 (12.5%)	36 (38.7%)	0.2 (0.042)	19 (30.2%)	19 (41.3%)	0.6 (0.228)
ASDH	6 (37.5%)	25 (26.9%)	1.6 (0.384)	19 (30.2%)	12 (26.1%)	1.2 (0.642)
SAH	10 (62.5%)	32 (34.4%)	3.1 (0.033)	26 (41.3%)	16 (34.8%)	1.3 (0.492)
Diffuse brain edema	1 (6.3%)	6 (6.5%)	0.9 (0.976)	5 (7.9%)	2 (4.3%)	1.8 (0.450)
Pneumocephalus	2 (12.5%)	14 (15.1%)	0.8 (0.790)	10 (15.9%)	6 (13.0%)	1.25 (0.680)

Abbreviations: ASDH, acute subdural hematoma; EDH, extradural hematoma; OR, odds ratio; SAH, subarachnoid hemorrhage; TBI, traumatic brain injury.
Notes: "+" indicates the presence of the variable at the time of the trauma; "-" indicates absence of the variable at the time of trauma; statistical significance was set at $p < 0.05$.

Table 2 Correlation regarding hospitalization, prognosis data of motorcyclists with moderate or severe TBI, and alcohol consumption before a TBI

Variables	Alcohol (+) N = 23	ALcohol (-) N = 16	OR	*p*-value
Need for admission – n (%)	15 (65.2%)	10 (62.5%)	1.1	0.866
Average length of stay (days):				
ICU (N = 25) – mean ± standard deviation	11.9 ± 14.5	6.6 ± 5.03		0.277
Hospital	15.8 ± 18.49	9.3 ± 8.25		0.197
In-hospital mortality rate (%)	34.8%	43.8%	0.6	0.583
Glasgow Prognostic Score (N = 29) – mean ± standard deviation	2.70 ± 1.89 (*N* = 17)	2.5 ± 1.88 (*N* = 12)		0.775

Abbreviations: ICU, Intensive Care Unit; OR, odds ratio; TBI, traumatic brain injury.
Notes: "+" indicates the presence of the variable at the time of the trauma; "-" indicates absence of the variable at the time of trauma; statistical significance was set at $p < 0.05$.

Discussion

The present study aimed to evaluate the association regarding alcohol consumption and helmet use with prognostic variables and injury patterns secondary to TBI on admission; moreover, we performed a prospective subgroup analysis of patients with moderate to severe TBI to evaluate the prognosis.

As observed, 93 patients (85.3%) were not wearing a helmet and 63 patients (57.8%) were intoxicated at the time of the accident. These data reflect the urgency of public policies aimed at raising awareness among the population, in addition to more effective inspection and punishment measures for those who fail to comply with these norms already established in Brazilian legislation.

In the present study, intoxicated patients had a higher rate of tomographic findings associated with greater severity on admission. Similarly, in a study[12] performed in Los Angeles with 479 seriously-injured patients, a higher incidence of severe TBI and lower GCS scores were observed in patients with high blood alcohol levels on admission.

When comparing the presence of bruises in motorcycle accidents according to helmet use, we observed that patients who were negligent presented a higher proportion of EDH in relation to acute subdural hematoma (ASDH). There is a statistical ($p = 0.042$) association between helmet use and a lower incidence of EDH, which can alter the ratio of hematomas (EDH and SDH), which have different injury mechanisms. In addition, there was an increase in the incidence of SAH in patients wearing a helmet at the time of the trauma ($p = 0.033$).

Thus, helmet use has been shown to be associated with a reduction in the incidence and severity of TBI in the motorcyclist population. It is believed that the reduction in morbidity and mortality when using the helmet correctly is due to the absorption and redistribution of kinetic forces during the impact. However, according to the study by Richter et al., in which the mechanisms of brain trauma in motorcyclists wearing helmets were evaluated, injuries caused by the effect of indirect forces (acceleration, deceleration, and

rotation) continue to be a problem. This finding reflects the inversion of the EDH and SAH/ASDH ratio.[13]

In an epidemiological study[14] performed in Cambodia, the authors also observed a reversal in the proportion of bruises related to helmet use or neglect. In this study, only 13% of the patients used a helmet during the trauma. As observed, the most common tomographic diagnosis was skull fracture. The ratio of ASDH to EDH was of 1:1.05.

Agrawal and Dawar[15] reported a strong association between tentorial hematomas and helmet use (89%). Thus, they suggested that although the helmet offers protection against direct brain injury, indirect transmission of rotational forces is still present. Gupta et al.[16] reported a lower rate of EDH in patients wearing helmets. However, patients with and without helmets presented similar rates of other types of intracranial hemorrhage, as well as fractures.

Regarding alcohol consumption, it is noteworthy that intoxicated patients had a higher incidence of all pathological tomographic findings on admission, except for EDHs. A correlation is suggested with the tendency of motorcyclists to drive at higher speeds (mechanism of inertial trauma) and to display greater neglect regarding helmet use (mechanism of trauma by direct contact) when intoxicated. However, such data were not statistically significant ($p > 0.05$).

Regarding the data on hospitalization and prognosis of the patients with moderate to severe TBI, antagonistic results regarding severity and outcome were observed in the present study. Although the intoxicated group of patients presented a higher severity index (with greater need for ICU admission, for example), they presented a lower in-hospital mortality rate, and a higher GPS. It is important to report the longer length of stay in the ICU and in the hospital among the intoxicated patients; their lower in-hospital mortality rate made hospital stay longer, but this was not statistically significant ($p > 0.05$).

The increase in interest in the role of alcohol and its repercussions on TBI outcome was based on laboratory results and animal studies,[8,9] which have demonstrated a lower mortality rate, better motor function, reduced size of intracranial lesions, and reduced cognitive dysfunction with alcohol consumption before the lesion.

However, the mechanism of this protective effect remains unclear. The binding of ethanol to N-methyl-D-aspartate receptors and the inhibition of the excitotoxicity pathway are presumed to be responsible for the neuroprotective effects of alcohol. The increase in postinjury hyperglycolysis and the reduction in the levels of catecholamines and inflammatory mediators have also been suggested as beneficial effects of alcohol intoxication in TBI.[7,17–19] Studies[7,18,20] have reported that the critical period for the benefits of alcohol in TBI occurs up to one hour after the injury.

Evidence of the Benefits of Alcohol in Moderate or Severe TBI

In 2009, the largest retrospective clinical study[6] to date on the relationship between alcohol and TBI was conducted; the authors that high serum levels of alcohol are independently associated with greater survival in patients with severe TBI. After this first study, the authors expanded the results and concluded that alcohol is also an independent factor for greater survival in patients with moderate TBI.[21]

Talving et al.[22] compared groups of patients with low and high blood alcohol levels, and they concluded that, in TBI patients, blood alcohol levels do not appear to be associated with the severity of the injury according to the GCS on admission, nor with the occurrence of major morbidities. However, hospital mortality was significantly lower in patients with high blood alcohol levels.

In a study conducted in Los Angeles,[12] the authors divided TBI patients according to blood alcohol levels into non-alcohol, low-alcohol, and high-alcohol groups; they reported an increase in the length of hospital stay in the low-alcohol group, but the high-alcohol group presented significantly better survival than the non-alcohol group.

In a retrospective study, Raj et al.[23] included TBI patients treated in the ICU of a large center, and they reported that low levels of alcohol on admission independently reduced the risk of long-term mortality when compared no alcohol or high levels of alcohol on admission. In addition, a trend toward better neurological evolution was observed in patients with some level of alcohol in their blood.[23]

On the contrary, Lin et al.[24] compared the in-hospital mortality rate of patients with blunt TBI with different blood alcohol concentrations, and they concluded that patients with moderate to high concentrations presented a lower mortality rate than those with low alcohol concentrations.

Studies have also demonstrated systemic benefits in patients with alcohol intoxication before a TBI. Lustenberger et al.[25] concluded that alcohol intoxication is associated with a lower incidence of early coagulopathy and in-hospital mortality. In addition, in a retrospective study,[4] the authors observed a significant decrease in the rate of pneumonia in intoxicated patients with moderate to severe TBI. However, Salim et al.[6] related alcohol to an increase in the rate of sepsis and in the indication for tracheostomy in intoxicated patients with severe TBI.

Does Alcohol Really Have a Neuroprotective Effect?

In a study[26] performed in a population of motorcyclists, the authors observed an increase in mortality of up to 4 times in the population who consumed alcohol before the TBI. Another study[27] on the impact of substance abuse, including alcohol, on the mortality of patients with severe TB found that the use of amphetamine was associated with lower in-hospital mortality; however, alcohol consumption did not affect mortality. Shandro et al.[11] did not report an association between alcohol consumption and mortality in patients with moderate or severe TBI.

Furthermore, in a study[28] performed with 137,950 alcohol-positive and 262,618 alcohol-negative patients, no statistically significant differences were found in the mortality rate between the two groups after a TBI.

In a retrospective study with patients included in the United States National Trauma Data Bank (NTDB), Pandit et al.[10] concluded that alcohol consumption is an

independent predictor of mortality in patients with TBI, and it is associated with higher complication rates.

Conclusion

The negligence regarding helmet use and alcohol consumption by motorcyclists is a serious health problem. Both variables play a role in the incidence and severity of TBI. Helmet use prevents brain injuries from direct contact, especially fractures and EDHs, but its role in relation to injuries caused by acceleration, deceleration or rotation is yet to be established. In the present study, we could not statistically correlate alcohol consumption before the TBI with any specific tomographic findings. In addition, alcohol consumption before a TBI seems to be related to a lower in-hospital mortality rate and better prognosis. However, further studies with a definition of risk are needed to reinforce these findings, but they. presents ethical difficulties, since it is not possible to guide groups to stop wearing helmets or drinking alcoholic beverages.

Limitations of the Study

The present study did not take into account variables that may interfere with tomographic findings, such as the helmet buckling condition at the time of the trauma. In addition, we found an association trend without statistical significance in the results regarding mortality and TBI prognosis when related to alcohol intake. Furthermore, in the prognostic evaluation of patients who were discharged from the hospital, we were unable to contact 10 patients, which represents 25.6% of the total sample, a fact that may interfere with the results herein reported. Association biases may be typical in studies with a retrospective design, such as in relation to patients with a better prognosis possibly having received better care in an ICU environment. The conduction of cohort studies to define risk is hampered by ethical issues, as it is not possible to guide groups to drink alcohol or not wear a helmet.

Funding
The authors declare that they have not received funding from any source for the conduction of the present study.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Albuquerque AM, Silva HCL, Torquato IMB, et al. Vítimas de acidente de moto com traumatismo. Rev enferm UFPE on line. 2016;10(5):1730–1738.
2 Canova JCM, Bueno MFR, Oliver CCD, et al. Traumatismo cranioencefálico de pacientes vítimas de acidentes de motocicletas. Arq Ciênc Saúde. 2010;17(01):9–14
3 Ministério da Saúde. Sistema de Informações Hospitalares do SUS (SIH/SUS).
4 Liz NA, Arent A, Nazário NO. Características clínicas e análise dos fatores preditivos de letalidade em pacientes com Traumatismo Crânio Encefálico (TCE) admitidos em Unidade de Tratamento Intensivo. Arq Catarin Med. 2012;41(01):10–15
5 Hadjibashi AA, Berry C, Ley EJ, et al. Alcohol is associated with a lower pneumonia rate after traumatic brain injury. J Surg Res 2012;173(02):212–215
6 Salim A, Teixeira P, Ley EJ, DuBose J, Inaba K, Margulies DR. Serum ethanol levels: predictor of survival after severe traumatic brain injury. J Trauma 2009;67(04):697–703
7 Gottesfeld Z, Moore AN, Dash PK. Acute ethanol intake attenuates inflammatory cytokines after brain injury in rats: a possible role for corticosterone. J Neurotrauma 2002;19(03):317–326
8 Goodman MD, Makley AT, Campion EM, Friend LA, Lentsch AB, Pritts TA. Preinjury alcohol exposure attenuates the neuroinflammatory response to traumatic brain injury. J Surg Res 2013;184 (02):1053–1058
9 Greiffenstein P, Mathis KW, Stouwe CV, Molina PE. Alcohol binge before trauma/hemorrhage impairs integrity of host defense mechanisms during recovery. Alcohol Clin Exp Res 2007;31 (04):704–715
10 Pandit V, Patel N, Rhee P, et al. Effect of alcohol in traumatic brain injury: is it really protective? J Surg Res 2014;190(02):634–639
11 Shandro JR, Rivara FP, Wang J, Jurkovich GJ, Nathens AB, MacKenzie EJ. Alcohol and risk of mortality in patients with traumatic brain injury. J Trauma 2009;66(06):1584–1590
12 Plurad D, Demetriades D, Gruzinski G, et al. Motor vehicle crashes: the association of alcohol consumption with the type and severity of injuries and outcomes. J Emerg Med 2010;38(01):12–17
13 Richter M, Otte D, Lehmann U, et al. Head injury mechanisms in helmet-protected motorcyclists: prospective multicenter study. J Trauma 2001;51(05):949–958
14 Peeters S, Blaine C, Vycheth I, Nang S, Vuthy D, Park KB. Epidemiology of Traumatic Brain Injuries at a Major Government Hospital in Cambodia. World Neurosurg 2017;97:580–589
15 Agrawal D, Dawar P. Traumatic tentorial hematoma in two-wheeler riders: Correlation with helmet use. Asian J Neurosurg 2016;11(04):392–395
16 Gupta S, Klaric K, Sam N, et al. Impact of helmet use on traumatic brain injury from road traffic accidents in Cambodia. Traffic Inj Prev 2018;19(01):66–70
17 Cebere A, Liljequist S. Ethanol differentially inhibits homoquinolinic acid- and NMDA-induced neurotoxicity in primary cultures of cerebellar granule cells. Neurochem Res 2003;28(08): 1193–1199
18 Kelly DF, Kozlowski DA, Haddad E, Echiverri A, Hovda DA, Lee SM. Ethanol reduces metabolic uncoupling following experimental head injury. J Neurotrauma 2000;17(04):261–272
19 Shahin H, Gopinath SP, Robertson CS. Influence of alcohol on early Glasgow Coma Scale in head-injured patients. J Trauma 2010;69 (05):1176–1181, discussion 1181
20 Türeci E, Dashti R, Tanriverdi T, Sanus GZ, Oz B, Uzan M. Acute ethanol intoxication in a model of traumatic brain injury: the protective role of moderate doses demonstrated by immunoreactivity of synaptophysin in hippocampal neurons. Neurol Res 2004;26(01):108–112
21 Salim A, Ley EJ, Cryer HG, Margulies DR, Ramicone E, Tillou A. Positive serum ethanol level and mortality in moderate to severe traumatic brain injury. Arch Surg 2009;144(09):865–871
22 Talving P, Plurad D, Barmparas G, et al. Isolated severe traumatic brain injuries: association of blood alcohol levels with the severity of injuries and outcomes. J Trauma 2010;68(02):357–362
23 Raj R, Skrifvars MB, Kivisaari R, Hernesniemi J, Lappalainen J, Siironen J. Acute alcohol intoxication and long-term outcome in patients with traumatic brain injury. J Neurotrauma 2015;32(02): 95–100
24 Lin HL, Lin TY, Soo KM, et al. The effect of alcohol intoxication on mortality of blunt head injury. BioMed Res Int 2014;2014:619231

25 Lustenberger T, Inaba K, Barmparas G, et al. Ethanol intoxication is associated with a lower incidence of admission coagulopathy in severe traumatic brain injury patients. J Neurotrauma 2011;28 (09):1699–1706
26 Luna GK, Maier RV, Sowder L, Copass MK, Oreskovich MR. The influence of ethanol intoxication on outcome of injured motorcyclists. J Trauma 1984;24(08):695–700
27 O'Phelan K, McArthur DL, Chang CW, Green D, Hovda DA. The impact of substance abuse on mortality in patients with severe traumatic brain injury. J Trauma 2008;65(03):674–677
28 Chen CM, Yi HY, Yoon YH, Dong C. Alcohol use at time of injury and survival following traumatic brain injury: results from the National Trauma Data Bank. J Stud Alcohol Drugs 2012;73(04): 531–541

Traumatic Brain Injury in Pregnancy

Traumatismo cranioencefálico na gravidez

Letícia Adrielle dos Santos[1] Carlos Umberto Pereira[2] Maycon Cristian Gomes de Paula[3] Gabriela Ferreira Kalkmann[4] Nicollas Nunes Rabelo[5]

[1] Department of Neurosurgery, Universidade Federal do Sergipe, Aracaju, SE, Brazil
[2] Department of Neurosurgery, Hospital de Urgência do Sergipe, Aracaju, SE, Brazil
[3] Department of Neurosurgery, Universidade do Vale do Sapucaí, Pouso Alegre, MG, Brazil
[4] Department of Neurosurgery, Universidade Federal do Paraná, Curitiba, PR, Brazil
[5] Department of Neurosurgery, Centro Universitário UniAtenas, Paracatu, MG, Brazil

Address for correspondence Nícollas Nunes Rabelo, MD, Department of Neurosurgery, Centro Universitário UniAtenas, Av. Antônio Diederichsen, n° 190, Ap. 193, Jardim América, 14.020-250, Ribeirão Preto, SP, Brazil (e-mail: nicollasrabelo@hotmail.com).

Arq Bras Neurocir 2024;43(3):e179–e186.

Abstract

Objective The present paper aims to provide a review on the main complications involving traumatic brain injury (TBI) during pregnancy and on the vegetative state after TBI.

Methods A systematic review was performed in concordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria checklist.

Results Seven studies were included, of which four were case reports, one was a follow-up, one was a comparative study, and one was a literature review.

Discussion Presence of neurological deficits such as hemiparesis, neonatal seizures, cerebral palsy, hemorrhage or hydrocephalus was observed in children of mothers who suffered trauma during pregnancy. The prolongation of a pregnancy in these victims, even in brain death, is within the reach of current medicine. Ethical issues must be considered when deciding to prolong a pregnancy of a woman in brain death.

Conclusion For the evaluation of pregnant women with TBI, there is a protocol that can be followed in the emergency care service. The cases reported in the literature suggest that there is no clear limit to restrict support to a pregnant patient in a vegetative state. Further studies should be done to elucidate this matter.

Keywords
- traumatic brain injury
- pregnancy
- management
- developmental disabilities
- persistent vegetative state

Resumo

Objetivo O presente artigo buscou revisar as principais complicações envolvendo lesão cerebral traumática durante a gravidez e sobre estado vegetativo após esse trauma.

Métodos Uma revisão sistemática foi realizada de acordo com o checklist dos critérios Principais itens para relatar Revisões sistemáticas e Metanálises (PRISMA, na sigla em inglês).

received
August 1, 2020
accepted
March 9, 2021
article published online
February 7, 2022

DOI https://doi.org/10.1055/s-0041-1733862.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resultados Sete estudos foram incluídos, dos quais quatro eram relatos de caso, um era um acompanhamento, um era um estudo comparativo, e um era uma revisão de literatura.

Discussão Presença de déficit neurológico como hemiparesias, convulsões neonatais, paralisia cerebral, hemorragia e hidrocefalia foram observadas em crianças cuja mãe sofreu trauma durante a gravidez. O prolongamento da gravidez nessas vítimas, mesmo nos casos de morte cerebral, está ao alcance da medicina atual. Dilemas éticos devem ser considerados na decisão de prolongar a gravidez em mulheres com trauma cerebral.

Conclusão Para avaliação de grávidas com trauma cerebral, existe um protocolo que pode ser seguido em serviços de emergência. Os casos relatados na literatura sugerem que não há um limite claro para restringir o suporte a uma paciente grávida em estado vegetativo. Mais estudos devem ser realizados para elucidar a questão.

Palavras-chave
- traumatismo cranioencefálico
- gravidez
- gestão
- deficiências de desenvolvimento

Introduction

Exposure of women to trauma in general has increased in recent years due to their more active lifestyle. Trauma is the main cause of nonobstetric death in females between 14 and 44 years old,[1,2] occurring more frequently during the 3rd trimester of pregnancy than at any other stage in life.[3,4] Severe trauma in a pregnant woman can be considered a lesion of double magnitude,[5] with significant fetal mortality.[6] Its occurrence varies from 6 to 7% of pregnancies,[1,5–7] with hospitalization in 0.3 to 0.4% of cases.[1,5]

The effect of trauma on a pregnant woman depends on the gestational age, on the intensity of maternal-fetal aggression, and on the type and severity of the injury,[5] and it is generally difficult to predict the possibility of fetal loss after trauma.[1,8] The extent of maternal injury does not correlate with the degree of fetal injury,[3,9] and it known that even small traumas can cause fetal death and premature labor.[3]

Nine out of 10 traumatic injuries during pregnancy are classified as minor trauma, that is, one that does not involve the abdomen, rapid decompression, deceleration or shear forces, and that the patient does not report pain, vaginal bleeding, fluid loss or decreased fetal movement; however, between 60 and 70% of the fetal losses associated with trauma are due to mild trauma.[10,11] Although the risk of fetal death can be as high in an apparently trivial trauma as in a severe accident,[12,13] most pregnancies continue with a relatively small intervention and are not followed-up.[14] The currently dominant attitude is to consider that the relative risk of having a child with cerebral palsy after exposure to trauma is not significant,[3] and that the result of pregnancy is normal when no early warning symptoms are recorded.[15]

Pregnant women are more susceptible to abdominal trauma than to traumatic brain injury (TBI);[1] however, the importance of the latter should not be disregarded, mainly because of the possibility of causing a permanent vegetative state.[16,17] Traumatic brain injury is the factor that most contributes to nonobstetric mortality in developing countries, with ~ 20% of cases of maternal mortality being directly correlated to TBI.[18] According to Suddaby et al., out of 252 brain deaths, only 2.85%, that is, 5 cases, involve pregnant women between 15 and 45 years old.[19]

In Brazil, it is estimated that ~ between 6 and 7% of pregnancies are complicated by trauma, which shows that the incidence of trauma in pregnant women is increasing every year. Despite the cases of permanent vegetative state or of maternal brain death, the progression of pregnancy is a possibility due to the recent improvements in life support technologies, critical care management, and obstetric monitoring techniques. Despite the cases of permanent vegetative state or of maternal brain death, the progression of pregnancy is a possibility due to the recent improvements in life support technologies, critical care management, and obstetric monitoring techniques. Due to this progression, it is becoming possible to maintain the vital functions of the patient after brain death.[20]

The present work aims to provide a detailed review on the main complications involving TBI in pregnancy and on the vegetative state after TBI.

Methods

The present systematic review has been performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (►**Fig. 1**).

Search Strategy

The following databases were inspected: Pubmed, LILACS, Scielo, and The Cochrane Database of Systematic Reviews. The search strategy utilized was as follows:

i: *"Pregnancy"*
ii: *"traumatic brain injury"*
iii: i AND ii

The last search was last updated in May 2020.

Study Selection

The inclusion criteria were:

1–Title with simultaneous presence of the two defined descriptors

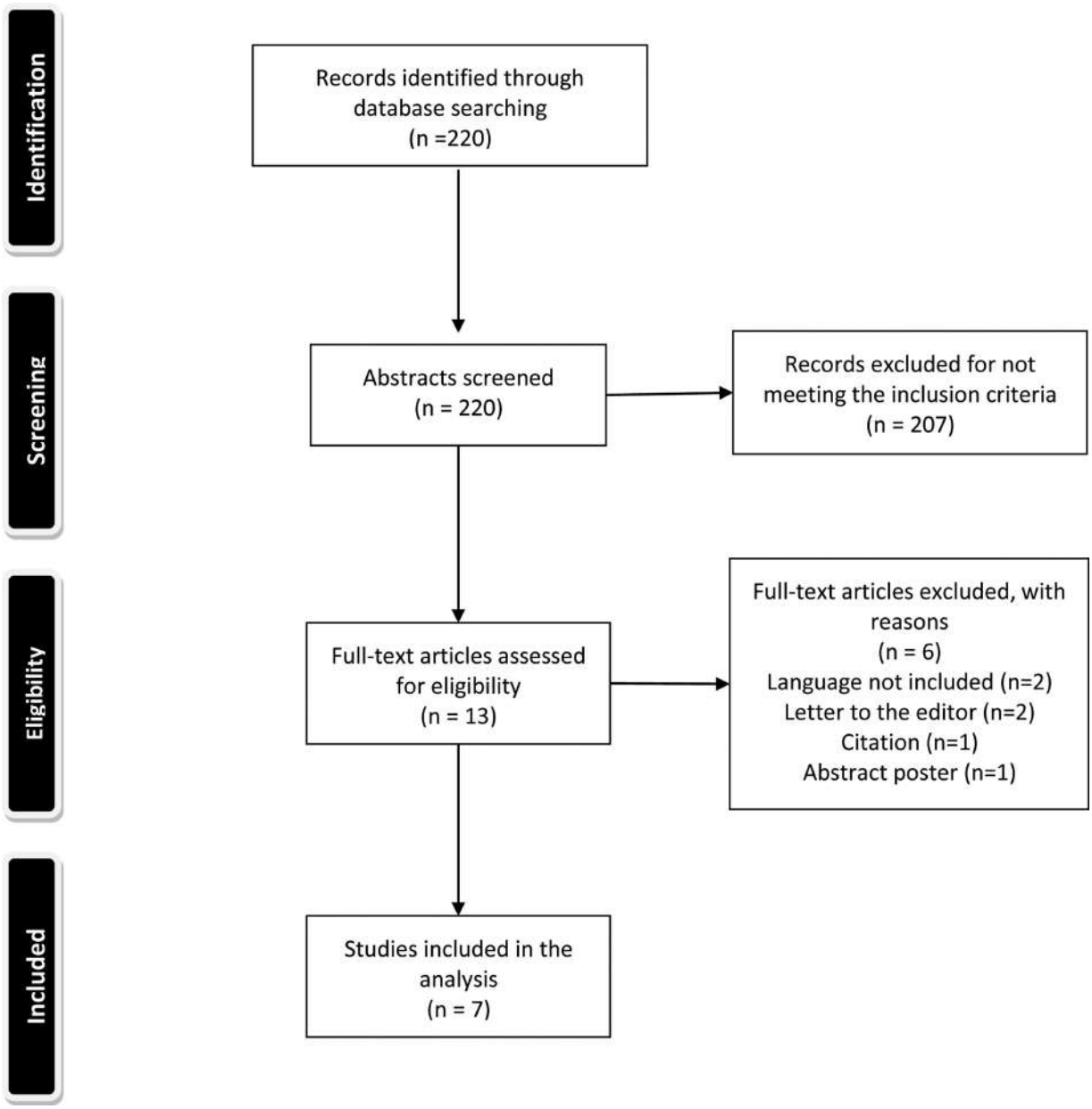


Fig. 1 PRISMA flow diagram.

2–Patient, Intervention, Control, Outcome and Study design (PICOS) criteria as below.

Patients: Pregnant women of all ages who suffered TBI. Patients who suffered nontraumatic brain injury were excluded.

Intervention/Control: Not required.

Outcomes: Recovery state based on the Glasgow Outcome Scale adapted for child, presence of injury on brain imaging, management, mortality and complications in women who suffered TBI, sequalae on fetus when the pregnant woman is in coma, and delivery route in these cases.

Study design: Full-text publications in the English language. Letter to the editor, abstract posters and citations were excluded.

Results

In our research, 4 (57.14%) of the 7 articles that met the inclusion criteria were case reports, which demonstrates the lack of studies focused on this theme and on this specific study population, making the subject lacking in data goals.

The study by Berry et al. was the only one that provided data; its objective was to investigate outcomes in pregnant trauma patients with isolated moderate to severe TBI, and it was concluded that besides being younger (24.9 ± 7.2 years versus 50.1 ± 23.8 years, p = 0.0001) and having a significantly lower systolic blood pressure on admission (126.9 mm Hg 17.5 versus 138.0 mm Hg 30.5, $p = 0.0004$), there were no other significant demographic and outcome differences

Table 1 Systematic review

	Authors	Year	Type	Conclusions
PubMed	Aderet et al[16]	1984	Case Report	Pregnancy patients need a special maternal and fetal intensive care unit, special nutrition, and fetal monitoring.
	Leroy-Malherbe et al[2]	2006	Follow-up	Fetal injury comes from a wide range of mechanisms. Post-traumatic evaluation of the fetus is often incomplete or absent.
	Berry et al[21]	2011	Comparative study	Pregnancy patients with traumatic brain injury had ↓ Age, ↓ Systolic Blood Pressure and ↑ mortality than their nonpregnant counterparts.
	Dawar et al[22]	2014	Case Report	Simultaneous craniotomy and cesarean section in the pregnant patient provide better outcome for both the mother and the baby.
	Tawfik et al[23]	2015	Case Report	Case of a term pregnant patient who suffered traumatic brain injury and was managed by cesarean delivery followed by craniotomy under general anesthesia
	Inoue et al[24]	2016	Case Report	Pregnancy and intrauterine fetal death can be a risk factor for paroxysmal sympathetic hyperactivity (PSH) exacerbation, and delivery can be useful to resolve refractory PSH and save the mother's life.
	Kho et al.[18]	2018	Literature Review	Every woman of reproductive age with significant damage is still pregnant until proven otherwise by a definitive pregnancy test or an ultrasound test.

between pregnant patients with TBI and their nonpregnant counterparts. Adjusting for confounding variables, pregnant patients with TBI had a tendency to increased mortality (adjusted odds ratio [AOR] 2.2; 95% confidence interval [CI], 0.9–5.1; $p = 0.07$).

Since all pregnant patients with TBI were between 15 and 47 years old, a separate analysis was performed with this specific age group. The only significant difference between the 2 groups was that pregnant women with TBI were younger (24.9 ± 7.2 years versus 29.0 ± 10.2 years, $p = 0.004$) than their nonpregnant counterparts with TBI.[21] The results are summarized in ►**Table 1**.

Discussion

Complications

For Leroy-Malherbe et al.,[2] in their study of 18 patients with neurological deficiency and with a history of accidents during pregnancy, it was shown that the score on the Glasgow results scale showed good recovery in 6% (1), moderate disability in 34% (6), severe disability in 34% (6), and persistent vegetative score in 20% (4). The neuroimaging was varied, ranging from normal in 17% (3) to injuries in 77% (14), of the most varied types: focal ischemic injury with congenital changes, ischemic injuries restricted to a vascular territory, diffuse ischemic injuries, periventricular leukomalacia, diffuse white matter abnormality, diffuse cortical and white matter atrophy, and a deceased patient had hemorrhagic lesions on pathological examination.

Presence of neurological deficits such as hemiparesis, neonatal seizures, cerebral palsy, hemorrhage or hydrocephalus were observed in children of mothers who suffered trauma during pregnancy.[3,8,9] A woman exposed to trauma, needing hospitalization during pregnancy, is under a 1.4 times higher risk of having a newborn with cerebral palsy when compared with a woman not exposed to trauma.[3]

It was observed that fetal injuries are more frequent after trauma in advanced pregnancy, with fractures of the skull bones and intracranial hemorrhage in the fetus being the most common, leading to death in most cases.[6,8] A traumatic origin is clear mainly for depressed skull fractures and cerebral hemorrhage.[2] Cranial fracture in the fetus is caused by the compression of the fetal head against the surrounding structures, such as the pubic symphysis, the pelvis (whole or fractured), the spine or the promontory.[8,9] Premature labor associated with trauma appears to be frequent, although it is rarely reported in the immediate postinjury period.[13,14] Diffuse axonal injury, as a result of strong accelerations/decelerations in the fetal brain, can result in the cessation of the growth of the head.[9]

Maternal hypovolemic shock, disseminated intravascular coagulation, and transient abnormalities of placental blood flow (reduced maternal-placental flow, placental embolization and detachment) can also be pointed out as the etiology for newborn brain injuries,[1,3,6,9,17] although there are no studies in the literature evaluating the effect of a hypercoagulable state and mortality in pregnant patients who suffered TBI; a hypercoagulable state, theoretically, puts patients at increased risk of complications and mortality.[21]

In addition, TBI-induced coagulopathy as an independent risk factor for increased mortality is well-described.[22] It is possible that the combination of the two can lead to a deep hypercoagulable state and worsen the result. Berry et al.,[21] in their study comparing pregnant and nonpregnant women who suffered TBI, demonstrated that although it is not

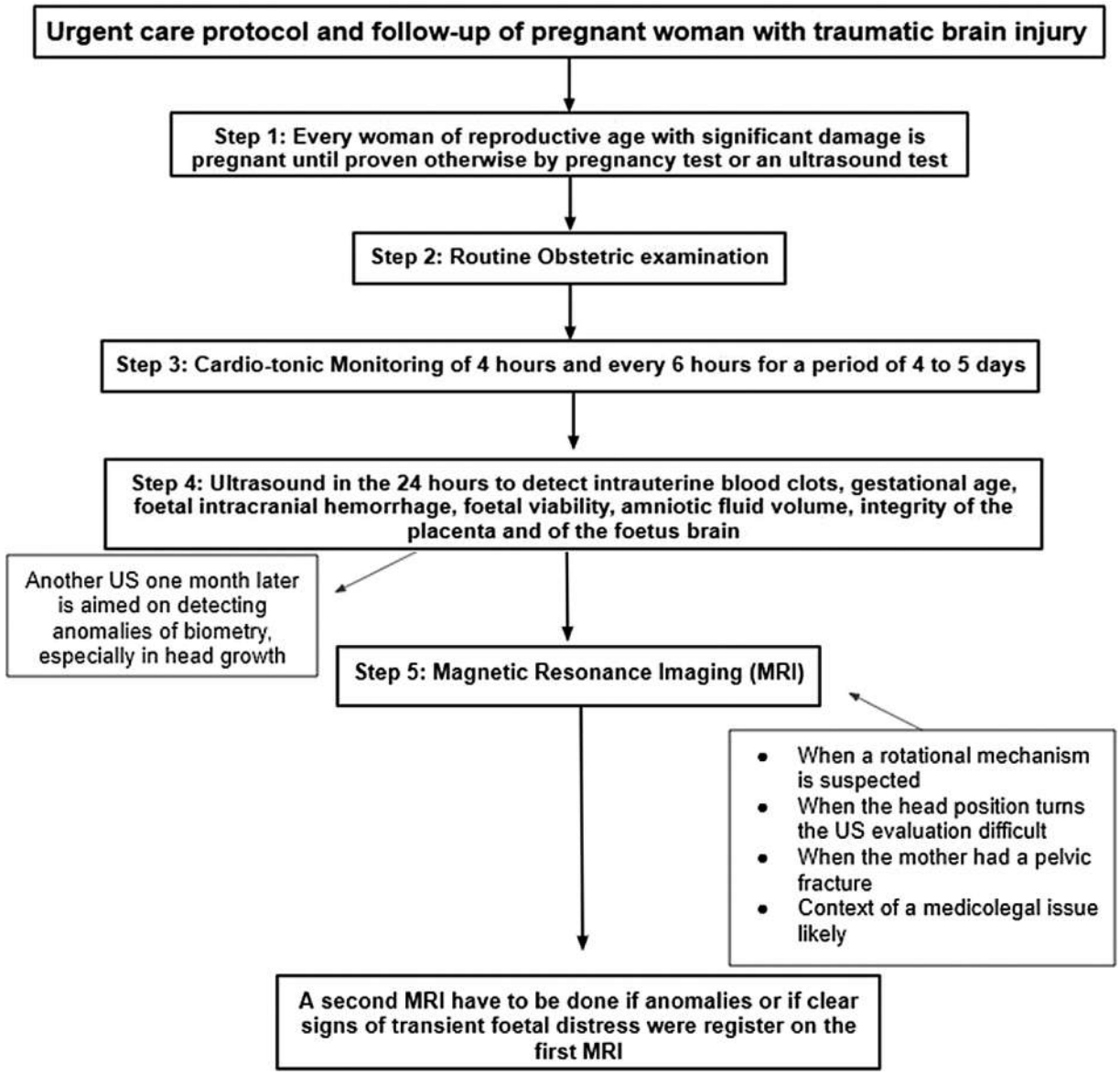


Fig. 2 Urgent Care Protocol and follow-up of pregnant women with traumatic brain injury. (own authorship).

significant, there was a tendency toward increased mortality in the pregnant TBI group (AOR: 2.0; 95%CI: 0.8–4.6; $p = 0.12$), which may be caused by a synergistic effect of a hypercoagulable state induced by pregnancy and coagulopathy induced by TBI.

As the etiologic agents for these types of lesions that should be pointed out as possible differential diagnoses, there are the other environmental factors, as well as perinatal anoxia and genetic factors.[9] Ultrasound tests are useful to assess the degree of brain damage in the newborn, as well as brain computed tomography (CT) and magnetic resonance imaging (MRI) exams.[5,8] Suggested protocol for emergency care and monitoring of pregnant women with TBI is shown in ►**Figure 2**.

Another complication is paroxysmal sympathetic hyperactivity (PSH), which is characterized by paroxysms of fever, hypertension, tachycardia, tachypnea, diaphoresis, and dystonic posturing. It was reported by Inoue et al. in a 16-year-old primiparous girl in the 11th week of gestation with who suffered a TBI during a motorcycle accident. From day 2, she developed intermittent episodes of tachycardia with tachypnea, fever, profuse sweating, and extensor posturing, and was diagnosed with PSH. Her condition only improved after delivery, after intrauterine fetal death was confirmed (16th week of gestation, on day 37 of hospitalization).[24]

Pregnant Women in Vegetative State

The prolongation of a pregnancy in a woman who has suffered severe brain trauma or who is brain dead is within the reach of current medicine. A fetus can develop normally in a comatose patient, despite the existence of complications of this condition (anemia, hypoxia, and digestive hemorrhage) and the use of medications.[5,17] The question that is not entirely clear, until now, is how long this pregnancy can be prolonged. Some authors have analyzed the use of intensive therapy to prolong a pregnancy for women with a

gestational age of at least 24 weeks, since there is evidence that somatic death accours 2 to 4 weeks after brain death.[17]

However, case reports have challenged this limit, demonstrating the possibility of prolonging pregnancies with a lower gestational age.[5,16,17] According to Slattery et al,[25] a fetus born before 24 weeks of gestation has a limited chance of survival, with the possibility of spontaneous abortion or intrauterine death, especially if the pregnant woman is between 13 and 19 weeks of gestation.[20] At 24, 28 and 32 weeks, a fetus has ~ 30, 80 and 98 chances of survival, respectively, with 40, 10 and $< 2\%$ chance of suffering from a severe disability, respectively.[20,25]

Many factors can cause sequelae to the fetus when the mother is comatose.[16] During extended life support, patients develop severe complications, including infection, hemodynamic instability, diabetes insipidus, panhypopituitarism, metabolic instability, acute respiratory stress syndrome, and disseminated intravascular coagulation.[17,20] Maternal malnutrition due to the high catabolism and negative nitrogen balance that occur in individuals immobilized for a long period can affect the weight and brain development of the fetus,[5,16,26] although some authors refer that the fetus is only affected when the conditions of calorie consumption or protein intake are extreme.[16]

According to the findings of the systematic literature review by Esmaeilzadeh et al,[20] prolonged somatic care can lead to the delivery of a viable child with a satisfactory Apgar score and birthweight. In addition, children can develop normally without problems resulting from their intrauterine conditions, as there were six children who underwent postneonatal follow-up up for 24 months in the study and they all developed normally and, apparently, had no problems related to their exceptional intrauterine circumstances. Ethical issues must be considered when deciding to prolong a pregnancy of a woman who is brain dead, requiring the active participation of family members.[5,17] It is also important to address the context of the cost of prolonged use of intensive care resources.

Monitoring and Management

Increased plasma volume and cardiac output are some of the numerous anatomical and physiological changes that occur during pregnancy, which, combined with the blood diversion provided by the uterus-placental circulation, can mask the signs of hypovolemia.[17] Compression of the aorta and of the vena cava through the pregnant uterus when the patient is in the supine position can also confuse the interpretation of vital signs. Pregnant patients in a permanent vegetative state require special maternal-fetal monitoring. Uterine activity and fetal heartbeat must be recorded every 8 hours for 30 minutes,[17] through cardiothoracic graph with manual detection of fetal movements in the mother's abdomen, serial ultrasound for the evaluation of fetal growth, and 24-hour urinary estriol dosage correlated with creatinine clearance are important for the assessment of fetal vitality.[16] Strict hemodynamic control, blood gas analysis, electrolyte balance, acid-base and nutrition must be performed throughout pregnancy.[5]

In maternal brain death, special attention should be paid to mechanical ventilation. To facilitate the elimination of carbon dioxide from the fetus as a result of the effect of progesterone on the respiratory center, the pregnant woman develops hypocarbia mediated by an increase in tidal volume and respiratory rate. Hypocarbia is compensated by an increase in the excretion of bicarbonate by the kidneys.[27] The carbon dioxide tension, the tidal volume, and the maternal respiratory rate must be maintained ~ between 29 and 31 mm Hg, between 6 and 8 ml/Kg, and between 10 and 12/min, respectively, in the normal pregnant woman.[281]

The use of medication may raise some doubts about its effect on the fetus. Few agents have a teratogenic action if administered in the first 12 weeks of pregnancy. The drugs that should be avoided are ergotamines and warfarin derivatives; antibiotics such as aminoglycosides and those containing sulfa should be used with caution due to their adverse effects.[5]

The nutritional support needed by a pregnant woman before and after brain death is not the same. A pregnant woman with brain death will spend ~ 75% of the baseline energy expenditure of a healthy pregnant woman.[29] The feeding route can be initially enteral, through a tube. The gastric emptying of the pregnant patient is slower and, if there is a large gastric residue, variations in the angle of the bed can be made.

The risk of developing deep venous thrombosis is higher during pregnancy because of the immobility and the flaccid paralysis that follows brain death. It is important to do prophylactic anticoagulation, which is effective for the mother and safe for the fetus, with low molecular weight heparin being the safest and most effective medication.[20,29,30] Prophylaxis of venous thrombosis can be performed using subcutaneous heparin (5000 U, twice a day).[17] Persistent anemia conditions occasionally require blood transfusion, so the maternal hemoglobin level should be monitored.[8,30]

The braindead patient is liable to contract pneumonia due to ventilatory support, kidney and bladder infections due to urinary catheters, and septicemia due to intravascular catheters.[20,31] Maternal infections should be treated aggressively with the most effective substances, rather than choosing to use substances safe for the fetus, which may not effectively treat the infection.[32–35]

If the patient develops pituitary insufficiency, replacement of thyroid hormone, corticosteroids and synthetic vasopressin should be performed. For fetal lung maturation, corticosteroids should be administered to the mother from the 26th week of gestation with cycles every 10 days.[17] To avoid prolonged exposure of the fetus to glucocorticoids during maternal support, which are necessary to treat the adrenal insufficiency that usually occurs in brain death and for pulmonarymaturation, prednisone or methylprednisolone should be used, given that they cannot cross the placental barrier.[20,25] Suggested protocol for monitoring and management of pregnant women in vegetative state is shown in ►**Figure 3**.

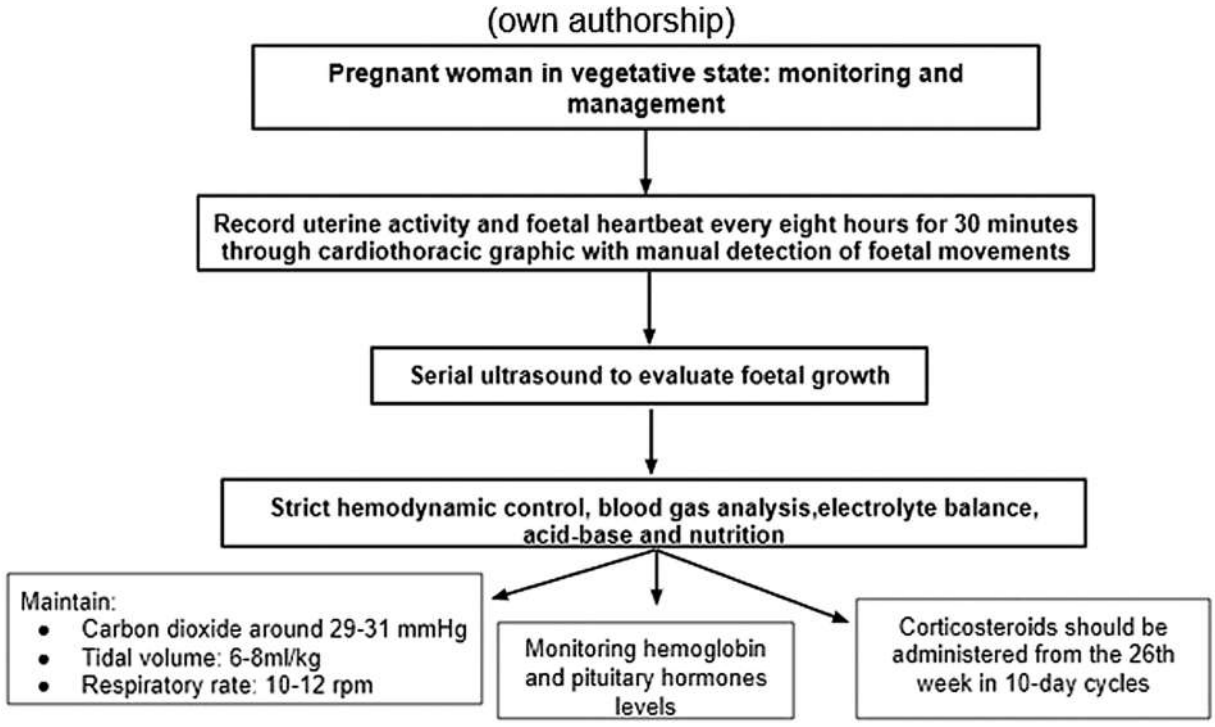


Fig. 3 Monitoring and management of pregnant woman in vegetative state. (own authorship).

Parturition

Much is questioned about the best route for delivery of mothers in a vegetative state. Even in the best of circumstances, a child with a gestational age < 24 weeks is unlikely to survive. Therefore, the risks and benefits of an induced delivery or cesarean section should be weighed, which should be reserved for the numerous complications resulting from the maternal state (fetal distress, placental detachment, uterine rupture, and anomalous presentations).[5] Cesarean sections are indicated in cases of recent maternal death or brain death, knowing that delivery should start within 4 to 5 minutes.[5] According to the study by Esmaeilzadeh et al,[20] all deliveries performed on pregnant women with brain death were cesarean, resulting in fetuses born alive.

Study Limitations

The present study has several limitations, since this is a topic that is rarely discussed in the literature. Due to the scarcity of more robust works on the subject, our casuistic had few works, most of which were case reports, which in fact impoverishes the quality of the meta-analysis.

Conclusion

For the evaluation of pregnant women with TBI, a protocol is suggested that can be followed in the emergency care service to predict or even minimize the possible future damage that the fetus may suffer. There is no clear limit to restrict support to a pregnant patient in a vegetative state. Therefore, a multidisciplinary approach to the case and strict monitoring of the patient and of the fetus are necessary. More clinical trials and cohort studies on the subject are needed for more accurate data and conclusions.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Shah KH, Simons RK, Holbrook T, Fortlage D, Winchell RJ, Hoyt DB. Trauma in pregnancy: maternal and fetal outcomes. J Trauma 1998;45(01):83–86
2 Leroy-Malherbe V, Bonnier C, Papiernik E, Groos E, Landrieu P. The association between developmental handicaps and traumatic brain injury during pregnancy: an issue that deserves more systematic evaluation. Brain Inj 2006;20(13-14):1355–1365
3 Gilles MT, Blair E, Watson L, et al. Trauma in pregnancy and cerebral palsy: is there a link? Med J Aust 1996;164(08): 500–501
4 Patterson RM. Trauma in pregnancy. Clin Obstet Gynecol 1984;27 (01):32–38
5 Sim KB. Maternal persistent vegetative state with successful fetal outcome. J Korean Med Sci 2001;16(05):669–672
6 Ali J, Yeo A, Gana TJ, McLellan BA. Predictors of fetal mortality in pregnant trauma patients. J Trauma 1997;42(05):782–785
7 Peckham CH, King RW. A study of intercurrent conditions observed during pregnancy. Am J Obstet Gynecol 1963;87(05): 609–624
8 Baethmann M, Kahn T, Lenard HG, Voit T. Fetal CNS damage after exposure to maternal trauma during pregnancy. Acta Paediatr 1996;85(11):1331–1338
9 Yamamoto T, Koeda T, Ishii S, Takeshita K. A patient with cerebral palsy whose mother had a traffic accident during pregnancy: a diffuse axonal injury? Brain Dev 1999;21(05):334–336
10 El-Kady D, Gilbert WM, Anderson J, Danielsen B, Towner D, Smith LH. Trauma during pregnancy: an analysis of maternal and fetal outcomes in a large population. Am J Obstet Gynecol 2004;190 (06):1661–1668

11 Murphy NJ, Quinlan JD. Trauma in pregnancy: assessment, management, and prevention. Am Fam Physician 2014;90(10):717–722
12 Farmer DL, Adzick NS, Crombleholme WR, Crombleholme TM, Longaker MT, Harrison MR. Fetal trauma: relation to maternal injury. J Pediatr Surg 1990;25(07):711–714
13 Goodwin TM, Breen MT. Pregnancy outcome and fetomaternal hemorrhage after noncatastrophic trauma. Am J Obstet Gynecol 1990;162(03):665–671
14 Pearlman MD, Tintinalli JE. Evaluation and treatment of the gravida and fetus following trauma during pregnancy. Obstet Gynecol Clin North Am 1991;18(02):371–381
15 Connolly AM, Katz VL, Bash KL, McMahon MJ, Hansen WF. Trauma and pregnancy. Am J Perinatol 1997;14(06):331–336
16 Ben AderetN, et al. Traumatic coma during pregnancy with persistent vegetative state. Case report. British Journal of Obstetrics and Gynaecology 1984;91(01):939–941. Doi: 10.1111/j.1471-0528.1984.tb03713.x
17 Bernstein IM, Watson M, Simmons GM, Catalano PM, Davis G, Collins R. Maternal brain death and prolonged fetal survival. Obstet Gynecol 1989;74(3 Pt 2):434–437
18 Kho GS, Abdullah JM. Management of severe traumatic brain injury in pregnancy: A body with two lives. Malays J Med Sci 2018;25(05):151–157
19 Suddaby EC, Schaeffer MJ, Brigham LE, Shaver TR. Analysis of organ donors in the peripartum period. J Transpl Coord 1998;8(01):35–39
20 Esmaeilzadeh M, et al. One life ends, another begins: Management of a brain-dead pregnant mother-A systematic review-. BMC Medicine 2010;8:74. Doi: 10.1186/1741-7015-8-74
21 Berry C, Ley EJ, Mirocha J, Margulies DR, Tillou A, Salim A. Do pregnant women have improved outcomes after traumatic brain injury? Am J Surg 2011;201(04):429–432
22 Dawar P, et al. Decompressive craniectomy in term pregnancy with combined caesarean section for traumatic brain injury. Neurology India 2013;61(04):423–425. Doi: 10.4103/0028-3886.117588
23 Tawfik MM, Badran BA, Eisa AA, Barakat RI. Simultaneous cesarean delivery and craniotomy in a term pregnant patient with traumatic brain injury. Saudi J Anaesth 2015;9(02):207–210
24 Inoue A, Ebina M, Atsumi T, Ariyoshi K. Refractory paroxysmal sympathetic hyperactivity following brain injury in a pregnant woman that dramatically improved after delivery. Acute Med Surg 2015;3(03):268–271
25 Slattery MM, Morrison JJ. Preterm delivery. Lancet 2002;360(9344):1489–1497
26 Luke B. Nutritional influences on fetal growth. Clin Obstet Gynecol 1994;37(03):538–549
27 Bhatia P, Bhatia K. Pregnancy and the lungs. Postgrad Med J 2000;76(901):683–689
28 Milliez J, Cayol V. Palliative care with pregnant women. Best Pract Res Clin Obstet Gynaecol 2001;15(02):323–331
29 Dominguez-Roldan JM, Murillo-Cabezas F, Santamaria-Mifsut JL, Muñoz-Sanchez A, Villen-Nieto J, Barrera-Chacon JM. Changes in resting energy expenditure after development of brain death. Transplant Proc 1995;27(04):2397–2398
30 Villa-Forte Gomes MP. Venous thromboembolism in pregnancy. Curr Treat Options Cardiovasc Med 2009;11(02):104–113
31 Farragher RA, Laffey JG. Maternal brain death and somatic support. Neurocrit Care 2005;3(02):99–106
32 Korzeniowski OM. Antibacterial agents in pregnancy. Infect Dis Clin North Am 1995;9(03):639–651
33 Einarson A, Shuhaiber S, Koren G. Effects of antibacterials on the unborn child: what is known and how should this influence prescribing. Paediatr Drugs 2001;3(11):803–816
34 Christensen B. Which antibiotics are appropriate for treating bacteriuria in pregnancy? The Journal of Antimicrobial Chemotherapy 2000;46(Suppl 1):29–34. Discussion 63–65
35 van Runnard Heimel PJ, Franx A, Schobben AFAM, Huisjes AJM, Derks JB, Bruinse HW. Corticosteroids, pregnancy, and HELLP syndrome: a review. Obstet Gynecol Surv 2005;60(01):57–70, quiz 73–74

What a Neurosurgeon Should Know about the Endolymphatic Sac: Part 1–Anatomy and Physiology

O que um neurocirurgião deve saber sobre o saco endolinfático: Parte 1–Anatomia e Fisiologia

Marco Antônio Schlindwein Vaz[1] Jander Monteiro[1] Francisco Luiz Souza Braga[1] Joel Lavinsky[2] Giuseppe Casella Santis[3] Lia Grub Becker[4] Marcelo Assis Moro da Rocha Filho[5] Carmen Austrália Paredes Marcondes Ribas[6] Ricardo Marques Lopes de Araújo[7] Eberval Gadelha Figueiredo[7] Gustavo Rassier Isolan[1]

[1] Department of Neurosurgery, Centro Avançado de Neurologia e Neurocirurgia (CEANNE), Porto Alegre, RS, Brazil
[2] Department of Otology and Otoneurology, The Center for advanced neurology and neurosurgery (CEANNE), Porto Alegre, RS, Brazil
[3] Department of Medicine, University of North Georgia, Dahlonega, GA, USA
[4] Department of Medicine, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil
[5] Department of Otology and Otoneurology, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil
[6] Department of Medicine, Faculdade Evangélica Mackenzie do Paraná, Curitiba, PR, Brazil
[7] Department of Neurosurgery, Universidade de São Paulo (USP), São Paulo, SP, Brazil

Address for correspondence Marco Antônio Schlindwein Vaz, Medical Student, Academic of Medicine, Department of Neurosurgery, Centro Avançado de Neurologia e Neurocirurgia (CEANNE), Av. Ceará, 212, Campo Bom, RS, Brazil (e-mail: marcoantoniosvaz@hotmail.com).

Arq Bras Neurocir 2024;43(3):e187–e193.

Abstract

Objective To describe the microsurgical anatomy and the physiology of the endolymphatic sac (ES) that a neurosurgeon should know.

Methods Review of previous studies from 1927 to 2021, from basic and translational research using human and animal ES tissue or cells, as well as previous reviews about the subject. The present article is divided into three parts. In this first part, we review the microsurgical anatomy and physiology of the ES.

Results The ES is a structure situated in the inner ear, together with the cochlea, the vestibular system, and other structures. Differently from its adjacent structures, the ES does not have a specialized epithelium; instead, it has mitochondria-rich cells and ribosomal-rich cells, which are responsible for ionic transportation and secretory activity. Apart from these functions, the ES is also responsible for homeostasis regulation of the inner ear, endolymphatic fluid volume control, immune response, elimination of inner ear cellular debris and floating otoconia, regulation of membranous labyrinth pressure, acid/basic transport, and secretion of substances. Its anatomy is not very variable, since in most studies no more than 20mm separates the location of the ES in the samples, in any direction.

Keywords
- endolymphatic sac
- anatomy
- physiology
- neurosurgery

received
November 16, 2021
accepted
August 1, 2022
article published online
October 9, 2023

DOI https://doi.org/10.1055/s-0042-1760210.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Conclusion The human ES has vital functions in the inner ear, and its anatomy is rarely variable. Knowing that, and the importance of this area for neurosurgery, the present study elucidates the exact location of the ES and the lost functions that a lesion in this structure must cause.

Resumo

Objetivo Descrever a anatomia microcirúrgica e a fisiologia do saco endolinfático (SE) que um neurocirurgião deve saber.

Métodos Revisão de estudos prévios de 1927 até 2021, de pesquisa básica até translacional usando tecidos ou células do SE humanas e animais, além de revisões sobre o assunto. O presente artigo é dividido em três partes. Nesta primeira, nós revisamos a anatomia microcirúrgica e a fisiologia do SE.

Resultados O SE é uma estrutura situada no ouvido interno, junto da cóclea, do sistema vestibular e outras estruturas. Diferentemente das estruturas adjacentes, o SE não tem um epitélio especializado; ao invés disso, possui células ricas em mitocôndrias e outras ricas em ribossomos, que são responsáveis por transporte iônico e atividade secretória. Além dessas funções, o SE é responsável por regulação homeostática do ouvido interno, controle do fluido endolinfático, resposta imune, eliminação de detritos e otólitos livres, regulação da pressão da membrana labiríntica, transporte ácido/básico e secreção de substâncias. Sua anatomia não é muito variável, já que na maior parte dos estudos a máxima diferença de localização entre as amostras do SE foi dada em 20 mm, em todas as direções.

Conclusão O SE humano tem uma função vital no ouvido interno e sua anatomia não é muito variável. Sabendo disso, e da importância dessa região para a neurocirurgia, o presente estudo elucida a localização exata do SE e as funções perdidas em uma eventual lesão dessa estrutura.

Palavras-chave
- saco endolinfático
- anatomia
- fisiologia
- neurocirurgia

Introduction

The endolymphatic sac (ES) is a structure situated in the inner ear, together with the cochlea and the vestibular system.[1] These two have the responsibility of, respectively, detecting sound frequencies and capturing angular and linear acceleration, therefore, acting in hearing and balance. To do that, the cochlea and the vestibular system have a specialized epithelium, which transforms external stimuli into electrical signals that will be interpreted by the brain.[1–4]

Differently from its adjacent structures, the ES does not have a specialized epithelium; instead, it has mitochondria-rich cells and ribosomal-rich cells, which are responsible for ionic transportation and secretory activity.[1] This way, the ES has a very different function if it is compared with the cochlea and the vestibular system.[3]

The ES, despite being only 3 mm in diameter, does not have a very variable location inside the inner ear.[2,5] Almost any alteration in this structure can cause a massive problem to the hearing, including its loss.[1]

In the present review, our goal is to elucidate the anatomy and the physiology of the ES.

Methodology

The present article is divided into three parts. In this first part, we review the microsurgical anatomy and physiology of the ES. We focused on evidence of PubMed (from 1927 to 2021) from basic and translational research using human and animal ES tissue or cells, as well as previous reviews about the subject, using the following terms individually and combined: *Endolymphatic sac*, *anatomy*, *physiology*, and *neurosurgery*. Literature inclusion criteria were articles in English; individual case studies and long-term follow-up studies were not excluded. duplicate studies were excluded. First, we made a detailed explanation of the ES anatomy, followed by a briefing of the endolymph circulation prioritizing their relationship with the ES, and in the end, we discussed the physiology of the ES.

Results

Endolymphatic Sac History

The discovery of the ES was made by Neapolitan Domenico Felice Antonio Cotugno in 1760, on his famous dissertation De Aquaeductibus Auris Humanae Internal (On the Aqueducts of the Human Internal Ear).[6] He described the presence of labyrinthine fluid in the various cavities of the inner ear and the existence of two aqueducts: the cochlear aqueduct and the vestibular aqueduct. As well as the structures, Cotugno described the path taken by the aqueduct from the posterior cranial fossa to the inner ear, the two leys of dura enclosing the ES, and that this sac is a continuation of the vestibular aqueduct.[7]

Fig. 1 Domenico Cotugno (1736–1822) by C. Nalli (wood engraving). Portrait no. 689. (Courtesy of the United States National Library of Medicine: Image ID172387)

Cotugno, despite having described the anatomy, was not the one that named the structure as an ES. This credit goes to German Hasse, who introduced the term in 1873, which has remained in use until today (►**Fig. 1**).[8]

Endolymphatic Sac Anatomy

The ES is divided into three regions. The proximal part, closer to the vestibule, is revested by an epithelium like the endolymphatic duct,[9] that is, epithelial cells with the cellular membrane folded, creating fingerlike cytoplasmic protrusions.[10] The middle region is revested by a high cylindrical epithelium with many papillae and crypts. The distal part is in a dura mater duplication, that is, connective tissue, with its surface all covered by the same type of simple pavement epithelium.[9] The vascularization of each part of the ES is made by the same vessels that irrigate its adjacent structures, proximal being the same of the endolymphatic duct, and middle and distal being the same of the dura mater vessels.[5,11–13]

The location of the ES stands in a dura mater duplication posteriorly to the petrous pyramid, thus ending up being a surgical area for many neurosurgical procedures in the posterolateral part of the skull base.[5] The average measurements in a study conducted by Ammirati et al. were 15.7 mm posterosuperior (superolateral) to the 11th nerve in the jugular foramen (range, 11.0–18.5 mm), and 13.3 mm posterior (lateral) to the internal auditory meatus (range, 10.0–18.0 mm). The center of the sac was 24.1 mm (mean value) (range, 20.0–28.0 mm) ahead of the petrosigmoid

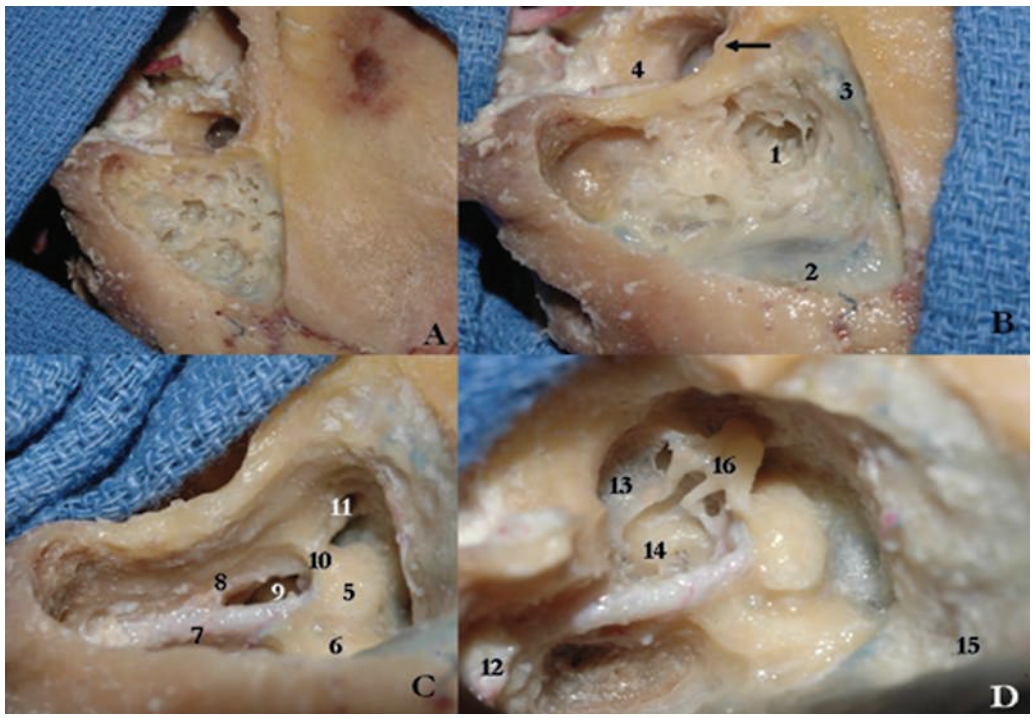


Fig. 2 Pictures of the inner ear showing: 1. Antrum, 2. Sinus Sigmoideus, 3. Mastoids segment of the dura mater, 4. External auditory meatus inferior wall, 5. Lateral semicircular canals, 6. Posterior semicircular canals, 7. Mastoids portion of the facial nerve, 8. Chorda tympani, 9. Facial recess, 10. Buttress, 11. Anvil, 12. Jugular bulb, 13. The tympanic membrane, 14. Promontory, 15. Citelli angle, 16. Ossicles. Mastoidectomy performed by Gustavo Isolan, MD, PhD.

intersection at a point 11.5 mm (mean value) (range, 8–17 mm) below the petrous ridge. The width and height of the sac were 3.83 (range, 2–6 mm) and 3.80 mm (range, 2.5–8 mm), respectively (►**Fig. 2**).[5]

There are some named structures that delimit the ES space. The Donaldson line is a surgical line that is parallel to the lateral semicircular canal (LSC) whereas it is vertical to the posterosuperior semicircular canal (SSC) and divides it into superior and inferior portions, from its most posterior point. Below this line, medial to the labyrinth, the endolymphatic sac is situated[5]–the Trautmann triangle is another important anatomic mark, bounded by the superior petrosal sinus (SPS) superiorly, the sigmoid sinus (SS) posteriorly, and a solid angle, which is formed by the bony labyrinth, anteriorly. In this triangle, the retrolabyrinthine tract from the mastoid antrum (MA), the ES, and the vestibular aqueduct are located.[13] Probably because of the bone limitation, the exact location of the sac is rarely variable.[2] In 85% of the cases studied by Ammirati, the sac was located between 10 and 15 mm posterior (lateral) to the internal auditory meatus. Similarly, the ES was never located < 11.5 or > 18.5 mm posterosuperior (superolateral) to the 11th nerve in the jugular foramen; in 80% of cases, the sac was located between 11 and 17 mm posterosuperior (superolateral) to the 11th nerve in the jugular foramen (►**Fig. 3**).[5]

The ES is attached to the endolymphatic duct, which is responsible for making the transit between the endolymph in the utricular saccular duct and in the endolymphatic sac.[14] The endolymphatic duct is vascularized by the accessory canal of the vestibular aqueduct, but there are no arteries in this structure.[9] The irrigation of the endolymphatic duct is made by adjacent capillaries that are in contact with the tissue through the lumen invagination of the duct.[9]

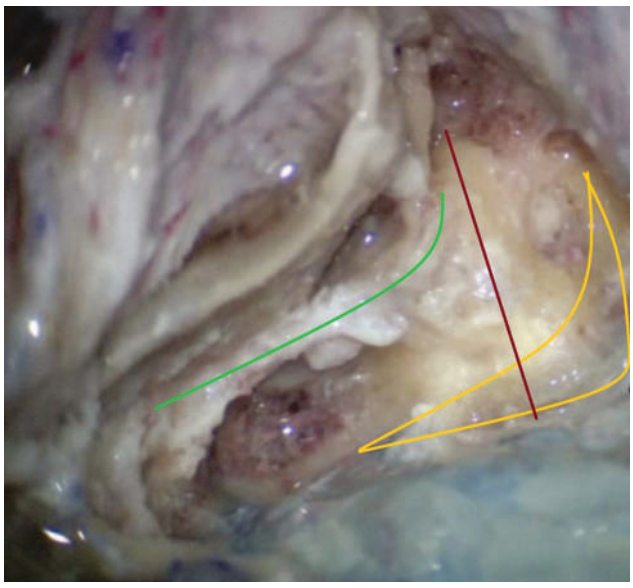


Fig. 3 Image showing the microanatomy of the inner ear. In red: Donaldson line. In yellow: Margins of the Trautmann triangle, in green: facial nerve. Mastoidectomy performed by Joel Lavinsky, MD, PhD.

Endolymph Way to the Endolymphatic Sac

The endolymph is a fluid with a composition very similar to the intracellular liquid.[1] The formation of this fluid is not a responsibility of one single structure; instead, all the blood capillaries in the membranous labyrinth work together in this goal.[9] Therefore, there is no unique way to the endolymph, as it can freely transit in the lumen of the canals. The orientation of the liquid will depend on the head orientation, the angle of the body, etc.[14] In this system, the ES is accountable, among other things, for storing the excess of endolymph.[1]

As said before, the endolymph does not have a single way to transit.[15] However, to explain the membranous labyrinth, let us take a portion of endolymph that is on the semicircular canals and go all the way to the ES. For that, we will always suppose that the endolymph heads to its next named structure. In the semicircular canals, the possibilities of the endolymph are to stay in it or reach the membranous ampullae of the semicircular canals. In the ampullae, the endolymph can return to the semicircular canals, stay in the ampullae, or move forward to the utricle. After reaching the utricle, the endolymph can stay in it, go back to the membranous ampullae of the semicircular canals, or proceed to the utricular saccular duct. In this stage, the endolymph is able to stay in the utricular saccular duct, flow back to the utricle, move to the saccule, or maintain itself in the way to the ES and go through the endolymphatic duct in the vestibular aqueduct. Once in the endolymphatic duct, which is sheltered by the vestibular aqueduct, the endolymph can only stay, go back to the utricular saccular duct, or move in the way to the ES (►**Fig. 4**).[14,16–18]

Starting from the cochlea, the differences are only at the beginning. The endolymph, if not remaining in the cochlea, can only go to the saccule through the canalis reuniens. In the saccule, the endolymph can stay, flow back to the cochlea by the canalis reuniens or move to the utricular saccular duct, and from there the way is the same if starting in the semicircular canals.[14,16–18]

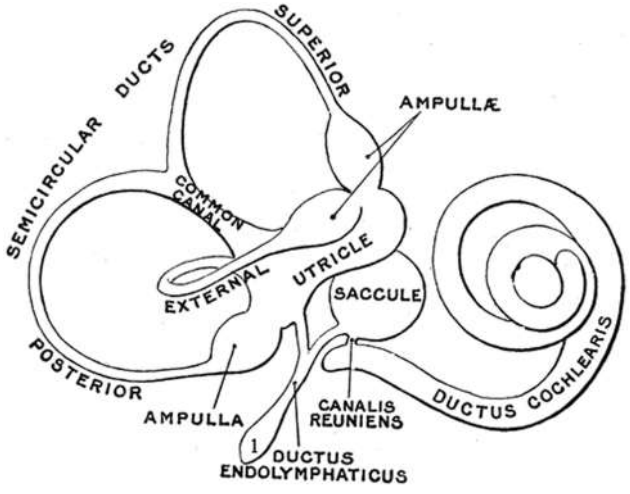


Fig. 4 Image showing the endolymphatic system. 1. Endolymphatic sac. Taken from the public domain: GRAY, H., & LEWIS, W. H. (1918). Anatomy of the human body. Philadelphia, Lea & Febiger, page 1052.

Endolymphatic Sac Physiology

The cochlea and semicircular canals or the vestibular system have the function of, respectively, detecting sound frequencies as well as angular and linear acceleration, acting therefore in hearing and balance. To do that, the cochlea and the vestibular system are provided with a sensorial epithelium, which transforms external stimulus in electric signals that will be interpreted by the brain.[1–4]

Differently from its adjacent structures, the ES does not have a specialized epithelium; instead, it has mitochondria-rich cells and ribosomal-rich cells, which are responsible for ionic transportation and secretory activity.[1] In this way, the ES has a very distinct function if compared with the cochlea and the vestibular system.[3]

In animals, it is suggested that the ES has an important role in the ionic homeostasis regulation of the internal ear and in the endolymphatic fluid volume control. Besides that, its involvement in immune response, elimination of inner ear cellular debris and floating otoconia, membranous labyrinth pressure, acid/basic transport, and substances secretion has been studied (►**Fig. 5**).[1,2,11,19–26]

Ionic Homeostasis

In the study by Mori et al.,[24] they show that mitochondria-rich cells in the ES intermediate portion have a higher activity of Na+, K+-ATPase, and higher Na+ permeability than other types of cells, implying that molecules related to Na+ transport, such as epithelial sodium channel, Na+–K+–2Clcotransporter 2 (NKCC2) and thiazide-sensitive Na+–Cl-cotransporter (NCC), may be present in mitochondria-rich cells.[24] Because of that, it is possible to suggest that the ES epithelium plays a role in the ionic transportation and composition of the endolymph.

Volume Regulation and Pressure Regulation

Also, in the study by Mori et al.[24] and supported by the study by Furuta et al.,[27] it is said that aldosterone may regulate Na+ transport in ES, resulting in endolymph volume regulation. Based on that, we can suggest that the ES is also a crucial part of the pressure regulation in the membranous labyrinth.[24,27]

Acid/Base Transportation

In the same study,[24] Mori suggests that the presence of molecules related to acid/base transport, such as H+-ATPase, Na+– H+ exchanger (NHE), pendrin (SLC26A4), Cl−–HCO3 - exchanger (SLC4A2), and carbonic anhydrase in ES epithelial cells may be a reason for the acid/base transport be another important role of the ES.

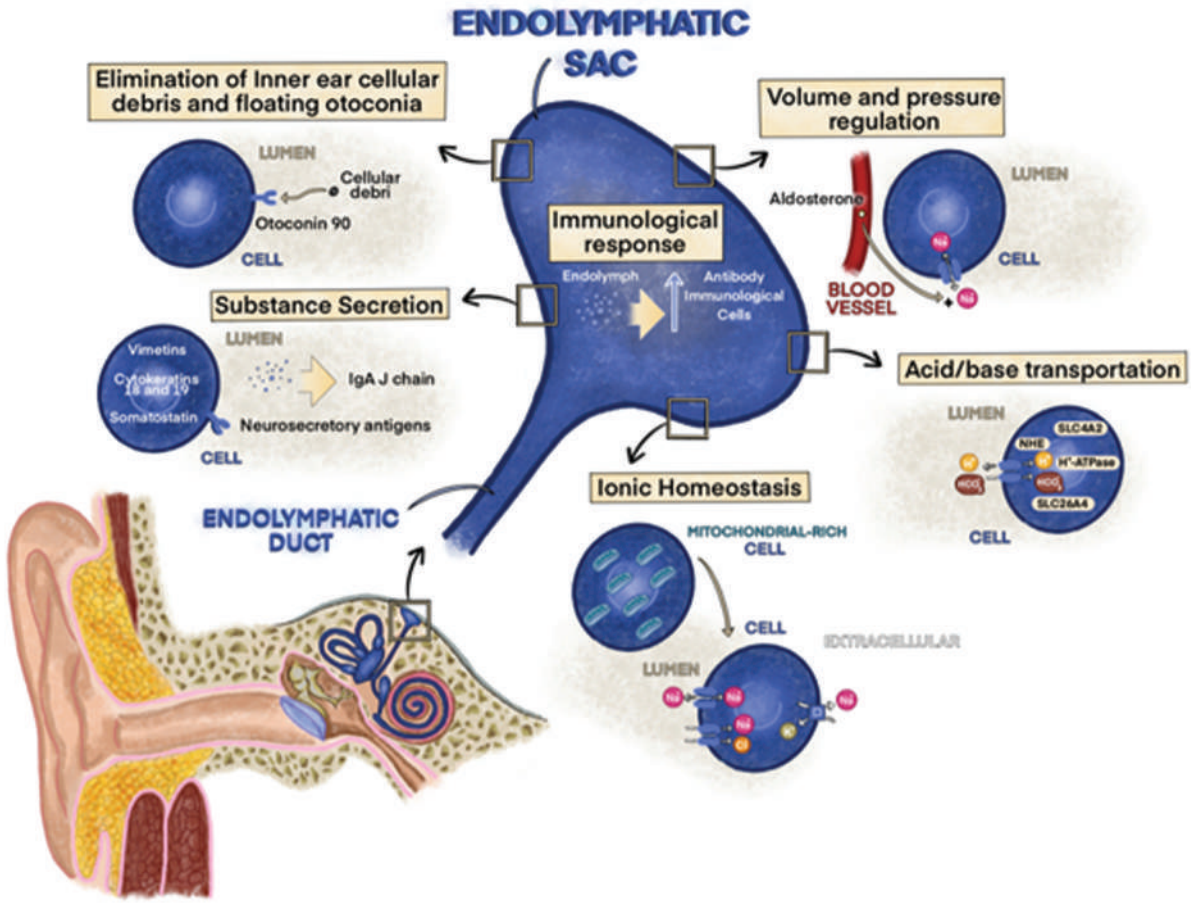


Fig. 5 Schematic representation of the endolymphatic sac physiology. "Created by Lia Grub Becker".

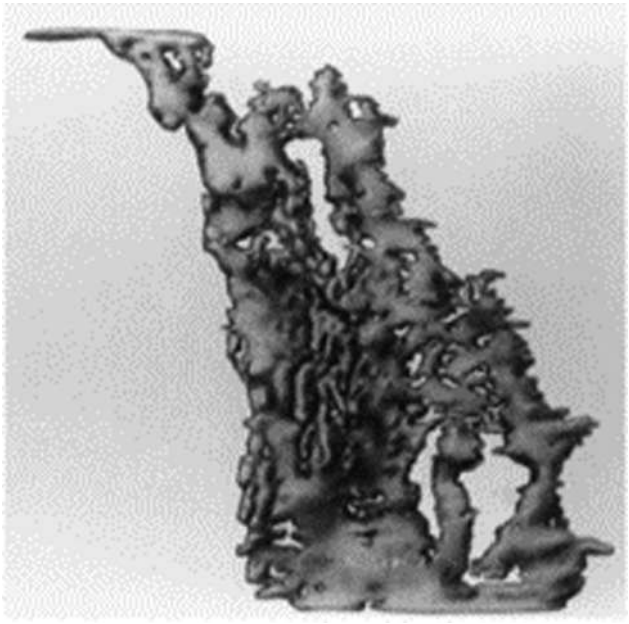


Fig. 6 3D image of the endolymphatic sac. Taken from: *Oehler MC, Chakeres DW, Schmalbrock P. Reformatted planar 'Christmas tree' MR appearance of the endolymphatic sac. AJNR Am J Neuroradiol. 1995 Aug;16(7):1525-8.* **FIG 1B**.

Immunologic Response

Recent studies demonstrated the presence of immunocompetent cells in the ES and its capability to respond to local primary and secondary antigen challenges.[3,21–23]

Measurements of serum and perilymph antibody levels, followed by inner ear immunization with keyhole limpet hemocyanin in guinea pigs with normal or obliterated ES, suggested that the ES plays a crucial role in the generation of local humoral immune responses.[25,26]

Also, these studies have searched for different types of cells in the ES and several, related to the immunologic system, have been found.[3,21–26]

Elimination of Inner Ear Cellular Debris and Floating Otoconia

According to the study by Ignatova et al.,[28] Otoconin-90 is the main otoconial matrix protein, and the endolymphatic sac of the embryonic chicks and guinea pigs contain otoconia. Otoconin-90 is also localized at the surface and inside epithelial cells lining the endolymphatic sac and is also incorporated into free-floating cells. Thus, the study concludes that the presence of these proteins can only be explained if there is an elimination process linked to it.[28]

Secretion of Substances

The presence of immunoglobulin A (IgA), secretory components like Cytokeratins 18 and 19, vimentins, as well as the J chain, was described within epithelial cells and in the lumen of the human ES.[19,20] Thus, the expression of these substances in the human ES epithelium supports the assumption that the ES is metabolically active and functionally related to a mesothelium that has both secretory, resorptive, and elimination capabilities[10,19,20]

A positive reaction for neuron-specific enolase and neurosecretory antigens was demonstrated in a few epithelial cells of the rugose part of the human ES.[19,20] In addition, neurosecretory granules and somatostatin were observed in cells of the human ES.[10,19,20] All this information contributes to the hypotheses of the secretory capacity of the ES.

Radiological Anatomy of the Endolymphatic Sac

The ES is a complex structure in terms of microscopic anatomy, which makes it difficult to visualize it in magnetic resonance imaging (MRI).[29] However, Oehler et al. [29] made a high-resolution three-dimensional Fourier transform technique and prototype bilateral dual phased-array surface coil technique, obtaining a 3D image of the ES (►**Fig. 6**).

Based on the results, it is possible to ensure that instead of a large confluent cavity, the ES is composed of multiple small channels that are interconnected, that in the study by Oehler et al is called by "Christmas tree" appearance.[29] However, Connor et al.[30] have shown that some ES pathologies can change its anatomy on MRI and computed tomography (CT). Individuals who have been diagnosed with large endolymphatic sac anomaly (LESA) and large vestibular aqueduct (LVAS) syndrome will probably have alteration on the scans, like the enlargement of the extraosseous ES (►**Fig. 7**).[30]

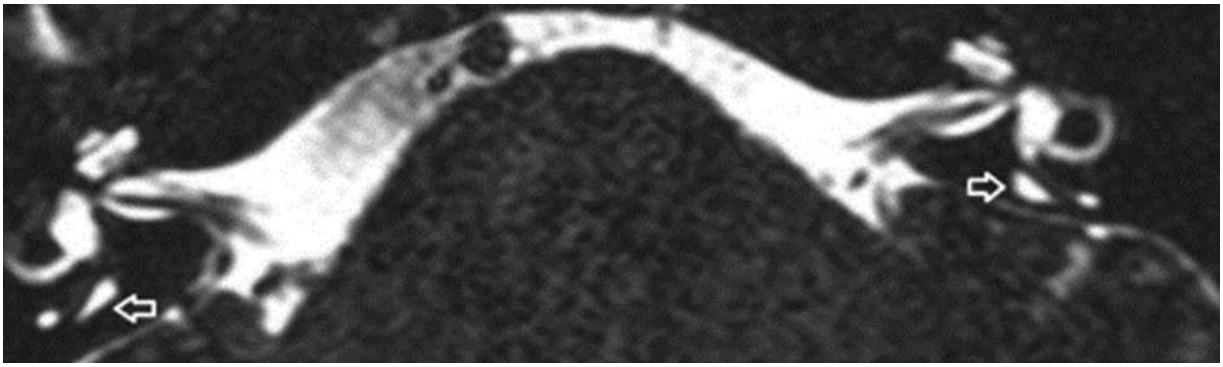


Fig. 7 T2 DRIVE axial images show an enlarged extra-osseous sac on the left. Taken from: *Connor SEJ, Dudau C, Pai I, Gaganasiou M. Is CT or MRI the optimal imaging investigation for the diagnosis of large vestibular aqueduct syndrome and large endolymphatic sac anomaly? Eur Arch Otorhinolaryngol. 2019 Mar;276(3):693-702.* ►**Figure 3**.

Conclusion

The human ES has vital functions in the inner ear, such as homeostasis regulation of the internal ear, endolymphatic fluid volume, immune response, elimination of inner ear cellular debris, and floating otoconia, membranous labyrinth pressure, acid/based transport, and secretion of substances.

The anatomy of the ES is rarely variable, since in $>80\%$ of the cases, in the reviewed studies, the maximum difference in the samples was <20 mm in any direction. Knowing that, and the importance of this area for neurosurgery, the present study elucidates the exact location of the ES and the function that a lesion in this structure must cause.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Kim SH, Nam GS, Choi JY. Pathophysiologic Findings in the Human Endolymphatic Sac in Endolymphatic Hydrops: Functional and Molecular Evidence. Ann Otol Rhinol Laryngol 2019;128 (6_suppl):76S–83S
2 Lundquist PG. Aspects on endolymphatic sac morphology and function. Arch Otorhinolaryngol 1976;212(04):231–240
3 Mogi G, Lim DJ, Watanabe N. Immunologic study on the inner ear. Immunoglobulins in perilymph. Arch Otolaryngol 1982;108(05): 270–275
4 Møller MN, Caye-Thomasen P, Qvortrup K. Oxygenated fixation demonstrates novel and improved ultrastructural features of the human endolymphatic sac. Laryngoscope 2013;123(08):1967–1975
5 Ammirati M, Spallone A, Feghali J, Ma J, Cheatham M, Becker D. The endolymphatic sac: microsurgical topographic anatomy. Neurosurgery 1995;36(02):416–419
6 Cotugno D. De aquaeductibus auris humanae internae. Neapoli: Somoniana; 1760
7 Corrales CE, Mudry A. History of the Endolymphatic Sac: From Anatomy to Surgery. Otol Neurotol 2017;38(01):152–156
8 Hasse C. Die Lymphbanen des inneren Ohres. Anat Studien 1873; 1:765
9 Friberg U, Rask-Andersen H, Bagger-Sjöbäck D. Human endolymphatic duct. An ultrastructural study. Arch Otolaryngol 1984;110 (07):421–428
10 Altermatt HJ, Gebbers JO, Müller C, Arnold W, Laissue J. Functional morphology of the human endolymphatic sac. A review. ORL J Otorhinolaryngol Relat Spec 1992;54(04):173–178
11 Altermatt HJ, Gebbers JO, Müller C, Arnold W, Laissue JA. Human endolymphatic sac: evidence for a role in inner ear immune defence. ORL J Otorhinolaryngol Relat Spec 1990;52(03):143–148
12 Altermatt HJ, Gebbers JO, Arnold W, Laissue JA. The epithelium of the human endolymphatic sac: immunohistochemical characterization. ORL J Otorhinolaryngol Relat Spec 1990;52(02):113–120
13 Anson BJ, Donaldson JA. Surgical anatomy of the temporal bone. W.B. Saunders Co 1973;2(01):176
14 Guild SR. The circulation of the endolymph. Am J Anat 1927;39 (01):57–81
15 Gibson WP. Hypothetical mechanism for vertigo in Meniere's disease. Otolaryngol Clin North Am 2010;43(05):1019–1027
16 Ferrary E, Sterkers O. Mechanisms of endolymph secretion. Kidney Int Suppl 1998;65(01):S98–S103
17 Tanioka H, Tanioka S, Kaga K. Vestibular Aging Process from 3D Physiological Imaging of the Membranous Labyrinth. Sci Rep 2020;10(01):9618
18 Wangemann P. Adrenergic and muscarinic control of cochlear endolymph production. Adv Otorhinolaryngol 2002;59(01):42–50
19 Arnold W, Altermatt HJ, Arnold R, Gebbers JO, Laissue J. Somatostatin (somatostatinlike) immunoreactive cells in the human inner ear. Arch Otolaryngol Head Neck Surg 1986 Sep;112(09):934–7
20 Arnold W, Altermatt HJ, Gebbers J-O, Laissue J. Secretory immunoglobulin A in the human endolymphatic sac. An immunohistochemical study. ORL J Otorhinolaryngol Relat Spec 1984;46(06): 286–288
21 Harris JP. Immunology of the inner ear: evidence of local antibody production. Ann Otol Rhinol Laryngol 1984;93(2 Pt 1):157–162
22 Harris JP. Immunology of the inner ear: response of the inner ear to antigen challenge. Otolaryngol Head Neck Surg 1983;91(01): 18–32
23 Kawauchi H, Ichimiya I, Kaneda N, Mogi G. Distribution of immunocompetent cells in the endolymphatic sac. Ann Otol Rhinol Laryngol Suppl 1992 Oct;157:39–47
24 Mori N, Miyashita T, Inamoto R, et al. Ion transport its regulation in the endolymphatic sac: suggestions for clinical aspects of Meniere's disease. Eur Arch Otorhinolaryngol 2017;274(04):1813–1820
25 Tomiyama S, Harris JP. The endolymphatic sac: its importance in inner ear immune responses. Laryngoscope 1986;96(06):685–691
26 Tomiyama S, Harris JP. The role of the endolymphatic sac in inner car immunology. Acta Otolaryngol 1987 Mar-Apr;103(01-04):182–188
27 Furuta H, Sato C, Kawaguchi Y, Miyashita T, Mori N. Expression of mRNAs encoding hormone receptors in the endolymphatic sac of the rat. Acta Otolaryngol 1999;119(01):53–57
28 Ignatova EG, Thalmann I, Xu B, Ornitz DM, Thalmann R. Molecular mechanisms underlying ectopic otoconia-like particles in the endolymphatic sac of embryonic mice. Hear Res 2004;194(1-2):65–72
29 Oehler MC, Chakeres DW, Schmalbrock P. Reformatted planar 'Christmas tree' MR appearance of the endolymphatic sac. AJNR Am J Neuroradiol 1995;16(07):1525–1528
30 Connor SEJ, Dudau C, Pai I, Gaganasiou M. Is CT or MRI the optimal imaging investigation for the diagnosis of large vestibular aqueduct syndrome and large endolymphatic sac anomaly? Eur Arch Otorhinolaryngol 2019;276(03):693–702

Pituitary Metastasis of Clear Cell Renal Carcinoma Mimicking Pituitary Macroadenoma – Case Report

Metástase de carcinoma renal de células claras em sela túrcica simulando macroadenoma hipofisário – Relato de caso

Lucas Caixeta Nogueira[1] Luciano Ricardo França da Silva[2] Luiz Eduardo Mendonça Tenório[1] Cleiton Onofre de Menezes[1] João Victor Franco de Oliveira Calado[1] Luiz Felipe Gomes Rosa[1] Guilherme Figner Moussalem[3] Nicolai Máximo Leventi[3]

[1] Departament of Neurosurgery, Hospital Santa Rosa, Cuiabá, MT, Brazil
[2] Departament of Neurosurgery, Hospital Santa Rosa, Cuiabá, MT, Brazil
[3] Department of Neurosurgery, Serviço de Cirurgia de Base de Crânio, Hospital Santa Rosa de Cuiabá, Cuiabá, MT, Brazil

Address for correspondence Lucas Caixeta Nogueira, MD, Neurocirurgião, Hospital Santa Rosa de Cuiabá, Adel Maluf Street, Jd Mariana 119, Cuiabá, Mato Grosso 78040600, Brazil (e-mail: nogueiraclucas@gmail.com).

Arq Bras Neurocir 2024;43(3):e194–e199.

Abstract

Introduction Pituitary tumors account for 25% of all primary brain tumors and for 15% of overall intracranial expansive masses. Pituitary metastases, in contrast, are a rare condition, estimated as 1.8% of all resected sellar lesions. We present here a rare case of clear cell renal carcinoma metastasis to the pituitary gland.

Case Report A 65-year-old patient with holocranial headache and diplopia, whose physical examination showed right eye abduction palsy and ipsilateral anisocoria. Magnetic resonance imaging (MRI) of the pituitary revealed a heterogeneous mass in T1 weighted imaging with mild peripheral contrast enhancement and considerable growth during follow-up. Prolactin levels were high and dropped to normal after use of cabergoline, but remained normal even after the medication was halted. Biopsy was compatible with clear cell renal carcinoma. After surgery, the patient underwent radiotherapy, which was effective in reducing the volume of the lesion.

Discussion Only 25 cases of pituitary metastasis arising from the kidney were reported in the literature between the years of 1957 and 2018. Metastases can reach the pituitary through hematogenous spread, cerebrospinal fluid, and contiguous bony lesions. Clinical presentation varies from vague complaints such as fatigue or headache to more specific signs like polyuria and polydipsia, and $\sim$ 60% of cases have clinical manifestations.

Conclusion Case reports of pituitary metastases are low worldwide, with only 25 case reports of kidney metastases in over a 60-year period. The rarity of the lesions and hormonal alterations due to pituitary stalk compression can mislead diagnosis, and some patients may even never be diagnosed regarding their lower life span. In this report, radiotherapy was effective postresection, and accounts for a treatment option. All these issues account for the relevance of these case reports.

Keywords
- pituitary metastasis
- renal clear cell carcinoma
- skull base
- sellar tumor
- neurosurgical oncology

received
April 14, 2023
accepted
July 5, 2023
article published online
October 18, 2023

DOI https://doi.org/10.1055/s-0043-1774748.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Introdução Os tumores hipofisários representam 25% de todos os tumores cerebrais primários e 15% das massas expansivas intracranianas totais. As metástases hipofisárias, por outro lado, são uma condição rara, estimada em 1,8% de todas as lesões selares ressecadas. Apresentamos aqui um caso raro de metástase de carcinoma renal de células claras para a glândula pituitária.

Relato de caso Paciente de 65 anos com cefaleia holocraniana e diplopia, cujo exame físico mostrou paralisia de abdução do olho direito e anisocoria ipsilateral. A ressonância magnética (RM) da hipófise revelou uma massa heterogênea na imagem ponderada em T1 com leve realce periférico de contraste e crescimento considerável durante o acompanhamento. Os níveis de prolactina estavam altos e caíram para o normal após o uso de cabergolina, mas permaneceram normais mesmo após a interrupção da medicação. A biópsia foi compatível com carcinoma renal de células claras. Após a cirurgia, o paciente foi submetido à radioterapia, que foi eficaz na redução do volume da lesão.

Discussão Apenas 25 casos de metástase hipofisária originada do rim foram relatados na literatura entre os anos de 1957 e 2018. As metástases podem atingir a hipófise por meio de disseminação hematogênica, líquido cefalorraquidiano e lesões ósseas contíguas. A apresentação clínica varia de queixas vagas, como fadiga ou dor de cabeça, a sinais mais específicos, como poliúria e polidipsia, e 60% dos casos têm manifestações clínicas.

Conclusão Os relatos de casos de metástases hipofisárias são baixos em todo o mundo, com apenas 25 relatos de casos de metástases renais em um período de mais de 60 anos. A raridade das lesões e alterações hormonais devido à compressão do pedúnculo hipofisário podem enganar o diagnóstico, e alguns pacientes podem nunca ser diagnosticados em relação à sua menor expectativa de vida. Neste relato, a radioterapia foi eficaz após a ressecção e representa uma opção de tratamento. Todas essas questões são responsáveis pela relevância desses relatos de caso.

Palavras-chave

- metástase hipofisária
- carcinoma renal de células claras
- base do crânio
- tumor selar
- neurocirúrgico oncologia

Introduction

Approximately 25% of primary benign brain tumors and 15% of all primary brain neoplasms are pituitary tumors. The annual incidence lies in an estimated range of 3 to 11 cases per 100,000 individuals, and they represent the third most common primary intracranial tumor, after gliomas and meningiomas.[1] On the other hand, pituitary metastases are rare, estimated to be 1.8% of all surgically resected sellar masses. In addition, only 25 cases of renal cell carcinoma metastasized to the pituitary were described between 1957 and 2018 in the largest meta-analysis to date, reinforcing the significance of the present case report.[2]

Regarding renal cell carcinoma, it accounts globally for 2 to 3% of all malignancies, with 338,000 new cases per year worldwide. Between 20 to 30% of the patients already have metastases at diagnosis.[3]

Autopsy studies demonstrated a prevalence of 1 to 4% of pituitary metastases in patients with advanced cancer, suggesting a higher prevalence than the diagnosed cases. These may be increasing due to enhancements in neuroimaging, laboratory testing, and higher lifespan of cancer patients over time. Treatment involves surgical decompression, chemotherapy, immunotherapy, radiotherapy, or even conservative approach.[2] The mostly described symptoms are visual field defects, panhypopituitarism, headache, and even diabetes insipidus (DI), but appear in only 7% of cases, as the rest of them are asymptomatic.[4]

Case Report

We present a female patient, 65 years old, reporting a holocranial headache and diplopia of insidious start and gradual worsening over 1 month. In physical examination, it was noted right abducens nerve palsy alongside anisocoria, whereas the right pupil was moderately more dilated and less reactive than the left pupil. Neuroimaging revealed a sellar mass, and laboratory testing presented elevated serum levels of prolactin (141 ng/mL, reference values 3 to 20 ng/mL). Cabergolin was initiated, and prolactin levels reduced (1.4 ng/mL), dropping to normal rates even though the dopaminergic agonist was halted.

Past medical history of the patient involved left nephrectomy and adrenalectomy 11 years before due to clear cell renal carcinoma, and right adrenalectomy 7 years later due to another metastasis. The patient sought medical assistance before neuroimaging due to upper abdominal pain in a band-like pattern, exams showing elevated lipase and

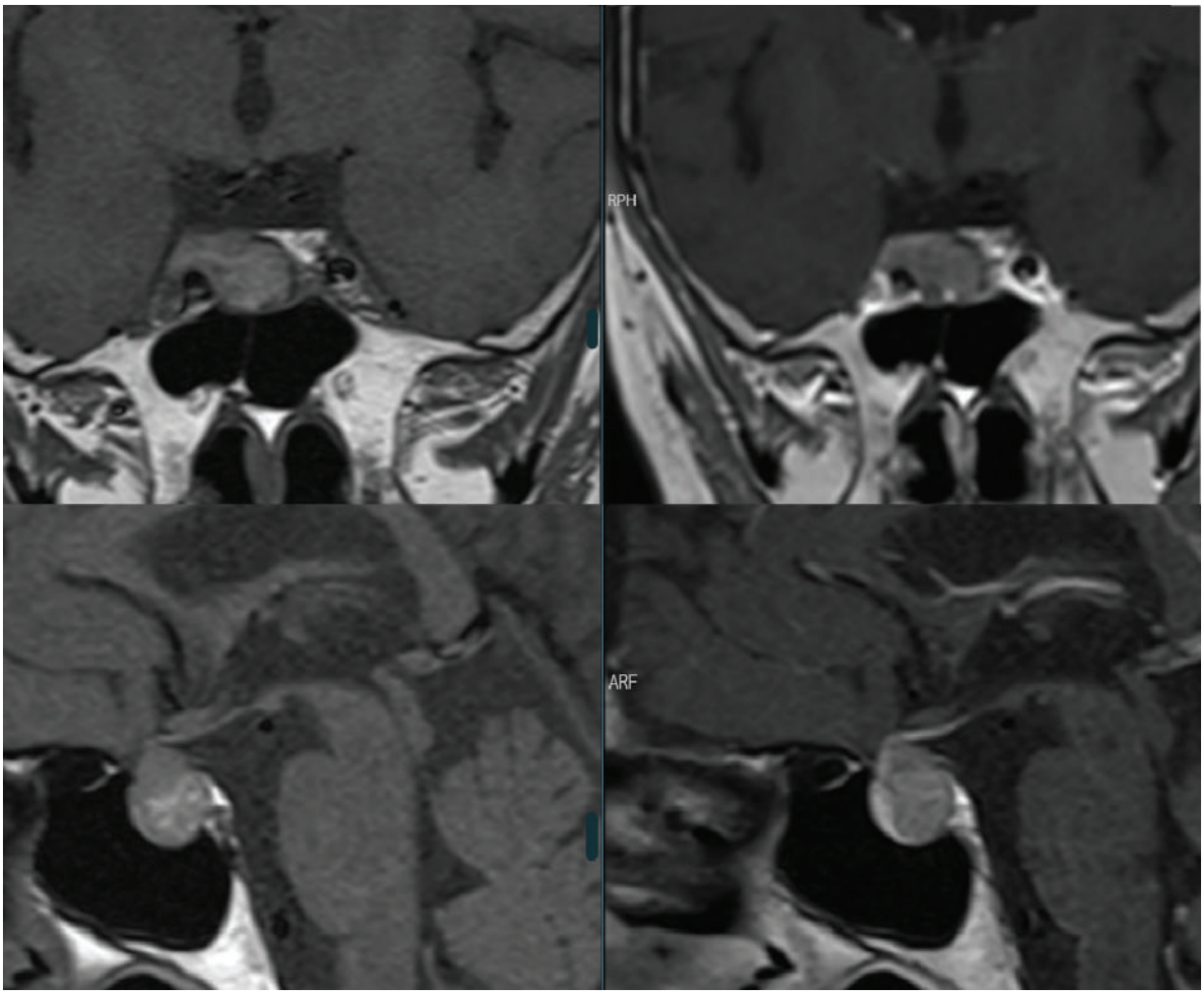


Fig. 1 First MRI of the patient, in coronal (superior half) and sagittal (inferior half) sections, precontrast T1 weighted images on the left and T1 postcontrast on the right. A sellar mass is observed with parasellar extension on the right over the cavernous carotid artery and surpassing it, therefore being classified as Knosp 3A. It is a heterogeneous lesion, with sparse high intensity spots in T1 and less postcontrast enhancement than the pituitary parenchyma surrounding it.

amylase serum levels. Abdominal imaging revealed a mass lesion invading the head of the pancreas causing pancreatitis, and biopsy confirmed it to be another site of metastasis of renal cell carcinoma. The comorbidities of the patient were type 2 diabetes mellitus and primary hypertensive disease.

Magnetic resonance imaging (MRI) of the brain of the patient revealed a heterogeneous mass in T1 weighted imaging with partial peripheral contrast enhancement (►**Fig. 1**). During follow-up and investigation, there was considerable growth in a period of 2 months, from 2.0 cm^3 to 3.1 cm^3 (►**Fig. 2**). The lesion extends lateral to the lateral tangent between the supracavernous and intracavernous internal carotid artery segments, advancing into the superior cavernous sinus compartment, therefore being classified as modified Knosp 3A.[5]

The patient underwent surgery with partial resection of the tumor because of its hardened consistency and involvement of cavernous sinus alongside the carotid artery. Nevertheless, there was progressive visual improvement, reported by the patient as reduction in diplopia. Immunohistochemistry was positive for PAX8 transcription factor and CD10 marker, both typically found in this type of tumor.[6] Histological study showed an epithelial neoplasm with clear cells (►**Fig. 3**), as correlated to the rarefied cytoplasm of a clear cell carcinoma usually described.[7]

Postoperative computed tomography scan (CT) soon after surgery showed hemostatic material inside the sella and sphenoid sinus. A small amount of residual tumor can be identified on the right side, but major reduction of the lesion volume is observed (►**Fig. 4**).

Oncologic follow-up after the procedure included chemotherapy with Axitinib and Pembrolizumabe. Radiosurgery was performed 3 months after surgical resection aiming for the residual tumor involving the right internal carotid artery, with even more reduction of its volume (►**Fig. 5**).

Discussion

According to a recent meta-analysis, only 25 cases of pituitary metastasis from kidney were reported from 1957 to 2018. The incidence of pituitary mass due to renal cell

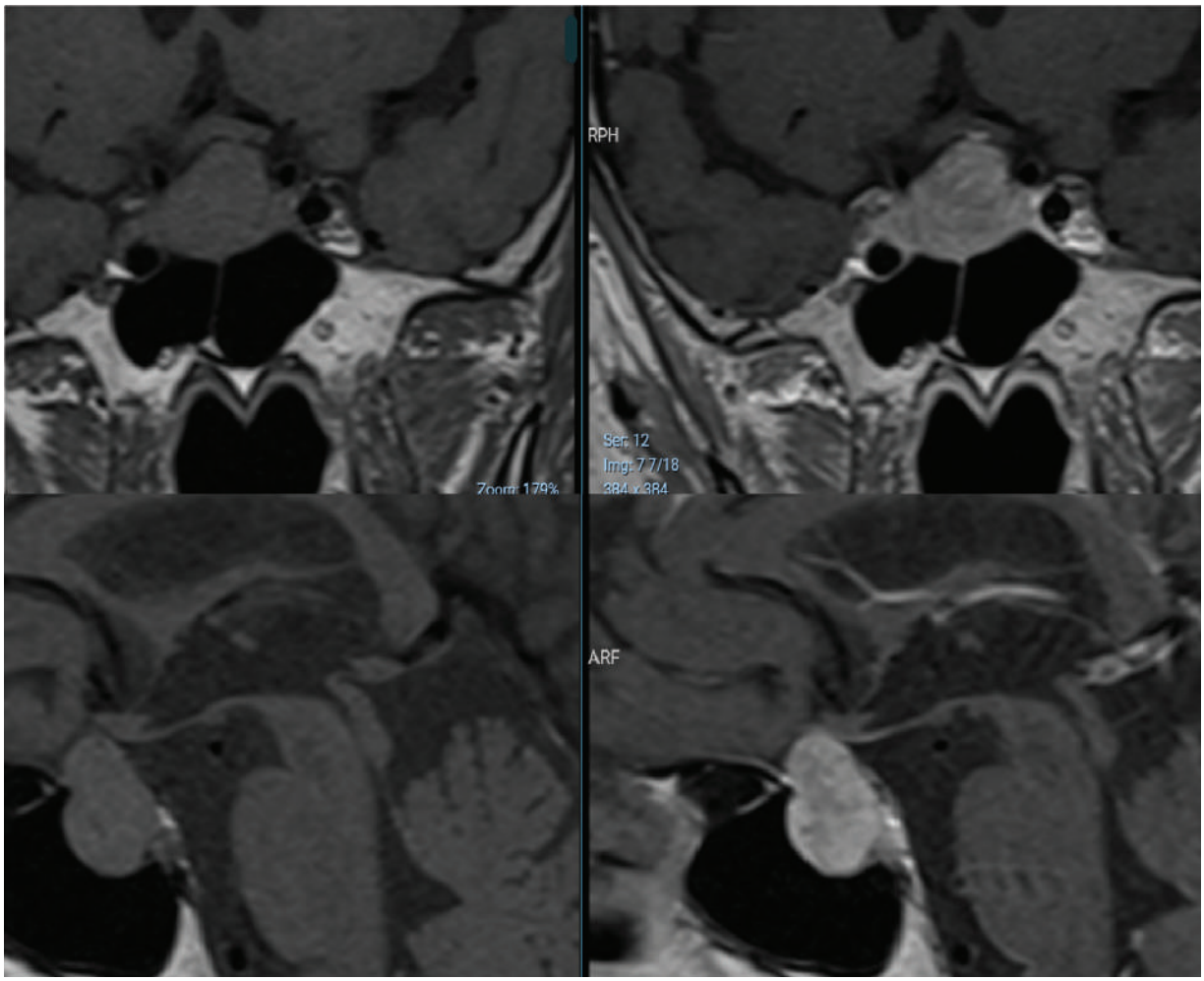


Fig. 2 MRI 2 months after initial imaging revealing growth of the tumor. Sagittal sections disposed inferiorly and coronal superiorly, in noncontrast T1 weighted images on the left and postcontrast on the right. It is noted higher contrast enhancement and growth of the lesion toward the suprasellar compartment with optic chiasm compression. Also, there is expansion bilaterally with greater involvement of the right cavernous sinus and extension to the left internal carotid artery. The mass grew from 2.0 cm^3 to 3.1 cm^3.

carcinoma is low worldwide, despite standing as the fourth most common primary site. The reported cases arise the possibility of interactions between the metastasis and renal cancers contributing to dissemination to the sella.[2]

Among patients with renal cell carcinoma in general, 21% have distant metastasis at the moment of diagnosis. Studies concur regarding frequency of the metastases, and according to an important prospective series, the

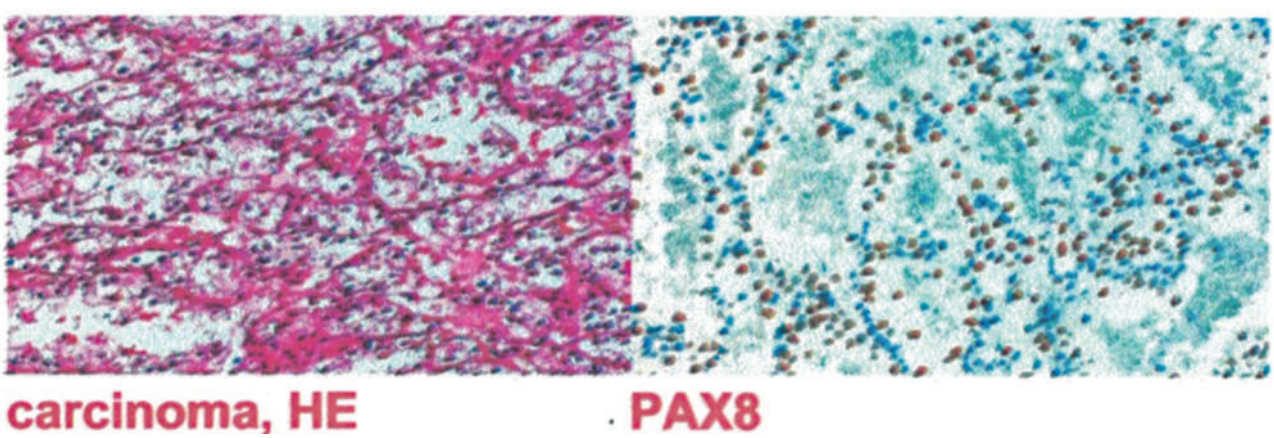


Fig. 3 Histological samples of anatomopathological and immunohistochemistry study of the lesion, where it is observed the presence of clear cells with scarce cytoplasm, typical of the clear cell renal carcinoma. There was expression of CD10 (not shown in the picture) and PAX8 factors, which corroborated the diagnosis.

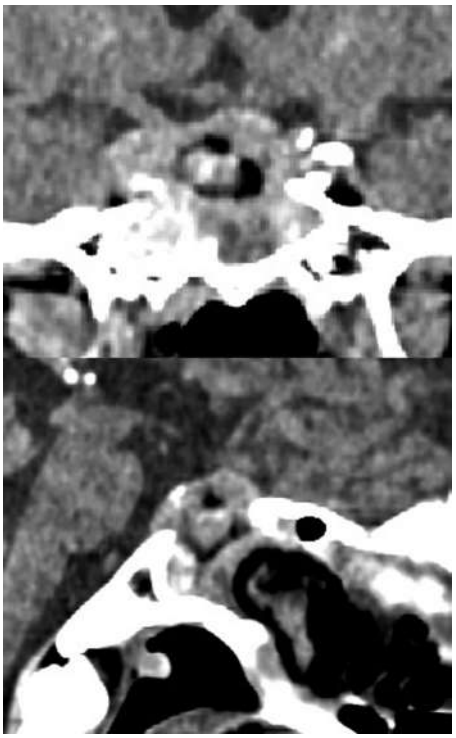


Fig. 4 Immediate postoperative CT scan with hemostatic material inside the sella and significant tumor reduction.

most frequent sites of metastases from renal cell carcinoma were lung (54%), lymph nodes (22%), and bone (20%). Moreover, 17% of patients without metastasis at diagnosis were affected by metastatic spread during follow-up.[3]

Breast and lung correspond to more than half of original tumor sites in all reported cases of pituitary metastasis. Kidney, prostate, and colon stand for 3 to 5% of the cases. Other rare causes include melanoma, thyroid, pancreas, hematologic neoplasms, and unknown primary cancers.[4]

There are four main ways of metastases to spread to the pituitary. Two of them involve conventional hematogenous spread, through the hypophyseal arteries supplying the posterior lobe and through the hypophyseal portal system of the anterior lobe. Cerebrospinal fluid can also carry malignant cells, and the final mechanism is direct compression or invasion of the gland by bony metastases of the skull base.[4]

Involvement of the posterior lobe alone occurs in 50.8% of cases, whereas only the anterior lobe is affected in 15.4%, and both of them in 33.8%.[7] The diminished flow of the portal system serves as a protection against dissemination to the adenohypophysis, while increased supply of the neurohypophysis favors its susceptibility when compared with the former. The posterior lobe is also smaller than the

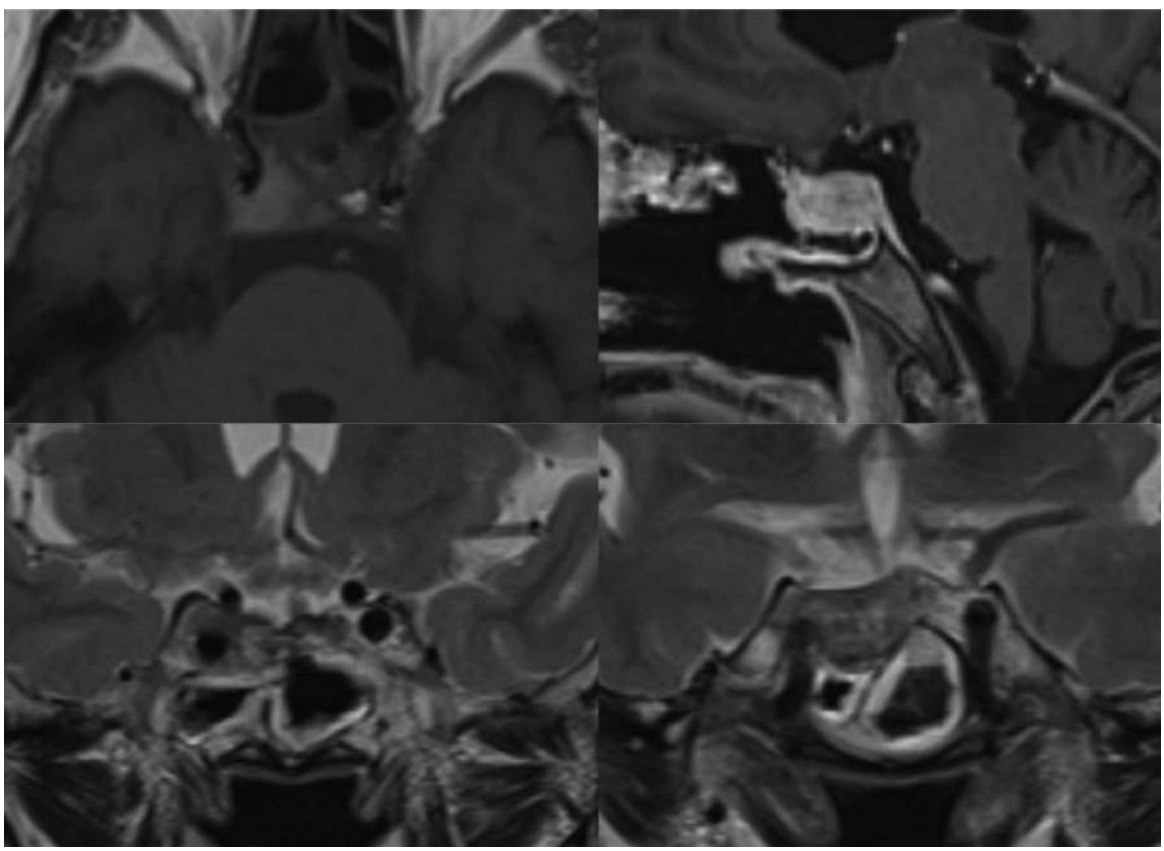


Fig. 5 MRI of the patient 4 months following radiotherapy. It is possible to note significant reduction of the volume of the metastasis, and therefore its responsiveness to the therapy. There is a smaller residual lesion hyperintense on T1 imaging in the upper left image that shows contrast enhancement in T1 postcontrast in the upper right picture, predominantly on the right side in close relation with the carotid artery in T2 images, in the lower half of the figure.

anterior, being more vulnerable to dysfunction than the anterior. Therefore, symptoms would be easier to identify through compression, leading to more cases diagnosed and accounted for. Another factor is that the posterior lobe has a larger surface area in contact with the adjacent dura, so cerebrospinal fluid dissemination is more prone to occur. Anterior lobe involvement is usually the result of a larger lesion of the posterior lobe or metastatic deposits through contiguous spread. The anterior lobe also seems to be susceptible to ischemic infarcts.[4,8]

Symptoms vary from vague complaints such as fatigue or headache to more specific signs like polyuria and polydipsia, and $\sim$ 60% of cases have clinical manifestations. Primary symptoms in descending order of importance with their respective frequencies are visual impairment (48.8%), DI (38.4%), panhypopituitarism (37.7%), and headache (35.3%). Extension of an infiltrating tumor to supraoptic and paraventricular nuclei in the hypothalamus can cause DI, as it is where the synthesis of neurohypophysis hormones takes place. It is also caused by compromised tracks convergence originating from hypothalamic nuclei, at the base of the hypothalamus at the origin of the pituitary stalk[2].

The patient also presented high prolactin levels. It is known that nonadenomatous pituitary or parasellar masses can cause hyperprolactinemia through inhibition of the release of hypothalamic dopamine, by compression of the infundibular stalk.[9] This can lead to misdiagnosis of the sellar mass, as prolactinoma would be considered a feasible diagnosis without proper care in propaedeutics. In this case, it was actually considered a differential diagnosis in a former investigation.

Surgery is a treatment option for confirming diagnosis and decreasing symptoms, but complete resection is difficult and may be risky when there is hypervascularization, invasion of nearby organs or even of the cavernous sinus,[2] which was the situation of this patient.

Even with current treatment, pituitary metastasis has poor prognosis, as metastases in other sites are commonly present at the moment of diagnosis. The estimated lifespan of the patients lies between 6 and 22 months, and no treatment has yet shown effectiveness in improving it. Factors that may lead to longer survival rates include younger age at presentation, smaller lesions, and less time between primary disease diagnosis and pituitary metastasis presentation[4].

Conclusion

Pituitary metastases are known as rare conditions, but of increasing awareness in spite of its rise in incidence favored by the improvement in diagnostic techniques. Metastases from clear cell renal carcinoma are even more rare, with only 25 described cases until 2018 from a large meta-analysis[2]. We present a case report of a 65-year-old woman with visual impairment and a sellar mass from which biopsy was consistent with clear cell renal carcinoma Acknowledging these cases is significant due to their rarity worldwide, their increasing incidence with the development of diagnostic tools and the pathogenesis of the disease, which is yet to be elucidated.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Gittleman H, Ostrom QT, Farah PD, et al. Descriptive epidemiology of pituitary tumors in the United States, 2004-2009. J Neurosurg 2014;121(03):527–535
2 Javanbakht A, D'Apuzzo M, Badie B, Salehian B. Pituitary metastasis: a rare condition. Endocr Connect 2018;7(10):1049–1057
3 Dabestani S, Thorstenson A, Lindblad P, Harmenberg U, Ljungberg B, Lundstam S. Renal cell carcinoma recurrences and metastases in primary non-metastatic patients: a population-based study. World J Urol 2016;34(08):1081–1086
4 Henry A, Nugent A, Wallace IR, Oladipo B, Sheehy O, Johnston PC. Pituitary metastasis: a clinical overview. Ulster Med J 2021;90 (03):146–150
5 Micko AS, Wöhrer A, Wolfsberger S, Knosp E. Invasion of the cavernous sinus space in pituitary adenomas: endoscopic verification and its correlation with an MRI-based classification. J Neurosurg 2015;122(04):803–811
6 Tong GX, Yu WM, Beaubier NT, et al. Expression of PAX8 in normal and neoplastic renal tissues: an immunohistochemical study. Mod Pathol 2009;22(09):1218–1227
7 McCormick PC, Post KD, Kandji AD, Hays AP. Metastatic carcinoma to the pituitary gland. Br J Neurosurg 1989;3(01):71–79
8 Komninos J, Vlassopoulou V, Protopapa D, et al. Tumors metastatic to the pituitary gland: case report and literature review. J Clin Endocrinol Metab 2004;89(02):574–580
9 Bi WL, Smith TR, Nery B, Dunn IF, Laws ER. Pituitary tumors: functioning and nonfunctioning. In: Winn HR (ed): *Youmans & Winn Neurological Surgery.* 7th ed. Philadelphia: Elsevier; 2016: 1155–1182

Surgical Treatment of Chronic Subdural Hematoma under Local Anesthesia: Case Report and Literature Review

Tratamento cirúrgico de Hematoma Subdural Crônico sob anestesia local: Relato de caso e revisão de literatura

Carlos Umberto Pereira[1] Débora Moura da Paixão Oliveira[2] Lauro Roberto de Azevedo Setton[3]

[1] Department of Neurosurgery, Emergency Hospital (HUSE), Aracaju, Sergipe, Brazil
[2] Brazilian Nursing Association in Neurology and Neurosurgery, Aracaju, Sergipe, Brazil
[3] Tiradentes University, Aracaju, Sergipe, Brazil

Address for correspondence Carlos Umberto Pereira MD, PhD, Department of Neurosurgery, Emergency Hospital (HUSE), Av. Augusto Maynard, 245/404, Bairro São José, 49015-380 Aracaju, Sergipe, Brazil (e-mail: umberto@infonet.com.br).

Arq Bras Neurocir 2024;43(3):e200–e203.

Abstract

Introduction Optimal surgical treatment for chronic subdural hematoma (CSDH) in the elderly has been controversial. Whenever possible, a less invasive technique should be used to avoid complications.

Case Report The patient was 82-years-old, with JPS; with diagnosis of liver cirrhosis due to alcohol abuse and history of recent myocardial infarction. He was admitted to the emergency room with temporal-spatial disorientation. The Glasgow coma scale (GCS) value on admission was 9. Left hemiparesis and osteotendinous hyperreflexia in the left side of the body. Noncontrast-enhanced cranial computed tomography (CT) showed right frontoparietal hypodense lesion with mass effect. Due to the clinical conditions of the patient, drainage of the hematoma was indicated through local anesthesia and sedation with midazolam. He was discharged after 8 days with improvement in his mental and neurological condition.

Conclusion Drainage of CSDH using local anesthesia in an elderly person with severe comorbidity can reach excellent results.

Keywords
- chronic subdural hematoma
- general anesthesia
- local anesthesia
- treatment

Resumo

Introdução O tratamento cirúrgico ideal para hematoma subdural crônico (HSDC) em idosos tem sido controverso. Sempre que possível uma técnica menos invasiva deve ser utilizada para evitar complicações.

Relato do Caso Paciente de 82 anos portadora de JPS; com diagnóstico de cirrose hepática por abuso de álcool e história de infarto do miocárdio recente. Foi admitido no pronto-socorro com desorientação espaço-temporal. O valor da escala de coma de Glasgow (ECG) na admissão era 9. Hemiparesia esquerda e hiperreflexia osteotendinosa no lado esquerdo do corpo. A tomografia computadorizada (TC) de crânio sem

Palavras-chave
- hematoma subdural crônico
- anestesia geral
- anestesia local
- tratamento

received
April 14, 2023
accepted
July 5, 2023
article published online
October 18, 2023

DOI https://doi.org/10.1055/s-0043-1774750.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

contraste mostrou lesão frontoparietal hipodensa direita com efeito de massa. Devido às condições clínicas do paciente foi indicada drenagem do hematoma através de anestesia local e sedação com midazolam. Teve alta após 8 dias com melhora do quadro mental e neurológico.
Conclusão A drenagem do HDC com anestesia local em idoso com comorbidade grave pode alcançar excelentes resultados.

Introduction

Chronic subdural hematoma (CSDH) is a common problem in neurosurgery and occurs mainly in the elderly.[1] In most cases, it results from mild cranioencephalic trauma.[2] Generally, the treatment is surgical. Anesthesia for this procedure can be general or local.[3] The elderly usually has systemic comorbidities and, in many cases, general anesthesia is contraindicated.[4–7] Drainage for this condition can be performed under local anesthesia, in previously selected patients, with excellent results.[8,9]

The authors review and discuss the indication of local anesthesia in the treatment of CSDH drainage.

Case Report

The patient is male, 82-years-old, with JPS; as well as a diagnosis of liver cirrhosis due to alcohol abuse and recent myocardial infarction, during which he underwent placement of two stents. There was no history of accidental fall. He presented with time and space disorientation. The Glasgow coma scale (GCS) score was 9. Lens clouding interfered with fundus examination. Other symptoms include hemiparesis and osteotendinous hyperreflexia on the left side. Computed tomography (CT) of the skull without contrast showed a hypodense lesion in the right frontoparietal region with mass effect. Due to the patient's comorbidities, a local anesthesia and sedation with midazolam maleate were chosen for drainage of the hematoma. A control cranial CT performed 5 days after the intervention showed a marked reduction in the hematoma. He was discharged from the hospital 8 days after the surgical procedure, with improvement to his mental and neurological condition. The patient was guided regarding the use of specific medication and outpatient return.

Discussion

Several neurosurgical procedures have been used in the surgical treatment of CSDH.[1] The best treatment method is still controversial today. Although the basic treatment for CSDH is surgical, conservative therapy can be chosen if there is no significant accumulation of blood that compromises the cerebral cortex and without any significant clinical manifestation.[10] Trepanation followed by drainage of the hematoma has been the most frequent surgical procedure in elderly with CSDH.[11–15] Whenever possible, the least invasive technique should be used to avoid complications.

General or local anesthesia, when carefully performed, has minimal complications in the surgical treatment of CSDH.[9,16–18] The indication of general or local anesthesia depends on the protocol established in the service, or on the medical professional's preference.[19,20] Systemic diseases coexist in the elderly, resulting in contraindications for general anesthesia.[3] In these cases, the use of local anesthesia is a favorable alternative for draining the CSDH.[8,9]

General anesthesia promotes complete immobility and good comfort, but it has been associated with a series of complications, especially among elderly patients with chronic systemic diseases such as diabetes mellitus, arterial hypertension, myocardial infarction, and the use of antiplatelet drugs.[21,22] General anesthesia can cause a delay in the preoperative level of consciousness, which has a negative impact, especially in cases that require an immediate postoperative evaluation, to exclude the need to repeat the procedure due to an early recurrence of the hematoma.[3,10]

Local anesthesia for draining the CSDH has been used by several authors; the main downside is that patients may become anxious and feel discomfort during the procedure.[23] The selection of the anesthetic method can be individualized.[5] For Surve et al.,[24] sedation consists of using midazolam with beneficial results.

Both coagulated blood and multiloculated hematoma were removed using local anesthesia in elderly patients.[2,20,25,26] Other authors have shown that local anesthesia with sedation for surgical drainage of the CSDH can reduce the risk of intraoperative brain activity, avoiding complications that could occur with the use of general anesthesia.[27,28] Mersha et al.,[1] in their sample of 195 patients, performed a burr hole, intraoperative lavage under local anesthesia, and a closed drainage system postoperatively, with a single professional; 95.2% of cases had good recovery, 13% were reoperated due to recurrence of the hematoma, and there were 4 deaths. These authors concluded that a single burr hole, intraoperative irrigation, and closed drainage system under local anesthesia, with occasional sedation in patients who are uncooperative due to altered mental status, is an easy, safe, and effective surgical technique in the treatment of CSDH. Seizur et al.[23] used two trepan holes to better determine the limits of the hematoma. The mean duration of the procedure using local anesthesia is

shorter compared with general anesthesia.[3,29] This reduction in procedure time may reduce the risk of thromboembolism, hypothermia, and other intraoperative adverse events.[3] According to Salama,[10] the treatment of CSDH through a single trepan hole under local anesthesia is careful, safe, being indicated mainly for cooperative patients who have unilocular CSDH and, as a result, have a shorter length of stay, lower hospital costs, and a lower rate of postoperative complications.

Many authors suggest that the treatment of CSDH by means of a single trepanation under monitored anesthesia is careful, effective, and sufficient for patients with cooperative unilocular CSDH, with a shorter mean duration of the procedure when compared with procedures under general anesthesia. Therefore, the use of local anesthesia results in shorter hospital stays, lower treatment costs, and lower rate of postoperative complications.[3,29]

In patients undergoing local anesthesia, easier early mobilization is observed, thus reducing the incidence of postoperative deep venous thrombosis and pulmonary atelectasis, which can make intensive care unit admission necessary.[10] be reduced in patients undergoing local anesthesia, making the procedure more economical and reducing the possibilities of developing nosocomial infection.[1,7,30] Despite the indication of surgical treatment for CSDH still being controversial, a less invasive surgical technique under local anesthesia should be encouraged in selected cases.[24]

Conclusion

The literature suggests that more cases should be performed with local anesthesia to better manage the less invasive treatment of CSDH, especially in high-risk elderly patients.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Mersha A, Abat S, Temesgen T, Nebyou A. Outcome of chronic subdural hematoma treated with single burr hole under local anesthesia. Ethiop J Health Sci 2020;30(01):101–106
2 Yadav YR, Parihar V, Namdev H, Bajaj J. Chronic subdural hematoma. Asian J Neurosurg 2016;11(04):330–342
3 Guzel A, Kaya S, Ozkan U, Ufuk Aluclu M, Ceviz A, Belen D. Surgical treatment of chronic subdural haematoma under monitored anaesthesia care. Swiss Med Wkly 2008;138(27-28): 398–403
4 Abe Y, Maruyama K, Yokoya S, et al. Outcomes of chronic subdural hematoma with preexisting comorbidities causing disturbed consciousness. J Neurosurg 2017;126(04):1042–1046
5 Atsumi H, Sorimachi T, Honda Y, Sunaga A, Matsumae M. Effects of preexisting comorbidities on outcomes in patients with chronic subdural hematoma. World Neurosurg 2019;122:e924–e932
6 Lee KS. How to treat chronic subdural hematoma? Past and now. J Korean Neurosurg Soc 2019;62(02):144–152
7 Mahmood SD, Waqas M, Baig MZ, Darbar A. Mini-craniotomy under local anesthesia for chronic subdural hematoma. An effective choice for elderly patients and for patients in a resource-strained environment. World Neurosurg 2017;106: 676–679
8 Deng XM, Xiao WJ, Luo MP, Tang GZ, Xu KL. The use of midazolam and small-dose ketamine for sedation and analgesia during local anesthesia. Anesth Analg 2001;93(05):1174–1177
9 Rohde V, Graf G, Hassler W. Complications of burr-hole craniostomy and closed-system drainage for chronic subdural hematomas: a retrospective analysis of 376 patients. Neurosurg Rev 2002;25(1-2):89–94
10 Salama H. Outcome of single burr hole under local anesthesia in the management of chronic subdural hematoma. Egyptian J Neurosurg 2019;34(01):8–13
11 Regan JM, Worley E, Shelburne C, Pullarkat R, Watson JC. Burr hole washout versus craniotomy for chronic subdural hematoma: patient outcome and cost analysis. PLoS One 2015;10(01): e0115085
12 Wakai S, Hashimoto K, Watanabe N, Inoh S, Ochiai C, Nagai M. Efficacy of closed-system drainage in treating chronic subdural hematoma: a prospective comparative study. Neurosurgery 1990; 26(05):771–773
13 Markwalder TM, Steinsiepe KF, Rohner M, Reichenbach W, Markwalder H. The course of chronic subdural hematomas after burr-hole craniostomy and closed-system drainage. J Neurosurg 1981; 55(03):390–396
14 Drapkin AJ. Chronic subdural hematoma: pathophysiological basis for treatment. Br J Neurosurg 1991;5(05):467–473
15 Santarius T, Kirkpatrick PJ, Kolias AG, Hutchinson PJ. Working toward rational and evidence-based treatment of chronic subdural hematoma. Clin Neurosurg 2010;57:112–122
16 Mori K, Maeda M. Surgical treatment of chronic subdural hematoma in 500 consecutive cases: clinical characteristics, surgical outcome, complications, and recurrence rate. Neurol Med Chir (Tokyo) 2001;41(08):371–381
17 Erol FS, Topsakal C, Faik Ozveren M, Kaplan M, Tiftikci MT. Irrigation vs. closed drainage in the treatment of chronic subdural hematoma. J Clin Neurosci 2005;12(03):261–263
18 Lee JY, Ebel H, Ernestus RI, Klug N. Various surgical treatments of chronic subdural hematoma and outcome in 172 patients: is membranectomy necessary? Surg Neurol 2004;61(06):523–527, discussion 527–528
19 Ajaya KA, Varghese G, Litte T. Serie study of subacute and chronic subdural hematoma. J Neurol Stroke 2016;5(02):00168
20 Lee JK, Choi JH, Kim CH, Lee HK, Moon JG. Chronic subdural hematomas : a comparative study of three types of operative procedures. J Korean Neurosurg Soc 2009;46(03):210–214
21 Van Der Veken J, Duerinck J, Buyl R, Van Rompaey K, Herregodts P, D'Haens J. Mini-craniotomy as the primary surgical intervention for the treatment of chronic subdural hematoma–a retrospective analysis. Acta Neurochir (Wien) 2014;156(05):981–987
22 Mehta V, Harward SC, Sankey EW, Nayar G, Codd PJ. Evidence based diagnosis and management of chronic subdural hematoma: A review of the literature. J Clin Neurosci 2018;50(01):7–15
23 Seizeur R, Abed-Rabbo F, Obaid S, et al. Chronic subdural haematomas in elderly population. Neurosurgical aspects and focus on the single-burr hole technique performed under assisted local anaesthesia. Br J Neurosurg 2017;31(02):258–261
24 Surve RM, Bansal S, Reddy M, Philip M. Use of dexmedetomidine along with local infiltration versus general anesthesia for burr hole and evacuation of chronic subdural hematoma. J Neurosurg Anesthesiol 2017;29(03):274–280
25 Rodziewicz GS, Chuang WC. Endoscopic removal of organized chronic subdural hematoma. Surg Neurol 1995;43(06):569–572, discussion 572–573
26 Khadka NK, Sharma GR, Roka YB, et al. Single burr hole drainage for chronic subdural haematoma. Nepal Med Coll J 2008;10(04): 254–257
27 Wang W, Feng L, Bai F, Zhang Z, Zhao Y, Ren C. The safety and efficacy of dexmedetomidine vs sufentanyl in monitored anesthesia care during burr-hole surgery for chronic subdural

hematoma: A retrospective clinical trial. Front Pharmacol 2016; 7:410

28 Srivastava VK, Agrawal S, Kumar S, Khan S, Sharma S, Kumar R. Comparative evaluation of dexmedetomidine and propofol along with scalp block on haemodynamic and postoperative recovery for chronic subdural hematoma evacuation under monitored anesthesia care. Turk J Anaesthesiol Reanim 2018;46(01):51–56

29 Ashry A, Al-Shami H, Gamal M, Salah AM. Local anesthesia versus general anesthesia for evacuation of chronic subdural hematoma in elderly patients above 70 years old. Surg Neurol Int 2022;13 (13):13

30 Kidangan GS, Thavara BD, Rajagopalawarrier B. Bedside percutaneous twist drill craniostomy of chronic subdural hematoma: a single-center study. J Neurosci Rural Pract 2020;11(01):84–88

Long-term Changes of Infrared Thermography in Successful Decompression of Carpal Tunnel Syndrome: A Case Report

Alterações a longo prazo da termografia infravermelha na descompressão bem-sucedida da Síndrome do Túnel do Carpo: Relato de caso

Matheus Henrique Oliveira Ferreira[1] Pedro Neves Borges[1] Paulo Roberto Bastos Fontinha[1] Marcus André Acioly[1,2]

[1] Division of Neurosurgery, Fluminense Federal University (UFF), Niterói, RJ, Brazil
[2] Division of Neurosurgery, Federal University of Rio de Janeiro (UFRJ), RJ, Brazil

Address for correspondence Marcus André Acioly, MD, PhD, Division of Neurosurgery, Fluminense Federal University, Niterói, RJ, Brazil (e-mail: marcusacioly@yahoo.com.br).

Arq Bras Neurocir 2024;43(3):e204–e207.

Abstract

Introduction Infrared thermography (IRT) has demonstrated high diagnostic accuracy for carpal tunnel syndrome (CTS) diagnosis in previous studies. However, the recovery of the autonomic function after treatment for CTS is rarely addressed in the literature, especially on the long-term.

Case Presentation A 59-year-old lady sought treatment for a long-term history of numbness, tingling, and hand and arm pain. CTS was diagnosed by clinical and electrophysiological means. After 6 months of conservative treatment, surgical treatment was offered. Preoperative IRT was performed by static and dynamic evaluations immediately and 5 minutes after the cold challenge test using the FLIR C2 camera with accuracy of 2°C or 2%. Fingers were consistently colder (mean of 3.76° C), which clearly represented an autonomic dysfunction in the patient's hand. The patient underwent mini-open carpal tunnel decompression and did great postoperatively. One year after surgery, the patient was fully recovered and completely asymptomatic. IRT imaging showed a remarkable improvement of fingers temperature (mean of 3.36°C).

Conclusion Our long-term results confirmed that functional recovery occurred concomitantly to autonomic recovery, which was demonstrated by consistent improvement in fingers' temperature. IRT has a strong potential at the evaluation of patients with CTS for both diagnosis and follow-up.

Keywords
- carpal tunnel syndrome
- infrared thermography
- peripheral nerve
- cold challenge test

received
February 20, 2023
accepted
July 5, 2023
article published online
October 18, 2023

DOI https://doi.org/10.1055/s-0043-1774751.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Introdução A termografia infravermelha (IRT) demonstrou alta precisão diagnóstica para o diagnóstico da síndrome do túnel do carpo (STC) em estudos anteriores. No entanto, a recuperação da função autonômica após o tratamento para STC é raramente abordada na literatura, especialmente a longo prazo.

Apresentação do caso Uma senhora de 59 anos procurou tratamento para um histórico de longo prazo de dormência, formigamento e dor nas mãos e braços. A STC foi diagnosticada por meios clínicos e eletrofisiológicos. Após 6 meses de tratamento conservador, o tratamento cirúrgico foi oferecido. A IRT pré-operatória foi realizada por avaliações estáticas e dinâmicas imediatamente e 5 minutos após o teste de provocação pelo frio usando a câmera FLIR C2 com precisão de 2 °C ou 2%. Os dedos estavam consistentemente mais frios (média de 3,76 °C), o que claramente representava uma disfunção autonômica na mão da paciente. A paciente foi submetida a uma mini descompressão aberta do túnel do carpo e teve um ótimo desempenho no pós-operatório. Um ano após a cirurgia, a paciente estava totalmente recuperada e completamente assintomática. A imagem IRT mostrou uma melhora notável na temperatura dos dedos (média de 3,36 °C).

Conclusão Nossos resultados de longo prazo confirmaram que a recuperação funcional ocorreu concomitantemente à recuperação autonômica, o que foi demonstrado pela melhora consistente na temperatura dos dedos. A IRT tem um forte potencial na avaliação de pacientes com STC para diagnóstico e acompanhamento.

Palavras-chave

- síndrome do túnel do carpo
- termografia infravermelha
- nervo periférico
- teste de provocação pelo frio

Introduction

Carpal tunnel syndrome (CTS) is considered the most frequent nerve entrapment syndrome of the upper limb.[1] The combination of a clinically compatible history together with abnormal electrophysiological findings are generally considered for the diagnosis of CTS.[1] Conventional neurological examination includes testing of motor and sensory functions, as well as provocative tests.[1] Generally, median nerve sympathetic function is overlooked.[2–4] Such autonomic component controls peripheral vasomotor activity and, ultimately, regional temperature, which can be assessed by infrared thermography (IRT) as a result of peripheral nerve lesion.[2–4]

IRT has demonstrated high diagnostic accuracy for CTS diagnosis in previous studies.[2–4] However, the recovery of the autonomic function after treatment for CTS is rarely addressed in the literature,[2] especially on the long-term. Herein, we present a typical patient affected by CTS who underwent surgery and improved clinically. Such clinical improvement occurred concurrently to autonomic function improvement, which was represented by a temperature recovery in median nerve distribution area one year after surgery.

Case Report

History, Clinical Findings, and Diagnostic Assessment

A 59-year-old lady experienced bilateral paresthesias, tingling, numbness, and pain in median nerve territory for five years. Symptoms were worse on the right hand and at night, which sometimes forced her awakening. Neurological examination revealed hand weakness (Grade ⅘) without thenar wasting, decreased sensation at the radial fingers, and positive provocative testing (Tinel, Phalen, and Durkan signs). Cervical imaging showed degenerative findings. CTS diagnosis was confirmed by electrophysiological examination. The patient was referred for surgical consultation after six months of conservative treatment (physical therapy, medication, and splinting).

Therapeutic Intervention, Follow up-and Outcomes

Bilateral staged carpal tunnel release was planned, in the way that the right hand was operated on first. Before proceeding with surgery in the left hand, the patient was examined with IRT with the following protocol: after acclimatization in a special room with stabilized temperature, thermal images were carried on a FLIR C2 camera (FLIR Systems, OR USA) with 2°C or 2% accuracy, and positioned ∼50cm from the hand. The regions of interest (ROIs) were the thenar region of the affected hand (Sp1), and the distal phalanx of the thumb (Sp2), forefinger (Sp3) and middle finger (Sp4). Temperature gradients (ΔT) were defined as the difference between the ROIs of the thenar region and the fingers (TSp1-TSpi). The cold challenge test (CCT) was used to provoke sympathetic sensitization, as previously described.[5] In short, the patient had her right lower limb immersed in a thermal container with cold water (between 11°C and 15°C for 5 minute). Thermal images of the left hand were obtained after acclimatization, immediately after CCT, and 5 minutes after CCT.

At baseline, fingers were consistently colder (mean ΔT of 3.76°C). CCT generally increased such a gradient, which clearly represented an autonomic dysfunction in the patient's hand. The patient was then submitted to mini-open carpal tunnel release three months after the first

Table 1 Temperature gradients of the left hand obtained before and one year after surgery

	ΔT2 (°C)		ΔT3 (°C)		ΔT4 (°C)	
	Preop	Postop	Preop	Postop	Preop	Postop
Baseline	4.5	0	3.2	-0.1	3.6	1.3
Immediately after CCT	3.1	0.1	4	0.1	4.8	0.4
5-minute recovery after CCT	3.7	0.6	4.9	0	5	1.6

Abbreviations: CCT, cold challenge test; (ΔTi) is defined as TSp1, TSpi (°C); Preop, preoperative; Postop, postoperative.

surgery in an outpatient setting with mild sedation and local anesthesia. She made an uneventful recovery. After one year, the patient was asymptomatic with complete resolution of symptoms on the operative side. Thermal images were obtained on the long-term, thereby demonstrating clear improvement in temperature gradients from median nerve distribution area at baseline and after CCT evaluations. Thermal images and temperature parameters of the operated hand obtained before and after surgery are demonstrated on ►**Table 1** and ►**Fig. 1**. The patient gave informed consent for the publication of this manuscript.

Interpretation

The assumption behind using IRT for an entrapment neuropathy consists in assigning the obtained thermographic responses to dysfunction of the autonomic nervous system. From the physiological standpoint, sympathetic nerves exist on the outer layer of the median nerve and are prone to compression injuries.[3] These fibers can be especially vulnerable in entrapment neuropathies because they are thin and unmyelinated.[4] Also, since the heat of the muscle or bone do not affect dermal tissue because of the dermal depth in most

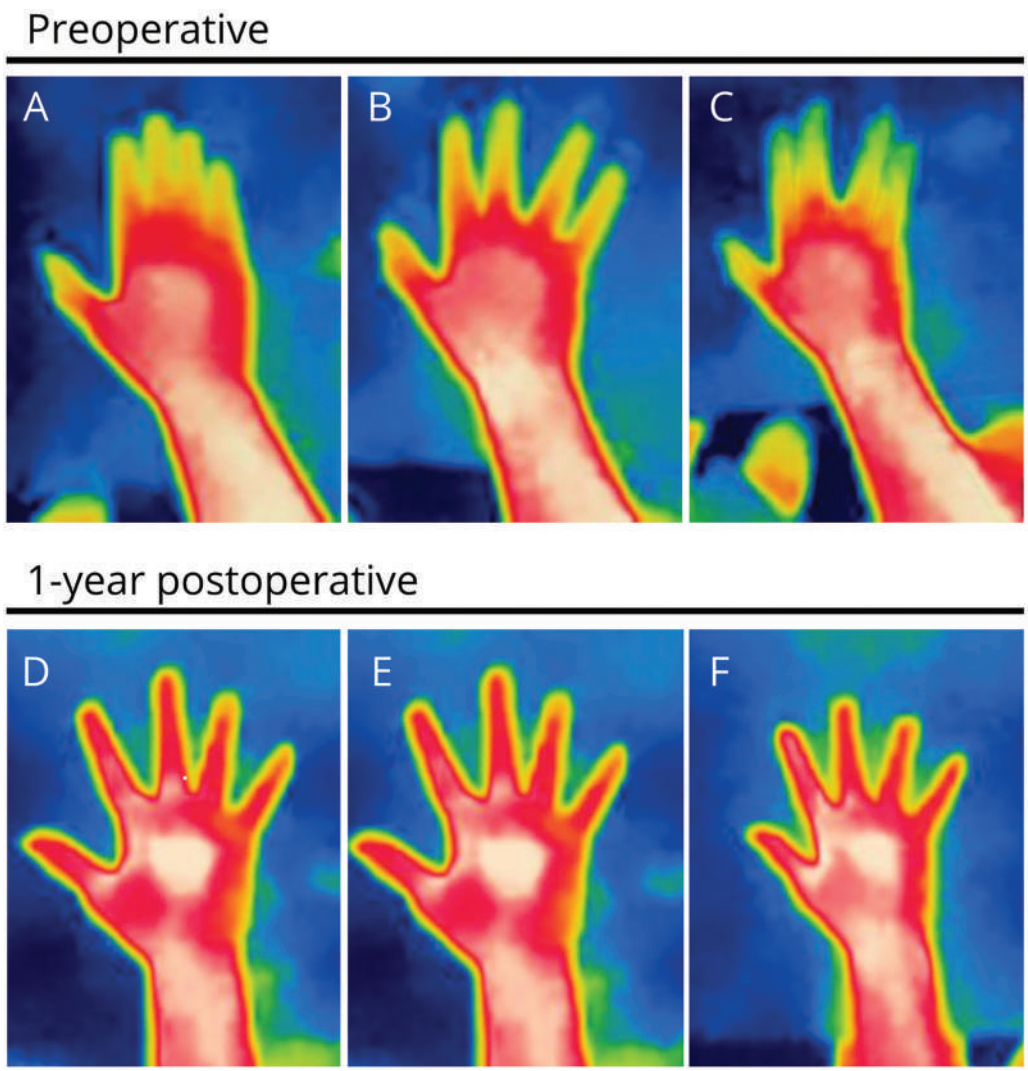


Fig. 1 Thermal images of the left hand obtained at baseline (A, D), immediately after the cold challenge test (B, E), and 5 minute after recovery (C,F) showing consistent improvement in fingers' temperature at the long-term (one year after surgery).

of the body, thermographic skin changes are presumed to occur as a result of the neurological status. Of note is that fingers are generally colder (mean of 0.3°C) than the thenar region and the shoulder in normal controls.[2,3]

The classical thermogram of a patient affected by CTS is a decreased area of vascular heating emission in median nerve territory.[3] In contrast, patients with severe or complete nerve injury generally demonstrate increased finger temperature.[3] The accuracy of IRT as a diagnostic method has been considered to be high, especially for patients with abnormal electrophysiological findings.[3,4] Major advantages of using IRT for CTS diagnosis are its non-invasiveness, it is less expensive than electrophysiological examination, and it can be used for screening, particularly in subclinical cases.[3]

IRT evaluations after carpal tunnel release are scarce in the literature. Baic et al. (X) studied 15 patients suffering from CTS and a control group. Thermographic examinations were performed before and 4 weeks after surgery. Baseline images demonstrated colder fingers (mean of 4.9° C), in comparison to thenar regions. Patients consistently recovered their hand temperatures after surgery (mean improvement of 4.5°C). At the end of their study, such temperatures were very similar to those observed in normal controls. Interestingly, the thumb presented a faster recovery in their evaluation.[2] This is not completely understood, since the authors suggested that the size of thenar musculature could have some impact in such recovery. Possibly, this is due to the position of the thumb, which is rather proximal than other fingers. Clinical outcomes were not cited, however.

Our thermographic results at baseline were in line with previous studies thereby suggesting the role of IRT in CTS diagnosis. Additionally, our long-term results confirmed that functional recovery occurred concomitantly to autonomic recovery. Interestingly, we have also observed that thumb thermal map presented the highest temperature improvement. CCT was found very useful to exacerbate autonomic dysfunction both before and after surgery. We are currently performing a study at our facility to confirm the findings we have demonstrated in this anecdotal case report.

In conclusion, we have evaluated the long-term changes of IRT in successful decompression of CTS demonstrating a consistent improvement in fingers' temperature, which might correlate to autonomic recovery. IRT has a strong potential at the evaluation of patients with CTS for both diagnosis and follow-up. However, more research is necessary to clarify the real usefulness of this technique.

Authors Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Matheus Henrique Oliveira Ferreira], [Pedro Neves Borges] and [Paulo Roberto Bastos Fontinha]. The first draft of the manuscript was written by [Marcus André Acioly] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None.

References

1 Wainner RS, Fritz JM, Irrgang JJ, Delitto A, Allison S, Boninger ML. Development of a clinical prediction rule for the diagnosis of carpal tunnel syndrome. Arch Phys Med Rehabil 2005;86(04): 609–618

2 Baic A, Kasprzyk T, Rżany M, et al. Can we use thermal imaging to evaluate the effects of carpal tunnel syndrome surgical decompression? Medicine (Baltimore) 2017;96(39):e7982

3 Herrick RT, Herrick SK. Thermography in the detection of carpal tunnel syndrome and other compressive neuropathies. J Hand Surg Am 1987;12(5 Pt 2):943–949

4 Ming Z, Zaproudina N, Siivola J, Nousiainen U, Pietikainen S. Sympathetic pathology evidenced by hand thermal anomalies in carpal tunnel syndrome. Pathophysiology 2005;12(02): 137–141

5 Bruehl S, Lubenow TR, Nath H, Ivankovich O. Validation of thermography in the diagnosis of reflex sympathetic dystrophy. Clin J Pain 1996;12(04):316–325

Delayed Posttraumatic Blepharocele: A Rare Case Report with Review of the Literature

Blefarocele Pós-traumática Tardia: Relato de caso raro com revisão da literatura

Amey P. Patankar[1] Shivani Chaudhary[2]

[1] Department of Neurosurgery, Baroda Medical College and SSG Hospital, Vadodara, Gujarat, India
[2] Department of Surgery, Baroda Medical College and SSG Hospital, Vadodara, Gujarat, India

Address for correspondence Amey P. Patankar, MBBS, MS, MCh, Department of Neurosurgery, Baroda Medical College and SSG Hospital, 703 Rajarshi Darshan Tower, Near Jalaram Mandir, Karelibag, Vadodara, Gujarat, 390018, India (e-mail: docapp@icloud.com).

Arq Bras Neurocir 2024;43(3):e208–e211.

Abstract

Though posttraumatic cerebrospinal fluid (CSF) rhinorrhea and otorrhea are fairly common, blepharocele and blepharoencephalocele are rare, with only 15 cases reported to date.

A 29-year-old female patient presented with a complaint of swelling of the right eyelid that had begun three months before. The patient had sustained a head injury 24 years prior to presentation.

Imaging studies revealed the presence of a craniopalpebral CSF fistula. The patient underwent successful surgical repair of the fistula with craniotomy and duroplasty by autologous fascia lata graft.

Delayed development of blepharocele 24 years after trauma is unusual, and, to our knowledge, the case herein reported is the first one in the literature.

Keywords

- blepharocele
- craniopalpebral fistula
- orbital encephalocele
- blepharoencephalocele

Resumo

Embora a rinorreia e a otorreia pós-traumática do líquido cefalorraquidiano (LCR) sejam bastante comuns, a blefarocele e a blefaroencefalocele são raras, com apenas 15 casos relatados até o momento.

Paciente do sexo feminino, 29 anos, apresentou queixa de edema em pálpebra direita com início há três meses. O paciente havia sofrido um traumatismo cranioencefálico 24 anos antes da apresentação.

Os exames de imagem revelaram a presença de fístula liquórica craniopalpebral. O paciente foi submetido com sucesso ao reparo cirúrgico da fístula com craniotomia e duroplastia com enxerto autólogo de fáscia lata.

O atraso no desenvolvimento de blefarocele 24 anos após o trauma é incomum e, até onde sabemos, o caso aqui relatado é o primeiro na literatura.

Palavras-chave

- blefarocele
- fístula craniopalpebral
- encefalocele orbital
- blefaroencefalocele

received
March 6, 2023
accepted
June 21, 2023
article published online
October 30, 2023

DOI https://doi.org/10.1055/s-0043-1776277.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Blepharocele is herniation of cerebrospinal fluid (CSF) into the eyelid. It is a rare condition, with only 15 cases reported to date.[1–15] It is usually traumatic in origin,[1–13] and very rarely congenital, without any history of trauma.[14,15] Traumatic blepharocele develops as a result of the breaching of an orbital bone fracture in the dura, leading to the formation of a craniopalpebral CSF fistula.

Case Presentation

A 29-year-old female presented with a complaint of swelling in the right eyelid that had begun three months before. The swelling appeared in the morning, upon waking up from sleep (►**Fig. 1**), and it gradually subsided as the day passed (►**Fig. 2**), only to reappear the next morning. The swelling was soft, with positive transillumination. The patient did not have any recent history of trauma or surgical procedures but had sustained a head injury 24 years before at the age of 5 years, for which she was managed conservatively. No radiological investigations were performed at the time of the injury.

A magnetic resonance imaging (MRI) scan of the orbit revealed a craniopalpebral CSF fistula in the right orbit (►**Fig. 3**). A computed tomography (CT) scan of the orbit showed a defect on the roof of the right orbit with irregular raised margins, suggestive of an old fracture (►**Fig. 4**).

Fundus examination and CSF manometry were performed to rule out raised intracranial pressure. The opening pressure of the CSF was of 12 cm of water, and the fundus examination was normal, without any signs of papilledema.

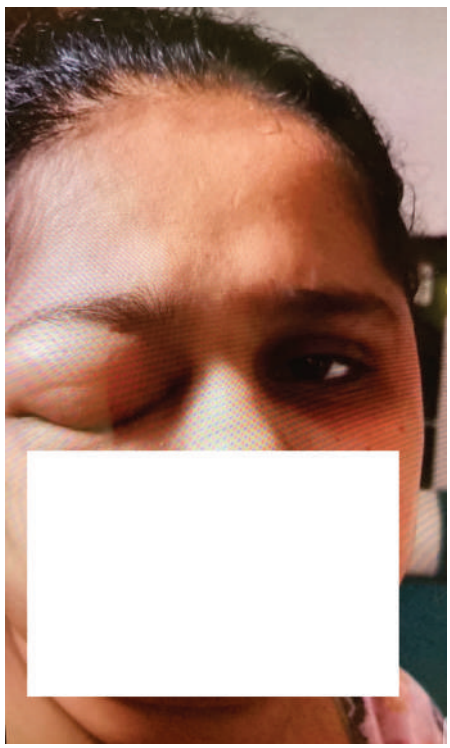


Fig. 1 Preoperative photograph of the patient in the morning showing right eyelid swelling.

Fig. 2 Preoperative photograph of the patient in the evening showing complete resolution of the right eyelid swelling.

The patient underwent surgical repair of the craniopalpebral CSF fistula under general anesthesia in the supine position. A right frontal craniotomy with an intradural subfrontal approach revealed that the gliotic brain tissue was adherent to the bony defect of the roof of the orbit. The gliotic brain tissue was separated from the bony defect, and the margins of the defect were defined. The irregular and raised bony edges of the roof of the orbit were flattened. The defect was repaired by autologous fascia lata graft, which was

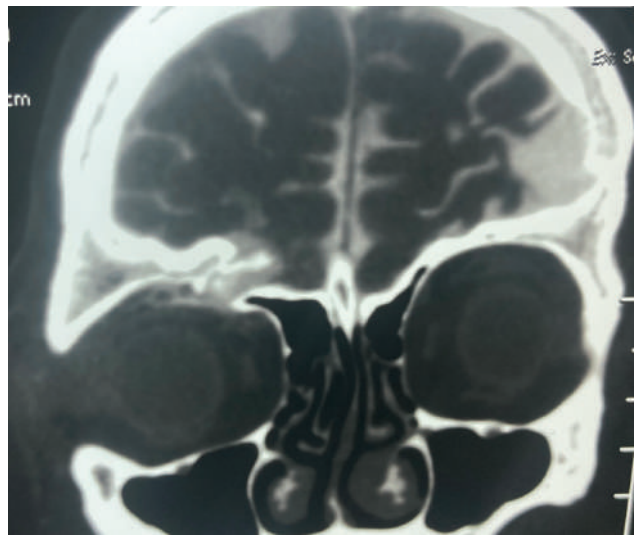


Fig. 3 T2-weighted magnetic resonance imaging scan of the brain in coronal view showing the craniopalpebral fistula.

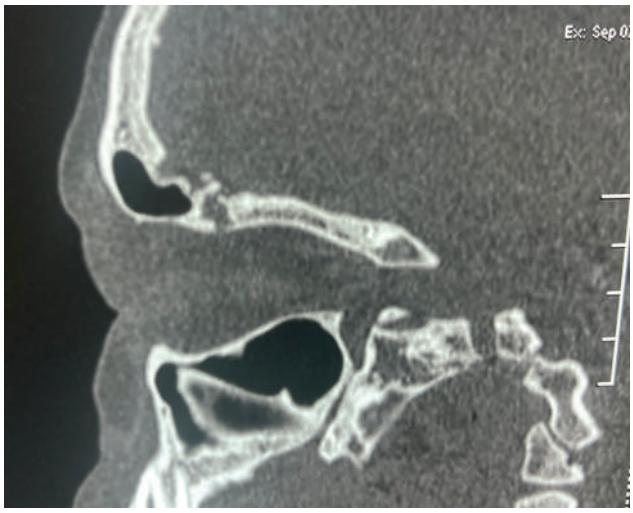


Fig. 4 Computed tomography scan of the brain and orbit showing the bony defect with irregular margins on the roof of the orbit.

anchored to the dura of the skull base by 2 stitches of 4-0 Vicryl suture (Ethicon, Inc., Raritan, NJ, United States). The postoperative course was uneventful, and in the early morning of the first postoperative day the eyelid swelling had disappeared (►**Fig. 5**). On the follow-up after 6 months, the patient remained asymptomatic (►**Fig. 6**)

Discussion

Cerebrospinal fluid fistulas complicate ~ 2% of all head injuries and ~ 12% to 30% of all skull base fractures;[11] CSF rhinorrhea and otorrhea are the most common forms of CSF fistulas after a head injury.

Fig. 5 Postoperative photograph of the patient in the morning of first postoperative day showing no eyelid swelling.

Fig. 6 Postoperative photograph of the patient six months after surgery showing no eyelid swelling.

Leakage of the CSF into the orbit (orbital encephalocele) is rare, and it can manifest as pseudolacrimation (CSF oculorrhea).[16–19] The rarity of craniopalpebral fistulas is due to the fact that the orbital walls are thicker and less fragile as compared with the thin bones of the frontal and ethmoidal sinuses and the cribriform plates.[4] Craniopalpebral fistulas are more commonly reported in children,[1,5,6,8,10,11,13,20] probably because their orbital walls are thinner. Additionally, frontal sinus agenesis has been hypothesized as one of the factors for the development of blepharoencephalocele.[2,9] Absence of the frontal sinus may enable the direct passage of CSF into the upper eyelid following a head injury. In the case herein reported, the frontal sinus was well developed (►**Fig. 4**).

The patient had right eyelid swelling, which was more intense the morning and gradually subsided as the day progressed. This is because the intracranial CSF pressure rises during the night in supine position, leading to more CSF egress into the eyelid through the fistulous tract. During the day, because of the upright posture, the decrease in intracranial pressure caused an outflow of CSF from the eyelid, leading to the disappearance of the swelling.

How the head injury sustained 24 years before led to blepharoencephalocele is a matter of conjecture. It is unlikely that that the defect was congenital, because its margins were irregular, rough and with raised edges, suggestive of callus formation after trauma. It is possible that the patient had sustained a fracture of the thin orbital roof at the time of the head injury, with entrapment of brain matter into the fracture. The pulsatile brain matter gradually eroded the periorbita,

leading to leakage of CSF into the upper eyelid. The case herein reported may be considered one of a small "internal growing skull fracture", which was not detected for 24 long years, as it was hidden from the external environment and not causing any orbital compression.

Diagnosis in this case was difficult, because craniopalpebral fistulas usually present within one to three months of trauma. Aspiration of CSF from the eyelid in such cases is strictly contraindicated, as it may cause meningitis. The disappearance of the swelling during the daytime and the history of trauma, though remote, provided a clue to the diagnosis, which was confirmed by imaging studies. The CSF manometry and fundus examination ruled out benign intracranial hypertension.

Though successful healing of the fistula by conservative means has been reported,[2,7,12] the treatment of this condition is almost always surgical, with repair of the fistula by pericranial or fascia lata grafts. Additional skull base repair by titanium mesh may be required in cases of large skull base defects.

Conclusion

Blepharocele, or craniopalpebral fistula, is rare, with only 15 cases reported to date. Cranioorbital and craniopalpebral fistulas should be suspected in patients with orbital fractures, in whom the posttraumatic orbital swelling or proptosis fails to resolve in two to three weeks. To the best of our knowledge, delayed presentation of blepharocele, 24 years after a head injury, has not been reported to date, this being the first such case.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Bagolini B. Leakage of spinal fluid into upper lid following trauma. AMA Arch Opthalmol 1957;57(03):454–456
2 Galzio RJ, Lucantoni D, Zenobii M, Grizzi LC. Traumatic craniopalpebral cerebrospinal fluid fistula. J Neurosurg Sci 1981;25(02):105–107
3 Garza-Mercado R, Aragon-Lomas J, Martinez-Garza J, Leal-Hernandez L. Cerebrospinal fluid blepharocele: an unusual complication of head injuries. Neurosurgery 1982;11(04):525–526
4 Bhatoe HS. Blepharocele after head injury. Skull Base 2002;12 (02):73–76
5 Arslantaş A, Vural M, Atasoy MA, Özsandik A, Topbaş S, Tel E. Posttraumatic cerebrospinal fluid accumulation within the eyelid: a case report and review of the literature. Childs Nerv Syst 2003;19(01):54–56
6 Bhatoe HS. Blepharocele following head injury in a child. Indian J Neurotrauma 2005;2(01):51–53
7 Borumandi F. Traumatic orbital CSF leak. BMJ Case Rep 2013;x: bcr2013202216
8 Chandra N, Ojha BK, Chandwani V, Srivastava C, Singh SK, Chandra A. A rare case of posttraumatic eyelid swelling: cerebrospinal fluid blepharocele. J Neurosurg Pediatr 2013;11(03):242–244
9 Govindaraju V, Bharathi R. Post-traumatic blepharocele in an adult. Sultan Qaboos Univ Med J 2013;13(03):E479–E481
10 Mishra A, Gupta DK, Gamangatti S, Sharma BS. Post-traumatic blepharocele: a rare manifestation of head injury. Neurol India 2014;62(05):568–570
11 Umerani MS, Bakhshi SK, Abbas A, Sharif S. Post Traumatic Transcalvarial Blepharoencephalocele: A Rare Entity. J Spine Neurosurg 2014;3:3
12 Soares A, Almeida C, Freitas C, Sales-Sanz M, Ribeiro S. Eyelid edema: a rare cause of a common sign. Case Rep Ophthalmol Med 2017;2017:9193706
13 Panigrahi AK, Senapati SB, Panda D, Panigrahi S. A Rare Case of Periorbital Edema and Conjunctival Prolapse Due to Traumatic Intraorbital CSF Leakage.
14 Germano RAS, Silva MV, Germano FAS, et al. Eyelid liquoric fistula secondary to orbital meningocele. Rev Bras Oftalmol 2015;74(01):46–48
15 Zurita M, Candanedo C, Moscovici S, Kaye AH, Spektor S. Spontaneous symptomatic orbital meningoencephalocele in an adult patient. Case report and review of the literature. J Clin Neurosci 2020;77:224–226
16 Apkarian AO, Hervey-Jumper SL, Trobe JD. Cerebrospinal fluid leak presenting as oculorrhea after blunt orbitocranial trauma. J Neuroophthalmol 2014;34(03):271–273
17 Salame K, Segev Y, Fliss DM, Ouaknine GE. Diagnosis and management of posttraumatic oculorrhea. Neurosurg Focus 2000;9 (01):e3
18 Joshi KK, Crockard HA. Traumatic cerebrospinal fluid fistula simulating tears. Case report. J Neurosurg 1978;49(01):121–123
19 Till JS, Marion JR. Cerebrospinal fluid masquerading as tears. South Med J 1987;80(05):639–640
20 Aggarwal A, Gupta AK, Aggarwal AK. Acute post-traumatic encephalocele in a child: CT and MRI features. BJR Case Rep 2016;2 (04):20150170

The Importance of Orthostatic Radiography in the Management of Thoracolumbar Fractures: Case Report

A importância do raio-X em ortostase no manejo das fraturas toracolombares: Relato de caso

Pedro Neves Fortunato[1] Yvens Barbosa Fernandes[1] Andrei Fernandes Joaquim[2]

[1] Department of Neurosurgery, Hospital Municipal Mario Gatti, Campinas, SP, Brazil
[2] Department of Neurology, Universidade de Campinas (UNICAMP), Campinas, SP, Brazil

Address for correspondence Pedro Neves Fortunato, MD, Department of Neurosurgery, Hospital Municipal Mario Gatti, Av. Prefeito Faria Lima, 340–Parque Itália, Campinas, SP 13036-902, Brazil (e-mail: pedronf95@gmail.com).

Arq Bras Neurocir 2024;43(3):e212–e216.

Abstract

Patients who are victims of traumatic injuries in the spine are evaluated by radiological protocols, as recommended by Advanced Trauma Life Support (ATLS), including a computed tomography (CT) scan with the patient in the decubitus position. Spine fractures considered *stable* with initial nonoperative management should be further evaluated with a standard simple plain radiograph in orthostasis and/or a magnetic resonance image (MRI), to exclude any associated ligament injury and avoid neurological damage caused by occult instabilities. We present an illustrative case with an injury diagnosed through orthostasis X-ray to discuss its importance in the management of thoracolumbar fractures.

Keywords
- thoracolumbar fracture
- orthostatic X-ray
- conservative management
- instrumented fusion

Resumo

Pacientes vítimas de lesões traumáticas na coluna são avaliados por protocolos radiológicos, conforme recomendado pelo Advanced Trauma Life Support (ATLS), incluindo uma tomografia computadorizada (TC) com o paciente em decúbito. Fraturas de coluna consideradas estáveis com tratamento inicial não operatório devem ser avaliadas posteriormente com uma radiografia simples padrão em ortostase e/ou uma ressonância magnética (RM), para excluir qualquer lesão ligamentar associada e evitar danos neurológicos causados por instabilidades ocultas. Apresentamos um caso ilustrativo com uma lesão diagnosticada por meio de raio-X em ortostase para discutir sua importância no tratamento de fraturas toracolombares.

Palavras-chave
- fratura toracolombar
- radiografia ortostática
- tratamento conservador
- fusão instrumentada

received
December 18, 2022
accepted
June 21, 2023
article published online
October 27, 2023

DOI https://doi.org/10.1055/s-0043-1776276.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Traumatic fractures of the thoracolumbar spine, specifically the thoracolumbar junction (T10–L2), represent the most affected site of spinal injuries in most studies due to the inherent biomechanical characteristics of the area—the junction of a mobile lumbar spine with a rigid thoracic spine.[1] The first radiological evaluation of these patients is usually made using simple plain radiographs. When a computed tomography (CT) scan is performed, up to 99% of diagnostic accuracy in detection of bone injuries can be achieved.[2] For this reason, CT scan is the most used and widespread radiological modality to diagnose spinal fractures.

The compression-type fractures of the AO Spine thoracolumbar classification system correspond to the majority of the injuries that affect the thoracolumbar spine; despite their high prevalence, there remains some controversies about the best treatment option (non-operative versus operative) for patients neurologically intact (N0) with *burst* fractures (currently classified as A3, or incomplete burst fractures, and A4, or complete burst fractures).[3,4] In this context, the final treatment is influenced by the anatomical characteristic of the fracture (degree of wedging of the vertebral body, degree of vertebral body comminution and segmental kyphosis), clinical status (pain or functional disability) and also surgeon's preferences.[5] In the absence of neurological damage, CT scan with the degree of canal compression and severe local kyphosis are potential characteristics related to failure of nonoperative management. Potential injury of the posterior ligamentous complex (PLC) may also influence the long-term outcome due to progressive kyphosis, leading to segmental deformity, pain, and neurological deterioration.[6]

Fractures considered stable, such as compression fractures and mild burst fractures (AO Spine type A) rarely need additional radiological evaluation after the CT scan.[7,8] Their management consists in thoracolumbar orthoses and analgesics that enable the patient to bear load of their own body weight during daily activities until vertebral healing.[6,9] However, some patients diagnosed with A3 and A4 fractures should not have be considered to have stable injuries when, in fact, they have an occult B2 fracture (AO Spine classification system – distraction fractures associated with posterior ligamentous complex injury),[10] which was not initially detected in the patient's exams in dorsal decubitus (without axial load) due to some postural reduction. We present an illustrative case to emphasize the importance of orthostatic simple, plain radiographs in detecting a hidden spine instability that had not been found in the conventional CT scan and how that fact impacted the case.

Methods

A 42 year-old male patient was admitted to the emergency department after a fall from a height of 10 m. Besides lacunar amnesia due to mild head injury, no other neurological function was affected—neurologically intact (N0). A spine CT scan revealed a thoracolumbar fracture at T12–A3 and L5–A0.[10]

►**Fig. 1** shows as sagittal CT image of an incomplete burst fracture (A3) at T12 without spinal dislocation (arrow).

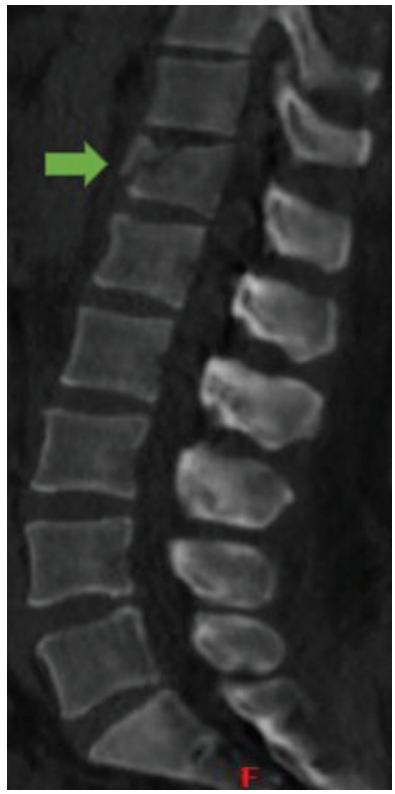


Fig. 1 Sagittal computed tomography.

Although the proposed initial treatment was nonoperative, a standing thoracolumbar simple, plain radiograph was performed and reported a clear increase of the interspinous distance (T11–T12), segment kyphosis (Cobb > 25°), and vertebral segment wedging (> 50%), along with severe back pain during the exam.

►**Fig. 2** shows an orthostatic simple plain lateral thoracolumbar spine radiograph with a clear spinal dislocation between T11 and T12, with increasing distance of the spinous

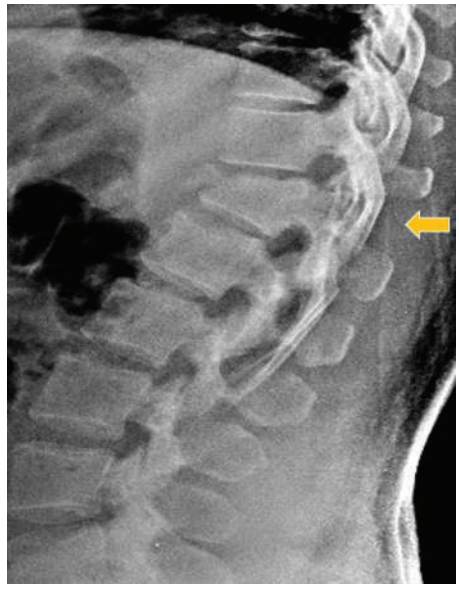


Fig. 2 Orthostatic simple, plain radiograph.

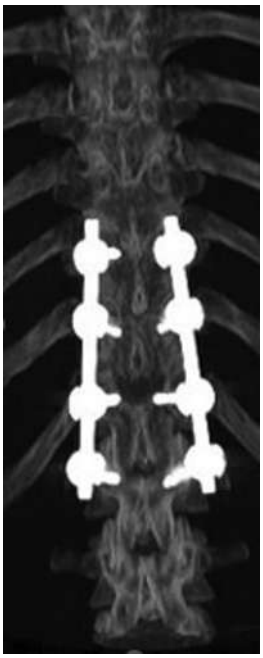


Fig. 3 Computed tomography reconstruction.

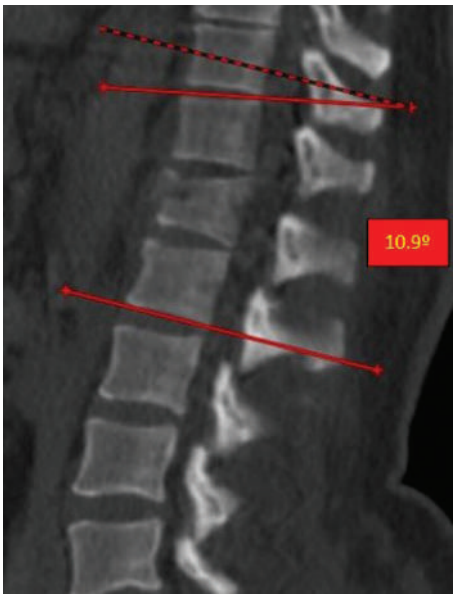


Fig. 4 Preoperative sagittal computed tomography scan showing kyphosis.

process (arrow). This injury should be better classified as a B2 injury with an A3 component of T12.

Based on this, a ligamentous failure was inferred, and we reclassified the injury as B2.[10] A thoracolumbar instrumented fusion was indicated and performed without complications. The procedure was uneventful, and the patient was discharged home 4 days later. After about 3 months, the patient returned to his job, without restrictions or additional medication for pain control.

►**Fig. 3** shows the postoperative CT scan of the reconstruction with a T10–11–12-L1 instrumented fusion with pedicle screws.

►**Fig. 4** shows the preoperative sagittal CT scan with a kyphosis angle between T11 and L1(red lines) of 10.9° in supine position.

►**Fig. 5** shows the orthostatic simple, plain lateral thoracolumbar spine radiograph with an increasing angle of the local kyphosis to 25.5° from T11 to L1 (red lines).

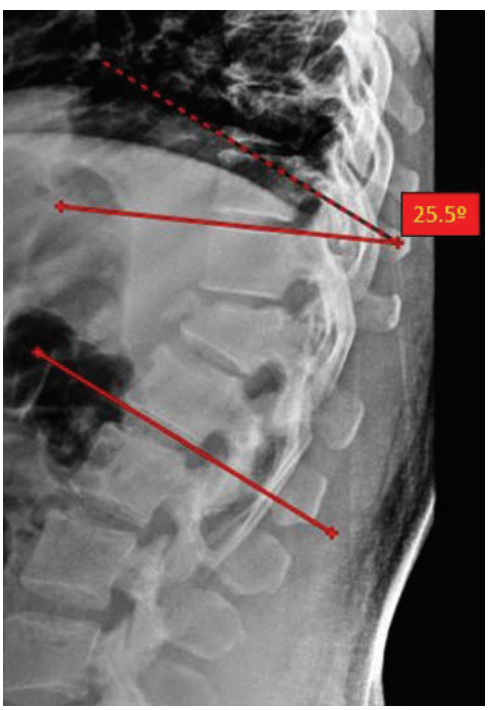


Fig. 5 Orthostatic simple, plain radiograph showing lateral local kyphosis.

Discussion

Clinical instability of the spine after a trauma occurs when the spinal ligaments and bones lose their ability to maintain normal alignment between vertebral segments while under a physiological load. Instability can lead to further injury, pain, or deformity, and can require further surgical stabilization.[11] Injuries to the posterior ligamentous complex (PLC) are often missed and may cause unexpected neurological deficits and complications. The diagnosis can be achieved using indirect signs of spinal radiographs and CT when the cuts are thinner (1–2 mm) with splaying of the spinous processes, avulsion of the superior or inferior margins of the spinous processes, widened facet joints, empty ("naked") facet joints, perched/dislocated facet joints, and vertebral translation/rotation, or with direct view of PLC injury using MRI.[4,12,13]

The use of the simple plain radiographies in the orthostatic position may be useful to obtain additional information for the evaluation of stability, especially at the level of controversial fractures.[14,15] Current trauma protocols are based in radiographs and decubitus CT scans that limit the visualization of soft tissues; therefore, PLC injuries may not be detected.[16,17]

Magnetic resonance imaging is the gold standard for detection of soft-tissue lesions or those[18,19] involving the

intervertebral disks and spinal ligaments.[20] It is also used to exclude occult injuries and helps to identify epidural space involvement or at the level of spinal cord.[1,21] The MRI protocol exam of the spine includes the sequences T1, T2, and short tau inversion recovery (STIR), especially the latter, which is particularly conspicuous to edema in the interspinous or supraspinous ligaments.[22] When MRI shows the rupture of the supraspinous ligament (SSL), one can infer PLC incompetence (signal *black-stripe* discontinuity).[23] The time interval defined as optimal between initial trauma and MRI should be less than 72 h. After that, the edema begins to reabsorb, and the hemorrhage reduces the sensitivity of imaging to reveal a ligament aggression. The hyperintensity at T2 is produced by edema or extravasation of blood into the injured extradural tissues, providing an excellent contrast medium and improving the definition of ligaments that are usually of low signal intensity on all imaging sequences.[24]

Some authors have proposed that injuries should be characterized as type A unstable when presenting segmental kyphosis values $\geq 25°$ and wedging of the vertebral body $\geq$ 50%—despite some criticism about their real significance in outcome.[21,25–27] They have also proposed that surgical intervention is considered in cases where a bone fragment (posterior wall disrupted) causes a canal compression greater than 50% of the its diameter.[28–30]

Considering its simplicity and low cost, we propose that an additional exam in the orthostatic position is included in patient radiological evaluation for burst fractures that are considered for nonoperative management.[28–30] An evaluation in decubitus may not be sensitive enough to detect posterior ligament instability in minor injuries.[31] The radiograph has the great convenience of being a less expensive equipment that is available in any healthcare or trauma center.[18] Of note, for those patients in whom clear spinal instability is documented in static exams as well as for those with neurological deficits (N2, N3, N4), standing or sitting X-rays should not be indicated due to the risk of additional neurological deficit. Finally, in our opinion, in an ideal scenario, both MRI and orthostatic radiographies can provide useful information for deciding the best treatment option in neurologically-intact patients with burst fractures.

Conclusion

An additional simple orthostatic plain radiography for patients with type A fractures who have a burst fractures without neurological deficits and are considered for nonoperative management should be an effective, available, and safe strategy to identify unstable lesions not clearly detected by radiological images in the supine position. An MRI is also recommended to detect potentially occult ligamentous injury. Further studies are necessary to study the safety and efficacy of this radiological modality in the management of thoracolumbar fractures.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Wood KB, Li W, Lebl DR, Ploumis A. Management of thoracolumbar spine fractures. Spine J 2014;14(01):145–164. Doi: 10.1016/j.spinee.2012.10.041Erratum in: Spine J. 2014 Aug 1;14(8): A18. Lebl, Darren S [corrected to Lebl, Darren R]. PMID: 24332321

2 Hauser CJ, Visvikis G, Hinrichs C, et al. Prospective validation of computed tomographic screening of the thoracolumbar spine in trauma. J Trauma 2003;55(02):228–234, discussion 234–235

3 Magerl F, Aebi M, Gertzbein SD, Harms J, Nazarian S. A comprehensive classification of thoracic and lumbar injuries. Eur Spine J 1994;3(04):184–201

4 Joaquim AF, Patel AA. Thoracolumbar spine trauma: Evaluation and surgical decision-making. J Craniovertebr Junction Spine 2013;4(01):3–9

5 Ferguson RL, Allen BL Jr. A mechanistic classification of thoracolumbar spine fractures. Clin Orthop Relat Res 1984;(189):77–88

6 Siebenga J, Leferink VJ, Segers MJ, et al. Treatment of traumatic thoracolumbar spine fractures: a multicenter prospective randomized study of operative versus nonsurgical treatment. Spine 2006;31(25):2881–2890

7 Keene JS. Radiographic evaluation of thoracolumbar fractures. Clin Orthop Relat Res 1984;(189):58–64

8 Dalinka MK, Kessler H, Weiss M. The radiographic evaluation of spinal trauma. Emerg Med Clin North Am 1985;3(03): 475–490

9 Alcalá-Cerra G, Paternina-Caicedo AJ, Díaz-Becerra C, Moscote-Salazar LR, Fernandes-Joaquim A. Orthosis for thoracolumbar burst fractures without neurologic deficit: A systematic review of prospective randomized controlled trials. J Craniovertebr Junction Spine 2014;5(01):25–32

10 Vaccaro AR, Oner C, Kepler CK, et al; AOSpine Spinal Cord Injury & Trauma Knowledge Forum. AOSpine thoracolumbar spine injury classification system: fracture description, neurological status, and key modifiers. Spine 2013;38(23):2028–2037

11 Benedetti PF, Fahr LM, Kuhns LR, Hayman LA. MR imaging findings in spinal ligamentous injury. AJR Am J Roentgenol 2000;175(03): 661–665

12 Bizdikian A, El Rachkidi R. Posterior Ligamentous Complex Injuries of the Thoracolumbar Spine: Importance and Surgical Implications. 2021

13 Schmidt OI, Gahr RH, Gosse A, Heyde CE. ATLS(R) and damage control in spine trauma. World J Emerg Surg 2009;4:9

14 Borba VC, et al. IMPORTANCE OF RADIOGRAPHY IN ORTHOSTATISM IN THE CONDUCT OF THORACOLOMBAR TRANSITION FRACTURES. Coluna/Columna 2021;20(01):60–63[online]

15 Cantor JB, Lebwohl NH, Garvey T, Eismont FJ. Nonoperative management of stable thoracolumbar burst fractures with early ambulation and bracing. Spine 1993;18(08):971–976. Doi: 10.1097/00007632-199306150-00004

16 Vaccaro AR, Lee JY, Schweitzer KM Jr, et al; Spine Trauma Study Group. Assessment of injury to the posterior ligamentous complex in thoracolumbar spine trauma. Spine J 2006;6(05): 524–528

17 Barcelos ACES, Joaquim AF, Botelho RV. Reliability of the evaluation of posterior ligamentous complex injury in thoracolumbar spine trauma with the use of computed tomography scan. Eur Spine J 2016;25(04):1135–1143

18 Haba H, Taneichi H, Kotani Y, et al. Diagnostic accuracy of magnetic resonance imaging for detecting posterior ligamentous complex injury associated with thoracic and lumbar fractures. J Neurosurg 2003;99(01):20–26

19 Wilmink JT. MR imaging of the spine: trauma and degenerative disease. Eur Radiol 1999;9(07):1259–1266

20 Parizel PM, Gielen JL, Vanhoenacker FM. 2007The spine in sports injuries: the cervical spine. In: Vanhoenacker FM, Maes M, Gielen JL (eds) Imaging of orthopedic sports injuries. SpringerBerlin, pp 377–390

21 Adams JM, Cockburn MI, Difazio LT, Garcia FA, Siegel BK, Bilaniuk JW. Spinal clearance in the difficult trauma patient: a role for screening MRI of the spine. Am Surg 2006;72(01):101–105
22 Linn M, Kim CW, Valente M. Compression fractures of the thoracic and lumbar spine. In: Zigler JE, Eismont FJ, Garfin SR, Vaccaro AR. Spine Trauma. Rosemont: American Academy of Orthopaedic Surgeons; 2011. p. 499–514.
23 Geck MJ, Yoo S, Wang JC. Assessment of cervical ligamentous injury in trauma patients using MRI. J Spinal Disord 2001;14(05): 371–377
24 Pizones J, Zúñiga L, Sánchez-Mariscal F, Alvarez P, Gómez-Rice A, Izquierdo E. MRI study of post-traumatic incompetence of posterior ligamentous complex: importance of the supraspinous ligament. Prospective study of 74 traumatic fractures. Eur Spine J 2012;21(11):2222–2231
25 Selden NR, Quint DJ, Patel N, d'Arcy HS, Papadopoulos SM. Emergency magnetic resonance imaging of cervical spinal cord injuries: clinical correlation and prognosis. Neurosurgery 1999; 44(04):785–792, discussion 792–793
26 Defino HLA, Fuentes AER, Remondi PH, Vallim EC. Tratamento conservador das fraturas da coluna toracolombar. Rev Bras Ortop 2000;35(08):301–308
27 Keynan O, Fisher CG, Vaccaro A, et al. Radiographic measurement parameters in thoracolumbar fractures: a systematic review and consensus statement of the spine trauma study group. Spine 2006;31(05):E156–E165
28 Keene JS, Lash EG, Kling TF Jr. Undetected posttraumatic instability of "stable" thoracolumbar fractures. J Orthop Trauma 1988;2 (03):202–211
29 Tsou PM, Wang J, Khoo L, Shamie AN, Holly L. A thoracic and lumbar spine injury severity classification based on neurologic function grade, spinal canal deformity, and spinal biomechanical stability. Spine J 2006;6(06):636–647
30 Garcia EB, Silva AL, Pimenta LG, et al. Fratura da coluna toracolombar do tipo explosão em T12/L1/L2. Rev Bras Ortop 2002;37(10):445–453
31 Petersilge CA, Pathria MN, Emery SE, Masaryk TJ. Thoracolumbar burst fractures: evaluation with MR imaging. Radiology 1995;194 (01):49–54

Charcot Arthropathy of the Shoulder Associated with Syringomyelia: A Report of 2 Cases

Artropatia do ombro de Charcot associada à Siringomielia: Relato de 2 casos

Mateus de Sousa Rodrigues[1] Camila Maciel Martins Coelho[2] Alexsandro da Silva Pereira[3] Fernanda Tavares Neto[4] Wanderson Ricardo Serapião da Silva[5] Heverty Rocha Alves Neto[5] Cícero do Juazeiro Job Maciel[6] Cícero Santos de Lima[5] Randson Ranilson Modesto Feitosa[3]

[1] Department of Neurosurgery, Universidade Federal do Vale do São Francisco (UNIVASF), Petrolina, PE, Brazil
[2] Nursing Department, Nursing Student Course, Universidade de Pernambuco (UPE), Petrolina, PE, Brazil
[3] Medical School Department, Universidade Federal do Vale do São Francisco (UNIVASF), Petrolina PE, Brazil
[4] Department of Pharmacy, Universidade Maurício de Nassau (UNINASSAU), Juazeiro do Norte, BA, Brazil
[5] Neurosurgical Department, Universidade Federal do Vale do São Francisco (UNIVASF), Petrolina, PE, Brazil
[6] Neurosurgical Department, São Camilo Hospital, Crato, CE, Brazil

Address for correspondence Mateus de Sousa Rodrigues, MD, Department Neurosurgery, Universidade Federal do Vale do São Francisco (UNIVASF), Av. José de Sá Maniçoba, s/n, Petrolina, PE 56330-400, Brazil (e-mail: mateus.kamloops@gmail.com).

Arq Bras Neurocir 2024;43(3):e217–e221.

Abstract

Charcot arthropathy of the shoulder caused by syringomyelia is a unusual degenerative disorder, frequently misdiagnosed and with few cases described in the literature. The diagnosis is made by clinical evaluation and radiological examinations with radiography and magnetic resonance imaging. However, the correct diagnosis and treatment is possible by carefully medical evaluation and can improve patient symptoms. Therefore, this study aimed to report two cases of Charcot arthropathy caused by syringomyelia. After achieving correct neurosurgical evaluation and magnetic resonance imaging, the diagnosis was made. The first case is a 53-year-old man with a click on his right shoulder for at least 12 months, associated with local edema, pain and limitation of joint range of motion. The second is a 45-year-old man with pain in the right upper limb and difficulty moving the joint for at least 24 months, associated with progressive worsening of the collection and edema in the ipsilateral upper limb. Posterior fossa decompression was performed, with symptoms relief after surgery. Posterior fossa decompression is a treatment that seems to be effective in reducing symptoms, especially when the diagnosis is early. However, this type of treatment still remains controversial, requiring further studies.

Keywords
- charcot arthropathy
- neurogenic arthropathy
- syringomyelia
- shoulder

Resumo

A artopatia de Charcot do ombro causada por siringomielia é uma doença degenerativa incomum, frequentemente subdiagnosticada e com poucos casos descritos na

received
November 15, 2022
accepted
June 21, 2023
article published online
May 10, 2024

DOI https://doi.org/10.1055/s-0044-1779437.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

literatura. O diagnóstico é feito pela avaliação clínica e exames radiológicos com radiografia e ressonância magnética. No entanto, o diagnóstico e tratamento corretos são possíveis mediante avaliação médica criteriosa e podem melhorar os sintomas do paciente. Portanto, este trabalho objetiva relatar dois casos de artropatia de Charcot causada por siringomielia. Após obter correta avaliação neurocirúrgica e ressonância magnética, o diagnóstico foi feito. O primeiro caso é um homem de 53 anos com clique no ombro direito por pelo menos 12 meses, associado a edema local, dor e limitação da amplitude do movimento articular. O segundo é um homem de 45 anos com dor em membro superior direito e dificuldade de movimentação articular há pelo menos 24 meses, associada a piora progressiva da coleção e edema em membro superior ipsilateral. A descompressão da fossa posterior foi realizada, com alívio dos sintomas após a cirurgia. A descompressão da fossa posterior é um tratamento que parece eficaz na redução dos sintomas, principalmente quando o diagnóstico é precoce. Porém, esse tipo de tratamento ainda permanece controverso, necessitando de mais estudos.

Palavras-chave
- artropatia de charcot
- artropatia neurogênica
- siringomielia
- ombro

Introduction

Charcot arthropathy is a chronic, normally progressive, degenerative disease caused by a sensorineural deficit that causes destruction of one or more joints.[1] Early diagnosis of Charcot neuroarthropathy is essential to prevent disease progression. Feet and ankle involvement are more prevalent in diabetics. The knee is most often affected in patients with syphilis. In syringomyelia, the shoulder and elbow joints are most commonly affected.[2] Syringomyelia is a chronic, progressive, and degenerative disorder of the spinal cord with formation and enlargement of a central fluid cavity (syrinx), affecting pain and thermal sensations, and generally sparing motor function and proprioception.[3] The etiology of the disease can be congenital, Arnold-Chiari malformation type I, communicating hydrocephalus, trauma, spinal tumors, infection, degeneration, or vascular disease.[4]

About 5% of Charcot arthropathy cases affect the shoulder joint.[5] Shoulder involvement in Charcot neuroarthropathy is commonly misdiagnosed and often confused with infections, rotator cuff tendon rupture, fractures, or pathological conditions with a better prognosis.[6] The most common cause of shoulder Charcot arthropathy is syringomyelia. A quarter of patients with syringomyelia develop neuropathic arthropathy.[7] In general, joint symptoms may appear earlier than neurological symptoms. Charcot arthropathy can develop insidiously as well as abruptly, causing rapid and progressive joint destruction.[3]

Despite the severity of Charcot arthropathy associated with syringomyelia if it is not diagnosed early, there are still few case reports on the subject, especially in cases related to syringomyelia. Thus, this study aimed to report two cases of Charcot arthropathy caused by syringomyelia.

Case Report

Case 1

A 53-year-old man from the rural area of Cabrobó, in the state of Pernambuco, Brazil, presented to the emergency department with clicking in the right shoulder for at least 12 months, associated with local swelling, pain, and limited range of joint motion. He was a former smoker (quit smoking more than 10 years prior) and had a previous prostate surgery due to urinary incontinence and benign prostatic hypertrophy. He denied high blood pressure and diabetes. Neurological examination showed predominance of right upper limb proximal monoparesis grade 3 muscle strength on the Medical Research Counsil (MRC) scale, and distal grade-4 muscle strength, abolished deep tendon reflexes in the upper right limb, hypotrophy of the suprascapular and lateral deltoid muscles, and inability to abduct above 90 degrees, ipsilaterally (►**Fig. 1**). A radiograph of the right shoulder in anteroposterior (AP) and profile views was performed, showing significant joint destruction, with

Fig. 1 Patient unable to abduct upper right limb of the arm from 90 degrees.

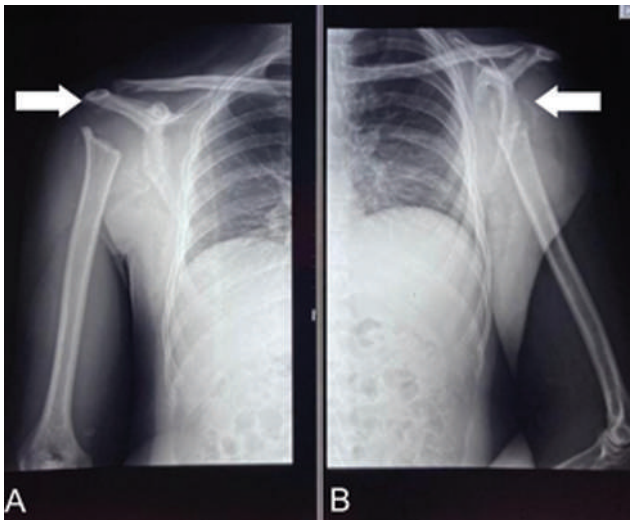


Fig. 2 Radiograph of upper limbs on coronal sections, showing destruction and absorption of the humeral head.

resorption of the head of the right humerus (►**Figs. 2A** and **2B**). The hypothesis of neoplasia and Charcot neuroarthropathy was raised, and magnetic resonance imaging (MRI) of the shoulder and cervical spine was requested. Right shoulder MRI showed bone destruction of the humeral head, with a liquid collection measuring $\sim 7.0 \times 4.7$ cm in the adjacent soft tissues (►**Fig. 3**). Cervical spine MRI showed syringomyelic cavity extending from the C2 to the T3 level and diffuse degenerative disc disease predominantly at the C5-to-T1 level (►**Fig. 4**). Neurosurgical treatment was proposed for occipitocervical decompression, but the patient refused the procedure, even though he was aware of the risks of possible neurological worsening. He is currently undergoing conservative treatment of neuroarthropathy with neuroleptics and non-steroidal analgesics.

Case 2

A 45-year-old man, a truck driver, from Salgueiro, in the state of Pernambuco, Brazil, arrived at the neurosurgical department with pain in the right upper limb and difficulty in joint motion for at least 24 months, associated with progressive worsening collection and edema in the ipsilateral upper

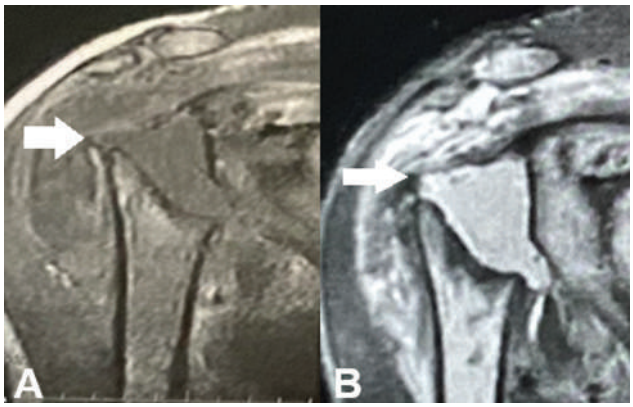


Fig. 3 Magnetic resonance imaging (MRI) of the right shoulder in T1- (A) and T2-weighted (B) sequence, in sagittal view, showing bone destruction of the humeral head with adjacent fluid collection.

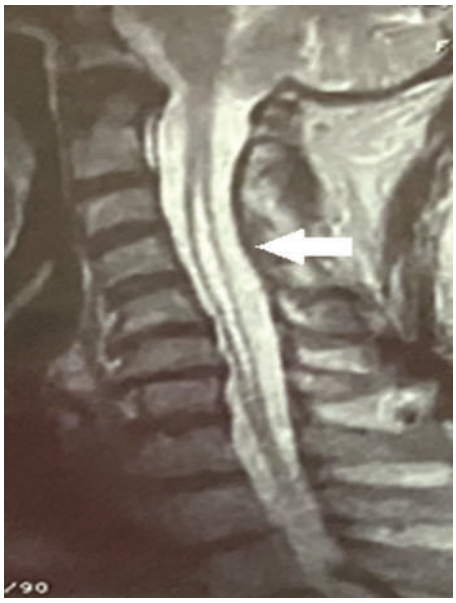


Fig. 4 Magnetic resonance imaging (MRI) of the cervical spine in T2-weighted sequence, in sagittal section, showing extensive syringomyelic cavity extending from the C2 to the T3 level.

limb. He also presented paresthesia, loss of strength, and inability to abduct the right upper limb (►**Fig. 5A**). He denied high blood pressure, smoking, or diabetes. He was referred to an orthopedist, who performed a puncture of the brachial collection. Laboratory analysis showed a nonspecific chronic inflammatory process. The orthopedist proceeded with corticosteroid infiltration and immunosuppressive treatment, with no improvement. On neurological examination, he had grade-3 strength (MRC scale) in the right upper limb, signs of hypotrophy in the deltoid muscle, and hyporeflexia grade 1 (National Institute of Neurological Disorders and Stroke scale) in the ipsilateral upper limb. The deep tendon reflexes in the other limbs were grade 3 on the National Institute of Neurological Disorders and Stroke scale. He was unable to abduct the right upper limb from 45 degrees. Humeral radiography showed complete destruction of the right humeral head with resorption and signs of a local inflammatory reaction (►**Fig. 6**). Right shoulder MRI showed marked heterogeneous fluid distension of the glenohumeral joint cavity, associated with destruction of the humeral head, glenoid and rotator cuff tendons, compatible with erosive inflammatory arthropathy (►**Fig. 7**). Cervical spine MRI showed mild invagination of the cerebellar tonsils through the foramen magnum, signs of diffuse degenerative disc disease, and extensive cervical hydrosyringomyelia from C1 to T2 (►**Fig. 8**). The right upper limb ultrasound showed a homogeneous collection involving the humerus, measuring $\sim 7.6 \times 7.0 \times 6.6$ cm ($186\,cm^3$) on its anterior view and $7.6 \times 7.0 \times 6.1$ on its posterolateral view ($172\,cm^3$). Thus, dissection of the biceps brachii muscle through the anterior collection (~ 3 cm above the elbow) was performed. The hypothesis of Charcot neuroarthropathy secondary to syringomyelia associated with humoral factors and chronic inflammatory response was raised. Neurosurgical treatment was performed for posterior fossa decompression, with

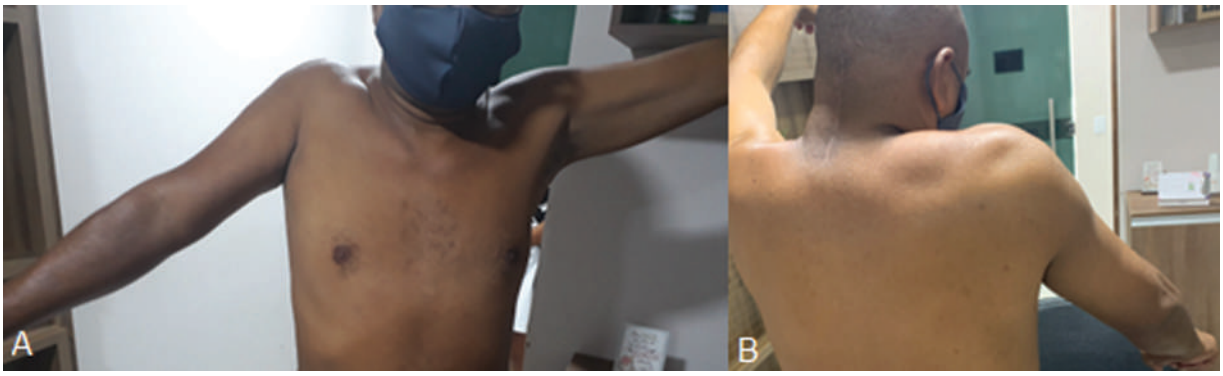


Fig. 5 Patient unable to elevate the right upper limb above 45 degrees before neurosurgical treatment (A); After posterior occipitocervical decompression (B).

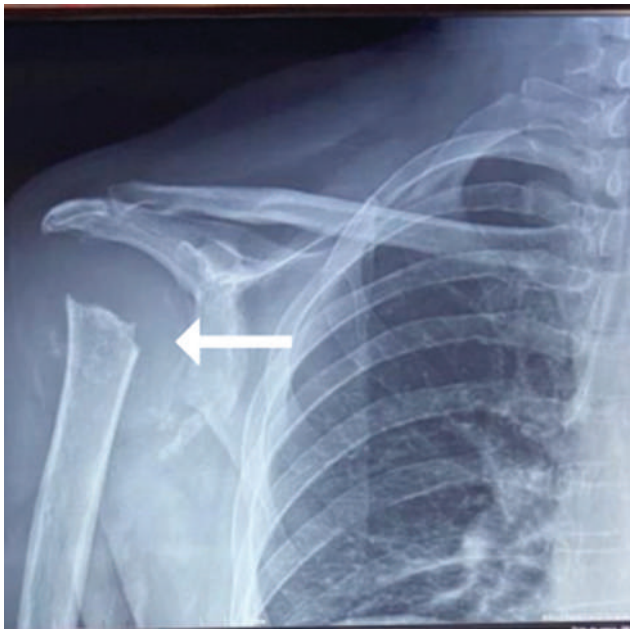


Fig. 6 Right upper limb radiograph on AP view, showing destruction and absorption of the humeral head.

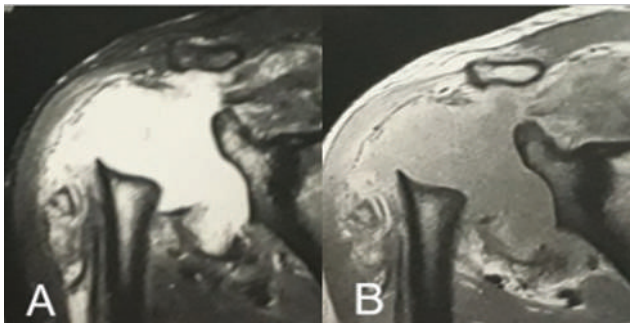


Fig. 7 Magnetic resonance Imaging of the right shoulder in T2-weighted (A) and short tau inversion recovery (STIR) (B) sequence, in sagittal view, showing destruction of the humeral head, glenoid and rotator cuff tendons, with a voluminous adjacent fluid collection.

suboccipital craniectomy, C1 vertebral arch resection and duraplasty. After surgery, the patient had complete resolution of the inflammatory collection of the right brachial soft tissues and improvement in distal muscle strength (grade 4 on the MRC scale). Currently, the patient maintains the neurological condition and no progression of osteoarticular disease of the humerus (►**Fig. 5B**).

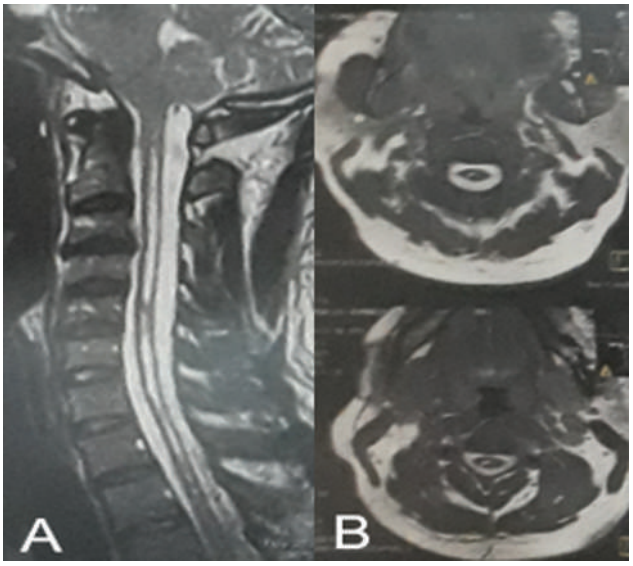


Fig. 8 Cervical spine magnetic resonance imaging in T2-weighted sequence, in sagittal (A) and axial (B) sections, showing extensive hydrosyringomyelia at the C1-to-T2 level.

Discussion

Neuropathic arthropathy was initially described by Mitchell in 1831, being fully characterized for the first time in 1868 by Jean-Martin Charcot, correlated, at the time, with neuropathy induced by tabes dorsalis (neurosyphilis). The first patient with neuropathic arthropathy caused by syringomyelia was described by Sokoloff in 1892.[8] Charcot arthropathy in the shoulder is a progressive joint degeneration that develops over years and is usually diagnosed only in advanced stages of neurological diseases, the main one being syringomyelia of the cervical segments of the spinal cord.[9]

In syringomyelia, central fluid cavity present in the spinal cord causes progressive destruction of the shoulder joint either by compression effects or by abnormal conduction.[10]

Approximately 20 to 30% of patients with syringomyelia develop a secondary arthropathy of the shoulder.[7] Syringomyelia is a rare disease that causes signs and symptoms such as massive bone loss, high inflammation, and neurological abnormalities such as weakness, loss of pain sensation, and arthropathy. In general, the affected shoulder presents a progressive degeneration of the humeral head and glenoid.[5]

The pathophysiology of neuropathic arthropathy is not completely proven, and there are two commonly accepted theories: neurovascular and neurotraumatic. The neurotraumatic theory claims that joint destruction is caused by repeated microtrauma, as a consequence of loss of proprioceptive and peripheral sensitivity resulting in macroscopic injuries such as fractures, dislocations, and joint deformities. The neurovascular theory suggests that peripheral neuropathy increases bone blood flow causing greater bone resorption and osteopenia by osteoclasts. Fragile bones are more susceptible to fractures, lesions, and joint destruction. Thus, it is believed that the junction of these two processes is responsible for the progression of the disease.[1,3,5]

Early diagnosis is essential to prevent progressive joint destruction, since treatment is based on the management of syringomyelia. Magnetic resonance imaging is the gold standard for the diagnosis of syringomyelia. The progression of the disease can vary from insidious cases, in which the patient is asymptomatic or with few symptoms, to rapid progressions.[6] The purpose of treatment for patients with neuropathic arthropathy is to slow the progression of the underlying disease and preserve joint functionality.[11] Conservative treatment consists of immobilizing the joint using orthosis and physical therapy to prevent further episodes of trauma. Pharmacological treatment is performed with nonsteroidal anti-inflammatory drugs (NSAIDs) to decrease synovial inflammation. Bisphosphonates and calcitonin are used to reduce osteoclastic activity.[12] In the case of surgical treatment, arthroplasty or arthrodesis is contraindicated for most cases considering the high failure rates due to muscle weakness. The central goal of neurosurgical treatment is to prevent cavity enlargement and damage to the remaining parts of the spinal cord caused by syringomyelia.[5]

Conclusion

Charcot arthropathy is a differential diagnosis of pain, swelling and limited range of motion in the shoulder joint. In patients with an unusual presentation of soft-tissue diseases, in order not to miss the disorder diagnosis, craniocervical MRI scan should be done to evaluate the presence of syringomyelia, in which the mainstay treatment is posterior fossa decompression. The correct diagnosis and treatment are possible by careful medical evaluation, and it can improve patient symptoms.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Wukich DK, Sung W. Charcot arthropathy of the foot and ankle: modern concepts and management review. J Diabetes Complications 2009;23(06):409–426
2 Kim DH. Charcot Shoulder in a Patient With Tetraplegia. PM R 2016;8(01):82–84
3 Klekamp J. How Should Syringomyelia be Defined and Diagnosed? World Neurosurg 2018;111:e729–e745
4 Fernández AA, Guerrero AI, Martínez MI, et al. Malformations of the craniocervical junction (Chiari type I and syringomyelia: classification, diagnosis and treatment). BMC Musculoskelet Disord 2009;10(Suppl 1, Suppl 1)S1
5 Rickert MM, Cannon JG, Kirkpatrick JS. Neuropathic Arthropathy of the Shoulder: A Systematic Review of Classifications and Treatments. JBJS Rev 2019;7(10):e1–e1
6 Alai A, Reddy CG, Amrami KK, Spinner RJ. Charcot arthropathy of the shoulder associated with typical and atypical findings. Clin Anat 2013;26(08):1017–1023
7 Nacir B, Arslan Cebeci S, Cetinkaya E, Karagoz A, Erdem HR. Neuropathic arthropathy progressing with multiple joint involvement in the upper extremity due to syringomyelia and type I Arnold-Chiari malformation. Rheumatol Int 2010;30(07):979–983
8 Yablon CM, Duggal N, Wu JS, Shetty SK, Dawson F, Hochman MG. A review of Charcot neuroarthropathy of the midfoot and hindfoot: what every radiologist needs to know. Curr Probl Diagn Radiol 2010;39(05):187–199
9 Chakraborty PP, Datta S, Ray S, Bhattacharjee R, Chowdhury S. Unilateral neuropathic arthropathy of the shoulder secondary to syringomyelia: Diagnostic challenges. World J Clin Cases 2015;3(12):1017–1020
10 Jones J, Wolf S. Neuropathic shoulder arthropathy (Charcot joint) associated with syringomyelia. Neurology 1998;50(03):825–827
11 Petrova NL, Edmonds ME. Medical management of Charcot arthropathy. Diabetes Obes Metab 2013;15(03):193–197
12 Rastogi A, Bhansali A, Jude EB. Efficacy of medical treatment for Charcot neuroarthropathy: a systematic review and meta-analysis of randomized controlled trials. Acta Diabetol 2021;58(06):687–696

Ventriculovesical Shunting in a Patient with Leptomeningeal Carcinomatosis: An Alternative to VP Shunts. A Technique Report

Derivação ventriculovesical em paciente com Carcinomatose Leptomeníngea: Uma alternativa às DVPs. Relato de técnica

Luiz Henrique Vargas de Andrade[1] João Pedro Motter de Carvalho[1] Arthur Garani Narciso[1] Alexandre Rossato Félix[2] Alisson Fucio[3] Leonardo Christiaan Welling[4] Nicolas N. Rabelo[5] Eberval Gadelha Figueiredo[5]

[1] Medicine Department, Faculty of Medicine, Universidade Estadual de Ponta Grossa, Ponta Grossa, PR, Brazil
[2] Neurological Surgery Department, Hospital Geral Unimed, Ponta Grossa, PR, Brazil
[3] Urologic Surgery Department, Hospital Geral Unimed, Ponta Grossa, PR, Brazil
[4] Neurological Surgery Department, Faculty of Medicine, Universidade Estadual de Ponta Grossa, Ponta Grossa, PR, Brazil
[5] Department of Neurology, Neurosurgery Service, Faculty of Medicine, Hospital das Clínicas, Universidade de São Paulo, São Paulo, SP, Brazil

Address for correspondence Luiz Henrique Vargas de Andrade, Medical student, Department of Medicine, Universidade Estadual de Ponta Grossa, PR, Brazil (e-mail: luizhva00@gmail.com).

Arq Bras Neurocir 2024;43(3):e222–e225.

Abstract

Leptomeningeal carcinomatosis (LC) is a rare but serious complication when cancer cells infiltrate the meninges. It is most commonly associated with breast cancer, but only 5% of breast cancer patients develop it. Leptomeningeal carcinomatosis typically presents with headaches, mainly due to hydrocephalus, and the diagnosis involves a cytological analysis of cerebrospinal fluid (CSF) and/or magnetic resonance imaging (MRI) scans. The treatment of LC consists of a combination of intra-CSF chemotherapy, systemic therapy, radiation therapy, and/or supportive care, including CSF drainage. In the case herein reported, a technique known as ventriculovesical shunting was performed on a female patient with LC and breast cancer who had hydrocephalus due to this condition. This procedure is not as common as ventriculoperitoneal shunts, which can lead, in this case, to serious complications such as peritoneal carcinomatosis.

Keywords
- meningeal carcinomatosis
- neoplasm metastasis
- hydrocephalus
- cerebrospinal fluid shunts
- neurosurgery

received
March 8, 2023
accepted
September 13, 2023
article published online
May 2, 2024

DOI https://doi.org/10.1055/s-0043-1777754.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Carcinomatose leptomeníngea (CL) é uma complicação infrequente, porém séria, que ocorre quando células cancerígenas infiltram as meninges. É mais comumente associada ao câncer de mama, mas apenas 5% dos pacientes com câncer de mama a desenvolvem. A CL apresenta-se tipicamente com dores de cabeça decorrentes principalmente da hidrocefalia, e o diagnóstico envolve uma análise citológica do líquido cefalorraquidiano (LCR) e/ou ressonância magnética (RM). O tratamento da CL envolve uma combinação de quimioterapia intra-LCR, terapia sistêmica, radioterapia e/ou cuidados de suporte, incluindo a drenagem do LCR. No caso aqui relatado, realizou-se uma técnica conhecida como derivação ventriculovesical em uma paciente feminina com CL e câncer de mama que tinha hidrocefalia em decorrência desta situação. Este procedimento não é tão comum em comparação com as derivações ventriculoperitoneais, as quais, nesse caso, podem levar à carcinomatose peritoneal.

Palavras-chave

- carcinomatose meníngea
- metástase neoplásica
- hidrocefalia
- derivações do líquido cefalorraquidiano
- neurocirurgia

Introduction

Leptomeningeal carcinomatosis (LC) occurs when a solid primary tumor infiltrates the meninges, including the pia mater, arachnoid, and subarachnoid space. This rare complication of breast cancer affects approximately 5% of patients. Given the high occurrence of breast cancer globally, in terms of sheer numbers, it is the most prevalent cause of LC.[1]

Patients with LC usually have a history of cancer, and most of them have already been diagnosed with metastatic disease. The signs and symptoms commonly observed include headache (80%), nerve pain that radiates from the spine, deficiencies in cranial nerves, visual loss, loss of hearing, seizures, and a condition known as cauda equina syndrome. Nausea, vomiting, headaches that worsen with changes in position, and even drowsiness, are symptoms associated with obstructive or communicative hydrocephalus, which may affect more than half of patients with LC due to impairment of the flow of cerebrospinal fluid (CSF). An additional potential clinical manifestation is the development of a new psychiatric disorder.[2,3]

The diagnosis is confirmed through positive (malignant) CSF cytology (gold standard), radiological evidence (nodular changes on computed tomography [CT] or magnetic resonance imaging [MRI] scans) that matches clinical observations, and symptoms indicating CSF involvement in a patient who has a known malignancy.[4,5]

The primary management goals for LC are to improve the neurological function and quality of life of the patients, prevent any further deterioration of neurological symptoms, and ultimately extend their lifespan. This may include radiation therapy, the use of bevacizumab, and ventriculoperitoneal shunt placement. In numerous cases, opting for a palliative and comfort-oriented approach may be appropriate, even starting from the initial diagnosis of leptomeningeal disease.[6,7]

Regarding CSF shunts, the current body of literature describes the possibility of diversion procedures in as many as 36 different sites, including areas such as the mastoid bone, the pleura, the right atrium, the peritoneum, the urinary tract (UT), and the fallopian tubes.[8] According to the literature, the UT may be considered a potential alternative to divert the CSF when the peritoneum or atrium is unavailable.[8,9] The primary advantage of using the UT as a diversion pathway for the CSF is that it does not rely on the absorption properties of the tissue, which is a factor in the case of the peritoneum. Moreover, the choice of this anatomical site for CSF diversion is based on elimination via micturition instead of absorption.[9,10]

Case Report

A 40-year-old female patient had been under oncological follow-up for breast carcinoma for 6 months. Due to the altered level of consciousness, nausea, and vomiting, a brain MRI scan was requested, which showed diffuse leptomeningeal inflammatory tissue in the posterior fossa (►**Figure 1**) with perineural extension, as well as in the supratentorial compartment, notably in the left frontotemporal region, with mild infiltration of the parenchyma edema and

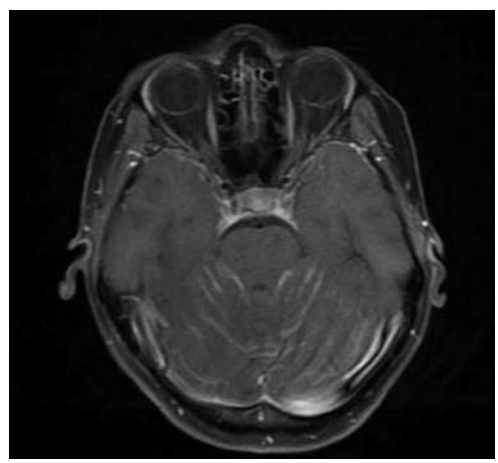


Fig. 1 Contrast-enhanced inflammatory tissue covering the leptomeningeal surface, mainly of the posterior fossa between the cerebellar folia, notably in the upper portion of the cerebellar vermis and mesencephalic aqueduct, with some areas of parenchymal infiltration causing local edema.

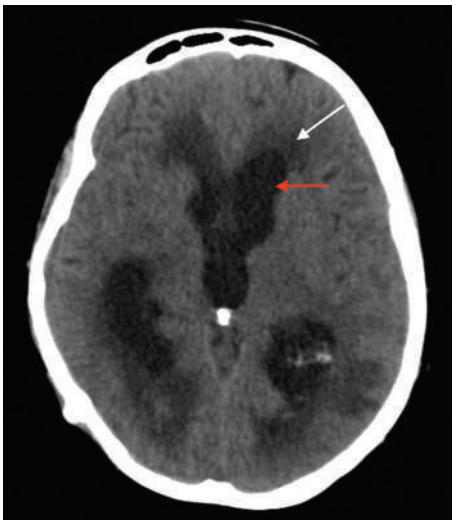


Fig. 2 Computed tomography (CT) scan showing hydrocephalus (white arrow) and transependymal edema (red arrow)

hydrocephalus (►**Figure 2**). Given the clinical context, the possibility of meningeal carcinomatosis, among other inflammatory and infectious diseases, was considered. Therefore, we decided to initiate radiation therapy.

Before the end of the radiation therapy, the patient was admitted to the emergency department with a sudden decreased level of consciousness. Thus, a brain CT scan showed supratentorial hydrocephalus and signs of transependymal transudation. Initially, external ventricular drainage was performed, and the definitive treatment was postponed until a discussion was held with the oncological team. Based on the clinical context, conditions, and prognosis, ventriculovesical shunting with the interposition of a low-pressure valve was proposed.

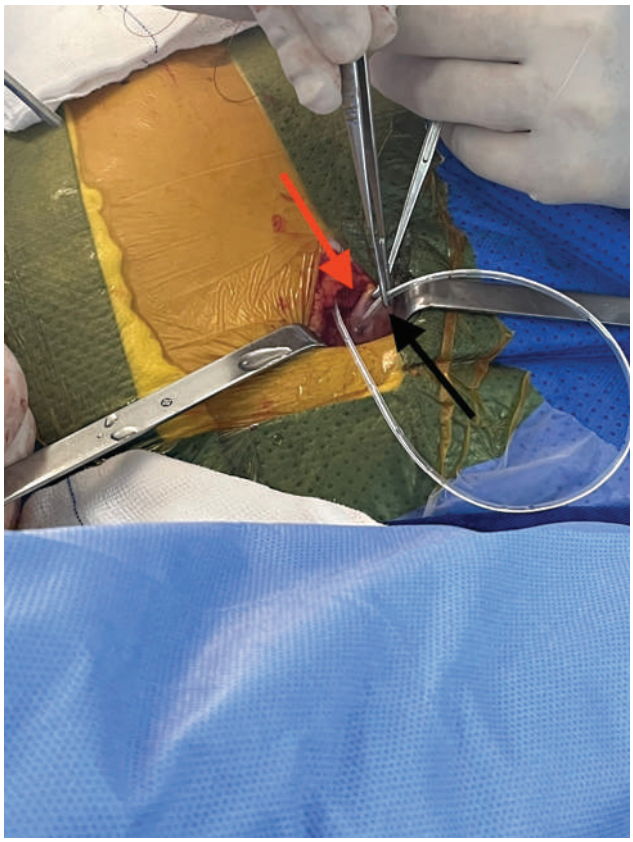


Fig. 3 A punctiform cystostomy (red arrow) is performed. The distal catheter is introduced for 7 cm to 8cm (black arrow).

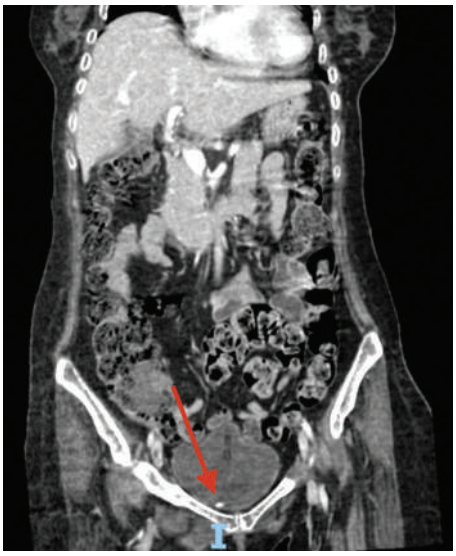


Fig. 4 Abdominal CT scan (coronal view): the distal catheter inside the bladder (red arrow).

The technique for the placement of the ventriculovesical shunt follows the same principles as those of ventriculoperitoneostomy. The patient must have an indwelling urinary catheter, and it must be open. A median suprapubic incision and tunneling of the subcutaneous tissue communicate with the cranial incision. The bladder wall is identified and repaired with a catgut suture. A punctiform cystostomy is performed. The distal catheter is introduced for 7 cm to 8cm, and the repair point is used to fix the catheter on the bladder wall (►**Figure 3**). Closure is performed conventionally, with sutures in layers. For the evaluation of the correct positioning of the urinary catheter, the patient undergoes an abdominal CT (►**Figures 4** and **5**). The indwelling bladder catheter is maintained for five days.

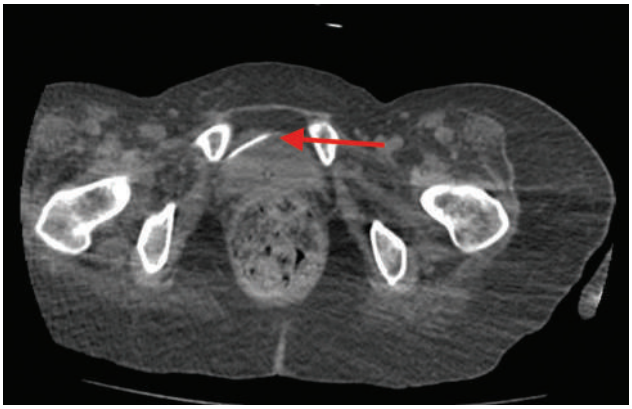


Fig. 5 Abdominal CT scan (axial view): the distal catheter inside the bladder (red arrow).

Discussion

The clinical manifestations of meningeal carcinomatosis are vast; patients may be asymptomatic (a minority of cases), as the findings may be accidental (~2% of the cases), or patients may present with severe symptoms (most cases). When symptomatic, the manifestations can be systemic and non-specific, involving headache (present in 80% of the cases), alteration in the level of consciousness, nausea, and vomiting, especially in cases in which there is hydrocephalus.[1,11] In the case herein reported, the patient was symptomatic, and her clinical history corroborated the diagnostic hypothesis developed after the imaging exams.

Cases that present with hydrocephalus, are typically treated with ventriculoperitoneal or ventriculoatrial shunts; however, due to the risks of dissemination of neoplastic cells, they can be replaced by a ventriculovesical shunt.[10] The first surgery that enabled a connection between CSF and the genitourinary system was performed in 1925 by Heinle, who connected the renal pelvis to the lumbar dura mater, a urethrodural anastomosis.[12] In 1949, Matson performed what was described as a lumboureterostomy at the ureterovesical junction using a polyethylene tube. This anatomical site has a valve mechanism that prevents backward flow and consequent ascending infections, but an ipsilateral nephrectomy was required.[13]

In 1980, West[14] reported the first ventriculovesical shunting, called ventriculovesicostomy. The bladder was initially opened on its front wall, and the shunt was rerouted obliquely, positioned above and to the side of the trigone. A suture was used to attach the catheter to the back wall of the bladder via a connecting component. A significant portion of the shunt tubing, measuring 15 cm in length, was left unsecured and hanging loosely inside the bladder. The aurthor[14] reported that the complication of recurrent obstruction was relieved by urethral instrumentation.

In 2001, Ames et al.[10] developed a new method of ventriculovesicostomy without sacrificing a kidney. They altered the first procedure described by creating a distal shunt catheter using a polyester cuff, which has antibacterial properties, at the end of a silicone catheter. A nonabsorbable suture was employed to fix this apparatus onto the front wall of the bladder. The authors[10] also created a deep tunnel running along the front wall of the bladder, which was then stitched over the catheter. This addition was intended to position the shunt slightly higher towards the dome of the bladder, thereby preventing trigonal irritation. To complete the procedure, a minor incision was performed in the bladder wall to enable the introduction of the distal shunt. There were no postoperative complications during the first year of follow-up; however, they[10] highlighted the need of awareness regarding dehydration, ascending infection, and the potential formation of encrustations on the shunt tube.

Conclusion

Ventriculovesical shunting is an alternative to other CSF diversion procedures, especially when CSF absorption is not desired. This option is particularly useful in cases of LC. More studies are necessary to define the incidence of complications and reoperations in ventriculovesical shunts.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Franzoi MA, Hortobagyi GN. Leptomeningeal carcinomatosis in patients with breast cancer. Crit Rev Oncol Hematol 2019; 135:85–94. Doi: 10.1016/j.critrevonc.2019.01.020

2 Le Rhun E, Galanis E. Leptomeningeal metastases of solid cancer. Curr Opin Neurol 2016;29(06):797–805. Doi: 10.1097/WCO.0000000000000393

3 Le Rhun E, Rudà R, Devos P, et al. Diagnosis and treatment patterns for patients with leptomeningeal metastasis from solid tumors across Europe. J Neurooncol 2017;133(02):419–427. Doi: 10.1007/s11060-017-2452-6

4 Lee JS, Melisko ME, Magbanua MJ, et al. Detection of cerebrospinal fluid tumor cells and its clinical relevance in leptomeningeal metastasis of breast cancer. Breast Cancer Res Treat 2015;154 (02):339–349. Doi: 10.1007/s10549-015-3610-1

5 Nevel KS, DiStefano N, Lin X, et al. A retrospective, quantitative assessment of disease burden in patients with leptomeningeal metastases from non-small-cell lung cancer. Neuro-oncol 2020; 22(05):675–683. Doi: 10.1093/neuonc/noz208

6 Taillibert S, Chamberlain MC. Leptomeningeal metastasis. Handb Clin Neurol 2018;149:169–204. Doi: 10.1016/B978-0-12-811161-1.00013-X

7 Le Rhun E, Taillibert S, Chamberlain MC. Carcinomatous meningitis: Leptomeningeal metastases in solid tumors. Surg Neurol Int 2013;4(Suppl 4):S265–S288. Doi: 10.4103/2152-7806.111304

8 Morosanu CO, Filip GA, Nicolae L, Florian IS. From the heart to the bladder-particularities of ventricular shunt topography and the current status of cerebrospinal fluid diversion sites. Neurosurg Rev 2020;43(03):847–860. Doi: 10.1007/s10143-018-1033-2

9 Negrete HO, Lavelle JP, Berg J, Lewis SA, Zeidel ML. Permeability properties of the intact mammalian bladder epithelium. Am J Physiol 1996;271(4 Pt 2):F886–F894. Doi: 10.1152/ajprenal.1996.271.4.F886

10 Ames CD, Jane JA Jr, Jane JA Sr, Campbell FG, Howards SS. A novel technique for ventriculovesical shunting of congenital hydrocephalus. J Urol 2001;165(04):1169–1171. Doi: 10.1016/S0022-5347(05)66458-0

11 Lukas RV, Thakkar JP, Cristofanilli M, et al. Leptomeningeal metastases: the future is now. J Neurooncol 2022;156(03): 443–452. Doi: 10.1007/s11060-021-03924-2

12 Sandvik U, Bartek J Jr, Edström E, Jönsson M, Stenman J. Percutaneously inserted ventriculo-ureteral shunt as a salvage treatment in paediatric hydrocephalus: a technical note. Childs Nerv Syst 2023;39(01):249–254. Doi: 10.1007/s00381-022-05673-7

13 Matson DD. A new operation for the treatment of communicating hydrocephalus; report of a case secondary to generalized meningitis. J Neurosurg 1949;6(03):238–247. Doi: 10.3171/jns.1949.6.3.0238

14 West CGH. Ventriculovesical shunt. Technical note. J Neurosurg 1980;53(06):858–860. Doi: 10.3171/jns.1980.53.6.0858

Syringe Port System as a Tubular Retractor Technique for Brain Lesions: Case Series and Review of the Literature

Sistema dilatador-seringa como técnica de retração tubular para lesões cerebrais: Série de casos e revisão de literatura

Carlos Augusto Vila Nova Moraes[1,2] João Augusto Gama da Sila Neto[1,2]
Breno William Mariz Guedes[1] Arthur Maynart Pereira Oliveira[1]
Bruno Fernandes de Oliveira Santos[1,2,3,4]

[1] Department of Neurosurgery, Fundação de Beneficência Hospital de Cirurgia, Aracaju, SE, Brazil
[2] Department of Medicine, Universidade Tiradentes, Aracaju, SE, Brazil
[3] Department of Medicine, Universidade Federal do Sergipe, Aracaju, SE, Brazil
[4] Health Sciences Graduate Program, Universidade Federal do Sergipe, Aracaju, SE, Brazil

Address for correspondence Bruno Fernandes de Oliveira Santos, Health Sciences Graduate Program, Universidade Federal do Sergipe, Aracaju, SE, Brazil (e-mail: brunofernandes.se@gmail.com).

Arq Bras Neurocir 2024;43(3):e226–e236.

Abstract

Objective To describe a tubular retractor technique for brain lesions through a series of cases and to conduct a literature review on intracranial tubular retractors with emphasis on the syringe port system.

Materials and Methods We described four cases of lesions with an intraventricular component and different pathological patterns. The surgeries were performed between April, 2021 and July, 2022. The images were acquired through computed tomography (CT) and magnetic resonance imaging (MRI) scans and transferred to the Horos software, version 1.1.7. To make the tubular retractor, a 20-mL syringe and a 14-Fr/Ch, 30-mL/cc Foley probe were used. The syringe was sectioned according to the planned depth based on preoperative imaging. The syringe was the retractor itself, while the probe served as a means of dilating the path to the lesion.

Results Gross total resection was achieved in all cases, and the samples collected were satisfactory regarding the results of the anatomopathological study. All patients evolved without any additional deficits and with adequate postoperative image control.

Conclusion The syringe as a tubular retractor associated with the Foley probe as a surgical port dilator was useful, and it enabled the radical resection of intracranial

Keywords
- tubular retractors
- brain microsurgery
- deep-seated brain lesions
- syringe port system

received
December 20, 2022
accepted
September 13, 2023
article published online
May 2, 2024

DOI https://doi.org/10.1055/s-0043-1777753.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

tumors related to the lateral ventricle, not limiting the use of auxiliary instruments, neither of microsurgical instruments; therefore, it is an affordable, secure, and inexpensive method.

Resumo

Objetivo Descrever uma técnica de retração tubular para lesões cerebrais por meio de uma série de casos e realizar uma revisão bibliográfica sobre retratores tubulares intracranianos com ênfase no sistema dilatador-seringa.

Materiais e Métodos Foram descritos quatro casos de lesões com componente intraventricular, com diferentes padrões patológicos. As cirurgias foram realizadas entre abril de 2021 e julho de 2022. As imagens foram adquiridas por tomografia computorizada (TC) e ressonância magnética (RM), e transferidas para o programa Horos, versão 1.1.7. Para fabricar o retrator tubular, foram utilizadas uma seringa de 20 mL e uma sonda Foley de 14Fr/Ch, 30mL/cc. A seringa foi seccionada de acordo com a profundidade planejada e com base na imagem pré-operatória. A seringa era o retrator em si, ao passo que a sonda servia como meio de dilatar o caminho para a lesão.

Resultados A ressecção total bruta foi alcançada em todos os casos, e as amostras recolhidas foram satisfatórias com relação aos resultados do estudo anatomopatológico. Todos os pacientes evoluíram sem quaisquer déficits adicionais e com controle de imagem pós-operatório adequado.

Conclusão A seringa como retrator tubular associado à sonda de Foley como dilatador cirúrgico foi útil e permitiu a ressecção radical de tumores intracranianos relacionados com o ventrículo lateral, e não limitou a utilização de instrumentos auxiliares, nem dos instrumentos microcirúrgicos, sendo assim um método acessível, seguro e pouco dispendioso.

Palavras-chave
- retratores tubulares
- microcirurgia cerebral
- lesões cerebrais profundas
- sistema de porta para seringas

Introduction

The advent of minimally invasive surgery in the twentieth century improved the extent of resection of deep brain lesions that were once difficult to manage. This was made possible by the introduction of several surgical techniques, such as microscopy and endoscopy in association with auxiliary tools, such as special retractors.

The use of tubular retractors in neurosurgery consists of placing a transparent tube in the brain parenchyma or in the vertebral column, which provides better visualization of the surgical site through both the endoscope and microscope.[1] The use of these techniques resulted in fewer intraoperative and postoperative complications when compared with the conventional techniques[2,3]

There are some commercial models of adjustable tubular brain retractors available, such as the Minimal Exposure Tubular Retractor (METRx, Medtronic, Memphis, TN, United States) system and ViewSite (Vycor Medical, Inc., Boca Raton, FL, United States). However, especially in lower- and middle-income countries, there is a need to develop techniques with lower costs, which could be done using resources already present in the local surgical environment. The aim of the present study was to describe a technical refinement of cerebral tubular retraction through a series of cases and to carry out a literature review on conventional intracranial tubular retractors and the syringe port method.

Materials and Methods

We described four cases of lesions with an intraventricular component and different pathological patterns. The surgeries were performed between April 2021 and July 2022. All patients consented to participate in the study. Brain magnetic resonance imaging (MRI) scans were acquired using a Discovery MR750w 3.0-T scanner (GE, Healthcare, Chicago, IL United States) with a 16-channel head coil and the following technical specifications: gradient – 40mT/m; matrix – 240 × 240 pixels; field of view – 240 × 240 mm; and cut thickness – 1 mm. The brain computed tomography (CT) scans were obtained using the Brilliance CT 64 System (Philips, Amsterdam, Netherlands with collimation of 20 × 0.625, 0.348 pitch, 512 × 512 matrix, 200-mm field of view, 140 kpV, 278 mA to 600 mA, and 1-mm thickness.

The image files were imported to the Horos software, version 1.1.7 (GNU General Public License, version 3), using the NeuroKeypoint[4] smart phone application to position the craniotomy in the planned location. Three-dimensional reconstructions of the sulci and gyrus along with the cortical veins were performed according to the previously described technique[5] for the exact definition of the corticectomy point. Intraoperative ultrasonography was used to assess any possible tumor residue. The Eximius neuronavigation system (Artis Tecnologia, Brasília, DF, Brazil) was used in cases 2 and 3.

During the operation, the head of the patient was fixed with Mayfield 3-point fixation. A small 3-cm craniotomy was performed, followed by opening of the dura mater and exposure of the brain parenchyma. The transsulcal route was chosen to minimize the volume of the transgressed cortex during the introduction of retraction. To make the tubular retractor, a 20-mL syringe with a diameter of 20 mm and a 14-Fr/Ch, 30-mL/cc Foley probe were used (►**Figure 1**). The syringe was sectioned according to the planned depth based on preoperative imaging. Initially, with the bipolar forceps, we made a small corridor through the white matter until reaching the lesion (►**Figure 2A**). After that, the Foley probe balloon is progressively inserted and smoothly inflated along the path to promote the necessary space to position the tubular retractor (►**Figure 2B**). The cut end of the syringe was trimmed with a drill to make it blunt. Once the path was ready, the probe was inflated with saline solution inside the syringe, obliterating it completely (►**Figure 2C**). This strategy is useful to prevent herniation of the brain parenchyma into the syringe. Once the retractor was positioned in the desired location, the probe was deflated, enabling access to the lesion (►**Figure 2D**). In this case, the syringe was the retractor itself, while the Foley probe served as a white matter route dissector.

The retractor was not externally fixed. This dynamic approach enabled us to angle the retractor in different directions for the procedure, considering the high volume of the lesions. After proper resection of the lesion, hemostasis was performed and the tube was carefully removed along the path in a straight line, with the performance of hemostasis, if necessary, along the white matter route. All resected material was sent for anatomopathological and immunohistochemical studies.

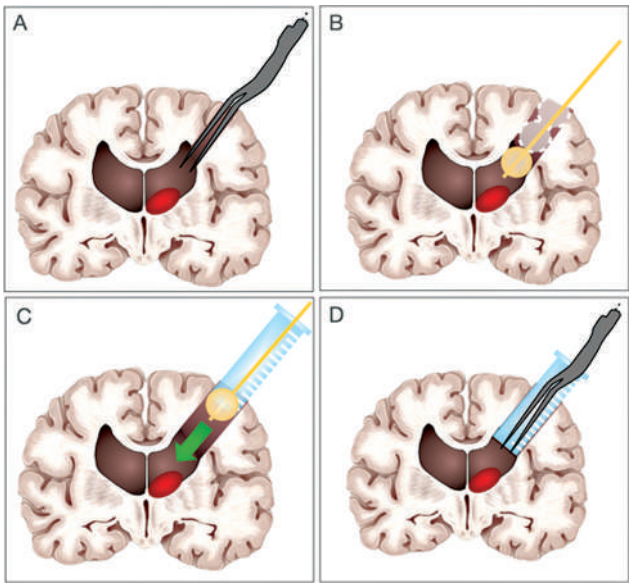


Fig. 2 The bipolar forceps being used to make a small corridor through the white matter until reaching the lesion (**A**). The Foley probe being progressively inserted and inflated along the path to promote the necessary space to position the tubular retractor (**B**). Insertion of the syringe over the tube to prevent herniation of the brain parenchyma into the syringe (**C**). Tubular retractor positioned to facilitate surgical handling of the intraventricular lesion (**D**).

Results

Case 1

Case 1 was that of a 36-year-old female patient with a 2-year history of holocranial and moderate progressive headache with normal neurological examination. Brain CT and MRI scans were performed (►**Figure 3**), which showed an intraventricular lesion (right ventricular atrium) with significant contrast enhancement. The surgical procedure was uneventful, using a tubular transparietal route with a piecemeal resection strategy (►**Figure 4**). The patient evolved in the follow-up without motor and sensory deficits. The pathological examination showed a grade-I meningioma according to the 2021 World Health Organization (WHO) grading system, and an immunohistochemical study revealed focal expression of epithelial membrane antigen (EMA) and positivity for progesterone receptor, confirming the meningothelial histogenesis of the lesion. The cell proliferation index (Ki-67) was estimated to be of 1%.

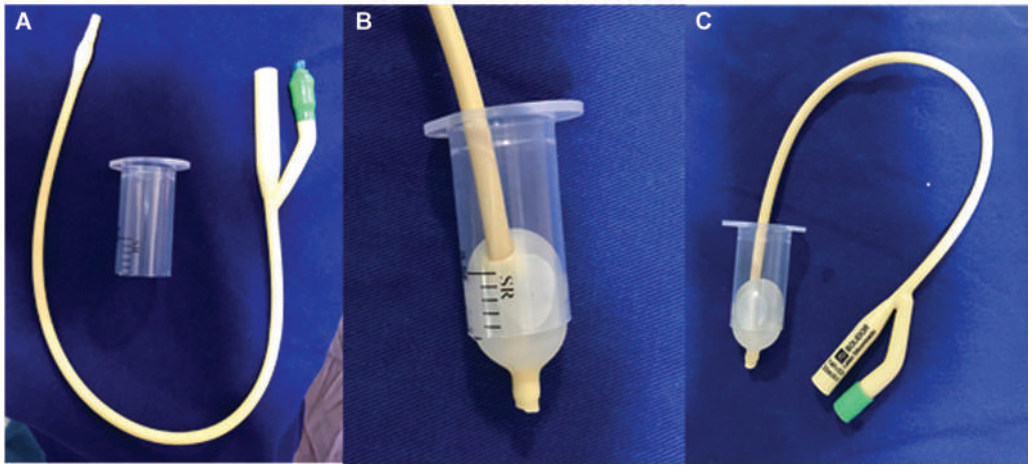


Fig. 1 The syringe used as the tubular retractor was sectioned based on the depth of the lesion acquired through neuronavigation and/or MRI scans (**A**). After the Foley probe balloon had been progressively inserted and smoothly inflated along the path to promote the necessary space to position the tubular retractor, the probe must be inflated with saline solution inside the syringe, obliterating it completely (**B**,**C**).

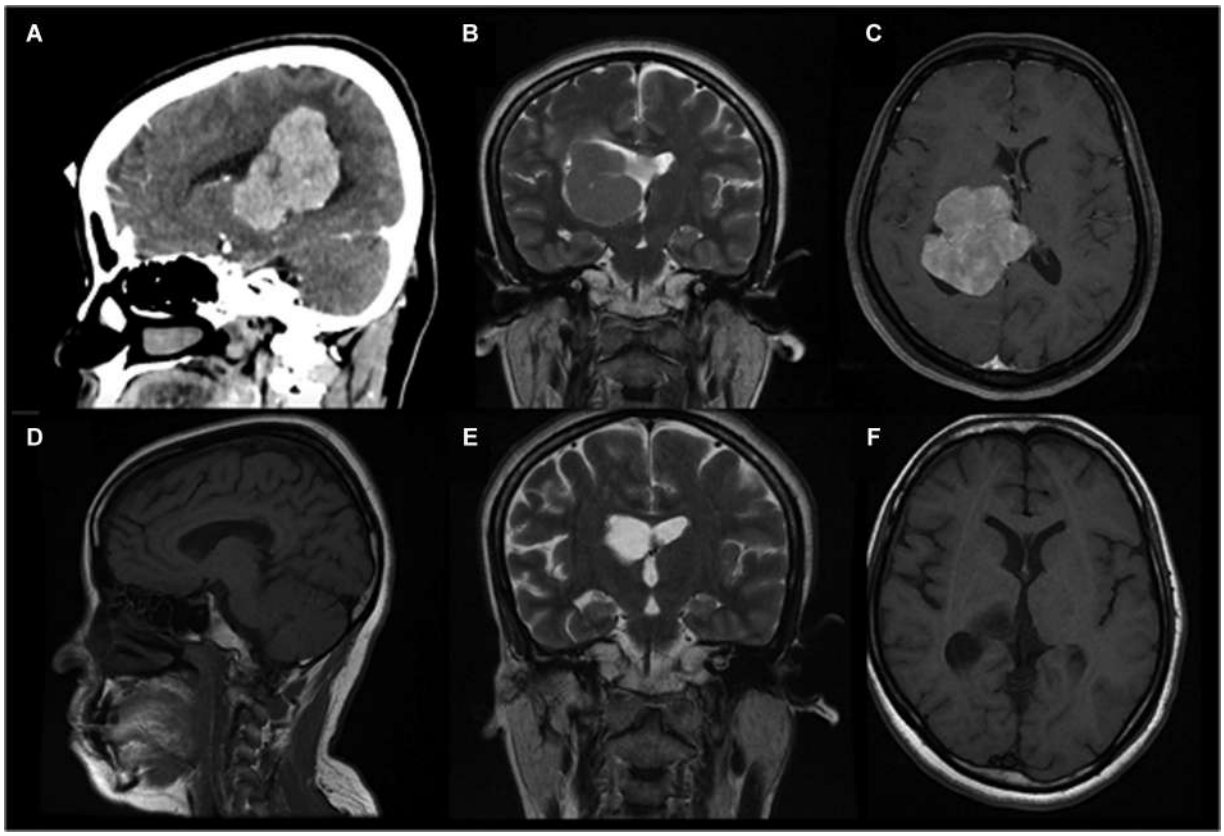


Fig. 3 Preoperative sagittal enhanced brain CT (**A**) scan. Preoperative MRI scans with coronal T2-weighted (**B**) and axial gadolinium-enhanced T1-weighted (**C**) images showing an expansive lesion in the right atrial region of the lateral ventricle. (**D-F**) Postoperative MRI scans.

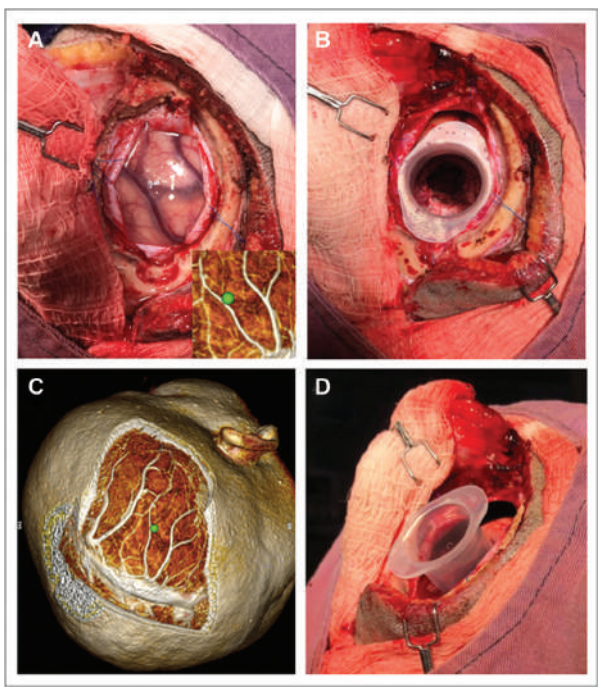


Fig. 4 Visualization of the cortical surface after craniotomy and opening of the dura mater and its relationship with the image of the 3D reconstruction. The green spot shows the surgical entry point in the brain parenchyma (**A**) after insertion of the tubular retractor with Foley probe dilatation and removal (**B**). Presurgical 3D reconstruction of the transparietal entry point (**C**). Syringe positioned to serve as a tubular retractor for tumor resection (**D**)

Case 2

Case 2 was that of a 17-year-old female patient with a previous history of headache, nausea, and syncope. The neurological examination revealed bilateral papilledema on funduscopy, and the motor and sensory functions were preserved. A Gadolinium-enhanced MRI scan with T1-weighted images (►**Figure 5**) showed an isointense expansive right ventricular/periventricular paramedian solidocystic lesion with central heterogenous contrast enhancement measuring approximately $4.0 \times 2.6 \times 3.8$ cm, in addition to a lesion with a right periventricular/frontal cystic component, with peripheral vasogenic edema, measuring $5.0 \times 4.0 \times 3.5$ cm. Resection was uneventful with the use of a tubular retractor, We initially approached the cystic component, followed by the solid component of the tumor. The immunohistochemical study revealed diffuse expression of glial fibrillary acidic protein (GFAP)/S100 protein and low cell proliferation index (Ki-67 $< 1\%$). The pathological findings were indicative of pilocytic astrocytoma (grade-I according to the 2021 WHO grading system). In the follow-up, the patient presented good recovery without any motor or sensory deficits or other complications, with regression of the papilledema.

Case 3

Case 3 is that if a 28-year-old male patient with a history of left paresthesia, severe headache, visual blurring, and loss of strength in the left side of the body, which was worse in the lower limb. A neurological examination showed preserved

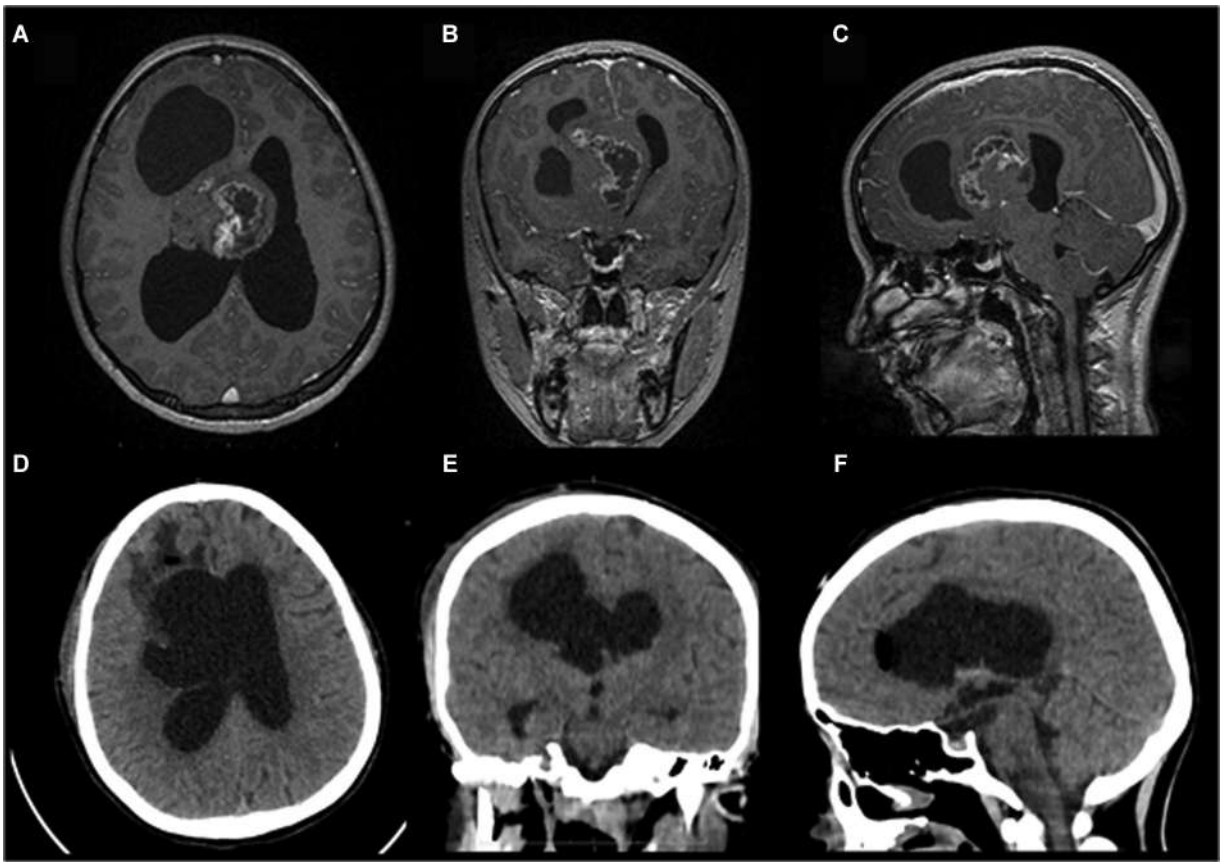


Fig. 5 (**A-C**) Gadolinium-enhanced T1-weighted MRI scans in the axial, coronal, and sagittal sections showing preoperative pilocytic astrocytoma measuring $9.0 \times 6.4 \times 7.4$, extensively compromising the corpus callosum. (**D-F**) Postoperative brain CT showing gross total resection.

cranial nerve functions, left grade-3 complete hemiparesis and left hemihypoesthesis with asymmetric deep tendon reflexes, with grade +2/4 on the right side of the body and grade +3/4 on the left side of the body. Coordination tests were preserved. A Brain MRI (►**Figure 6**) showed a deep and large right frontoparietal lesion, infiltrating the right cingulate gyrus and corpus callosum, intralesional high signal in the T1-weighted image suggestive of a hemorrhagic component and small areas of contrast enhancement. Its local expansive effect determined compression of the lateral ventricles and third ventricle. The tubular surgery was performed as previously described, achieving gross total resection (►**Figure 7**). The patient evolved without any complications or additional motor or sensory deficits, maintaining hemiparesis in the left side. The pathological examination showed a hypercellular neoplasm of anaplastic morphology, with a fibrillar background, frequent mitotic figures, including atypical forms. Vascular proliferation and foci of necrosis were also observed. The immunohistochemical study revealed GFAP and S100 protein expression, confirming the glial histogenesis of the neoplasia. We also observed expression of the p53 protein in a mutated pattern, positivity for isocitrate dehydrogenase 1 (IDH1) R132H mutation and a Ki-67 cell proliferation index of 20%. The pathological findings were compatible with an IDH-mutated grade-IV astrocytoma (according to the 2021 WHO grading system).

Case 4

Case 4 was that of a 51-year-old female patient with history of frontal headache with associated vertigo who was refractory to medication use. A neurological examination showed diplopia, right abducens nerve paresis, and grade-4 left hemiparesis. A brain MRI showed expansive intraventricular lesions. Surgery was performed uneventfully with the help of a tubular retractor, and the patient evolved maintaining hemiparesis in the left side, with no cranial nerve deficit. A pathological examination showed a low-grade fusocellular neoplasm, with immunohistochemical findings of a grade-II CD34 positive hemangiopericytoma/solitary fibrous tumor, with a Ki-67 cell proliferation index $< 1\%$. The preoperative images and step-by-step surgery of this case are illustrated in a video with a narration of the tubular retraction technique.

All microsurgical instruments, in addition to the ultrasonic aspirator, were used through the tube without ergonomic issues or viewing limitations. Radical resection was achieved in all cases, and the samples collected were satisfactory regarding the results of the anatomopathological study. All patients evolved without any additional deficits and with adequate postoperative image control.

The lack of an external fixation system did not limit the procedure. Positioning of the standalone tubular retractor was feasible, and the workability of the syringe facilitated the surgical procedure, and it could be repositioned whenever necessary, enabling freedom of angulation of approximately

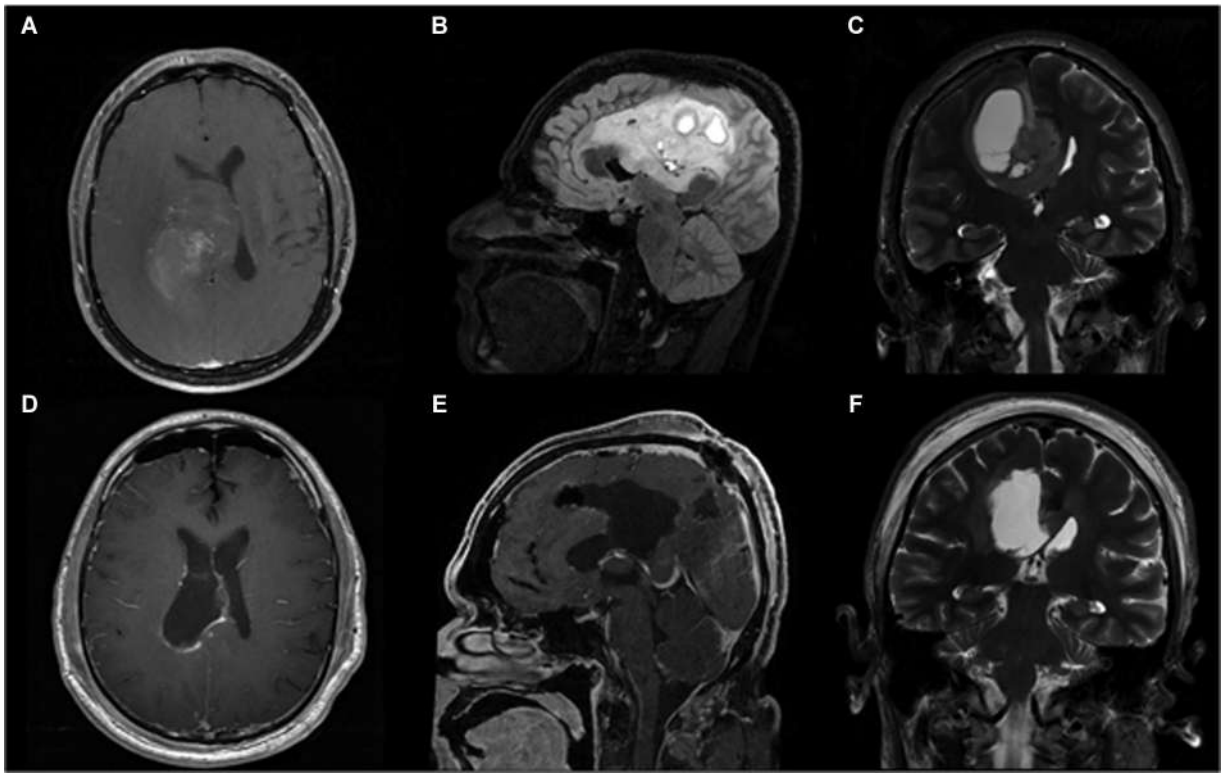


Fig. 6 Axial gadolinium-enhanced T1-weighted (**A**), sagittal FLAIR (**B**) and coronal T2 weighted MRI (**C**) showing a right deep frontoparietal lesion with infiltration of the right cingulate gyrus and corpus callosum. Postoperative images: axial gadolinium-enhanced T1-weighted (**D**), sagittal gadolinium-enhanced T1-weighted (**E**) and coronal T2 weighted MRI (**F**) showing postoperative result with gross total resection without complications.

30° in all directions. Neuronavigation can be useful to define the path to the injury. Due to the dilation provided by the Foley probe, which worked as a dissector the white matter fibers prior to placement of the syringe retractor, the pressure exerted through the syringe was minimized during its introduction into the brain parenchyma. The entire retracted parenchyma could be visualized through the transparent surface of the syringe. When it was removed, the parenchyma returned to its original shape, with no apparent damage.

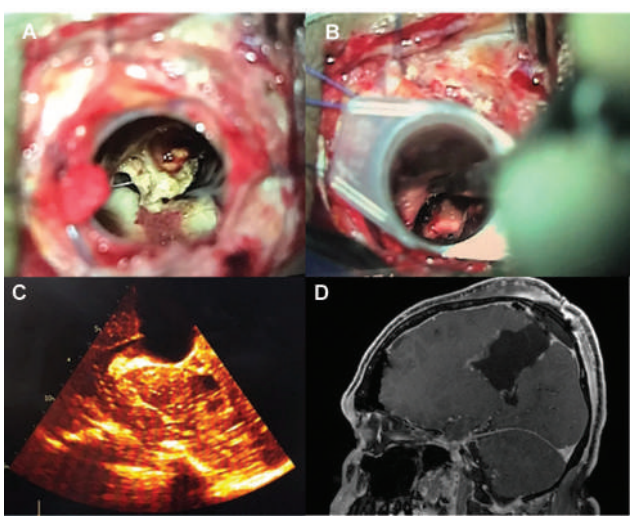


Fig. 7 Lesion visualized through the microscope tubular view (**A**); intraoperative mobilization of the syringe retractor enabling different angles of work (**B**); postoperative ultrasound image showing hypoechoic area and the path to the tumor (**C**); and corresponding sagittal gadolinium-enhanced T1-weighted MRI (**D**).

The technique herein reported was in line with other methods of tubular retraction described in the literature due to the pressure exerted radially on the parenchyma, making this retraction mechanism unlikely to cause damage to the brain tissue, as described in ►**Table 1**.

Discussion

The use of the tubular retractor described in the present study proved to be a low-cost, simple, and effective technique to visualize deep lesions, especially when located in or related to the lateral ventricle. The approaches were less invasive compared with the classic microsurgical alternative with fixed retractors. Furthermore, the transparent surface of the retractor made it possible to view the retracted parenchyma, in addition to protecting it throughout the procedure. This approach enabled the resection of difficult-to-access lesions with different histology (glioblastoma, meningioma, and pilocytic astrocytoma).

In the mid-nineteenth century, there was a significant change in the field of neurosurgery, involving advances in concepts such as antisepsis, asepsis, anesthesia, brain localization, and intracranial pressure control. These were of paramount importance to reduce morbidity and mortality

Table 1 Literature review of syringe port as a tubular retractor technique for neurosurgical procedures

Author	Number of patients	Diameter of syringe	Insertion technique and path dilatation	Navigation system	Phathology	Complications
Vaish et al. 2014[26]	20	13 mm (5mL)	Syringe introduced with a Teflon trocar	Under navigation guidance (Brainlab system)	Colloid cysts	No complications or postoperative morbidity related
Almubarak et al. 2018[22]	9	17 mm (10 mL)	Syringe introduced through transsulcal or transgyral approach, without pior dilation	Under navigation guidance	Glioblastoma, gliosarcoma, toxoplasmosis	Transient afasia ($n = 2$), weakness ($n = 3$), 6th cranial nerve palsy ($n = 1$), memory impairment ($n = 1$)
Singh et al. 2018[23]	62	2.06 mm (5mL); 14.5 mm (10mL); and 19.3mm (20 mL)	Syringe introduced with plastic trocar	Under navigation guidance	Gliomas, cavernomas, metastasis, lymphomas, intracranial bleeding	No complications or postoperative morbidity related
Sharif et al. 2019[24]	Not reported	14 mm (5 mL); 17 mm (10 mL); and 20 mm (20 mL)	Syringe introduced with plastic trocar	Under navigation guidance	Malignant tumors and intracerebral hematomas	No complications or postoperative morbidity related
Zhenzhu et al. 2020[25]	7	5-mL and 10-mL syringes	Glove-syringe introduced with trocar	Under navigation guidance	Intracerebral hematomas	No complications or postoperative morbidity related
Moraes et al. (present study)	4	20mm (20 mL)	Prior dilation with Foley probe	Under navigation guidance (Horos software, version 1.1.7)	Meningioma, astrocytoma, metastasis	No complications or postoperative morbidity observed

in patients who underwent neurosurgery, which encouraged professionals in the area to turn their attention to more effective procedures and methods. With intracranial surgery becoming more accessible, there was a progressive increase in the need for techniques for brain retraction to better visualize the surgical field.[6]

At the beginning of the twentieth century, the first fixed retractors were created, which did not require fixed handling by an assistant. The first fixed retractor, called the Weitlaner retractor, was created in 1905 by Franz Weitlaner.[6] The use of tubular retractors became popular in the late twentieth century, and it was first described by Kelly et al.,[7] from the Mayo Foudation's Department of Neurosurgery, in Rochester, Minnesota, United States, in the late 1980s, as a useful alternative in minimally-invasive surgery, especially in cases of patients with deep tumors in the brain parenchyma. The use of this technique in neurosurgeries for lesions in anatomical areas such as the ventricles, the basal nuclei, the posterior thalamus, the insular cortex, and the basal cisterns is well described in the literature,[8] with a reduction in morbidity associated with the approach to these lesions.[2,9]

The first commercial model of tubular retractor to be used was the METRx (Medtronic) system, created in 1985, which consists of alternating conjugated tubes of variable lengths and widths, which is more used in spinal surgeries.[1] Before that, devices such as syringes or tube speculums made of polyethylene were used as a form of tubular retractor.[1] Another well-known commercial model available is the ViewSite (Vycor Medical), which is a clear plastic retractor that also offers the possibility to change the length in 3 different sizes (3 cm, 5 cm and 7 cm) and 4 widths (12 cm, 17 cm, 21 cm, and 28 mm).[10] There is no statistical difference reported in the literature between the different commercial types of tubular retractors regarding the rate of postoperative complications.[11,12]

Studies show an equivalence in effectiveness when different types of retractors were compared. A meta-analysis performed by Marenco-Hillembrand et al.[11] on four different types of tubular retractors, including models such as the ViewSite and METRx, showed a complication rate of 9% in 309 surgeries performed, with no higher percentage linked to one type over another.

There is a report[13] on the use of tubular retractors in the surgical management of different types of pathologies in the brain parenchyma, such as intracranial hemorrhages, gliomas, vascular lesions such as cavernomas and arteriovenous malformations, meningiomas, and brain metastases, among others.

Despite being an extremely useful method to access deep lesions, the improper and careless use of this technique can result in cerebral edema and ischemia, generating new iatrogenic lesions.[14] In order to avoid such complications, it is necessary to correctly plan the surgical path, the diameter of the retractor, and the pressure exerted by it on the brain structures. In relation to damage to the brain parenchyma, an animal study[15] has shown that pressures of 25 mmHg exerted focally in a region of the brain parenchyma can cause electroencephalographic alterations. Furthermore, Rosenørn[16] reports that focal pressures $>$ 30 mmHg can cause a decrease in local blood flow in the cerebral parenchyma, especially if this pressure is maintained for more than 2 hours.[17] Ogura et al.[14] showed that the pressure exerted by a tubular retractor did not exceed 10 mmHg, which did not result in ischemic complications in the brain tissue.

A study[18] using MRI, which evaluated the damage caused by tubular retractors in the postoperative period of intraparenchymal lesions through T2 fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging DWI sequences, did not show a statistically significant increase in hypersignal images in the FLAIR sequence, suggesting a lower risk of vasogenic edema due to brain damage in the postoperative period. This reinforces the concept that the use of tubular retractors are potentially less traumatic than other brain retraction techniques, although there is not enough data in the literature for comparison purposes.[18] However, this same study[18] also demonstrated, through DWI, evidence of edema of cytotoxic origin in the tissue around the retracted area. Despite this finding, much of the brain damage caused by tubular retractors is transitory and self-limited.[19]

The lower probability of traumatic events in tubular retraction may be due to the reduced pressure exerted by tubular retractors, which is circumferentially distributed across the cylindrical surface of the tube, unlike other types of retractors such as blades, which exert a nonuniform pressure on the brain.[7,20] Furthermore, with tubular retractors, white matter tracts can be divulged and, consequently, preserved, rather than sectioned, through the passage of the blunt tip of the retraction instrument and progressive dilation technique.[21] It has been described[15,16] that tubular retractors can be harmful to the parenchyma if they exceed pressures between 25 and 30 mmHg. Due to the technical refinement described in the present case series, with path dilation performed by the Foley probe and the diameter of the syringe used (20 mm), which is compatible with other tubular retraction instruments described in the literature and commercially available, these pressures were most likely not exceeded in the cases herein reported.

Compared to other studies, the use of tubular structures as brain retractors resulted in fewer intraoperative and postoperative complications, such as lower levels of blood loss and shorter hospital stay, when compared with conventional techniques.[2] In addition, it presents other advantages such as smaller corticectomy (of only 2 cm), no thin edges like mobile retractors, and less brain damage due to the malleability of the tube, not to mention the fact that it is simple to position, safer, easy to use, and low-cost.[3]

It is also worth highlighting the versatility of tubular techniques. There is the possibility of angulation of the tube in different directions, with a range of approximately 30°, as well as the possibility of associating auxiliary techniques such as endoscopy, further facilitating the visualization of the lesion in any perspective desired by the neurosurgeon. Furthermore, the 20-mm diameter of the syringe enabled the use of 2 microsurgical instruments at the same time, such as bipolar forceps and ultrasonic aspirator. The syringe was also an easy-to-handle method, as it did not need a permanent fixation such as other retractors. The flanges of the syringe served as its own retainer and were supported on the cortical surface without any additional damage. The lack of an external fixation system did not limit the procedure. This method can also be conveniently associated with neuronavigation and intraoperative ultrasound. Ultrasonography was particularly useful in assessing the degree of lesion resection in real time. It is one of the main strategies, besides neuronavigation, to optimize the use of tubular retractors in the intraoperative period and increase the extent of resection.[9]

There are reports in the literature of tubular retraction methods with syringes associated with microsurgical techniques such as endoscopy or microscopy, which are used in the resection of lesions such as intracerebral hematomas, glioblastomas, and gliosarcomas, among others (►**Table 1**). Almubarak et al.[22] described a technique similar to ours, in which a retraction system with a syringe and a Foley probe was used, which has been shown to be useful in preventing trauma to the brain parenchyma in the path to the injury. Other articles[23–25] have also shown syringe techniques associated with trocar designed from medical-grade plastic dilators or gloves as an alternative. None of them showed significant rates of intraoperative or postoperative complications.[22–26] We believe that our technique shares the same advantages even with important differences, such as previous dilatation with the Foley probe, which provides security in preventing brain damage and probably less damage to the white matter fibers. Futhermore, our technique did not need an external fixator to secure the retractor, since the flanges of the syringe served as its own retainer. In addition, the tube itself did not cause damage due to the trim of the cut surface prior to surgery, the radial pressure exerted by the tube on the parenchyma resulted in reduced risk of ischemia, and because its 20-mm diameter is similar to that of other forms of tubular retraction with low complication rates described in the literature and commercially available, such as the ViewSite.[11] Additionally, the probe did not cause thermal injury to the brain parenchyma due to the material the syringe was made of, which presented low heat absorption.

Neuroradiological planning in this approach is of paramount importance. The neurosurgical team must have acquired brain MRI and/or CT scans following a volumetric

protocol. Therefore, oblique reconstructions in the coronal and sagittal planes, perpendicular to the approach, are possible. Thus, the exact location for corticectomy and insertion of the tubular retractor can be planned, as well as the size that the syringe must have for its correct intraoperative positioning and to estimate the tube angulation.

Despite being commercially available, tubular retractors are not easily present in public services and are hardly available through health insurances. It is a problem present in low-to-middle-income countries, such as Brazil. As a result, there is a demand to develop creative alternatives to fulfill this need. Due to this necessity, this method can be a way to bypass those difficulties.

Conclusion

The use of the syringe as a tubular retractor associated with the Foley probe as a surgical port dilator was useful in enabling gross total resection of intracranial tumors related to the lateral ventricle, not limiting the use of auxiliary instruments, neither of microsurgical instruments; therefore, it is an affordable, safe, and inexpensive method. More studies with a higher number of patients are needed to evaluate the possible damage caused by tubular retractors, especially in comparison with older retraction methods, to better guide the technique and use of tubular retractors.

Competing Interests and Funding

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in the present manuscript. No funding was received for the present research.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgements

The authors would like to thank José Pinto Cardoso Junior for his assistance with copyediting and reviewing of the manuscript. We would also like to acknowledge the patients for their paramount contribution to making the present article possible.

References

1 Kim YB, Hyun SJ. Clinical applications of the tubular retractor on spinal disorders. J Korean Neurosurg Soc 2007;42(04):245–250. Doi: 10.3340/jkns.2007.42.4.245
2 Assina R, Rubino S, Sarris CE, Gandhi CD, Prestigiacomo CJ. The history of brain retractors throughout the development of neurological surgery. Neurosurg Focus 2014;36(04):E8. Doi: 10.3171/2014.2.FOCUS13564
3 Yadav YR, Yadav S, Sherekar S, Parihar V. A new minimally invasive tubular brain retractor system for surgery of deep intracerebral hematoma. Neurol India 2011;59(01):74–77. Doi: 10.4103/0028-3886.76870
4 Fernandes de Oliveira Santos B, de Araujo Paz D, Fernandes VM, et al. Minimally invasive supratentorial neurosurgical approaches guided by Smartphone app and compass. Sci Rep 2021;11(01):6778. Doi: 10.1038/s41598-021-85472-3
5 Santos BFO, Costa MDS, Centeno RS, et al. Clinical Application of an Open-Source 3D Volume Rendering Software to Neurosurgical Approaches. World Neurosurg 2018;10:864–872. Doi: 10.1016/j.wneu.2017.11.123
6 Lener S, Wipplinger C, Hernandez RN, et al. Defining the MIS-TLIF: A Systematic Review of Techniques and Technologies Used by Surgeons Worldwide. Global Spine J 2020;10(2, Suppl)151S–167S. Doi: 10.1177/2192568219882346
7 Kelly PJ, Goerss SJ, Kall BA. The stereotaxic retractor in computer-assisted stereotaxic microsurgery. Technical note. J Neurosurg 1988;69(02):301–306. Doi: 10.3171/jns.1988.69.2.0301
8 Bosnjak R, Antolin A, Jeglic A, Felbabic T, Velnar T. Navigated Endoport in the Purely Endoscopic Microsurgery of Intraventricular and Other Deep-Seated Brain Lesions: A Case Report. Acta Med Acad 2020;49(Suppl 1):70–77. Doi: 10.5644/ama2006-124.309
9 Zammar SG, Cappelli J, Zacharia BE. Utility of tubular retractors augmented with intraoperative ultrasound in the resection of deep-seated brain lesions. Cureus 2019;11(03):e4272. Doi: 10.7759/cureus.4272
10 Otani Y, Kurozumi K, Ishida J, et al. Combination of the tubular retractor and brain spatulas provides an adequate operative field in surgery for deep-seated lesions: Case series and technical note. Surg Neurol Int 2018;9:220. Doi: 10.4103/sni.sni_62_18
11 Marenco-Hillembrand L, Prevatt C, Suarez-Meade P, Ruiz-Garcia H, Quinones-Hinojosa A, Chaichana KL. Minimally invasive surgical outcomes for deep-seated brain lesions treated with different tubular retraction systems: a systematic review and meta-analysis. World Neurosurg 2020;143:537–545.e3. Doi: 10.1016/j.wneu.2020.07.115
12 Echeverry N, Mansour S, MacKinnon G, Jaraki J, Shapiro S, Snelling B. Intracranial Tubular Retractor Systems: A Comparison and Review of the Literature of the BrainPath, Vycor, and METRx Tubular Retractors in the Management of Deep Brain Lesions. World Neurosurg 2020;143:134–146. Doi: 10.1016/j.wneu.2020.07.131
13 Marenco-Hillembrand L, Alvarado-Estrada K, Chaichana KL. Contemporary surgical management of deep-seated metastatic brain tumors using minimally invasive approaches. Front Oncol 2018;8:558. Doi: 10.3389/fonc.2018.00558
14 Ogura K, Tachibana E, Aoshima C, Sumitomo M. New microsurgical technique for intraparenchymal lesions of the brain: transcylinder approach. Acta Neurochir (Wien) 2006;148(07):779–785, discussion 785. Doi: 10.1007/s00701-006-0768-7
15 Greenberg IM. Self-retaining retractor and handrest system for neurosurgery. Neurosurgery 1981;8(02):205–208. Doi: 10.1227/00006123-198102000-00009
16 Rosenørn J. The risk of ischaemic brain damage during the use of self-retaining brain retractors. Acta Neurol Scand Suppl 1989;120:1–30. Doi: 10.1111/j.1600-0404.1989.tb08017.x
17 Zagzoog N, Reddy KK. Modern Brain Retractors and Surgical Brain Injury: A Review. World Neurosurg 2020;142:93–103. Doi: 10.1016/j.wneu.2020.06.153
18 Bander ED, Jones SH, Kovanlikaya I, Schwartz TH. Utility of tubular retractors to minimize surgical brain injury in the removal of deep intraparenchymal lesions: a quantitative analysis of FLAIR hyperintensity and apparent diffusion coefficient maps. J Neurosurg 2016;124(04):1053–1060. Doi: 10.3171/2015.4.JNS142576
19 Eliyas JK, Glynn R, Kulwin CG, et al. Minimally Invasive Transsulcal Resection of Intraventricular and Periventricular Lesions Through a Tubular Retractor System: Multicentric Experience and Results.

World Neurosurg 2016;90:556–564. Doi: 10.1016/j.wneu.2015.12.100

20 Eichberg DG, Buttrick S, Brusko GD, Ivan M, Starke RM, Komotar RJ. Use of tubular retractor for resection of deep-seated cerebral tumors and colloid cysts: single surgeon experience and review of the literature. World Neurosurg 2018;112:e50–e60. Doi: 10.1016/j.wneu.2017.12.023

21 Greenfield JP, Cobb WS, Tsouris AJ, Schwartz TH. Stereotactic minimally invasive tubular retractor system for deep brain lesions. Neurosurgery 2008;63(4, Suppl 2)334–339, discussion 339–340. Doi: 10.1227/01.neu.0000334741.61745.72

22 Almubarak AO, Alobaid A, Qoqandi O, Bafaquh M. Minimally Invasive Brain Port Approach for Accessing Deep-Seated Lesions Using Simple Syringe. World Neurosurg 2018;117:54–61. Doi: 10.1016/j.wneu.2018.05.236

23 Singh H, Patir R, Vaishya S, Miglani R, Kaur A. Syringe Port: A Convenient, Safe, and Cost-Effective Tubular Retractor for Transportal Removal of Deep-Seated Lesions of the Brain. World Neurosurg 2018;114:117–120. Doi: 10.1016/j.wneu.2018.03.019

24 Sharif S, Shaikh MY, Ali SM. Novel Tool for Minimally Invasive Brain Surgery-Syringe Port System. World Neurosurg 2019;131:339–345. Doi: 10.1016/j.wneu.2019.06.202

25 Zhenzhu L, Ruiyu X, Wei C, et al. Novel Cost-Effective Tubular Port Based on Glove and Syringe for Endoscopic Surgery of Intracerebral Hematomas. World Neurosurg 2020;135:367–374.e1. Doi: 10.1016/j.wneu.2019.11.097

26 Vaish M, Patir R, Prasad R, Agrawal A. Single port microsurgical technique for excision of third ventricular colloid cysts. Asian J Neurosurg 2014;9(04):189–192. Doi: 10.4103/1793-5482.146599

ISSN 0103-5355

Instruções aos Autores

Muito obrigado por contribuir com a Arquivos Brasileiros de Neurocirurgia. Por favor, leia cuidadosamente as instruções a seguir. A falta de concordância com essas instruções pode causar atrasos desnecessários na publicação de seu artigo. Esta revista não cobra taxas de submissão e publicação de artigos.

Arquivos Brasileiros de Neurocirurgia, publicação científica oficial da **Sociedade Brasileira de Neurocirurgia** e das **Sociedades de Neurocirurgia de Língua Portuguesa**, destina-se a publicar trabalhos científicos na área de neurocirurgia e ciências afins, inéditos e exclusivos. **Serão publicados apenas trabalhos redigidos em inglês, com resumos em inglês e em português**. Os manuscritos devem ser escritos de forma clara e concisa.

Os artigos submetidos serão classificados em uma das categorias abaixo:

- ***Artigos originais:*** resultantes de pesquisa clínica, epidemiológica ou experimental. Resumos de teses e dissertações.
- ***Artigos de revisão:*** sínteses de revisão e atualização sobre temas específicos, com análise crítica e conclusões. As bases de dados e o período abrangido na revisão deverão ser especificados.
- ***Relatos de caso:*** apresentação, análise e discussão de casos que apresentem interesse relevante.
- ***Notas técnicas:*** notas sobre técnica operatória e/ou instrumental cirúrgico.
- ***Artigos diversos:*** são incluídos nesta categoria assuntos relacionados à história da neurocirurgia, ao exercício profissional, à ética médica e outros julgados pertinentes aos objetivos da revista.
- ***Cartas ao editor:*** críticas e comentários, apresentados de forma resumida, ética e educativa, sobre matérias publicadas nesta revista. O direito à réplica é assegurado aos autores da matéria em questão. As cartas, quando consideradas como aceitáveis e pertinentes, serão publicadas com a réplica dos autores.

Normas gerais para publicação

- Os arquivos dos artigos para publicação deverão ser enviados ao Editor, no endereço eletrônico http://www.editorialmanager.com/bns/.
- Todos os artigos serão avaliados pelo processo de revisão por pares do tipo duplo-cego, e não há cobrança de taxa pelo processamento da publicação (APC). Para saber mais sobre *Open Access*, acesse http://open.thieme.com.
- Serão aceitos apenas os artigos inéditos não publicados previamente. Os artigos, ou parte deles, submetidos à publicação em **Arquivos Brasileiros de Neurocirurgia** não deverão ser submetidos, concomitantemente, a outra publicação científica.
- Compete ao Corpo Editorial recusar artigos e sugerir ou adotar modificações para melhorar a clareza e a estrutura do texto e manter a uniformidade conforme o estilo da revista.
- Os direitos autorais de artigos publicados nesta revista pertencerão exclusivamente à **Arquivos Brasileiros de Neurocirurgia à Thieme Revinter Publicações Ltda**. É vetada a reprodução de artigos ou ilustrações publicadas nesta revista sem o consentimento prévio da Editora.

Normas para submeter os artigos à publicação

Os autores devem enviar os seguintes arquivos:

1. Carta formal ao Editor (arquivo de texto) explicitando que o artigo não foi previamente publicado no todo ou em parte ou submetido concomitantemente a outro periódico. Deve conter Título do artigo, nome completo dos autores, filiação em ordem crescente de hierarquia e autor correspondente.

2. Manuscrito Anônimo (arquivo de texto deve conter o nome do artigo em inglês, nome do artigo em português, resumos em inglês e português, sem identificação de autores e filiações).

3. Figuras (*Tiff, Jpeg, Pdf, Indd*), enviadas em arquivos individuais para cada ilustração, com resolução mínima de 300 dpi.

4. Tabelas, quadros e gráficos (arquivo de texto), enviados em **arquivos individuais**.

Normas para a estrutura dos artigos

Os artigos devem ser estruturados com todos os itens relacionados a seguir e paginados na sequência apresentada:

1. Página-título: título do artigo em português e em inglês; nome completo de todos os autores; sem abreviações, títulos universitários ou profissionais dos autores principais (máximo de dois títulos por autor); nomes das instituições onde o trabalho foi realizado; título abreviado do artigo, para ser utilizado no rodapé das páginas; nome, endereço completo, *e-mail* e telefone do autor responsável pelas correspondências com o Editor, juntamente com o **Formulário ICMJE** disponível em (http://www.icmje.org/conflicts-of-interest/).

2. Resumo: para **artigos originais**, deverá ser estruturado, utilizando cerca de 250 palavras, descrevendo **objetivo, métodos, principais resultados e conclusões**; para Revisões, Atualizações, Notas Técnicas e Relato de Caso o resumo não deverá ser estruturado; abaixo do resumo, indicar até seis palavras-chave, com base no MeSH (Medical Subject Headings), publicado pelo Medline e disponível em: www.ncbi.nlm.nih.gov/mesh/.

3. Abstract: título do trabalho em inglês; versão correta do resumo para o inglês; indicar até seis palavras-chave, com base no DeCS (Descritores em Ciências da Saúde), publicado pela Bireme e disponível em http://decs.bvs.br.

4. Texto principal: introdução; casuística ou material e métodos; resultados; discussão; conclusão; agradecimentos.

5. Referências: numerar as referências de forma consecutiva **de acordo com a ordem em que forem mencionadas pela primeira vez no texto**, utilizando-se números arábicos sobrescritos. Utilizar o padrão de Vancouver; listar todos os nomes até seis autores, utilizando "*et al*." após o terceiro quando houver mais de seis autores; as referências relacionadas devem, obrigatoriamente, ter os respectivos números de chamada indicados de forma sobrescrita, em local apropriado do texto principal; no texto, quando houver citação de nomes de autores, utilizar "*et al.*" para mais de dois autores; dados não publicados ou comunicações pessoais devem ser citados, como tal, entre parênteses, no texto e não devem ser relacionados nas referências; utilizar abreviatura adotada pelo *Index Medicus* para os nomes das revistas; siga os exemplos de formatação das referências (observar, em cada exemplo, a pontuação, a sequência dos dados, o uso de maiúsculas e o espaçamento):

Artigo de revista

Agner C, Misra M, Dujovny M, Kherli P, Alp MS, Ausman JI. Experiência clínica com oximetria cerebral transcraniana. Arq Bras Neurocir 1997;16(1):77–85

Capítulo de livro

Peerless SJ, Hernesniemi JA, Drake CG. Surgical management of terminal basilar and posterior cerebral artery aneurysms. In: Schmideck HH, Sweet WH, editors. Operative neurosurgical techniques. 3rd ed. Philadelphia: WB Saunders; 1995:1071–86.

Livro considerado como todo (quando não há colaboradores de capítulos)

Melzack R. The puzzle of pain. New York: Basic Books Inc Publishers; 1973.

Tese e dissertação

Pimenta CAM. Aspectos culturais, afetivos e terapêuticos relacionados à dor no câncer. [tese]. São Paulo: Escola de Enfermagem da Universidade de São Paulo; 1995.

Anais e outras publicações de congressos

Corrêa CF. Tratamento da dor oncológica. In: Corrêa CF, Pimenta CAM, Shibata MK, editores. Arquivos do 7º Congresso Brasileiro e Encontro Internacional sobre Dor; 2005 outubro 19–22; São Paulo, Brasil. São Paulo: Segmento Farma. p. 110–20.

Artigo disponível em formato eletrônico

International Committee of Medial Journal Editors. Uniform requirements for manuscripts

submitted to biomedical journals. Writing and editing for biomedical publication. Updated October 2007. Disponível em: http://www.icmje.org. Acessado em: 2008 (Jun 12).

6. Tabelas e quadros: devem estar numerados em algarismos arábicos na sequência de aparecimento no texto; devem estar editados em espaço duplo, utilizando folhas separadas para cada tabela ou quadro; o título deve ser colocado centrado e acima; notas explicativas e legendas das abreviaturas utilizadas devem ser colocadas abaixo; apresentar apenas tabelas e quadros essenciais; os arquivos devem ser submetidos separadamente do texto principal.

8. Figuras: elaboradas nos formatos TIFF, JPEG, PDF, Indd; a resolução mínima aceitável é de 300 dpi (largura de 7,5 ou 15 cm).

9. Legendas das figuras: numerar as figuras, em algarismos arábicos, na sequência de aparecimento no texto; editar as respectivas legendas, em espaço duplo, utilizando arquivos separados; identificar, na legenda, a figura e os eventuais símbolos (setas, letras etc.) assinalados; reprodução de ilustração já publicada deve ser acompanhada da autorização, por escrito, dos autores e dos editores da publicação original e esse fato deve ser assinalado na legenda.

10. Declaração de ética: Negrito nenhum dado ou imagem identificando um paciente pode ser utilizado sem consentimento formal (**os formulários de permissão do paciente estão disponíveis em: www.thieme.com/journal-authors**); estudos utilizando seres humanos ou animais devem obrigatoriamente seguir os padrões do ***International Committee of Medical Journals Editors* – ICMJE, bem como deve obter a aprovação do Comitê de Ética da Instituição onde foi realizado o trabalho; todos os autores devem assinar e anexar o seu próprio o formulário de conflitos de interesse (disponível em: http:// www. icmje. org/ conflicts-ofinterest/**); deve ser evitada a citação de marcas comerciais; os autores serão os únicos responsáveis pelas opiniões e conceitos contidos nos artigos publicados, bem como pela exatidão das referências bibliográficas apresentadas.

11. Os editores e Thieme combatem o plágio, dupla publicação, e má conduta científica atravé do uso do software CrossCheck distribuído por iThenticate. Seu manuscrito pode estar sujeito a investigação e retratação caso haja suspeita de plágio.

12. Os autores devem divulgar qualquer relação financeira no ato da submissão, e quaisquer divulgações devem ser atualizadas pelos autores antes da publicação. Informações que podem ser percebidas como potencial (is) separar conflito (s) de interesse deve ser declaradas. Esta informação inclui, mas não se limita a, subvenções ou financiamento, emprego, afiliações, patentes, invenções, honorários, consultorias, royalties, ou testemunho de especialista.

13. Outras informações: provas PDF serão enviadas aos autores correspondentes para resposta sobre eventuais dúvidas e/ou aprovação **dentro de 72 horas**; exceto para unidades de medida, abreviaturas devem ser evitadas; abreviatura utilizada pela primeira vez no texto principal deve ser expressa entre parênteses e precedida pela forma extensa que vai representar.

Thieme Publishers

Acquisitions Editor
Ana Bluhm

Production Coordinator
Paula Di Sessa Vavlis
paula.disessa@thieme.com.br

Junior Production Coordinator
Tamiris Moreira Rudolf
tamiris.rudolf@thieme.com.br

Journals Intern
Caroline Bianchi Ávila
carol.avila@thieme.com.br

ISSN 0103-5355

Instructions to Authors

Thank you for contributing to Brazilian NeuroSurgery (BNS). Please read the instructions carefully and observe all the directions given. Failure to do so may result in unnecessary delays in publishing your article. There are no submission charges to submit your manuscript to this journal..

Brazilian Neurosurgery (Arquivos Brasileiros de Neurocirurgia), an official journal of the Brazilian Society of N**eurosurgery (Sociedade Brasileira de Neurocirurgia) and Portuguese Language Neurosurgery Society (Sociedades de Neurocirurgia de Língua Portuguesa)**, aims to publish scientific works in Neurosurgery and related fields, unpublished and exclusive. As from January 2018, the journal **only publishes papers written in English with English and Portuguese abstracts**. Manuscripts must conform to acceptable English usage.

Submitted articles shall be placed as one of the following categories:

- ***Original:*** result of clinical, epidemiological or experimental research. Abstracts of theses and dissertations.
- ***Review:*** review and update synthesis of specific themes, with critical analysis and conclusions. Databases and the period range must be specified.
- ***Case Report:*** presentation, analysis and discussion of cases that present relevant interest.
- ***Technical Note:*** note on surgery techniques and/or surgical instruments.
- ***Miscellaneous:*** neurosurgery history, professional practice, medical ethics and other pertinent matters to the journal purpose.
- ***Letter to the Editor:*** critics and comments presented in a brief ethical and instructive manner about published content in this journal. The copyright is safe to authors of the aimed subject. Letters, when accepted, will be published with authors reply.

General standards for publishing

- Article files for publishing must be submitted to the Editor, via https://www.editorialmanager.com/bns/.
- All articles will have a double blinded peer-review process, and no Article Publishing Charge (APC) – society funded. More about Open Access at http://open.thieme.com.
- Only new unpublished manuscripts will be acceptable. Submitted articles **must not be** fully or partially submitted to any other journal.
- The editorial board may reject or suggest changes in order to improve the clarity and structure of the text and maintain uniformity with the journal policy.
- Copyrights of articles published in the journal will belong exclusively to the **Brazilian Neurosurgery and Thieme Revinter Publicações Ltda**. The reproduction of articles or illustrations without prior consent is prohibited.

Standards for submission

Authors must send the following files:

1. Pub Letter (formal text file) stating the article has not yet been published partially or fully or submitted concomitantly to other journal. Must contain Article Title, authors names in full (without abbreviations) and affiliations in ascending order of hierarchy and corresponding author (full address for correspondence, email, telephone).

2. Blind Manuscript (text file must contain article name in English, article name in Portuguese, abstracts in English and Portuguese, without identification of authors and affiliations).

3. Figures (*Tiff, Jpeg, Pdf, Indd*) sent in separate files with minimum resolution of 300 dpi.

4. Tables, charts and graphics (text file) sent separately.

Standards for articles structure

Articles must be structured with all the following items and paginated accordingly:

1. Title page: article title both in Portuguese and English; full name of all authors; academic or professional affiliation of each author; institutions names where the study took place; running title; corresponding author name, degree, full address, e-mail and phone number; followed by **ICMJE COI forms** (COI forms are available at: http://www.icmje.org/conflicts-of-interest/).

2. Abstract: original articles need structured abstract with 250 words at the most: **objective, methods, results and conclusions**; review articles, case reports, technical notes and miscellaneous need no structured abstract. Following the abstract comes keywords (six at the most), based on MeSH (Medical Subject Headings), published in Medline and available at: www.ncbi.nlm.nih.gov/mesh/.

3. Portuguese abstract: Portuguese version of title, abstract and keywords based on DeCS (Descritores em Ciências da Saúde, http://decs.bvs.br).

4. Main text: introduction; casuistry or material and methods; results; discussion; conclusion; acknowledgments.

5. References: number references as they are **first cited** in the text with Arabic numerals. Use Vancouver style; list all authors until the sixth, using *et al*. after the third when more than six; when reference authors are cited in the text cite the first and et al. for references with more that two authors; unpublished data or personal communication must be cited as such between parentheses and cannot be listed as reference; use journal abbreviation from *Index Medicus*; use the following examples:

Journal Article

Agner C, Misra M, Dujovny M, Kherli P, Alp MS, Ausman JI. Experiência clínica com oximetria cerebral transcraniana. Arq Bras Neurocir 1997;16(1):77–85

Book Chapter

Peerless SJ, Hernesniemi JA, Drake CG. Surgical management of terminal basilar and posterior cerebral artery aneurysms. In: Schmideck HH, Sweet WH, editors. Operative neurosurgical techniques. 3rd ed. Philadelphia: WB Saunders; 1995:1071–86.

Book

Melzack R. The puzzle of pain. New York: Basic Books Inc Publishers; 1973.

Theses and dissertations

Pimenta CAM. Aspectos culturais, afetivos e terapêuticos relacionados à dor no câncer. [thesis]. São Paulo: Escola de Enfermagem da Universidade de São Paulo; 1995.

Annals and other congresso publications

Corrêa CF. Tratamento da dor oncológica. In: Corrêa CF, Pimenta CAM, Shibata MK, editores. Arquivos do 7º Congresso Brasileiro e Encontro Internacional sobre Dor; 2005 outubro 19–22; São Paulo, Brasil. São Paulo: Segmento Farma. pp. 110–20.

Available Article in ahead of print

International Committee of Medial Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. Writing and editing for biomedical publication. Updated October 2007. Available at: http://www.icmje.org. Access in: June 12, 2008.

6. Tables and charts: numbered by Arabic numerals according to its citation in the text; edited in double space, using separate sheets per table/chart; title right above; note, abbreviations, legends must follow right under; introduce only essential tables and charts; files must come separately.

8. Figures: digital formats (TIFF, JPEG, PDF, Indd) with minimum resolution of 300 dpi (trim 7.5 or 15 cm).

9. Legends and captions: numbered by Arabic numerals according to its citation in the text; edited in double space, using separate files; identify eventual labels present in the figure

(arrows, characters, lines etc.); image previously published must have publisher authorization and credits.

10. Ethics standards: No data or image identifying a patient can be used without ***formal consent*** (**patient permission forms are available at: www.thieme.com/journal-authors**); studies using human beings or animal trials must follow ethical standards from the International Committee of Medical Journals Editors – ICMJE, as well as approval of original institution's Ethics Committee; conflicts of interest must have a ICMJE form filled in by all authors (available at: http://www.icmje.org/conflicts-of-interest/); commercial marks should be avoided; authors are the sole responsible for opinions and concepts in the published articles, as well as for the reference accuracy.

11. The editors and Thieme combat plagiarism, double publication, and scientific misconduct with the software CrossCheck powered by iThenticate. Your manuscript may be subject to an investigation and retraction if plagiarism is suspected.

12. Authors must disclose any financial relationship(s) at the time of submission, and any disclosures must be updated by the authors prior to publication. Information that could be perceived as potential confl ict(s) of interest must be stated. This information includes, but is not limited to, grants or funding, employment, affiliations, patents, inventions, honoraria, consultancies, royalties, stock options/ownership, or expert testimony.

13. Other information: PDF proof will be sent to corresponding author for eventual queries and/or approval within 72 hours; except measure units, acronyms must be spelled out after its first time mentioned.

Thieme Publishers

Acquisitions Editor
Ana Bluhm

Production Coordinator
Paula Di Sessa Vavlis
paula.disessa@thieme.com.br

Junior Production Coordinator
Tamiris Moreira Rudolf
tamiris.rudolf@thieme.com.br

Journals Intern
Caroline Bianchi Ávila
carol.avila@thieme.com.br